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50 Clarence Street
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Complimentary Copy

ISSN (ONLINE): 2208-3693
ISSN (PRINT): 2208-3685

Journal of Clinical and Nursing Research

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ISSN (ONLINE): 2208-3693
ISSN (PRINT): 2208-3685

Submission open for July 2023

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Journal of Clinical and Nursing Research

Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Research Progress of Traditional Chinese and Western Medicine Dressing Change on Wound Healing After Anal Fistula Surgery

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Abstract: With the change of people's lifestyle and diet, the incidence of anorectal diseases is increasing year by year. Anal fistula is a common anorectal disease. Because it cannot heal by itself, surgery has become the main treatment method. Due to the particularity of wound location and physiological structure, the wound is easily contaminated by bacteria, so dressing change after surgery plays a decisive role in wound healing. Modern western medicine and traditional Chinese medicine have different dressing changing methods respectively. In this paper, we reviewed commonly used dressing changing methods of traditional Chinese and western medicine after anal fistula surgery.

Keywords: Chinese and Western medicine; Anal fistula; Treatment methods; Wound healing

Online publication: April 19, 2023

1. Introduction

Anal fistula is a relatively refractory anorectal benign disease [1]. It is an abnormal infectious passage between the anorectal canal and the perianal skin, which is mostly composed of three parts: the inner opening, the fistula, and the outer opening [2]. Persistence of anal fistula will not cause physical and psychological pain, but also lead to a significant reduction in the quality of life. Therefore, surgical resection is the gold standard for treatment [3]. Surgical treatment puts forward higher requirements for the physician team in order to reduce the occurrence of postoperative complications [4], to speed up the postoperative wound healing [5]. Due to the particularity of the surgical site, the postoperative wound is generally not sutured, and the postoperative defecation will easily cause irritation to the wound, which is prone to infection symptoms. In addition, the deep and large wound cavity leads to slow wound healing [6]. Therefore, dressing change after anal fistula surgery plays a crucial role in the healing of surgical wounds. It can not only prevent the formation of pseudo-healing of wounds, but also accelerate the healing of wounds in the operated area. At the same time, it also significantly reduces the pain of patients [7].

2. Understanding of anal fistula in traditional Chinese and western medicine

2.1. Views of traditional Chinese medicine

"Anal fistula" is also known as "anal leakage" and "fistula sores" in traditional Chinese medicine. The word "fistula" was first put forward in the *Shanhai Jing · Zhongshan Jing*. The water comes from its Yin and flows north into Luo. There exist many fishes like red-tailed *Siniperca chuatsi*, which can prevent carbuncle

when eaten and can be used to treat fistula. Here, "fistula" includes many parts of the body where fistula can occur and does not refer to anal fistula alone [8]. The symptoms and prognosis of anal fistula were recorded in the book *Keke Zhengzhi Quanshu*, namely, "It starts from the root of the anterior perineum of the anus near the junction of the posterior perineum. At the beginning, it is like small particles, gradually growing into the size of a lotus seed and then a peach in a few days, red and painful. After the syndrome breaks out, the tube will leak, and stool and urine will leach out. Finally, the patient will die from the blood vessels draining out. The symptoms are the same, all leakage could be treated but this one. If treated, the leakage will be more serious [9].

Traditional Chinese medicine believes that anal leakage is the gradual onset of anal carbuncle. In the *Introduction to Medicine, the General Preface of Medicine*: "The two heats combat and turn into pus, which results from heat but not damp, heat cannot rot the muscles." The anal carbuncle is the acute stage of the conflict between pathogens, and as time passes, it will become anal leakage. Patients with anal leakage are those whose constitution is hot and humid, or who is always fond of meat or spicy and irritating food, or whose lifestyle is not "clean," leading to the endogenous heat and humidity, accumulated poison, rotten meat, pus and finally leakage. The wound surface of anal leakage is difficult to heal due to the long-term existence of "moisture," "heat," and "poison." Surgery and postoperative external treatment is needed to fully treat anal leakage. Since ancient times, various schools of traditional Chinese medicine (TCM) have accumulated rich experience and clinical cases in external treatment of wounds. In the field of wound healing, most practitioners have developed a variety of traditional Chinese medicine surgical classic drugs on the basis of promoting qi and activating blood circulation, clearing heat and detoxifying, drying dampness and relieving pain, and astringing and regenerating muscles.

2.2. Views of modern western medicine

The full name of "anal fistula" in western medicine is "anorectal fistula." As early as the 4th century BC, Hippocrates defined anal fistula. In 1962, Parker and his colleagues proposed a more detailed classification according to the relationship between anal fistula and sphincter [10]. About 90–95% of the pathogenesis is caused by anorectal perianal space infection, and 3.5% is caused by injury and other factors. The two reasons above connect anorectal and perianal and perineal skin to form a pathological channel. In addition, the incidence of anal fistula male is higher than that of female [11]. Its clinical manifestations are recurrent perianal abscess, and the course of disease is long. In particular, complex anal fistula has a very high probability of recurrence even after appropriate treatment, and even after surgical treatment, there might be different degrees of anal incontinence and other conditions [12]. Although there are a variety of surgical methods for the treatment of anal fistula, there is still no clear definition of success, failure, and recurrence [13].

Modern western medicine believes that anal fistula is a benign anorectal disease caused by perianal abscess, which occupies a very large proportion in anorectal diseases. The surgical method of anal fistula is mostly done in a way of "low cut and high hanging," that is, the low anal fistula is treated by one-time resection, and high anal fistula is treated by seton placement. Due to the unique anatomical structure of the anus, anal incontinence and complications are prone to occur after surgery. Moreover, as the anus is an organ for excreting feces, most of the wounds are open after surgery, and many factors will lead to slow wound healing. Wound dressing change is an important factor affecting the quality and speed of wound healing in patients with anal fistula after surgery. Therefore, keeping the wound clean and wound drainage unimpeded is crucial for the full recovery of anal fistula [14].

3. Concept of wound dressing of traditional Chinese and western medicine after anal fistula surgery

3.1. Dressing concept of traditional Chinese medicine

Traditional Chinese medicine has a variety of theories and thoughts on wound healing. “If the decayed flesh is not removed, new flesh will not be created” has always been the method of traditional Chinese medicine for wound treatment. *Surgery Enlightenment* from the Ming dynasty writes: “The muscle is not born (...) when the paste is stuck, pus will be simmered, and flesh grows.” “Simmering pus and growing flesh” can be considered as the further development and supplement of removing pus and rot, or the next stage of removing pus and rot. “Simmering pus and growing flesh” mainly refers to the external application of traditional Chinese medicine to promote the simmering of pus, flesh growth, and healing after the removal of decaying flesh from the wound. The simmering pus here is not an early necrotic substance, but a manifestation of sufficient and unblocked qi and blood. It provides a good wet environment for the wound to grow better while protecting the wound [15].

Traditional Chinese medicine mainly relies on the combination of “clearing heat and promoting blood circulation, relieving swelling and pain, and astringing and myogenic methods” to promote wound healing, which focus on dialectical treatment and nursing and utilizes the characteristics of traditional Chinese medicine [16].Traditional Chinese medicine has a long history and accumulated a lot of experience, especially in the treatment of trauma wounds, and has its own unique understanding and advantages [17]. Relying on the collective methods and experience of Chinese medicine, many Traditional Chinese medicine specialized hospitals have developed special ointment for postoperative patients with anorectal diseases, which have been proven effective.

3.2. Concept of dressing change in modern western medicine

The concept of dry healing in modern western medicine believes that only a dry and clean environment is conducive to creating a high oxygen concentration environment that promotes wound repair and healing. Cotton pad and gauze can well absorb exudate and isolate external pollution and keep the wound relatively clean in cleaning and suturing the wound. However, the dressing tend to stick to the wound when removed, which may tear the new granulation tissue on the surface, and cause unintentional secondary mechanical injury [18].

In 1962, Dr. Jorge Winter from the United Kingdom proposed the “wet healing environment theory,” which is the source of the “wet therapy” theory [19]. The Food and Drug Administration defined the standard approach to wound management as “wet therapy” in the business guidance in 2000. The main method of “wet therapy” is to provide a closed, micro-oxygen or no oxygen, moist, and slightly acidic environment for the wound, so as to better promote wound healing. With the development of modern biotechnology, more research has been done on the mechanism of wound repair, and new biological dressings have emerged in western medicine, such as alginate dressings and hydrocolloid dressings.

4. Different methods of traditional Chinese and western medicine for postoperative dressing change in patients with anal fistula

4.1. Methods of dressing change of Traditional Chinese medicine

Liu [20] discussed and analyzed of the clinical effect of Shengjiyuhong ointment on promoting wound healing after low anal fistula surgery by randomly dividing the patients into the control group (treated with conventional Vaseline gauze dressing) and the study group (treated with Shengjiyuhong ointment gauze dressing). The results showed that the duration of secretion, the duration of largest amount of secretion, duration of epithelial growth, and duration of wound healing in the study group were shorter than those in the control group. In general, Shengjiyuhong ointment can significantly accelerate the growth rate of granulation and epithelial tissue, promote local blood perfusion and capillary growth rate, and accelerate

wound healing after low anal fistula surgery.

Xie [21] randomly divided 90 patients with damp-heat anal fistula after surgery into Vaseline group (surgical wound dressed with Vaseline gauze) and Coptis oil group (surgical wound dressed with Coptis oil gauze), with 45 cases in each group. The wound dressings of both groups were changed once a day. The results showed that Coptis oil can accelerate wound healing and shorten the length of hospital stay and the effect is safe and reliable.

Traditional Chinese medicine has a long history in the treatment of anorectal diseases. Ointments that are developed based on the principles of traditional Chinese medicine are safe and reliable for dressing change in patients with anal fistula after operation, and their therapeutic effect is better than conventional western medicine dressing change. However, the formula of traditional Chinese medicine preparation is not standardized, so the treatment formula varies from hospital to hospital.

4.2. The method of dressing change in modern western medicine

Guo [22] studied the clinical effect of alginate dressing applied to the wound dressing after low anal fistula surgery by first dividing the patients into the observation group and the control group by random number table method, with 121 patients in each group. The wound was covered by alginate dressing after surgery in the observation group, and the wound was covered by Vaseline gauze in the control group. The results showed that alginate dressing could significantly reduce the frequency of dressing change, the amount of wound secretion, and shorten the healing time compared to Vaseline dressing.

Liu [23] observed the application effect of hydrocolloid dressing in superficial skin injury, and divided 100 patients with superficial skin injury into two groups by random number table method, with 50 patients in each group. The control group was treated with routine surgical dressing change, and the experimental group was treated with hydrocolloid dressing change. The results showed that hydrocolloid dressing can relieve the pain of patients during dressing change, reduce the frequency of dressing change, accelerate the recovery of skin injury, and reduce the incidence of scar formation and wound infection.

Alginate dressing and hydrocolloid dressing are new types of dressing that have similar effects. They are biological substances widely used for healing and regeneration of human tissues [24]. Because they are new types of wet dressing, the frequency of dressing change is less than conventional dressings, and are more effective in promoting wound healing, so they are expensive.

4.3. Combination traditional Chinese and western medicine in wound dressing

To observe the effect of Qudu-Shengji ointment gauze combined with Teding Dianci Pu irradiation on promoting wound healing after complex anal fistula surgery and on serum tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), and interleukin 10 (IL-10), Wang [25] divided the patients into an observation group and two control groups according to the numerical expression method. The observation group was treated with Qudu-Shengji ointment gauze packing combined with TDP irradiation; one control group was treated with Qudu-Shengji ointment gauze packing, while the other control group was treated with Vaseline gauze packing. After treatment, the VAS score of pain, the weekly change in the proinflammatory factor content of TNF-α and IL-6 in serum, the scores of various symptoms (including wound secretion, granulation morphology, redness, and degree of swelling), the shedding of decaying flesh, and the wound healing time of the observation group were shorter than those of the two control groups. After treatment, the changes of IL-10 anti-inflammatory factor, wound reduction rate, and clinical efficacy in the observation group were higher than those in the two control groups. Therefore, the combination of traditional Chinese and western medicine in wound dressing can relieve the pain of patients and promote the metabolism of wound healing, which achieve the purpose of removing the decaying flesh and generating new flesh.

The treatment of combining traditional Chinese and western medicine will become a new development trend of medicine, which is not only the combination of the two fields but also their cultures. This is a new field which needs to be further explored and excavated, so that the two can be better combined to benefit more patients [26].

5. Summary and prospects

Anal fistula is a common anorectal disease [27]. The result of postoperative dressing change plays a decisive role in the wound recovery of patients. Due to the special location of the wound and the complex structure of anal tissues, many complications, such as microcirculation barrier, local inflammatory response, oozes, exudation and pain, may occur at the wound, which will significantly affect wound healing [28,29]. In the treatment of postoperative anal fistula, modern western medicine mainly focuses on controlling inflammation, but adverse symptoms are prone to occur, such as postoperative infection and inflammation [30]. Wet healing is a new concept of wound healing. Combined with the new dressing and dressing change method, the drug can be fully fitted to the wound, so that the necrotic flap tissue can loosen and fall off more easily [31], which is conducive to rapid wound healing. The new dressing is a breakthrough in the theory and practice of traditional dressing and viewpoints [32]. At present, compared to conventional dressing, the new dressings have not been widely used in clinical practice, and the price of the new dressings are slightly more expensive than conventional dressing, which increases the economic burden of some patients. Traditional Chinese medicine has accumulated a lot of experience in the treatment of anorectal diseases, and the treatments are simple, convenient, cheap, and green, and its clinical efficacy has been proven [33]. However, the treatment of traditional Chinese medicine is mostly based on experience, and the mechanism of some drugs is not clear without standardized prescriptions [34]. In view of this situation, medical and nursing staff should reasonably integrate the treatment methods of traditional Chinese medicine into western medicine, drawing on each other's strengths to complement each other's weaknesses, and design a method suitable for postoperative dressing change in patients with anal fistula and apply them in clinical work, so that more patients with anal fistula can be benefited.

Funding

Shaanxi Provincial Key Research and Development Program (Project number: 2021SF-351)

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Patient Safety Risks and Measures for Pediatric Neurosurgery Nursing

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Abstract: The aim of this study was to determine the patient safety risks and measures for pediatric neurosurgery nursing. A total of 564 pediatric patients admitted to the hospital from June 2020 to June 2023 under the neurosurgery department were included in this study. We analyzed the safety incidents in pediatric neurosurgery nursing and their causes and proposed corresponding measures for pediatric neurosurgery nursing in hope to reduce the occurrence of patient safety incidents in pediatric neurosurgery nursing and establish harmonious nurse-patient relationships.

Keywords: Neurosurgery; Pediatric patients; Patient safety risks; Countermeasures

Online publication: May 22, 2023

1. Introduction

With the progress of modern medical technology and people's higher demand for health, the nursing of neurosurgical patients has gained widespread attention. Safe nursing is the basis to guaranteeing high-quality nursing services and an important index to measure the quality of nursing work. Neurosurgery is a department that deals with many critical and emergency cases. The majority of patients in neurosurgery have complex problems, are unstable, and are in critical conditions, accompanied by varying degrees of consciousness and limb movement disorders, as well as prolonged bed rest, all of which would increase the patient safety risks. Younger age patients, *i.e.*, pediatric patients, pose a greater challenge to neurosurgical care [1]. For example, a child's reaction to narcotic drugs is more unpredictable than an adult's reaction, so special care is needed. Close monitoring of breathing, heart rate, and blood pressure is necessary in pediatric neurosurgery cases, and nurses must ensure that these patients remain stable during procedures. In neurosurgery, bleeding and thrombosis may occur; therefore, blood loss and clotting indicators should be closely monitored, so that timely measures can be taken to prevent bleeding or thrombosis. It is of great significance to analyze the patient safety risks in pediatric neurosurgery and take appropriate nursing measures.

2. Data and methods

A total of 564 pediatric patients admitted to the hospital from June 2020 to June 2023 under the neurosurgical department were included in this study. We conducted a retrospective analysis of patient safety incidents in pediatric neurosurgery nursing and proposed corresponding measures.

3. Patient safety risks in pediatric neurosurgery nursing

3.1. Choking

Children who are unconscious or intubated may develop asphyxia due to aspiration of sputum. Once asphyxia is noted, the child's head should be tilted backward, while lifting the chin up, to open the airway. Oxygen should be given via artificial respiration, which helps maintain breathing, to improve oxygenation [2]. Foreign bodies or secretions blocking the respiratory tract should be removed immediately. The patient's vital signs, including heart rate, respiration, and blood pressure, should be closely monitored, along with the patient's state of consciousness. Drugs or tracheal intubation should be considered depending on situation.

3.2. Skin injury

Skin injury is one of the common patient safety issues in pediatric neurosurgery. The reasons for skin injury in children undergoing neurosurgery are as follows: (i) friction or compression during surgery (since incisions are made on the skin during surgery, there may be friction or compression on the skin, resulting in skin injury) [3]; (ii) prolonged bed rest after surgery (since patients are required to rest in bed for a period of time after surgery, especially in neurosurgery, skin damage may occur as a result of pressure on certain parts of the body); (iii) malnutrition (patients may be malnourished due to improper diet or complications after surgery, which may also affect their skin health, thus increasing their risk of skin damage; (iv) skin infection (patients are prone to infection after surgery due to decreased immunity; a delay or neglect in cleaning or disinfecting the skin may cause infection and lead to skin damage).

3.3. Falls

Falls, especially falls from the bed, are common patient safety issues in pediatric neurosurgery. Children with neurological disorders, such as those with brain tumor and cerebral hemorrhage, which may affect their balance and gait, are prone to falls [4]. Following neurosurgery, patients are required to stay in bed for extended periods of time, which may cause muscle atrophy and decreased muscle strength due to prolonged immobility, thus making the patient more likely to lose balance when standing or walking. Certain drugs, such as sedatives, anesthetics, *etc*., which affect balance and reflexes, are often administered to children undergoing neurosurgery. These drugs increase the risk of falls among children. If care is not provided, such as failing to check patient's position on bed, not fixed bedpan or urinal pot, it may also lead to patients falling down.

4. Analysis of the causes of patient safety risks in pediatric neurosurgery nursing

4.1. Nursing staff lack nursing skills

The lack of nursing skills among nurses in neurosurgery is one of the main reasons leading to the occurrence of patient safety incidents in pediatric neurosurgery nursing. The diseases are more complex in pediatric neurosurgery, which requires nurses to have certain professional knowledge and skills to carry out effective nursing. If the nursing staff lacks understanding of the disease, misdiagnosis and mistreatment are bound to occur, leading to the deterioration of the patient's condition [5]. In addition, neurosurgical care requires the use of special equipment and instruments, such as ventilators, monitors, electroencephalograph, *etc*. The lack of skills in operating these devices among the nursing staff may lead to improper operations,

equipment failure, and other adverse situations, which may affect the safety of these patients. When nursing pediatric patients in neurosurgery, emergency situations, such as sudden loss of consciousness and difficulty in breathing, may occur, and without proper training, the nursing staff may not be able to handle these emergencies quickly and correctly, thus putting patients' lives at risk.

4.2. Disease factors

Disease factors are also one of the important reasons leading to patient safety incidents in pediatric neurosurgery nursing. Firstly, neurosurgical diseases are often accompanied by severe neurological damage, including increased intracranial pressure, cerebral hemorrhage, *etc*. These conditions pose a threat to the life of children and thus require timely and effective nursing and monitoring [6]. Secondly, neurosurgery often involves complex operations and excision; thus, various complications may occur after surgery, such as infection and cerebral edema. These complications require timely observation and treatment; otherwise, the recovery and rehabilitation of patients may be affected. Thirdly, neurosurgical conditions, such as brain injury, epilepsy, *etc*., often require long-term care and monitoring. Such conditions require continuous observation and care by the nursing staff to ensure the safety and health of patients.

4.3. Behavioral factors

Children's own behavior may also lead to certain patient safety risks. Patients with neurosurgical problems may have cognitive impairment, movement disorders, and other issues, resulting in poor awareness of self-protection. Thus, if the nursing staff do not pay adequate attention to these patients, injury or accidents may occur. Neurosurgical conditions may affect the behavioral and emotional control of children, making them susceptible to external stimuli; thus, they may elicit symptoms of anxiety and irritability [7]. In this context, if the nursing staff do not carry out timely and effective intervention and control, accidental injuries or other life-threatening concerns are bound to happen.

In addition, some children may elicit improper behaviors, such as self-extubation, removal of monitoring instruments, and other behaviors that may pose a threat to their own health and safety.

5. Measures for nursing in pediatric neurosurgery

5.1. Improve the nursing staff's nursing skills

The nursing staff should be trained and educated to enhance their understanding and skills in pediatric neurosurgical care, *i.e*., their knowledge of neurological diseases, common neurosurgical procedures, *etc*. The nursing staff should improve their communication skills, so as to help caregivers understand the needs of patients and their families; in addition, they should work with physicians and other caregivers as a team to develop the best care plan for patients. Other than that, they should ensure an effective shift and record-keeping system [8]. The condition and treatment of each patient should be recorded in a timely and detailed manner in order to better track and evaluate the patient's progress. In addition, nursing operation procedures and standards of practice should be standardized to ensure compliance to correct operating procedures and hygiene measures. It is also necessary to strengthen the training of nursing staff in the management of drug therapy, including the proper use and storage of drugs, in order to prevent the occurrence of safety incidents caused by improper use or storage of drugs. In order to strengthen risk assessment and prevention, the nursing staff must identify and deal with the possible risks of patients as quickly as possible to prevent adverse events from occurring.

5.2. Improve the nursing staff's attitude

It is important to strengthen the training of nurses' service attitude and professional ethics by establishing a professional ethics and service awareness training plan; implement nursing quality control; develop strict

nursing standards and process specifications; improve the nursing quality; and reduce medical errors. Medical institutions should implement scientific and reasonable medical nursing management systems, establish scientific nursing plans and demonstrations, as well as guide nurses in carrying out nursing operations. The nursing staff should strengthen communication with the patients and their parents, establish a close relationship with them, and provide timely and comprehensive nursing services. It is necessary to evaluate the nursing effect on a regular basis, improve the quality of nursing service, provide timely feedback on the nursing effect, continuously improve on the basis of the feedback, and provide optimization measures. Establishing a scientific nursing research and education system, improving the professional skills and nursing level of the nursing staff, as well as strengthening the nursing quality and service attitude of the nursing staff would also be beneficial.

5.3. Establish a prevention mechanism for patient safety risks

(i) Establish a comprehensive risk assessment system

A comprehensive risk assessment system should be developed based on the characteristics of pediatric neurosurgery nursing to investigate and evaluate the potential safety risks in pediatric neurosurgery.

(ii) Develop standardized nursing norms

In view of the particularity of pediatric neurosurgery patients, standardized nursing norms and operating procedures that require the compliance of the nursing staff should be formulated in order to ensure that nursing operations are standardized, scientific, and reasonable.

(iii) Strengthen nursing staff training

It is important to provide special training for pediatric neurosurgery nursing staff and strengthen the knowledge and skills of the nursing staff to ensure that the patients receive safe and effective services.

(iv) Improve the information exchange mechanism

Various forms of information exchange, including regular meetings, safety prevention notification, experience sharing, *etc*., should be carried out. The communication and exchange among pediatric neurosurgery nursing staff should be strengthened, along with their ability to identify and solve patient safety risks in their nursing work.

(v) Strengthen supervision and management

A scientific and standardized supervision mechanism should be established. With this mechanism, it is possible to supervise the work of the nursing staff, and timely corrections can be made in cases of violations, thus guaranteeing the safety and safeguarding the rights of pediatric patients in neurosurgery.

6. Conclusion

With the advancements in modern medical technology, the demand for safety in nursing is increasing. There are difficulties and risks in pediatric neurosurgery nursing. In this study, we analyzed the causes of patient safety incidents in pediatric neurosurgery and put forward corresponding measures to provide better nursing services for patients.

Disclosure statement

The authors declare no conflict of interest.

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Publisher's note

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Experience in Surgical Coordination of Type III Cesarean Scar Pregnancy Removal with Combined Assistance of Hysteroscopy and Laparoscopy

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Abstract: *Objective:* This paper aims to summarize the operative nursing coordination essentials of type III cesareans car pregnancy removal. *Methods:* Six patients were recruited for this study, and the patient's condition was fully evaluated before the operation. In addition, the personnel, environment, and materials were well prepared before the operation, and the preparation of special intraoperative instruments and equipment was perfected. *Results:* The operation is successfully performed in all six patients. Each surgery lasted 70 to 120 minutes with an average duration of 90 minutes. Postoperative blood loss was about 100-500 ml. Postoperative recovery was good without complications in all the patients. *Conclusion:* In summary, laparoscopic removal of gestational tissue from type III cesareans car pregnancy in conjunction with hysteroscopy ensures compete removal of gestational tissue, while avoiding damaging the surrounding organs and tissues, thus greatly avoiding common complications which usually occur during the surgery. Effective surgical coordination is helpful to further improve the success rate of the operation.

Keywords: Cesarean scar pregnancy (CSP); Hysteroscopic assistance; Surgical coordination; Gestational tissue

Online publication: May 22, 2023

1. Introduction

In recent years, with the comprehensive implementation of the family planning policy, the cesarean section rate in women of childbearing age is extremely high. The number of women with second pregnancy after cesarean delivery increased sharply, and the incidence of cesarean scar pregnancy (CSP) exhibits a significant rising trend. According to foreign reports, the incidence of CSP among women with a history of cesarean section is 1 in 2500 to 1 in 1800 pregenancies. According to domestic reports, the incidence of CSP is 1 in 2221 pregnancies, accounting for 1.05% of ectopic pregnancy [1-3].

CSP is a relatively new type and a rare form of ectopic pregnancy which happened at the scar region forms from previous cesarean delivery, resulting in the implantation of a blastocyst within myometrial scar tissue in the anterior lower uterine segment. It is a long-term complication after a cesarean section. Studies have shown that poor muscle healing at the uterine incision scar after cesarean section, which forms a wide uterine scar diverticulum, or the formation of tiny pores in the incision scar under the action of inflammatory factors, may contribute to the development of CSP. A fertilized egg that moves too fast or is underdeveloped does not have a good implantation capacity when it passes through the uterine cavity. CSP may develop when the fertilized egg reaches the scar and enters the myometrium through the tiny pores for implantation. Abnormal vaginal bleeding after cessation of menstruation, with or without lower abdominal pain is the most common clinical manifestation. Indeed, some patients do not show typical clinical manifestations and

symptoms. If it is misdiagnosed as a common intrauterine pregnancy and blindly undergoes an abortion, the patient is susceptible to massive hemorrhage that is difficult to control effectively during operation. In a worse situation, the uterus may need to be removed by surgery. Therefore, doctors should be highly vigilant about the possibility of CSP in women with a second pregnancy after cesarean delivery in clinical. Once diagnosed with CSP, the pregnancy should be terminated as soon as possible. However, traditional dilation and curettage have significantly increased the risk of direct damage to the scar, massive bleeding, and uterine rupture [4]. At the same time, it is more likely to result in a hysterectomy, which affects women's reproductive health and endangers their lives in serious cases. In type III CSP, (1) the gestational sac usually implants completely in the muscular layer at the uterine incision scar and protrudes toward the bladder; (2) the uterine cavity and cervical canals are often empty; (3) the myometrium at the scar is significantly thinner (with a thickness ≤ 3 mm) or absent; and (4) if transvaginal surgery is done, it is prone to massive bleeding, which cannot be controlled effectively during the surgery, and may even require hysterectomy.

There are few reports on the surgical options and nursing coordination in these patients. How to complete the perioperative nursing preparation, ensure tacit operative cooperation and the smooth implementation of surgery, avoid surgical complications as much as possible, and improve the success rate of the surgery has become a huge challenge facing surgical nurses. From January 1, 2020 to January 1, 2023, six patients with type III CSP successfully underwent the laparoscopic removal of uterine scar pregnancy assisted by hysteroscopy in our hospital with good clinical results.

2. Perioperative nursing

2.1. Preoperative visit

The day before the operation, operating room nurses should fully familiar with the medical record, understood the patient's previous medical history, history of present illness, and the results of various routine examinations, as well as the patient's preoperative basic information and problems in nursing. Through the preoperative interview, we found that the biggest psychological stress facing by the six patients before the surgery was "anxiety and worry about the impact of the disease to their health and fertility." CSP may injure the bladder during excision with a risk of massive bleeding. Therefore, we conducted targeted specialist education knowing the patient's concerns. We walked them through the procedures, told them about the techniques that we use to avoid complications, and that the surgeons are quite experienced and have conducted many surgeries successfully in the past. We introduced the operating room environment to the patients, and showed them the workflow from the time the patient enters the operating room until before anesthesia, i.e., pre-operative safety check by the surgeon, the anesthesiologist, and operating room nurses, signing of anesthetic consent, venipuncture, body positioning (while completing limb function assessment). We told them that they would be under anesthesia during the operation, that the anesthesiologist would adjust the dosage of drugs according to the needs of the operation and the patient's vital signs, and that the whole process of monitoring would ensure that the patient receives the operation safely and painlessly, as well as how should patients cooperate during the postoperative anesthetic period to get through the recovery. We did our utmost to enhance patients' sense of trust and security, and relieve their perioperative tension and anxiety, thus enabling them to cooperate in the surgical treatment and nursing with an optimistic attitude.

2.2. Preoperative discussion

The operating room nurses took the initiative to participate in the preoperative discussion of the gynecologist team. We fully understood the conception of the surgeons, and get familiar with the surgical steps. We made the final confirmation of the patient's preoperative preparation such as the signing of surgical consent, preoperative hair removal, surgical medication instructions, preoperative blood allocation, preoperative fasting, and preoperative education. According to the discussion and the needs of the surgeon,

the circulating nurse discussed with the head of the operating room specialist and the head nurse about the manpower arrangement, the preparation of special equipment and materials, and the emergency cooperation process of intraoperative emergencies.

2.3. Preoperative coordination

2.3.1. Personnel preparation

Medical staff in the operation including the anesthesiologist, the nurse anesthetist, the surgeon, 3 assistant doctors, the scrub nurse (who are familiar with all kinds of difficult and critical surgery cooperation in gynecology), and the circulating nurse (senior specialist nurses). All surgical team members participated in the preoperative discussion, familiarized themselves with the patient's situation and the surgical plan, and identified the surgical risks.

2.3.2. Environment, goods, and equipment preparation

The proposed surgical procedures before surgery are as follows: Initially, a hysteroscopy is performed to have a grasp of the location of retained products of conception, and then pelvic adhesion release and removal of the uterine scar pregnancy are performed by laparoscopy. Therefore, various equipment and materials are required. On the day of the operation, the circulating nurse should complete the environment arrangement and materials preparation 30 minutes before accepting the patient into the operating room. The bed unit should be pre-insulated in advance, and the disinfectant, dilatation liquid, peritoneal washing liquid, and rehydration liquid for operation should be placed into the warm tank in advance. It is essential to reconfirm that the operating bed, postures, electrosurgical equipment, camera system, etc. are in good condition and in standby condition. The endoscopy (hysteroscope, 30-degree laparoscope) includes hysteroscope (vaginal speculum, cervical forceps, curet, uterine probe, cervical dilator of different sizes, abortion aspirator, etc.); surgical instruments include common instruments (towel clips, pneumoperitoneum needles, knife handle, sponge forceps, etc.), laparoscopic special instruments (elastic separating plier, non-invasive ureteral forceps, stomach clamp, various types of hemostatic clamps, endoscopic needle holder, etc.), and disposable consumables (No. 11 sharp blade, 3 to 4 sets of puncture instrument, endoscope yarn strip, double channel catheter, injection syringe, urine bag, 2-0/3-0 absorbable sutures, various types of vascular sutures, and methylene blue solution); hemostatic materials such as ultrasonic knife, bipolar electric coagulation forceps, hemostatic clamps, etc. are sufficient in quantity, intact in packaging, effectively sterilized, and within the validity period.

2.3.3. Intraoperative coordination

First, the hysteroscopy was performed to determine the shape and size of the uterine cavity, and the location and size of the gestational tissue. Then, a laparoscopic exploration was performed to determine the site of the scar pregnancy lesion and its adhesion to the surrounding tissue. The surgeon separated the ovaries and pelvic wall on both sides with an ultrasonic knife, opened the anterior lobe of the ligament to find the internal iliac artery and uterine artery on both sides, and identified the ureter, and lastly cut the uterine artery with a hemostatic clamp. The vesicouterine pouch was opened from the left and right sides, if the bladder is found to be closely attached to the lesion during the process, it should be filled with normal saline, the uterus should be lifted and the bladder should be pushed down with the manipulator to expose the scar pregnancy lesion, then the ultrasound knife is used to cut the scar into the uterine cavity and remove the gestational tissue. After thorough hemostasis, the wound was sutured continuously with 2-0 absorbable thread, and the incision was sutured by locking. Examination: There was no active bleeding spot on the bladder wound, and the methylene blue test was performed. The peritoneum was sutured, the wound was stopped by electrocoagulation, the pelvic cavity and abdominal cavity was completely washed, and no

bleeding was seen. A hysteroscopy was performed again to confirm that the gestational tissue in the uterine cavity was completely cleared and there was no bleeding. The operative materials were checked and the abdomen was closed after the operation.

3. Discussion

In type III CSP, (1) the gestational sac usually implants completely in the muscular layer at the uterine incision scar and protrudes toward the bladder; (2) the uterine cavity and cervical canals are often empty; (3) the myometrium at the scar is significantly thinner (with a thickness ≤ 3 mm) or absent; and (4) if transvaginal surgery is done, it is prone to massive bleeding, which cannot be controlled effectively during the surgery, and may even require a hysterectomy. Therefore, once diagnosed, the CSP should be terminated as soon as possible. The principles of the treatment are as follows: under the premise of ensuring the life safety of patients, we will control bleeding, remove the lesion, and preserve the reproductive function of patients. Studies have shown that hysteroscopy in conjunction with laparoscopy has an irreplaceable role in the treatment of type III CSP compared with hysteroscopy alone or uterine artery embolization with curettage, which integrates the advantages of both for further diagnosis, reduction of bleeding, removal of the lesion, and evaluation of the suture effect after the laparoscopic scar repair. It has the advantages of safety, effectiveness, short operation time, less bleeding, fast recovery, shorter hospital stays, etc. Meanwhile, patients' reproductive function preserved with these procedures, may reduce the risk of uterine rupture in patients with CSP who have a demand for re-birth and a thin muscle layer at the scar [6-7].

Based on this case, the medical group discussed and concluded before the operation that there is a risk of intraoperative uterine and bladder rupture, which may even cause massive hemorrhage and endanger the patient's life if not handled promptly. Therefore, the patient's perioperative safety poses a higher challenge to nursing care. The cooperation of the paramedics in the operating room in this type of surgery is particularly important.

The preoperative tripartite safety check reconfirmed the recent relevant imaging data and the patient's readiness, such as whether deep venipuncture was established for emergency transfusion to avoid the uterine and bladder rupture; a hysteroscopy and a laparoscopic exploration were performed before surgery, combined with preoperative B-ultrasonography to comprehensively understand the implantation position of the gestational sac and the vulnerable part of the uterus, to achieve targeted and successful operation; circulating and scrub nurses should understand the surgical procedures before surgery, and prepare the corresponding equipment and instruments in advance to prevent the delay of rescue during emergencies, including the establishment of unobstructed venous access before surgery, the preparation of surgical materials, and the signing of the blood transfusion consent and blood allocation order. Since type III CSP is characterized by a gestational sac that often lies completely in the myometrium of the uterine incision scar and protrudes toward the bladder, the separation of the peritoneum of the bladder from the uterus is the key to the procedure. To expose the uterus as wide as possible without damaging the bladder, we need to prepare the lifting cup in advance, leave a urinary catheter in place, fill the bladder with melphalan solution if necessary to facilitate the separation of the peritoneum, and confirm that there is no leakage of urine from the bladder after separation. And, because the gestational sac was embedded next to the bladder, the ureter was closely associated with the uterine artery even in normal anatomy. The surgeon has to open the anterior lobe of the broad ligament on the affected side and the peritoneal reflection of the bladder and push down on the bladder to separate and ligate the uterine artery and free the ureter to the entrance of the ureteral tunnel to avoid damage to the uterine artery and ureter, and ultimately, avoid complications.

The development and implementation of a rational surgical plan are important, as well as the impact of patients' perioperative anxiety on their recovery. At present, with the transformation of the bio-psycho-

social medical model, human health and diseases are affected by biological factors, and are closely connected with psychological factors. Study by Li [8] suggests that apart from improving the satisfaction of patients, the implementation of a series of humanistic care for perioperative patients and patients in the intensive care unit reduces patients' psychological pressure, and prompts them to cooperate in the treatment positively. We found from the patient during their preoperative visit that they are more worried about the complications of surgery than the pain caused by surgery, such as massive bleeding of the uterus and bladder resulting from surgical injury, bladder injury, and even afraid that it may affect the fertility function. We established a good trust relationship with the patient through psychological intervention during the perioperative period, and an explanation of accessible surgical knowledge, and also encouraged the patient to express their feelings in the whole process. We provided the patient with information about treatment and prognosis, and helped them by clarifying misconceptions. The patient's mental stress is relieved, encouraging them to cooperate with medical treatment and care throughout the perioperative period, which may accelerate postoperative rehabilitation.

The laparoscopic removal of the CSP requires comprehensive nursing by nurses before, during, and after the operation to ensure the safety and effectiveness of the operation. The results of this study indicate that the laparoscopic removal of CSP is a safe and effective treatment with a good postoperative recovery, which is recommended to be applied in clinical treatments.

The success of the operation is inseparable from the tacit cooperation of operation and nursing. Only when the paramedics have a comprehensive understanding of the surgical plan formulated by the operator and the possible emergencies during the operation, have formulated a contingency plan in advance, and have a comprehensive assessment and adequate preparation of all factors of human, machine, material, method, and environment, coupled with the close monitoring of the patient by the anesthesia and nursing team during the operation, can the operation be completed with close cooperation with the medical team during emergencies.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Application of Heuristic Method to the Clinical Teaching of Internal Medicine

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Abstract: There is an old saying, "Give a man a fish, and he will eat for a day. Teach a man to fish, and he will eat for the rest of his life." In clinical teaching, students should not only be taught about diseases, but their intelligence should also be cultivated, along with their analytical, comprehension, and independent learning skills. The ability to solve problems enables students to think independently and acquire knowledge. This is known as the heuristic method of teaching. In this study, we mainly analyze the application value of the heuristic method in the clinical teaching of internal medicine.

Keywords: Heuristic method of teaching; Internal medicine clinical teaching; Application

Online publication: May 26, 2023

1. Introduction

The heuristic method of teaching is an advanced educational concept and teaching method, which can enlighten students' thinking, prompt students to carry out targeted learning according to the teaching objectives, and strengthen the teaching effect. The application of this method in clinical teaching is relatively valuable.

2. Overview of the heuristic method of teaching

The heuristic method of teaching is based on the tasks given and the learning rules, beginning from the actual needs of the students, and adopting various means to stimulate students' thinking and mobilize students' enthusiasm for learning. This is not only a teaching method, but also an educational idea. In talent training, stimulating students' thinking has always been the focus of attention. The implementation of this method requires clear goals, diverse models, and rich methods.

3. Heuristic method of teaching

3.1. Contrastive heuristic method

In the clinical teaching of internal medicine, common diseases need to be explained to students. Although there are some similarities in the manifestations of common diseases, each disease has its own characteristics. For students who have never experienced actual clinical situations, they often face certain difficulties in the learning process. The application of contrastive heuristic method mainly stimulates students' thinking and follows the basic principles of seeking differences within similarities and seeking

similarities within differences. For example, when explaining the clinical manifestations of pneumothorax, a detailed explanation should be given according to different clinical characteristics; for instance, if a patient has simple pneumothorax, air does not enter nor exit; if a patient has communicating pneumothorax, air enters and exits; if a patient has tension pneumothorax, air only enters and does not exit. When explaining the clinical features of pleural effusion and pneumothorax to students, the comparison and similarity method can be used to summarize as follows: (i) upon inspection, the patient's chest appears full, and the degree of respiratory activity decreases to a certain extent; (ii) upon palpation, the position of trachea has shifted to the healthy side; (iii) upon auscultation, reduced breath sounds are heard on the affected side. The difference is in percussion; when percussing for pleural effusion, the affected side will appear dull, but when percussing for pneumothorax, there is hyperresonance.

3.2. Activity heuristic method

In order to broaden the horizons of students, teaching activities such as case discussions can be carried out. When discussing cases, students are encouraged to speak and express their own ideas. This method cultivates and improves students' independent thinking and problem-solving skills. The application of this method not only improves students' expressiveness, but also fully mobilizes students' enthusiasm for learning. Visitations can also be organized, so that students would be inspired through practical activities. For example, after explaining about hemodialysis, a visitation to an artificial kidney center can be organized. This allows students to familiarize themselves with dialysis equipment and its operation methods in person, so as to deepen their theoretical understanding.

3.3. Image heuristic method

Physical objects, charts, and languages are commonly used "images," which can effectively stimulate students' thinking. Teachers can combine the explanation contents to create corresponding images, provide intuitive feelings to the students, inspire the students, and deepen their understanding of relevant knowledge points. For example, when explaining about internal medicine diagnosis and treatment technology as well as cardiopulmonary resuscitation-related knowledge, videos can be used for intuitive teaching to effectively stimulate students' interest, followed by physical operations to strengthen students' understanding.

3.4. Action heuristic method

In the process of teaching, teachers can use gestures to create certain enlightening effects. Especially for the symptoms and signs of diseases, gestures can be used for explanation. For instance, by asking students to stretch out and open their hands, showing their ten fingers, and then close their eyes and move their metacarpophalangeal joints, this action would deepen the impression on students. Other than that, when explaining about bronchial diseases, the corresponding actions and expressions of patients with bronchial asthma can be simulated to help students have a better understanding of the clinical manifestations of the disease.

4. Application and practice of heuristic method in the clinical teaching of internal medicine

There are many types of diseases in internal medicine that are relatively complex. One of the difficulties faced by students is to give accurate diagnoses and treatment plans for specific cases. In this regard, the heuristic method of teaching should be adopted through multi-form and multi-directional methods to stimulate students' thinking, so as to encourage them to think actively about clinical problems and improve their knowledge of cases through the interaction between teachers and students. It is also necessary to address the issue of participation among students and mobilize their enthusiasm, so as to cultivate a scientific clinical thinking mode among students.

Li [1] chose to apply this method to the teaching of nursing in internal medicine. By comparing with the traditional teaching method, Li found that the use of this method can improve students' theoretical knowledge and practical skills as well as strengthen their ability. He *et al*. [2] also applied this method to the teaching of nursing in internal medicine. Through heuristic lesson preparation, students were taught in accordance with their aptitude to stimulate their motivation for learning. The study concluded that the heuristic method can deepen students' understanding, as evident by the favorable results achieved. Ye *et al*. [3] applied this method to the clinical teaching of internal medicine, comparing it with the traditional teaching method, and found that it can improve students' skills and stimulate learning interest.

Yang *et al*. [4] proposed the use of this method for case teaching in internal medicine and incorporated it with action orientation, insinuating that the leading role of teachers and the main role of students can be fully realized through this method. The streamline approach of dividing cases into sections, selecting typical cases, collecting data, constructing preliminary solutions, discussing and analyzing, further collecting and reading data, drawing final solutions, and reporting to teachers can improve the mastery of clinical knowledge in internal medicine. Chang *et al*. [5] chose the analogy method to be used in conjunction with this method and applied it to the teaching of nursing in internal medicine; they found that on the basis of the knowledge and skills that have been mastered, students' subjective initiative can be brought into play, changing the unknown into known and abstraction into image, as well as minimizing the difficulty of knowledge points, thus completing knowledge transfer and successfully achieving the teaching objectives.

Ye *et al*. [6] applied the case heuristic method to the clinical teaching of nurses in general practice wards. There were significant improvements in the score and teaching satisfaction. On the other hand, Ma *et al*. [7] applied the heuristic method combined with the case teaching method to the clinical teaching under the department of endocrinology. Compared with the traditional teaching method, they found that the theoretical and practical assessment scores of the observation group were higher than those of the control group. At the same time, the scores obtained by the observation group for active learning, communication skills, innovative practice, and teamwork were significantly higher than those obtained by the control group ($P < 0.05$). Jiang *et al*. [8] used the problem-oriented heuristic method and applied it to the pre-job training of new nurses in the anesthesiology department. They found that satisfaction with the teaching method can promote the rapid adaptation of new recruits to the position.

Yang *et al*. [9] used the case heuristic method to manage the teaching of junior nurses and found that it can effectively improve the theoretical knowledge, practical skills, and satisfaction of nurses with the teaching management. Wang *et al*. [10] applied the case heuristic method to the teaching of nursing students in gastrointestinal surgery and found that it can improve their theoretical operation assessment scores and satisfaction level with the teaching management. Yao *et al*. [11] used this teaching method to cultivate critical thinking skills among nursing school students and found that it can improve students' ability to discover the truth and think openly, analytically, and systematically; boost students' self-confidence in decision-making; inspire curiosity among students; and improve students' cognitive maturity, overall score, and teaching satisfaction.

Huang *et al*. [12] applied the heuristic method to the teaching of formula science through the heuristic process of induction, analogy, questioning, case reflection, and case discussion to improve students' enthusiasm for learning, innovate traditional Chinese medicine (TCM) thinking, effectively improve the quality of teaching, and cultivate TCM talents. Ren [13] applied the heuristic method combined with case-based learning and found that it can improve the theoretical performance, case analysis skills, comprehensive ability, and teaching satisfaction of doctors trained in TCM dermatology. Chen [14] used this method combined with action learning and found that it can improve the theoretical and nursing skill assessment scores of nursing interns in TCM gynecology and strengthen the overall teaching effect and teaching satisfaction. Li [15] used this method in combination with the discussion teaching method and found

that it can improve students' active participation and classroom response to the theoretical knowledge of digestive internal medicine, which not only improves learning efficiency, but also helps exercise students' thinking skills and improves the teaching quality.

5. Conclusion

In the clinical teaching of internal medicine, the application of heuristic method has achieved good outcomes. Compared with the traditional teaching method, it can better stimulate students' learning initiative and improve the learning effect.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Study on the Effectiveness of the Application of Perineal Wound Model in Teaching Midwife Interns

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Abstract: *Objective:* To discuss and analyze the effectiveness of the application of perineal wound model in teaching midwife interns. *Methods:* The research subjects in this study were 40 midwife interns who enrolled in our hospital from January 2020 to December 2022, which were divided into a control group (consisted of 20 interns, taught with the conventional method) and a research group (consisted of 20 participants, taught with the perineal wound model) using the random number table method. The outcomes of these two groups were compared. *Results:* The examination results of the research group were better than control group ($P < 0.05$); the interns of the research group were more satisfied towards the teaching method compared to the control group ($P < 0.05$). *Conclusion:* Applying the perineal wound model in teaching midwife interns could effectively improve their examination achievements and teaching satisfaction, which brings a significant clinical value.

Keywords: Midwife intern; Perineum wound; Examination results; Teaching satisfaction

Online publication: March 29, 2023

1. Introduction

Obstetrics is a highly practical and specialized field. Therefore, the improvement of quality of obstetric healthcare is crucial in obstetric healthcare. As the "Put People First" initiative advocated in contemporary education emphasizes cultivating the innovative, practical, communicative abilities of healthcare professionals, it is crucial to improve the competencies of midwife interns, so as to fully achieve the purpose of obstetrics teaching [1]. In this study, we investigated and researched the effectiveness of the application of perineal wound model in teaching midwife interns.

2. Materials and Methods

2.1. Materials

The research subjects of this study are 40 midwife interns who have enrolled in our hospital from January 2020 to December 2022. They were divided into a control group and a research group using the random number table method. The control group has 20 participants including 1 male and 19 female, with average age of 22.25 ± 2.23. Meanwhile, the research group has 20 participants, who were all female, with average age of 22.19 ± 2.15. The baseline information of interns before the study was $P > 0.05$. All participants of this study have signed an informed consent.

2.2. Research methods

The participants in control group were taught with regular methods: regular syllabus, classroom presentation combined with textbooks and typical case studies, and periodically visiting and learning in inpatient wards.

The participants in research group were taught with the perineal wound model. (1) A unified teaching plan created by the collaboration of the institution and intern hospital, where teaching tasks can be divided into a weekly schedule and a specific delivery and nursing procedure is taught to each intern. (2) After 4 weeks of basic teaching in delivery room, interns began to review the relevant knowledge and participate in the process of delivery, perineum protection, and suture under the guidance of teachers and tutors. (3) The interns watched the presentation of delivery and perineum suture and practiced making perineum lateral incision and the complex perineum lacerated wound model with oxtongues, making levator ani model with chicken legs, and making rectum and anus with small intestines of pigs, so that they could better understand the perineum anatomy. After the wound model was completed, the interns practiced their suturing until they were proficient. (4) During the training, the teachers explained the common and difference between practice suture and real suture, so as to improve their skills and adaptability towards real surgeries.

2.3. Research objectives

Theoretical and practical tests were given to the participants, 50 marks each, an increase in the score indicates improvement in the results [2]; self-making the teaching satisfaction questionnaire, online anonymous filled and statistics analysis after integrating.

2.4. Data analysis

This study used the statistics software SPSS 21.0 as a data processing tool, of which the counting data were described as (%), the verification was calculated by χ^2; measurement data were described as (mean ± SD), the verification was calculated by t, $P < 0.05$ has statistical significance.

3. Results

3.1. Comparison of test scores between two groups

As shown in **Table 1**, the theoretical and practical tests scores in the research group were higher than that of control group.

Table 1. Comparison of the test scores between the two groups

Project	Theoretical test score	Practical test score
Research group (n = 20)	41.25 ± 2.13	40.25 ± 1.12
Control group (n = 20)	34.26 ± 1.21	33.25 ± 1.45
t	8.5682	10.0271
P	< 0.05	< 0.05

3.2. Comparison of interns' satisfaction towards the teaching between the two groups

Based on **Table 2**, the teaching satisfaction of interns in research group was higher than control group.

Table 2. Comparison of the teaching satisfaction between the two groups

Project	Satisfied	Neutral	Unsatisfied	Degree of satisfaction
Research Group (n = 20)	13 (65.00)	7 (35.00)	0 (00.00)	20 (100.00)
Control Group (n = 20)	8 (40.00)	6 (30.00)	6 (30.00)	14 (70.00)
x^2	-	-	-	4.5836
P	-	-	-	< 0.05

4. Discussion

Midwifery is a highly specialized field, and midwife training plays a crucial role developing the skills of midwives. For midwives, clinical internship is where they deal with their patients and society, and it is where they learn and be proficient in midwifery technologies, which are the fundamentals of nursing students [4]. However, as midwifery is a high-risk occupation, together with recently increasing legal and consumer awareness of puerperae and their families, interns may counter many issues during their internship, for example, some puerperae and families are unwilling to undergo surgeries by nursing interns, thus some tutors choose to not let interns handle deliveries to avoid getting complaints. This results in reduction of internship opportunities and also severely impact teaching quality. Therefore, it is important to mediate the contradiction between protecting patients' rights and improving clinical teaching.

The results in this study showed that the scores of both theoretical and practical tests in the research group were higher than that of the control group ($P < 0.05$). Therefore, it is clear that perineal wound model can effectively improve the internship outcomes in nursing students. Hospital internship focuses on treating the perineum wound, providing better effects on clinical practice. While medical college provides a combination of both theory and practical education, which helps in visualizing the abstract knowledge. With repeated practice, the skills of the midwifes can be enhanced and improved, which lays a foundation for clinical practice. Besides, in medical colleges there is a lack of personal bond between the students and the patients, and the communication methods are highly standardized [5]. However, by directly being involved in surgeries, the interns can experience the whole process of a delivery, which will help in linking their theoretical and practical knowledge. Due to the complexity of maternal care, repeated practice alone is not enough. With college education and hospital internship, interns will have a comprehensive understanding of human anatomy, maternal morbidity, and suture techniques guided by clinical tutors. However, they are not capable of performing operations. Therefore, with the perineal wound model and oxtongue model, they can understand the difference between model practice and real operations, hence improving adaptability and confidence. After reworking, their operation skill has significantly improved. In this study, the teaching satisfaction of interns of the research group was higher than that of the control group ($P < 0.05$). In this program, midwife interns performed required procedures in a delivery on the perineal wound models repeatedly, which enhanced their perceptual awareness, stimulated their passion and potential in learning, and also allowed them to better understand suture techniques and related theories. In order to improve the clinical teaching quality, it is important to have reason analysis, clear objectives, appropriate management, evaluation, and feedback, and each procedure should be well-connected to ensure rapid development [6].

In conclusion, the application of perineal wound model could improve the test results of midwife interns and has high teaching satisfaction, with clear clinical benefits.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Analysis of Serum Cys-C, TBA, and Routine Blood Parameters of Patients with Hepatitis B-Related Decompensated Cirrhosis

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Abstract: *Objective:* To study the levels of serum cystatin C (Cys-C), total bile acid (TBA), and other routine blood parameters on patients with decompensated hepatitis B cirrhosis. *Methods:* Study group 1 consisted of 30 patients with hepatitis B-related decompensated cirrhosis, and study group 2 consisted of 30 patients with hepatitis B; while the control group consisted of 30 healthy people who underwent physical examination. The blood parameters were used to evaluate the clinical treatment effect of patients. *Results:* The TBA, Cys-C, alanine transaminase (ALT), total bilirubin (TBIL), aspartate aminotransferase (AST), and international normalized ratio (INR) in study group 1 were significantly higher than those of study group 2 and the control group; while the platelet count (PLT), hemoglobin (Hb), albumin (ALB), and estimated glomerular filtration rate (eGFR) were significantly lower in the study group 1 compared to the control group and study group 2 ($P < 0.05$). The Cys-C, PLT, TBA, AST, TBIL, and INR of patients in study group 1 who were successfully treated were significantly lower than the patients who were not successfully treated ($P < 0.05$). *Conclusion:* Serum Cys-C, TBA, and routine blood parameters are useful in predicting the condition and the prognosis of patients of hepatitis B-related decompensated cirrhosis.

Keywords: Serum Cys-C; TBA; Routine blood parameters; Hepatitis B-related decompensated cirrhosis

Online publication: May 29, 2023

1. Introduction

Liver cirrhosis is a common chronic liver disease, commonly caused by hepatitis B and other hepatitis virus infections. Decompensated liver cirrhosis is a serious condition that has a high mortality rate. Therefore, early detection and effective diagnosis and treatment of patients with decompensated liver cirrhosis are very important to improve their survival rate and quality of life [1-3]. Currently, the levels of serum cystatin C (Cys-C), total bile acid (TBA), and routine blood parameters in patients with decompensated hepatitis B cirrhosis have been increasingly highlighted. These indicators have certain sensitivity and specificity and are helpful for the diagnosis and treatment of patients [4-6]. This article aims to explore the serum Cys-C, TBA and routine blood parameters in patients with hepatitis B-related decompensated cirrhosis, in order to provide reference for clinical practice. In this paper, 30 patients with hepatitis B-related decompensated

cirrhosis, 30 patients with hepatitis B, and 30 healthy people with physical examination were selected, and the following reports are made:

2. Materials and methods

2.1. Information

30 patients with decompensated hepatitis B cirrhosis in the Department of Infectious Diseases and Gastroenterology of Shaanxi Provincial People's Hospital were selected from January to December 2021 and grouped as study group 1; study group 1 consisted of 15 males and females each, aged 36–59 years old, with an average age of 41.25 ± 0.65 years old; they were diagnosed in accordance with the "Chinese Guidelines on the Management of Liver Cirrhosis (2019 Edition) [7]. Meanwhile, 30 patients with hepatitis B were selected to form study group 2, and then 30 healthy people who underwent physical examination were selected to form a control group. The number of men and women in the study group 2 was 16 and 14, respectively, aged 35–58 (41.21 ± 0.61) years old. The number of men and women in the control group was 17 and 13, respectively, aged 32–60 (41.22 ± 0.62) years old. The research protocol has been approved by the Ethics Committee of Shaanxi Provincial People's Hospital, and all participants of this study signed the informed consent.

2.2. Methods

Serum Cys-C, TBA and blood routine indicators were measured to evaluate the effect of the clinical treatment.

2.3. Treatment effect

The treatment was effective: the symptoms were significantly relieved, the systemic edema disappeared, the ascites subsided, the alanine transaminase (ALT) and total bilirubin (TBIL) were restored to less than 2 times the normal value, and the 24-hour urine sodium was 78 mmol/L and above.

2.4. Data inspection

The SPSS25.0 statistical software was used to carry out χ^2 test, where the discrete variables were expressed in the form of percentage, and carry out *t* test, where the continuous variables were expressed in the form of mean ± s. When $P < 0.05$, it is considered to be statistically significant.

3. Results

As shown in **Table 1**, The TBA, Cys-C, ALT, TBIL, aspartate aminotransferase (AST), and international normalised ratio (INR) of study group 2 and the control group were lower than those of the study group 1. However, the platelet count (PLT), haemoglobin (Hb), albumin (ALB), and estimated glomerular filtration rate (eGFR) were significantly lower in study group 1 compared to those of study group 2 and the control group ($P < 0.05$).

In study group 1, Cys-C, PLT, TBA, AST, TBIL, and Hb in patients who were successfully treated were significantly lower than those who were not successfully treated ($P < 0.05$).

Table 1. Comparison of clinical indicators among the three groups

Group	TBA (μmol/L)	Cys-C (mg/L)	ALT (U/L)	TBIL (mmol/L)	AST (U/L)	INR	PLT ($\times 10^9$/L)	Hb (g/L)	ALB (g/L)	eGFR (mg/mL)
Study group 1 (n = 30)	32.51 ± 2.51	1.44 ± 0.75	245.17 ± 52.11	91.37 ± 25.95	255.22 ± 64.14	1.51 ± 0.41	76.01 ± 5.55	101.01 ± 2.55	29.02 ± 4.88	88.26 ± 17.42
Study group 2 (n = 30)	15.21 ± 0.22*	0.87 ± 0.44*	80.24 ± 17.44*	22.15 ± 4.84*	90.42 ± 22.75*	1.32 ± 0.42*	104.02 ± 5.21*	125.05 ± 3.25*	32.72 ± 5.81*	91.11 ± 25.70*
Control group (n = 30)	2.41 ± 0.55*	0.71 ± 0.12*	18.87 ± 2.62*	10.26 ± 3.95*	28.42 ± 6.95*	0.91 ± 0.32*	133.05 ± 2.51*	130.05 ± 2.55*	48.16 ± 5.28*	105.72 ± 28.42*

Note: *P < 0.05 compared to study group 1

Table 2. Comparison of various indicators between patients who were successfully treated and not successfully treated in study group 1

Group	TBA (μmol/L)	Cys-C (mg/L)	WBC ($\times 10^9$/L)	ALT (U/L)	TBIL (mmol/L)	AST (U/L)	INR	PLT ($\times 10^9$/L)	Hb (g/L)	ALB (g/L)	eGFR (mg/ml)
Patients who were successfully treated (n = 19)	20.11 ± 1.22	1.22 ± 0.55	4.11 ± 1.11	222.55 ± 45.16	87.61 ± 9.62	230.11 ± 52.95	1.41 ± 0.43	80.11 ± 5.22	115.31 ± 5.22	29.62 ± 5.11	90.85 ± 15.26
Patients who were not successfully treated (n = 11)	40.11± 2.55	1.84 ± 0.61	4.61 ± 1.12	245.92 ± 55.24	98.22 ± 3.22	299.62 ± 55.22	1.55 ± 0.34	71.11 ± 5.22	95.21 ± 11.55	27.65 ± 5.55	83.72 ± 15.42
t	29.1516	2.8602	1.1851	1.2589	3.5228	3.4120	0.9234	4.5508	6.5723	0.9864	1.2286
P	< 0.05	< 0.05	> 0.05	> 0.05	< 0.05	< 0.05	> 0.05	< 0.05	< 0.05	> 0.05	> 0.05

4. Discussion

In patients with hepatitis B-related decompensated cirrhosis, the increase of serum Cys -C level is closely related to the degree of liver function damage and the prognosis of patients [8-10] .

In patients with hepatitis B-related decompensated cirrhosis, elevated TBA levels usually mean severe damage to liver function and cholestasis, and also indicate that liver cell function is damaged [11-14].

In patients with hepatitis B-related decompensated cirrhosis, indicators such as white blood cell count and C-reactive protein usually increase, while indicators such as red blood cell count and hemoglobin decrease, which are related to the degree of liver function damage and the prognosis of the patient. At the same time, platelet count is also an important indicator to assess the severity of a liver disease, because in patients with decompensated liver cirrhosis, impaired liver function can lead to thrombocytopenia [15].

Detection of serum Cys-C, TBA and routine blood parameters can improve the diagnostic accuracy and therapeutic effect of patients with hepatitis B-related decompensated cirrhosis [16].

The experiments in this group showed that compared with the TBA, Cys-C, ALT, TBIL, AST, and INR of of study group 1 were significantly higher than those of study group 2 and the control group. However, the PLT, Hb, ALB, and eGFR of study group 1 were significantly lower than study group 2 and the control group (P < 0.05). The Cys-C, PLT, TBA, AST, TBIL, and Hb of the patients who were successfully treated in study group 1 were significantly lower than those who were not successfully treated (P < 0.05).

The levels of Cys-C, TBA, and routine blood parameters is helpful in predicting the condition of patients with hepatitis B-related decompensated cirrhosis and their prognosis.

Funding

This work was supported by SPPH Incubator Fund for Development of Science and Technology (2021YJY-19), SPPH Foundation for Development of Science and Technology (2021BJ-26), and International Science and Technology Cooperation Projects of Shaanxi Province (2022KW-14).

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Right Sub-Axillary Incision for Right Pulmonary Vein Atresia in a Child: A Case Report and Literature Review

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Abstract: Unilateral pulmonary vein atresia (UPVA) in children is a rare disease that is characterized by a recurrent pulmonary infection and hemoptysis in childhood. This paper is a report of a case of pulmonary venous atresia treated by a right sub-axillary incision. Hopefully, more literature can be produced to improve the awareness and treatment level of pulmonary vein atresia.

Keywords: Right sub-axillary incision; Unilateral pulmonary vein atresia; Children; Pulmonary collateral vessels

Online publication: May 30, 2023

1. Introduction

Unilateral pulmonary vein atresia (UPVA) in children is a rare disease that is characterized by recurrent pulmonary infection and hemoptysis in childhood. Adult patients occasionally have chest pain or cough, recurrent pleural effusion, and decreased activity tolerance, and some patients have pulmonary hypertension. Pulmonary venous atresia lacks specific clinical manifestations. The types of pulmonary vein atresia include common cava pulmonary vein atresia, bilateral pulmonary vein atresia, unilateral pulmonary vein atresia, and single pulmonary vein atresia. UPVA can be on the left or right side, and there is no reports on which side is more prone to UPVA [1]. There is currently no standard clinical treatment for pulmonary vein atresia, and if patients are not treated in time, the long-term case fatality rate is high [2]. This paper is a report of a case of pulmonary venous atresia treated by a right sub-axillary incision. Hopefully, more literature can be produced to improve the awareness and treatment level of pulmonary vein atresia.

2. Case presentation

The child was 3 years and 2 months old, weighed 13.5 kg, and admitted to the hospital with SpO_2 of 97%. He was hospitalized with the chief complaint of "intermittent cough and fever for more than one month." Children with pulmonary atresia usually have heavier breathing, poor physique, and sweating and are prone to repeated pneumonia. There was no obvious cyanosis and no history of operations or allergies in the past. Physical examination upon admission showed that the patient's breath sounds were rough, the respiratory rate was 30 times/minute, there was no cyanosis of lips, intermittent fever, and the child's peak temperature was 39.0 ℃. No pathological murmur was heard in the auscultatory areas of the heart, the breath sounds in the right lung were softer than the left lung, and no dry and wet rales were heard. Echocardiography showed that the right pulmonary vein was not detected, cardiac catheterization was recommended, and systemic

and pulmonary collaterals were formed near the diaphragm on the posterior wall of the right atrium. The chest anteroposterior radiograph showed a large high-density shadow in the right lung, the heart shadow deviated to the right, and the mediastinum was shifted to the right (**Figure 1**). Cardiac CT showed that the development of the right pulmonary artery and its branches was normal, and no right pulmonary venous return was found. The left pulmonary artery was dilated, and the left pulmonary venous return was normal (**Figure 2**). Cardiac catheterization and pulmonary angiography showed that the diameter of the right pulmonary artery was 7.5 mm, the pressure of the right pulmonary artery was 23/15/17 mmHg, the diameter of the left pulmonary artery was 12 mm, and the pressure of the left pulmonary artery was 18/14/15 mmHg. The systolic pressure of the right pulmonary artery was 5 mmHg higher than that of the left pulmonary artery, and the mean pressure was 2 mmHg higher. However, there was no pulmonary hypertension. Pulmonary arteriography showed that the right pulmonary artery was poorly developed with thin branches; no clear development of the right pulmonary vein was found, the emptying of contrast medium was delayed, and the contrast medium could flow back into the left pulmonary artery from the right pulmonary artery. Embedding angiography of the right pulmonary artery revealed the presence of a common trunk and branches of the right pulmonary vein, which was thinly developed and had a delayed emptying of contrast (**Figure 3**). Descending aortography showed the formation of systemic and pulmonary collateral vessels. The systemic and pulmonary collateral vessels were occluded with coils during cardiac catheterization (**Figure 4**). The patient required surgery, and after communication with his family, the patient and his family opted for surgery, including a right axillary incision and right pulmonary vein, and left atrial connection under extracorporeal circulation. During surgery, the right lung was found to be hypoplastic, and there were many enlarged veins on the surface of the lung and pericardium. The junction of the superior and inferior veins of the right lung and the left atrium was atresia, showing a fibrous cord-like atresia without blood flow. The aortic atresia was longitudinally incised, and the pericardial patch of the right pulmonary vein and left atrium was enlarged to restore the blood flow from the right pulmonary vein to the left atrium. Intraoperative ultrasound showed that the flow velocity at the junction of the right pulmonary vein and left atrium was 1 m/s. The patient fully recovered after the operation, and his physique was better than before. Echocardiography and cardiac CT showed that the blood flow of the right pulmonary vein and left atrium was unobstructed, and the patient was discharged. The patient is still undergoing long-term follow-up.

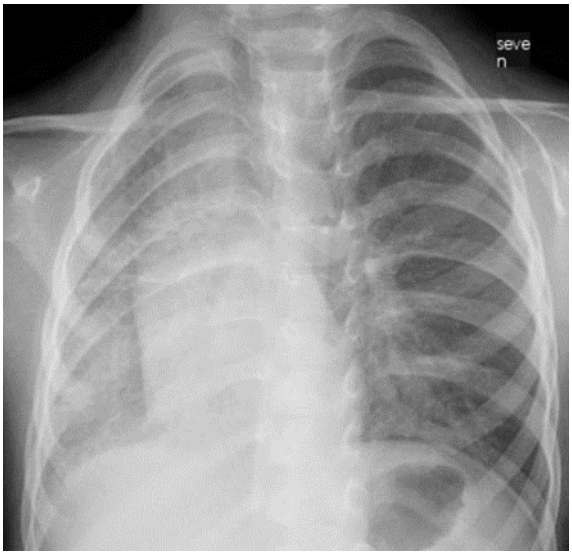

Figure 1. Chest X-ray. Note: The patient's right thorax was slightly smaller, the mediastinum was shifted to the right, the right lung markings were thickened, and the heart shadow was to the right.

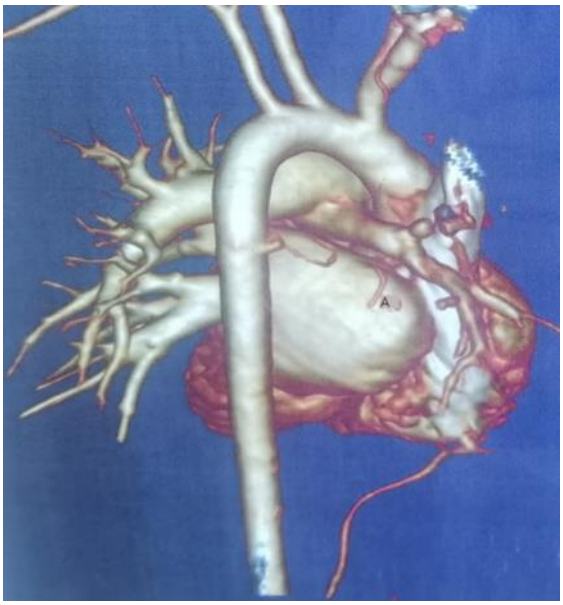

Figure 2. CT three-dimensional reconstruction of the heart of the child. Note: The right pulmonary artery of the patient is narrow, the branches of pulmonary vessels are sparse, the connection between the right pulmonary vein and the left atrium was not seen, and systemic and pulmonary collateral vessels formed in the descending aorta.

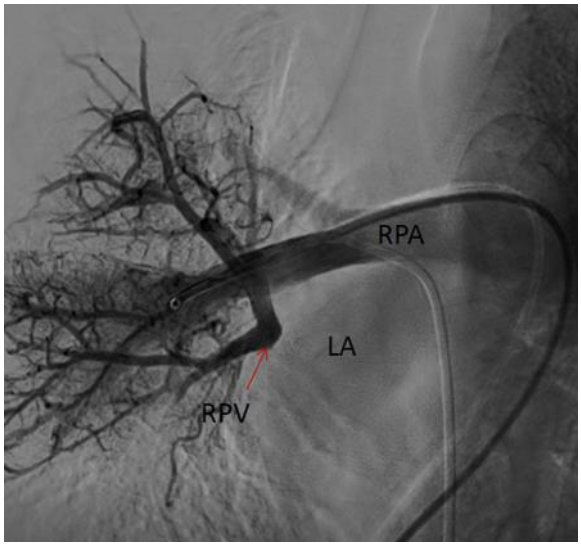

Figure 3. Embedding angiography of the patient's right pulmonary artery. Note: The right pulmonary artery was sparsely marked, the junction of the right pulmonary vein and the left atrium was atretic, and the diffusion of the contrast agent was delayed.

Figure 4. Patient aortography. Note: Angiography of the descending aorta showed the formation of two pulmonary collateral vessels, both supplying the right lung tissue, which were occluded with coils during the operation.

3. Discussion

3.1. Etiology

UPVA is a rare disease, and its morbidity is unknown. At present, most UPVA cases are individual case reports. Fifty percent of the cases occur without any other concurrent conditions, and the remaining 50% of the cases are associated with congenital heart disease [3]. Pulmonary venous atresia can occur on the left or right side, and although it is usually unilateral, there is no significant site advantage. At present, UPVA is considered to be the main cause of congenital diseases. Most patients develop symptoms at a young age of 2 years old, when the probability of congenital heart disease is higher. Histological evidence of active inflammation is rare in cases of UPVA. Har-Even Cohn *et al.* [4] reported that three patients with left pulmonary dysplasia and hemoptysis were diagnosed with rare familial UPVA. It was thought that this disease might be related to autosomal dominant inheritance, but the family refused to undergo genetic testing. However, some scholars believe that UPVA is a secondary vascular occlusion change, and the causes of secondary UPVA include postoperative complications of congenital heart disease [5], mediastinal tumor, pericardial or mediastinal infection, cardiac tumor, and thrombosis. Mohammed Firdouse *et al.* [6] reported a case where a child had a normal pulmonary artery and pulmonary vein before examination, but UPVA was found during follow-up. The patient had not undergone surgery because there were no obvious clinical manifestations. Right pulmonary vein atresia was found in this patient, along with recurrent pneumonia; right pulmonary hypoplasia was found during the operation; and the right pulmonary artery was more underdeveloped than the left pulmonary artery. The patient had no previous history of surgery, which excludes the possibility of a secondary occlusion. More research would be needed to determine whether it was a repeated infection that led to UPVA. Therefore, it is unclear whether UPVA is a congenital disease, and further study is needed.

3.2. Clinical manifestations

Unilateral pulmonary vein atresia has no specific clinical manifestations. Patients usually show different degrees of clinical signs and symptoms, ranging from repeated pulmonary infection, exertional dyspnea, and hemoptysis to no symptoms at all. Pulmonary hypertension may occur in only some patients, and a case report from the United States was the first to report that a 16-year-old patient did not have concurrent pulmonary hypertension [7]. The initial symptoms of UPVA are easily misdiagnosed as tuberculosis or

secondary malignant tumors of the lung. In Vietnam, Cung-Van Cong et al. [8] reported that a 19-year-old patient had been misdiagnosed with tuberculosis and was treated for tuberculosis without laboratory evidence. Hemoptysis is caused by the rupture of bronchial varices or the systemic and pulmonary collaterals, which often indicates that the condition is serious and there is a higher possibility of resection of the affected lung. Some patients may not have obvious clinical signs or symptoms, and only occasional chest pain in a patient can allow for a definite diagnosis [7].

3.3. Diagnosis

The gold standard of clinical diagnosis of unilateral pulmonary vein atresia is cardiac catheterization and angiography. The contrast medium of the pulmonary vein would show that blood cannot flow back into the left atrium and that emptying is delayed. Chest antero-posterior radiography may show mediastinal displacement, lung dysplasia on the affected side, thickening of lung markings, and patchy shadows. The chest CT and echocardiography results showed that there was no blood flow between the pulmonary veins and the left atrium. Some patients were complicated with congenital heart disease. Submucosal bronchial varices in the affected lung can be observed through bronchoscopy, which is a definite manifestation of unilateral obstruction of pulmonary venous return [9]. Bronchial varices may not be present if the patient has other bulky collateral pathways. Therefore, bronchial varices should be considered a possibility in cases of UPVA.

3.4. Treatment

At present, there are no clear treatment guidelines or mature treatment plans. It has been reported that some patients had no obvious symptoms and were followed up for a long time [1,7,8]. If the patient has repeated pulmonary infections and hemoptysis and is older at the time of diagnosis, pneumonectomy on the affected side is helpful to improve the quality of life [4,10]. It is believed that cardiac catheterization and angiography should be performed to evaluate the development of the pulmonary veins and the distance between the obturator end of pulmonary veins and the left atrium. There are surgical options such as noncontact suture of pulmonary veins and left atrium or expanded anastomosis of patches, which is selected based on the patient's condition. For patients with hemoptysis, interventional occlusion of collateral vessels can be considered to alleviate the symptoms of hemoptysis to improve their quality of life. In this case, right axillary incision was chosen to anastomose the right pulmonary vein with the left atrium, which had a clear field of vision, minimized the surgical trauma, and made the axillary incision more concealed and beautiful, and this method had not been reported in previous literature.

3.5. Conclusion

UPVA is a rare disease. Whether it is a congenital disease or acquired disease remains debatable. It is important to raise awareness for patients with repeated pulmonary infection and hemoptysis, especially infants, to avoid a missed diagnosis or misdiagnosis. Early detection, definite diagnosis, and appropriate treatment are helpful for the long-term prognosis of patients.

Disclosure statement

The author declares no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Effect of Rituximab Versus Mycophenolate Mofetil or Cyclophosphamide as Control in Lupus Nephritis: A Meta-Analysis

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Abstract: *Objective:* To evaluate the effects of rituximab versus mycophenolate mofetil or cyclophosphamide as control in lupus nephritis by meta-analysis. *Methods:* A systematic search was carried out up to January 2022, obtaining 7 studies involving 645 participants with lupus nephritis at the commencement of the investigation; 198 of them were treated with rituximab, while 447 were treated with mycophenolate mofetil or cyclophosphamide. We determined the odds ratio (OR) and mean difference (MD) with 95% confidence index (CI) to compare rituximab's efficacy to that of mycophenolate mofetil or cyclophosphamide as control in lupus nephritis using random- or fixed-effects model by dichotomous or continuous techniques. *Results:* The rituximab group showed significantly higher complete renal remission rate (OR = 2.52; 95% CI 1.30–4.91, P = 0.006) and total renal remission rates (OR = 2.22; 95% CI 1.36–3.63, P = 0.001) than the control group. However, there was no significant difference in terms of end Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score (MD -1.16; 95% CI -2.88–0.57, P = 0.19), proteinuria (MD -0.31; 95% CI -0.70–0.09, P = 0.013), and serum creatinine (MD 0.01; 95% CI -0.04–0.07, P = 0.64) between the rituximab group and the control. *Conclusion:* Rituximab exhibited significantly greater complete renal remission rate and total renal remission rates, with no significant difference in terms of shorter-end SLEDAI, proteinuria, and serum creatinine, compared with the control in individuals with lupus nephritis.

Keywords: Rituximab; Mycophenolate mofetil; Cyclophosphamide; Lupus nephritis; Complete renal remission rate; Total renal remission rates; End Systemic Lupus Erythematosus Disease Activity Index; Proteinuria; Serum creatinine

Online publication: May 30, 2023

1. Introduction

Lupus nephritis occurs in up to 40% of individuals with systematic lupus erythematosus [1] and is a main contributor to illness and mortality. At present, the suggested treatment for lupus nephritis comprises prednisolone with intravenous cyclophosphamide or oral mycophenolate mofetil [2]. However, these treatments are not always effective, and recurrent relapses would require further continual management. Ultimately, long-term organ damage occurs as a consequence of drug toxicity. B-lymphocyte has a role in the development of systematic lupus erythematosus and lupus nephritis [3]. Rituximab, a monoclonal antibody against CD20, prevents pathogenic B cells from producing autoantibodies and antigens [4]. Rituximab is effective in some individuals with lupus nephritis, whether it is used solely or in combination with other immunosuppressants, comprising those who are unresponsive or with poor response to cyclophosphamide or oral mycophenolate mofetil treatment [2,5,6]. However, current data from a randomized controlled trial in which rituximab or placebo was used as an adjuvant to glucocorticoids and oral mycophenolate mofetil for lupus nephritis reported that rituximab, in comparison with placebo, had no

effect on the improvement of clinical outcomes after one year of follow-up [7]. Hence, we intended to determine the effect of rituximab in comparison with that of mycophenolate mofetil or cyclophosphamide as a control on lupus nephritis in our current study.

2. Methodology

This meta-analysis followed the accepted technique and was organized according to the epidemiology statement [8].

2.1. Study selection

The search was limited to studies in English, and the inclusion criteria were not restricted by the study type or size.

The main goal of the studies was to compare the effect of rituximab to that of mycophenolate mofetil or cyclophosphamide as a control in lupus nephritis, utilizing odds ratios (ORs), mean differences (MDs), frequency rates, or relative risks, with a 95% confidence index (CI). Editorials, review articles, letters, and comments were excluded from the analysis, as they had no correlation. **Figure 1** shows the mode of analysis.

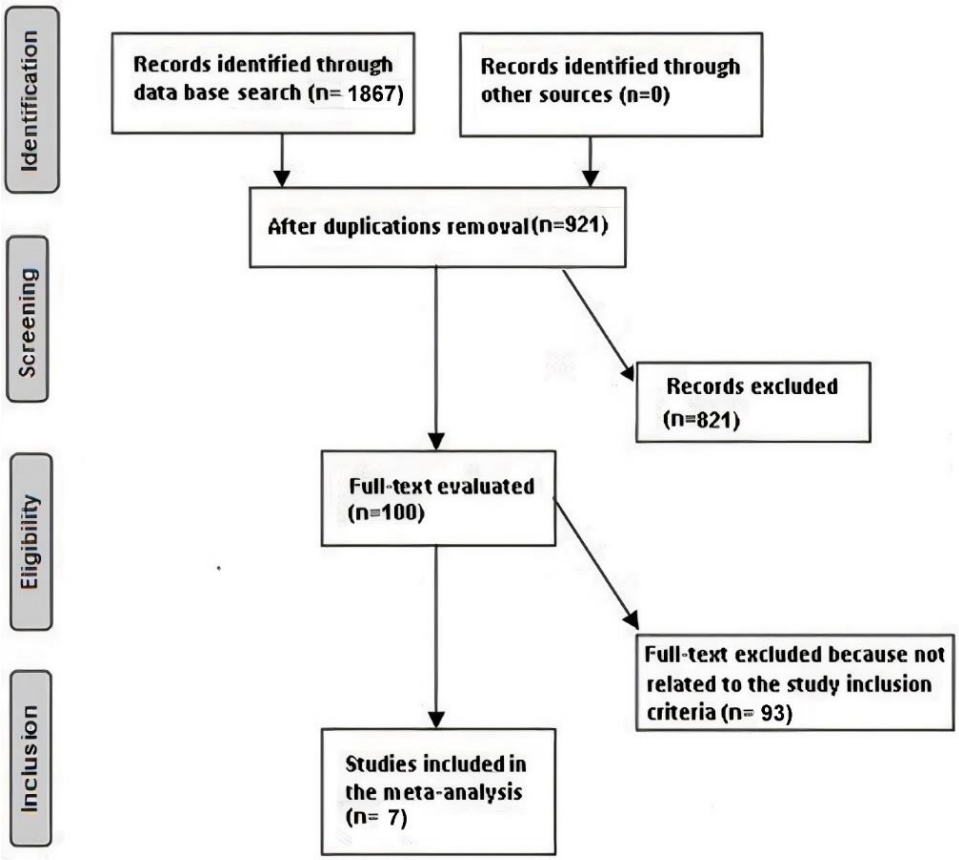

Figure 1. Schematic diagram of the study method

In this meta-analysis, we classified and integrated the inclusion criteria as follows:

(i) prospective study, randomized controlled trial, or retrospective study;
(ii) individuals with lupus nephritis;
(iii) rituximab and control as interventions;
(iv) research work comparing rituximab with mycophenolate mofetil or cyclophosphamide as control in lupus nephritis.

The exclusion criteria were as follows:

(i) research work with management other than rituximab and mycophenolate mofetil or cyclophosphamide as control;
(ii) research work that did not focus on the impact of comparative outcomes;
(iii) research work that did not evaluate the effect of rituximab compared to that of mycophenolate mofetil or cyclophosphamide as control in lupus nephritis.

2.1.1. Identification

The PICOS approach was used. We established the crucial parts of PICOS: P (population), lupus nephritis patients; I (intervention/exposure), rituximab; C (comparison), mycophenolate mofetil or cyclophosphamide as control; O (outcome), complete renal remission rate, total renal remission rates, end SLEDAI, proteinuria, and serum creatinine; S (study design), without limitation [9]. A systematic and quick search on MEDLINE/PubMed, Google Scholar, Embase, OVID, and Cochrane Library up to January 2022 was conducted by using keywords and correlated words, such as rituximab, mycophenolate mofetil, cyclophosphamide, lupus nephritis, complete renal remission rate, total renal remission rates, end SLEDAI, proteinuria, and serum creatinine (**Table 1**). EndNote was used to pool the relevant investigations to eliminate duplication. The gathering of information was done from the remaining studies. A comprehensive evaluation of the title and abstracts was also carried out to rule out any data that did not show any effect of rituximab, in comparison with mycophenolate mofetil or cyclophosphamide as control, on the outcomes investigated in individuals with lupus nephritis.

Table 1. Search strategy for each database

Database	Search strategy
PubMed	#1 “rituximab” [MeSH Terms] OR “mycophenolate mofetil” [MeSH Terms] OR “cyclophosphamide” [MeSH Terms] OR “lupus nephritis” [All Fields] #2 “complete renal remission rate” [MeSH Terms] OR “proteinuria” [All Fields] OR “serum creatinine” [All Fields] OR “total renal remission rates” [All Fields] OR “end Systemic Lupus Erythematosus Disease Activity Index score” [All Fields] #3 #1 AND #2
Embase	#1 “rituximab”/exp OR “mycophenolate mofetil”/exp OR “cyclophosphamide”/exp OR “lupus nephritis”/exp #2 “complete renal remission rate”/exp OR “proteinuria”/exp OR “serum creatinine”/exp OR “total renal remission rates”/exp OR “end Systemic Lupus Erythematosus Disease Activity Index score”/exp #3 #1 AND #2
Cochrane Library	#1 (rituximab):ti,ab,kw OR (mycophenolate mofetil):ti,ab,kw OR (cyclophosphamide):ti,ab,kw OR (lupus nephritis):ti,ab,kw (word variations have been searched) #2 (complete renal remission rate):ti,ab,kw OR (proteinuria):ti,ab,kw OR (serum creatinine):ti,ab,kw OR (total renal remission rates):ti,ab,kw OR (end Systemic Lupus Erythematosus Disease Activity Index score):ti,ab,kw (word variations have been searched) #3 #1 AND #2

Abbreviations: /exp, explosion; ti,ab,kw, terms in either title, abstract, or keyword fields.

2.1.2. Screening

The data characteristics about the subject and study were collected, categorized, and aggregated into a uniform format. In order to categorize the data in a standardized form, the first author’s surname, length of study/trial, place of practice, study design, subject type, sample size, categories, demography, methods of

treatment, information source, method of evaluation (both qualitative and quantitative), statistical analysis, and primary outcome evaluation were used [10].

In order to assess the methodological quality, the Cochrane risk-of-bias tool from the Cochrane Handbook for Systematic Reviews of Interventions version 5.1.0 was utilized.

The extent of bias risk was taken into account in the assessment criteria. If all criteria of quality are satisfied, the risk is low; if one of the criteria of quality is not met or is partially met, the risk is moderate; but if one of the criteria of quality is not met or included, the risk is high. Any inconsistencies in the original article were double-checked.

In order to ensure the reliability of methodology, discussions were held to address any disagreement that occurred between the two reviewers while gathering data and, if necessary, by the corresponding author when the inclusion criteria of a study/trial were found to be dependent on previously indicated standards [11]. When several types of data were found in a single study based on the evaluation of relationship, they were extracted independently.

2.1.3. Eligibility

The primary eligibility criterion was the effect of rituximab on lupus nephritis when compared to mycophenolate mofetil or cyclophosphamide as control. In lupus nephritis, the effect of rituximab, compared to mycophenolate mofetil or cyclophosphamide as control, on the complete renal remission rate, total renal remission rates, end SLEDAI, proteinuria, and serum creatinine was evaluated, and the extraction of these data was done.

2.1.4. Inclusion

Studies comparing rituximab's effect on lupus nephritis with that of mycophenolate mofetil or cyclophosphamide as control were included in the sensitivity analysis. The effect of rituximab in comparison with mycophenolate mofetil or cyclophosphamide as control in lupus nephritis was deemed a subgroup of sensitivity analysis.

2.2. Statistical analysis

At a 95% CI, the OR and MD for a fixed-effects or random-effects model were estimated using dichotomous or continuous approaches. The I^2 index ranged from 0 to 100%, with the I^2 index for heterogeneity being defined as no (0%), low (25%), moderate (50%), and high (75%) [10]. The random-effects model was used when $I^2 > 50\%$, whereas the fixed-effects model was used when $I^2 < 50\%$. In sub-group analysis, a significant difference in *P*-value was stated at 0.05 in the initial evaluation of the outcome. By evaluating the funnel plots of the logarithm of ORs compared to their standard errors, publication bias was evaluated objectively and subjectively by Egger's regression test (if $P \geq 0.05$) [10]. All of the *P*-values were two-tailed. Review Manager version 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used to perform statistical analysis and produce graphs.

3. Results

Seven studies (from 2008 to 2022) that met the inclusion criteria were selected from 1,867 different studies [2,5,6, 12-15]. Based on the seven studies, there were 645 participants with lupus nephritis, among which 198 were treated with rituximab, while 447 were treated with mycophenolate mofetil or cyclophosphamide as control for lupus nephritis. All past works evaluated the effect of rituximab in comparison with mycophenolate mofetil or cyclophosphamide as control in lupus nephritis. All seven studies reported data stratified by complete renal remission rates and total renal remission rates, five studies reported data stratified by end SLEDAI, five studies reported data stratified by proteinuria, and five studies reported data

stratified by serum creatinine. At the commencement of investigation, there were between 24 and 222 individuals with lupus nephritis. **Table 2** shows the results of the seven investigations.

Table 2. Characteristics of the selected studies for meta-analysis

Study	Country	Total	Rituximab	Control	Type of control
Moroni, 2012 [6]	Italy	24	10	14	Cyclophosphamide
Rovin, 2012 [13]	USA	144	72	72	Mycophenolate mofetil or cyclophosphamide
Moroni, 2014 [2]	Italy	54	17	37	Mycophenolate mofetil or cyclophosphamide
Zhang, 2015 [5]	China	84	42	42	Cyclophosphamide
Goswami, 2019 [14]	India	222	22	200	Mycophenolate mofetil or cyclophosphamide
Roccatello, 2021 [15]	Italy	60	30	30	Mycophenolate mofetil or cyclophosphamide
Gururani, 2021 [16]	India	57	5	52	Mycophenolate mofetil or cyclophosphamide
	Total	**645**	**198**	**447**	

The rituximab group showed significantly higher complete renal remission rate (OR = 2.52; 95% CI 1.30–4.91, P = 0.006), with moderate heterogeneity (I^2 = 50%), and total renal remission rates (OR = 2.22; 95% CI 1.36–3.63, P = 0.001), with no heterogeneity (I^2 = 0%), in comparison with the control group, as shown in **Figures 2** and **3**.

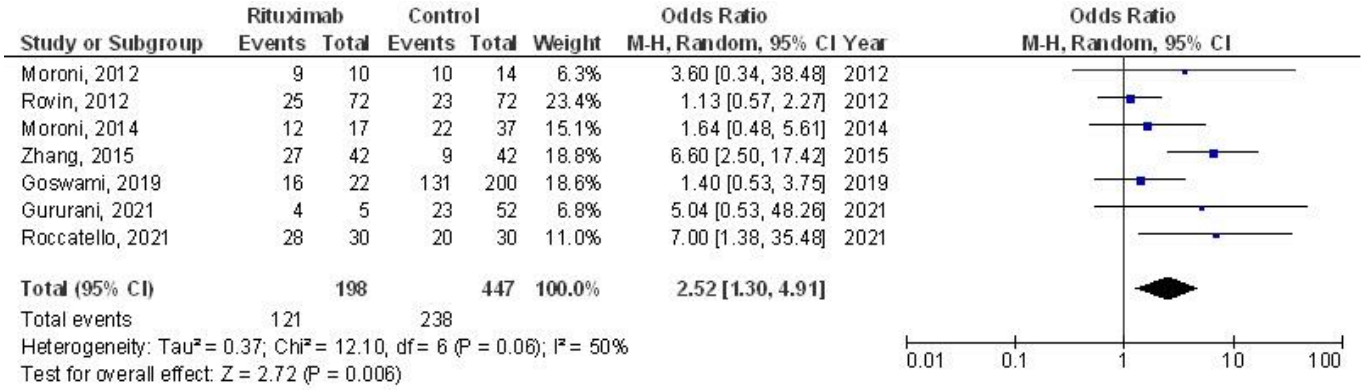

Figure 2. A forest plot showing the complete renal remission rate of rituximab versus control in individuals with lupus nephritis

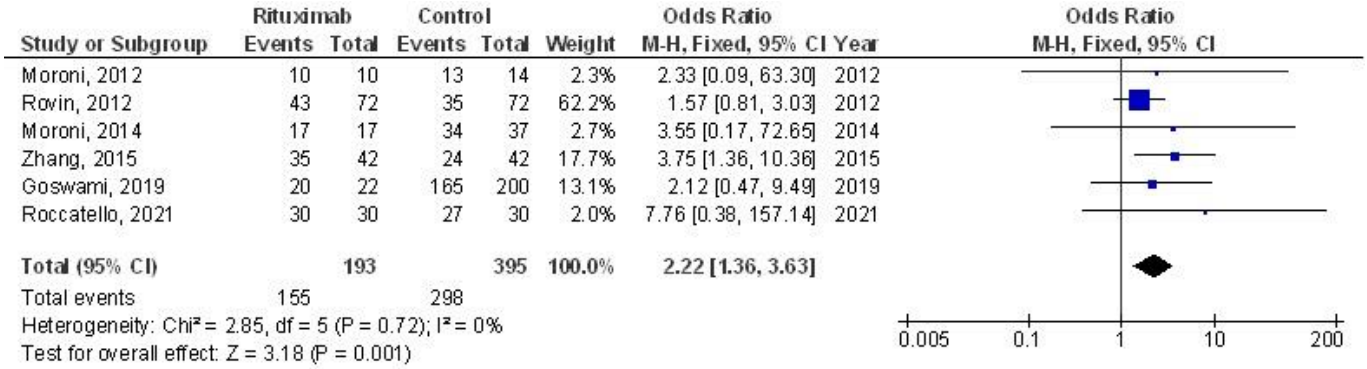

Figure 3. A forest plot showing the total renal remission rates of rituximab versus control in individuals with lupus nephritis

There were no significant differences in terms of end SLEDAI (MD -1.16; 95% CI -2.88– 0.57, P = 0.19), with high heterogeneity (I^2 = 83%), proteinuria (MD -0.31; 95% CI -0.70–0.09, P = 0.013), with

high heterogeneity (I^2 = 87%), and serum creatinine (MD 0.01; 95% CI -0.04–0.07, *P* = 0.64), with no heterogeneity (I^2 = 0%), between rituximab and control in individuals with lupus nephritis, as shown in **Figures 4–6**.

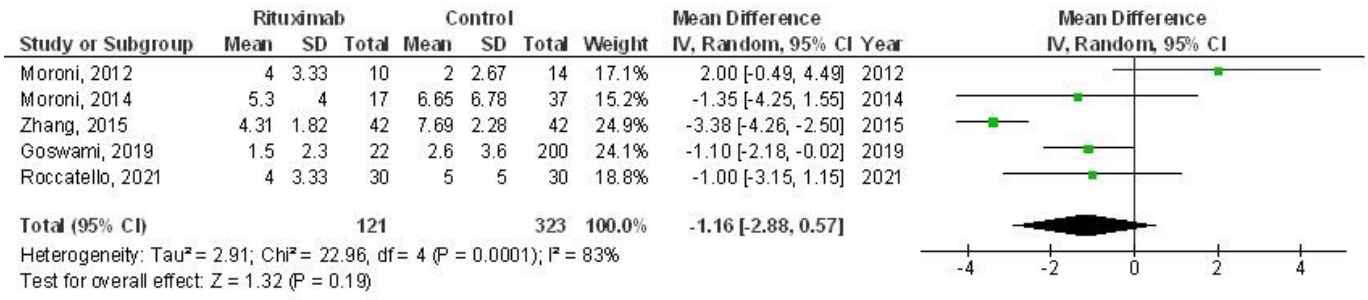

Figure 4. A forest plot showing the end SLEDAI score of the rituximab group versus the control group

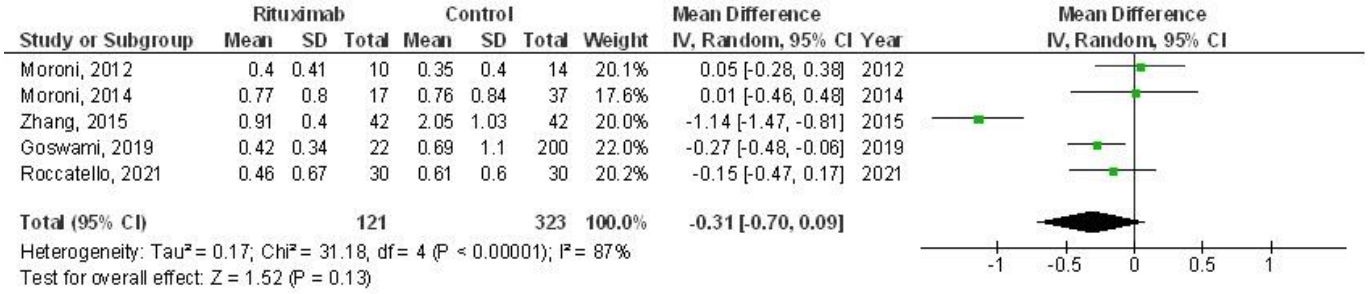

Figure 5. A forest plot showing the proteinuria of the rituximab group versus the control group

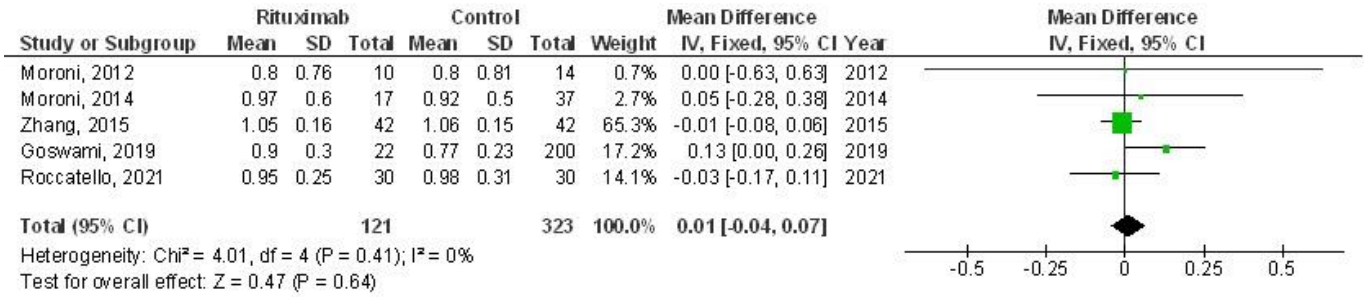

Figure 6. A forest plot showing the serum creatinine of the rituximab group versus the control groups

Since none of the studies adjusted or specified these characteristics, the stratified data did not evaluate age, gender, or ethnicity differences between the two groups. When quantitative measurement was performed via Egger's regression test and the evaluation of the funnel plot, no publication bias (*P* = 0.87) was found. However, some randomized controlled trials demonstrated poor methodological quality. There was no biased reporting or incomplete data in any of the studies, indicating that they were free of selective reporting bias.

4. Discussion

In the seven studies selected, 645 participants were included in our meta-analysis, among which 198 of them were treated with rituximab at the commencement of the study, while the remaining 447 were treated with mycophenolate mofetil or cyclophosphamide as control for lupus nephritis [2,5,6, 12-15]. The rituximab group showed significantly higher complete renal remission rate and total renal remission rates when compared to the control group. However, there was no significant difference in terms of end SLEDAI,

proteinuria, and serum creatinine between the rituximab group and the control group. The analysis of outcomes ought to be conducted with care in view of the small number of studies selected and the small sample size in more than half of the included studies; 5 out of 7 studies had a sample size of less than 100, suggesting the need for additional research to either validate these findings or perhaps contribute to the confidence in the effect assessment.

Lately, a growing number of studies have revealed that the addition of rituximab appears to be of benefit to the management of lupus nephritis [2,5,6]. Kotagiri *et al*. [16] demonstrated a partial or complete renal response to rituximab therapy in 79% of participants with refractory illness who did not respond to standard treatment (steroids plus cyclophosphamide, mycophenolate, or azathioprine) at a median period of five months. The results from a multicentered observational study in Italy demonstrated that the renal remission rates, both complete and partial response, to rituximab in individuals with systematic lupus erythematosus refractory to standard treatment reached 94.1%, and the complete renal remission rate was 30.9% after a 12-month follow-up period [17]. This meta-analysis supported the effectiveness of rituximab as demonstrated in previous studies. Nevertheless, the lupus nephritis assessment in rituximab research on individuals suffering from active lupus nephritis has reported that the rates of renal remission, either partial or complete response, were not statistically different between the group treated with rituximab and the control group [12]. The reason for this may be the different baseline characteristics of patients in the lupus nephritis assessment with rituximab study. The patients enrolled in the lupus nephritis assessment with rituximab study were individuals with first occurrence of lupus nephritis, as opposed to the participants in our meta-analysis who had been treated with various immunosuppressive drugs and were typically resistant to standard therapy. This inconsistency may have been caused by the substantially greater sample size in our study, which may be another factor. We also pooled further renal outcomes at the end of the follow up, but no significant difference was found between them on which the addition of more studies perhaps could significantly affect the confidence level. A relative improvement in end SLEDAI and proteinuria was observed in individuals treated with rituximab. Lowering proteinuria and serum creatinine is crucial to treating lupus nephritis. However, no significant difference or relative difference in serum creatinine was observed at the end of the follow-up. The possible reason for this inconsistency is that only five studies included information on proteinuria at the end of the follow-up period, whereas the other two did not provide detailed values that might have had an impact on the results. The results indicated that the group treated with rituximab had lower proteinuria at the end of the follow-up period, although the difference was not statistically significant. However, if more cases were recognized and analyzed, rituximab may be effective at reducing proteinuria. Contis *et al*. [18] demonstrated that rituximab contributes to the improvement of proteinuria in individuals with lupus nephritis, from 3 g/24 h at baseline to 0.5 g/24 h after 12 months of follow-up. Hence, greater, properly designed, prospective, and controlled investigations are required to evaluate and assess these influences. The safety of rituximab for induction in individuals with lupus nephritis requires additional assessment.

This meta-analysis demonstrated the association between rituximab and mycophenolate mofetil or cyclophosphamide as control in individuals with lupus nephritis. In order to confirm this potential relationship and obtain outcomes that are clinically significant, additional research is required. Clinically significant outcomes have been indicated in other meta-analyses that demonstrated similar effects [7, 19-22], but a clear justification has yet to be offered to explain these outcomes, thereby necessitating further investigation. Our study did not establish whether these factors are related to the outcomes. Therefore, well-designed clinical trials are needed to evaluate these factors in different age groups, genders, and ethnicities.

5. Limitations

Since many studies were excluded from this meta-analysis, there is a possibility of collection bias. The

eliminated studies did not meet the inclusion criteria of the meta-analysis. Furthermore, we were unable to ascertain if the outcomes were associated with age, gender, or ethnicity. The goal of the study was to see if there is a link between the effect of rituximab and mycophenolate mofetil or cyclophosphamide as control in lupus nephritis on the outcomes of individuals with lupus nephritis. Since the study was based on data from previous studies, it may be bias due to missing details. This meta-analysis was based on seven studies, five of which had small sample size (under 100 participants). In addition, the type of rituximab, mycophenolate mofetil, or cyclophosphamide used in the included studies for lupus nephritis treatment varied. Individual characteristics such as age, gender, obedience, nutritional status, and ethnicity were unlikely to cause bias. As a result of multiple unpublished research and missing data, there could be a pooled influence bias. Various pharmacological drugs, treatment schedules, and dosages in addition to healthcare plans were used. Moreover, the included studies did not provide a sufficient assessment of the hospital expenses covered by the individuals studied.

6. Conclusions

When compared to controls, patients with lupus nephritis treated with rituximab had significantly higher complete and total renal remission rates. However, there was no significant difference in proteinuria, serum creatinine, or SLEDAI score between the rituximab group and the control group. Since more than half of the studies included in our meta-analysis have small sample size, the analysis of outcomes should be performed with care, along with the recommendation of other studies to verify these outcomes and perhaps contribute to the confidence in the effect evaluation.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Effect of Nursing Intervention Based on Caprini Risk Assessment Scale for Venous Thromboembolism in Perioperative Patients with Liver Cancer

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Abstract: *Objective:* To explore the effect of nursing intervention based on Caprini risk assessment scale for venous thromboembolism (VTE) in perioperative patients with liver cancer. *Methods:* A total of 128 hepatocellular cancer (HCC) patients who were hospitalized in our department from January 2021 to March 2022 and met the research criteria were selected. According to odd and even numbers in the order of inclusion, 64 cases were divided into two groups: a control group and an observation group. The control group received routine nursing intervention during perioperative period, while the observation group received nursing intervention based on Caprini risk assessment scale for VTE. The incidence of VTE and complications were compared between the two groups. *Results:* The incidence of VTE and postoperative complications in the observation group were lower than those in the control group ($P < 0.05$). *Conclusion:* Nursing intervention based on Caprini risk assessment scale for VTE can reduce the incidence of perioperative deep vein thrombosis and complications in patients with liver cancer; thus, it is worthy of clinical application.

Keywords: Thrombotic risk assessment scale based on Caprini model; Deep vein thrombosis; Liver cancer; Nursing intervention

Online publication: May 30, 2023

1. Introduction

Venous thromboembolism (VTE) is a common clinical disorder caused by abnormal aggregation of blood in veins. It includes deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT is more common in the lower extremities, and the detachment of thrombus may cause pulmonary embolism, which endangers the life of patients. The incidence of VTE in patients with malignant tumors is about 5%–60%, which is about 4 times that of healthy people [1]. Liver malignancy ranks fourth in the incidence of malignant tumors in China. At present, surgical resection is an effective treatment. It is of great clinical significance to conduct perioperative VTE screening and intervention in patients with liver cancer, so as to achieve early detection and prevention. The Caprini risk assessment scale is an individualized VTE risk assessment model developed by American surgeons based on the clinical characteristic assessment of surgical patients by Caprini [2]. Relevant research results have shown that Caprini risk assessment scale can effectively screen high-risk, medium-risk, and low-risk patients with VTE, so as to facilitate the adoption of targeted, graded prevention measures and thus effectively reduce the incidence of VTE in patients [3]. In this study, we explored the effect of nursing intervention based on Caprini risk assessment scale for VTE in perioperative

patients with liver cancer.

2. Data and methods

2.1. General information

A total of 128 patients who received surgical treatment for liver cancer in our department from January 2021 to March 2022 were selected as the research subjects. Inclusion criteria: (1) surgical treatment for liver cancer; (2) no venous thrombosis on admission; (3) no sensory, language, motor, cognitive, intellectual, or other dysfunction before surgery; and (4) informed consent given. Exclusion criteria: (1) patients with confirmed venous thrombosis at admission; (2) patients with contraindications at admission and no intervention measures can be taken; (3) patients using anticoagulants, such as low molecular weight heparin and warfarin; and (4) patients with communication disorders and poor compliance. Patients who met the criteria were divided into two groups (a control group and an observation group) according to odd and even numbers of inclusion order, with 64 cases in each group. The control group consisted of 38 male and 26 female patients with an average age of 59.3 ± 3.65 years, while the observation group consisted of 34 male and 30 female patients with an average age of 62.1 ± 2.11 years. There were no deaths in the two groups during hospitalization, and no statistically significant differences were observed between the two groups in terms of age, gender, surgical method, operation time, Autar [4] score, and other data ($P > 0.05$), as shown in **Table 1**.

Table 1. Comparison of general data between the two groups

Factors	Control group	Observation group	*P*-value
Gender			
Male	38	34	
Female	26	30	
Age (mean ± SD, years)	59.3 ± 3.65	62.1 ± 2.11	> 0.05
Operation time (mean ± SD, h)	3.56 ± 1.23	3.72 ± 1.06	> 0.05
Autar score on postoperative day			
Medium-risk group (11–14 points)	23	21	
High-risk group (≥ 15 points)	41	43	

2.2. Methods

2.2.1. Control group

Routine nursing was adopted in the perioperative period, *i.e.*, the nurses explained to the patients and their families the purpose and method of preventing venous thrombosis, ensured that the patients maintained proper lower limb position, turned over the patients and patted their backs regularly, avoided the lower limb intravenous line, ensured moderate fluid replacement to avoid blood from being too concentrated, taught the patients ankle pump exercises in bed, encouraged them to drink more water, *etc*.

2.2.2. Observation group

On the basis of routine nursing, the Caprini risk assessment scale for VTE was used for scoring and intervention. The specific measures were as follows: a VTE intervention core group consisting of 2 chief physicians, 4 attending physicians, 1 head nurse, and 5 nurses was established in the department of which the 2 chief physicians in the team were responsible for training the team members on VTE-related knowledge and the application of the risk assessment scale. Each team member mastered the evaluation methods and preventive measures of the risk assessment scale. The first assessment of each patient was

done by the doctor and nurse in charge within 24 hours of admission using the Caprini risk assessment scale. The patient/family member was required to provide informed consent, and the results were recorded in the course of disease and nursing record sheet. High-risk and extremely high-risk patients were assessed every 8 hours, dynamically when their condition changes, and again within 6 hours after surgery. 0–1 was classified as low risk, 2 as medium risk, 3–4 as high risk, and 5–7 as very high risk (**Table 2**). According to the score, corresponding nursing and treatment orders were provided by the doctor in charge (**Table 3**). For high-risk and extremely high-risk patients with a score of 3 or more, the chief physician of the group was invited to participate in the review of the treatment plan. The specific measures are stated below.

(1) Basic measures: Suitable for low-risk patients with a score of 0–1. The doctors and nurses in charge educated and encouraged the patients to quit smoking and drinking, keep their stools soft, drink more water (> 2,500 mL/d), perform deep breathing exercises, blow up balloons, get out of bed more often, perform ankle pump and quadriceps exercises, prevent lower limb infusion, *etc*.

(2) Basic measures + physical measures: Suitable for medium-risk patients with a score of 2. On the basis of basic measures, intermittent pneumatic compression device was used and elastic socks were worn. Pneumatic therapy was performed twice a day for one hour each time. The nurses assisted the patients in selecting medical elastic socks with appropriate specifications and instructed the patients to wear them before getting up or 8 minutes after elevating their lower extremities, with a slight sense of tightness as appropriate, observe the temperature and color of their lower extremities, wear them for no more than 12 hours a day, and relax once every 4 hours.

(3) Basic measures + physical measures + drug: Suitable for high-risk patients with a score of 3–4. On the basis of basic measures + physical measures, oral warfarin and rivaroxaban or injection of low molecular weight heparin were followed by medical advice to ensure timely and accurate anticoagulant therapy. In drug treatment, patients were encouraged to avoid injury or falls and brush their teeth with a soft-bristled toothbrush, observed for bleeding tendency, regularly tested to determine their coagulation function, and given low molecular weight heparin according to the results; their body temperature was closely monitored, and the color and swelling of their limbs were also monitored on a daily basis; a subcutaneous injection of 4000 IU low molecular weight heparin was administered 12 hours before surgery.

(4) Basic measures + physical measures + drugs + others: Suitable for extremely high-risk patients with a score of 5. On the basis of implementing the aforementioned measures, vascular surgeons and other specialists were invited for consultation when necessary to conduct individualized intervention programs and regularly review the patients' coagulation function and other indicators.

Table 2. Caprini risk assessment scale

Score	Description
1 point	Age 41–60; obese (BM1 ≥ 25 kg/m^2); abnormal pregnancy; pregnancy or postpartum (1 month); on birth control pills or hormone replacement therapy; bedbound; history of inflammatory bowel disease; lower limb edema; varicose veins; severe lung disease, including pneumonia (within 1 month); abnormal pulmonary function, chronic obstructive pulmonary disease; acute myocardial infarction; congestive heart failure (within 1 month); sepsis (within 1 month); planning for minor surgery; major surgery (within 1 month); other risk factors
2 points	Age 61–74; plaster fixation (within 1 month); in bed for > 72 hours; malignant tumor (past or present); central vein catheterization; laparoscopic surgery (> 45 minutes); major surgery (> 45 minutes); arthroscopic surgery
3 points	Age ≥ 75; deep vein thrombosis/pulmonary embolism; family history of thrombosis; heparin-induced thrombocytopenia (HIT); congenital or acquired thrombosis; anticardiolipin antibody positive; prothrombin 20210A positive; factor V Leiden positive; Lupus anticoagulant positive; elevated serum homocysteine.

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5 points	Stroke (within 1 month); acute spinal cord injury (paralysis) (within 1 month); selective lower limb joint replacement; multiple trauma to hip, pelvic, or lower limb fractures (within 1 month)

Note: Low risk 0–1 point; medium risk 2 points; high risk 3–4 points; extremely high risk ≥ 5 points

Table 3. Corresponding treatment strategy

Surgical and invasive procedures	Venous thromboembolism risk classification	Prevention strategy
0–1	Low risk	Basic measures
2	Medium risk	Basic + physical measures
3–4	High risk	Basic + physical + drug
≥ 5	Extremely high risk	Basic + physical + drug + other
(1) Basic measures: □ Elevation of affected limb □ Ankle movement □ Quadriceps contraction		
□ Turn over or actively flex lower limbs every 2hours □ Drink more water		
□ Quit smoking and drinking □ Keep bowels open □ Deep breathing exercises or blow balloons		
□ Get out of bed and exercise □ Others: _____		
(2) Physical measures: □ Intermittent inflation pressure device □ Wear elastic socks		
(3) Drug: □ Low molecular weight heparin subcutaneous injection		
□ Rivaroxaban □ Warfarin □ Other		

2.2.3. Observation indicators

The incidence of VTE and its complications were compared between the two groups. Lower limb vascular ultrasonography was performed 3–5 days after surgery to determine the presence of DVT. Complications included pulmonary infection, gastrointestinal bleeding, pressure sore, *etc*., and gastrointestinal bleeding included blood in gastric fluid from gastric tube drainage, positive stool occult blood, and black stool.

2.2.4. Statistical analysis

SPSS 17.0 was used. Statistical data were compared by chi-square test with two independent samples, and rank data were compared by Wilcoxon rank-sum test with a test level of $\alpha = 0.05$.

3. Results

3.1. Incidence of venous thromboembolism

The occurrence of VTE in the two groups was compared (see **Table 4**). Postoperative VTE occurred in one case (3.12%) in the observation group and five cases (7.81%) in the control group, with four cases of DVT involving the lower extremity and one case of pulmonary embolism. The incidence of thrombus in both the observation group and the control group was consistent with the findings of Jing *et al*. [5].

Table 4. Comparison of venous thromboembolism incidence between the two groups

Group	Number of cases	With VTE	No VTE
Control group	64	5 (7.81)	59 (92.19)
Observation group	64	1 (1.56)	63 (98.43)
χ^2 value			9.714
P-value			0.002

Abbreviation: VTE, venous thromboembolism.

3.2. Complications

The comparison of complications between the two groups is shown in **Table 5**.

Table 5. Comparison of rate of complications between the two groups

Group	Number of cases	Bleeding from gastric tube drainage	Stool occult blood	Tarry stool	Pulmonary infection	Pressure sore
Control group	64	2 (3.92)	4 (7.84)	2 (3.92)	2 (3.92)	3 (5.88)
Observation group	64	0 (0.00)	1 (1.96)	1 (1.96)	1 (1.96)	1 (1.96)
χ^2 value						5.718
P-value						0.017

4. Discussion

VTE is a high-incidence complication after major surgery and also one of the important causes of perioperative deaths and unexpected deaths in hospital. According to Nam *et al*. [6], prevention and control should be carried out according to the level of VTE risk to ensure appropriate prevention and control; both safety and efficacy should be taken into account. Patients with liver cancer after surgery may be at high risk of thrombosis due to prolonged immobilization, as well as surgical and tumor-related factors. A survey of 32 countries around the world has shown that the evaluation process by nurses is time-consuming, patients have poor compliance, and nearly half of the patients at high risk for VTE do not take any preventive measures [7]. The Caprini risk assessment scale requires doctors and nurses to participate in assessment and intervention, so as to ensure that patients receive both clinical and nursing intervention, effective communication between medical care, dynamic observation of the condition, and timely adjustment of intervention measures. Through whole-course and professional health guidance and intervention, patients are more likely to accept it, thus achieving the purpose of preventing VTE. The American College of Chest Physicians (ACCP) clinical practice guidelines recommend risk stratification based on Caprini score [8], followed by standardized care and treatment. The Caprini risk assessment scale accurately reflects the degree and level of risk of patients by assessing the risk of VTE. Targeted nursing interventions based on the level of risk can effectively reduce the possibility of VTE occurrence in patients [9] and improve the quality of life and satisfaction of patients. In the present study, the incidence of VTE and its complications in the observation group were lower than those in the control group, and the satisfaction of patients in the observation group was higher than that of patients the control group.

In conclusion, the overall diagnostic accuracy of VTE risk assessment for patients with liver cancer surgery based on Caprini risk assessment scale is high. Caprini risk assessment scale can be used to effectively screen out patients with risk of venous thrombosis and ensue targeted intervention measures, which can effectively reduce the incidence of VTE and its complications, improve patients' quality of life, and increase patient satisfaction. Therefore, it is worth promoting and using in clinical settings.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Influence of Heparin on Fibrinogen Assay by Clauss Method

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Abstract: *Objective:* To investigate the effect of heparin on fibrinogen detection by Clauss method. *Methods:* A normal plasma pool (NPP) of 20 healthy people was prepared with 3.2% sodium citrate anticoagulant. For experimental group 1, samples containing different concentrations of heparin were prepared. For experimental group 2, samples of experimental group 1 were diluted twice. For experimental group 3, samples of experimental group 1 were diluted 4 times. For the control group, samples of normal saline with the same volume as heparin in experimental group 1 were prepared. The fibrinogen contents of experimental group 1, experimental group 2, experimental group 3, and control group were detected by Clauss method and prothrombin time (PT)-derived method, and the fibrinogen detection results of different groups were analyzed. *Results:* The trend of fibrinogen detected by Clauss method and PT-derived method in experimental group 1 was different; there was significant difference between the results of experimental group 1 and the control group ($P < 0.05$); there was no significant difference between the results of experimental group 2 and the control group ($P > 0.05$); there was no significant difference between the results of experimental group 3 and the control group ($P > 0.05$); there was no significant difference between the results of experimental group 2 and experimental group 3 ($P > 0.05$); the relative deviation between experimental group 1 and the control group was higher in high-concentration heparin sample. *Conclusion:* Heparin affects fibrinogen detection by Clauss method, and the effect can be reduced by sample dilution.

Keywords: Heparin; Clauss method; PT-derived method; Fibrinogen

Online publication: May 30, 2023

1. Introduction

Heparin is often used in the treatment of venous thrombosis, arterial thrombosis, and disseminated intravascular coagulation (DIC) caused by various factors [1], as well as in the prevention of thrombosis after major surgery and thrombosis recurrence. It is the first choice of anticoagulant in cardiac surgery and vascular surgery. Activated partial thromboplastin time (APTT) is usually monitored 6 hours after administration of heparin, and it is generally prolonged to 1.5–2.0 times the baseline level. Heparinized patients should be monitored with whole-blood clotting time (CT) or activated clotting time (ACT).

Fibrinogen detection is one of the commonly used coagulation function tests in clinical practice. Fibrinogen can be detected by various methods, including Clauss method, prothrombin time (PT)-derived method, immunoturbidimetry, *etc.* [2,3]. Clauss method is based on solidification time and is widely used in laboratories. The PT-derived method is a fibrinogen detection method based on the change of absorbance when PT is measured. The change of absorbance of the reaction system during PT detection is positively correlated with the concentration of fibrinogen [4]. Immunoturbidimetry is a quantitative test based on

antigen-antibody reaction. However, it is not a routine test in clinical laboratories. The detection of fibrinogen by Clauss method is affected by direct thrombin inhibitors, such as bivalirudin, and dabigatran. In addition, Zhang demonstrated that argatroban can also affect the detection of fibrinogen by Clauss method [5]. The effect of heparin on fibrinogen detection is unclear. This study might help clinicians understand the effect of heparin on fibrinogen, so as to better evaluate the status of patients. This study provides some reference to the understanding of the effects of other drugs on fibrinogen.

2. Materials and methods

2.1. General information

The blood of 20 healthy people was collected into 3.2% sodium citrate anticoagulant to prepare a normal plasma pool (NPP). Supernatant was extracted after centrifugation at 1500 g for 15 min. Experimental group 1 was prepared by adding NPP and heparin (heparin sodium for injection, Ma'anshan Fengyuan Pharmaceutical Co., Ltd.) to make 0 U/mL, 0.25 U/mL, 0.5 U/mL, 0.75 U/mL, 1 U/mL, 1.25 U/mL, 1.5 U/mL, 1.75 U/mL, 2 U/mL, 3 U/mL, and 4 U/mL heparin samples. Experimental group 2 was prepared with the sample of experimental group 1 after 2-fold dilution, experimental group 3 was prepared with the sample of experimental group 1 after 4-fold dilution, and the sample prepared by replacing the heparin used in the experimental group with saline was assumed as the control group.

2.2. Fibrinogen detection

2.2.1. Experimental equipment

The equipment used in the experiment was the ACL TOP 750 automatic coagulation analyzer (Werfen, Instrumentation Laboratory, MA, USA).

2.2.2. Experimental reagents

The reagents used were Fibrinogen-C XL (Werfen, Instrumentation Laboratory, MA, USA) and RecombiPlasTin 2G (Werfen, Instrumentation Laboratory, MA, USA).

2.3. Statistical analysis

IBM SPSS 23.0 was used to process data. Paired sample *t*-test was used for comparison between groups, and the test level was $\alpha = 0.05$. $P < 0.05$ was considered statistically significant.

2.4. Experimental procedure

Fibrinogen in experimental group 1 was detected by Clauss method and PT-derived method, while fibrinogen in experimental group 2, experimental group 3, and the control group was detected by Clauss method; the results were recorded.

The relative deviation of fibrinogen between experimental group 1, experimental group 2, experimental group 3, and the control group was compared, respectively.

3. Results

3.1. Trend of fibrinogen detected in the experimental groups and the control group

The fibrinogen detected by Clauss method and PT-derived method in experimental group 1 and the fibrinogen detected by Clauss method in experimental group 2, experimental group 3, and the control group are shown in **Table 1**. The trend of fibrinogen detected by Clauss method in experimental group 1, experimental group 2, experimental group 3, and the control group as well as the trend of fibrinogen detected by PT-derived method in experimental group 1 are shown in **Figure 1**.

Table 1. Fibrinogen detected in experimental group 1, experimental group 2, experimental group 3. and the control group

		Heparin concentration (U/mL)										
		0	**0.25**	**0.5**	**0.75**	**1**	**1.25**	**1.5**	**1.75**	**2**	**3**	**4**
Fibrinogen results (mg/dL)	Experimental group 1 Clauss method	305	289	280	272	268	249	226	206	191	123	59
	Control group Clauss method	305	301	288	287	288	287	287	294	284	276	272
	Experimental Group 1 PT-derived method	357	356	359	355	360	348	347	358	354	295	285
	Experimental group 2 Clauss method	311	294	300	296	288	288	288	287	271	254	241
	Experimental group 3 Clauss method	308	302	302	302	298	288	286	284	288	256	264

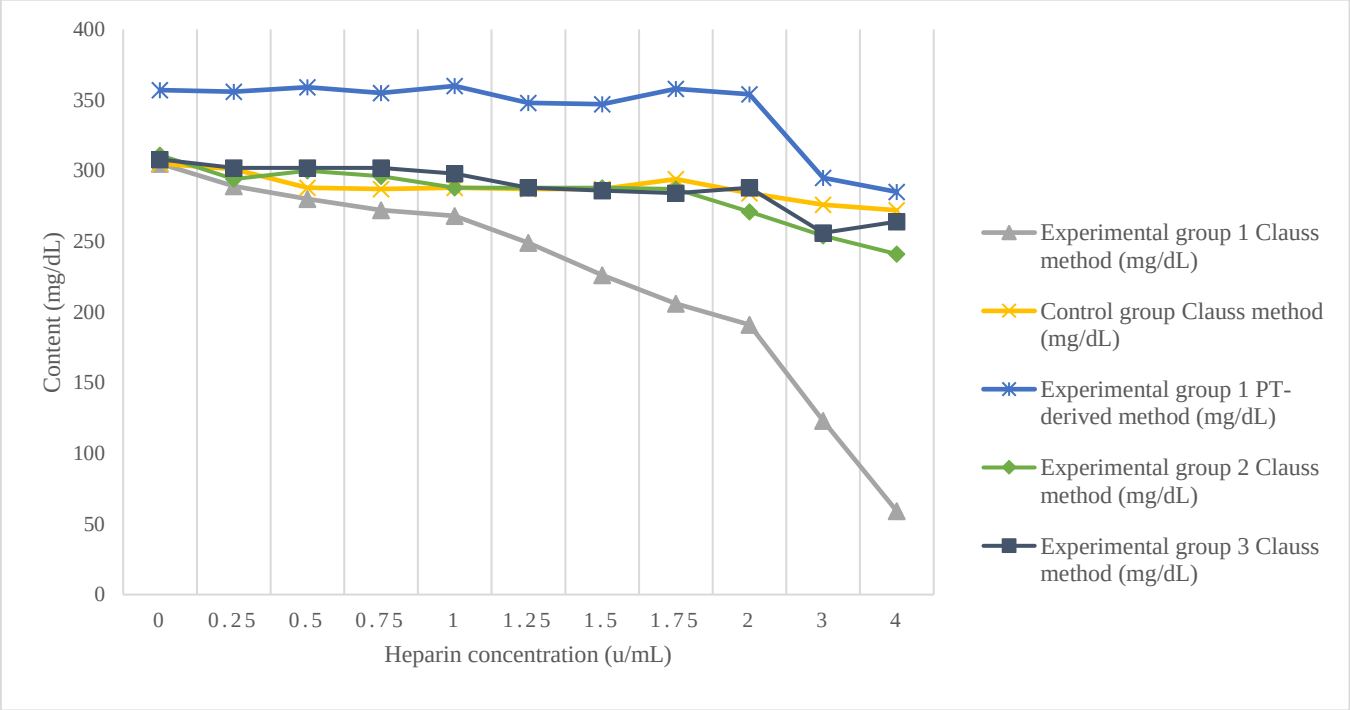

Figure 1. Trend of results of fibrinogen detection by Clauss method in experimental group 1, experimental group 2, experimental group 3, and the control group, as well as the trend of results of fibrinogen detection by PT-derived method in experimental group 1

3.2. Relative deviation of fibrinogen detected by Clauss method in the experimental groups and the control group

The fibrinogen detected by Clauss method in the experimental groups and the control group was statistically analyzed using paired sample *t*-test. The results are shown in **Table 2**. When comparing the results of experimental group 1 with those of the control group, *P* was less than 0.05, indicating that the difference was significant; when comparing the results of experiment group 3 with those of the control group, *P* was more than 0.05, indicating that the difference was insignificant; when comparing the results of experimental group 3 with those of the control group, *P* was more than 0.05, indicating that the difference was insignificant; when comparing the results of experimental group 2 with those of experimental group 3, *P* was more than 0.05, indicating that the difference was insignificant.

Table 2. Relative deviation of fibrinogen detected by Clauss method in the experimental groups and the control group

		Heparin concentration (U/mL)										
		0	**0.25**	**0.5**	**0.75**	**1**	**1.25**	**1.5**	**1.75**	**2**	**3**	**4**
Relative deviation (%)	Experimental group 1 and control group	0.00	-3.99	-2.78	-5.23	-6.94	-13.24	-21.25	-29.93	-32.75	-55.43	-78.31
	Experimental group 2 and control group	1.97	-2.33	4.17	3.14	0.00	0.35	0.35	-2.38	-4.58	-7.97	-11.40
	Experimental group 3 and control group	0.98	0.33	4.86	5.23	3.47	0.35	-0.35	-3.40	1.41	-7.25	-2.94

4. Discussion

The research results showed that heparin has a certain influence on the detection of fibrinogen by Clauss method and the influence of heparin on the results can be weakened by 2-fold dilution and 4-fold dilution. The influence of heparin on the detection of fibrinogen by Clauss method is based on the principle of heparin action and the principle of the method itself. Heparin binds to antithrombin (AT), causing it to undergo conformational change and further forming a triplex complex with thrombin, thereby irreversibly inhibiting serine proteases with coagulation activity, including thrombin, and interfering with the clotting time. The working principle of Clauss method is that thrombin acts on the fibrinogen in the plasma and converts it into fibrin, and the plasma coagulates. The fibrinogen content in the plasma is negatively correlated with the clotting time, and the fibrinogen content can be obtained by comparing the test results with the standard curve prepared from the reference plasma [6]. The main component of the reaction reagent in Clauss method is thrombin, and heparin is an indirect thrombin inhibitor. When the sample contains a high concentration of heparin, it is believed that it will also inhibit the thrombin in the reagent, thus affecting the detection of fibrinogen to a certain extent. In this study, there was significant difference in the fibrinogen Clauss assay results between the experimental group and the control group, which demonstrated the above inference; the results of the experimental group were lower than those of the control group, indicating that heparin has a role in reducing fibrinogen Clauss assay results.

In addition, based on the trend of the results, with the increase in heparin concentration, especially when heparin concentration is above 1 U/mL, the graph showed a gradual downward trend. This trend was not apparent in the control, 2-fold dilution, 4-fold dilution, and PT-derived method groups until the concentration of heparin reached 2 U/mL.

By calculating the relative deviation between the experimental groups and the control group (**Table 2**), it can be seen that the relative deviation between experimental group 1 and the control group is within an acceptable range (±10%) when the heparin concentration is 1 U/mL or below; the relative deviation between experimental group 2 and the control group is within an acceptable range when the heparin concentration is 3 U/mL and below; and the relative deviation between experimental group 3 and the control group is within an acceptable range when the heparin concentration is 4 U/mL and below. This shows that the influence of heparin on the results can be weakened by moderate dilution.

The PT-derived method is based on the change of absorbance when PT is measured. PT reagent contains a certain amount of heparin antagonist, which can theoretically antagonize heparin at a concentration of 1 U/mL. As observed in **Figure 1**, the trend of fibrinogen detected by PT-derived method decreased significantly when heparin was at a concentration of 2 U/mL. This may be attributed to the 1:8 ratio of sample to reagent in the final reaction system of ACL TOP 750, indicating that the sample was diluted to a certain extent and the concentration of heparin was reduced in the final reaction system. The

effect on the results of the PT-derived method was also reflected after the heparin concentration in the sample reached 2 U/mL. However, the results of the PT-derived method are for reference only. Shapiro *et al*. [7] used blood coagulation analyzers and supporting reagents from different manufacturers to detect fibrinogen and found that the fibrinogen Clauss results were significantly lower than the PT-derived results in 35 patients with hereditary dysfibrinogenemia. Miesbach *et al*. [6] reported that the fibrinogen detected by PT-derived method in 27 patients with inherited abnormal fibrinogen was approximately 5-fold higher than that detected by Clauss method, independent of the reagents and instruments used. In another study, the specificity and sensitivity of fibrinogen antigen/activity ratio (PT-derived result/Clauss result) greater than 1.43 were both found to be 100% for the diagnosis of hereditary dysfibrinogenemia [8]. The present study did not compare the PT-derived results with those of the control group but only observed the trend of fibrinogen PT-derived results in different concentrations of heparin samples. The effect on PT-derived method was smaller than that of Clauss method.

In the fibrinogen Clauss detection reaction process of the present study, the sample was first diluted 1:10, and thrombin was added. The ratio of the sample to the fibrinogen reagent containing thrombin was in fact 1:14. The thrombin content in Fibrinogen-C XL was 35 U/mL. We believe that when the sample is diluted and the same amount of thrombin is added, the ratio of thrombin to heparin will be higher than that without dilution, thereby weakening the effect of heparin. This statement is supported by the experimental results of this study. When comparing the results of experimental group 2 and the control group, P was more than 0.05, indicating that the difference was insignificant; and when comparing the results of experimental group 3 and the control group, P was more than 0.05, indicating that the difference was also insignificant. Therefore, when there is heparin interference in the sample, dilution should be considered. However, when comparing the results of experimental group 2 and experimental group 3, P was more than 0.05, indicating that the difference was not significant. This suggests that the dilution factor has no effect on the results, but the linearity of the instrument should be considered when diluting.

Molinaro *et al*. [9] and Zhang [5] showed that it is not only the drug concentration that affects the detection of fibrinogen, but also the thrombin concentration in the reagent. Laboratory testing personnel should have full understanding of the instruments and reagents used. The dearth of the present study is the failure to explore whether fibrinogen reagents containing high concentrations of thrombin will also be affected and whether the detection of fibrinogen by immunoturbidimetry is also affected by heparin. There have been reports on other thrombin-inhibiting anticoagulant drugs, such as argatroban, dabigatran, and bivalirux, that affect the detection of fibrinogen by Clauss method [5,9,10].

This study might help clinicians obtain more accurate detection results. Although there are now many anticoagulant drugs that have emerged, including indirect thrombin inhibitors (low molecular weight heparin, vitamin K antagonist warfarin, *etc*.), direct thrombin inhibitors (lepirudin, bivalirudin, argatroban, dabigatran, *etc*.), and factor Xa inhibitors (direct factor Xa inhibitor rivaroxaban, *etc*.; indirect factor Xa inhibitor fondaparinux sodium) [11], heparin still plays an irreplaceable role in the European Society of Cardiology (ESC) guidelines. Enoxaparin is recommended with high-quality evidence as an anticoagulant therapy in patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) [12]. Therefore, it is of great significance to study the influence of heparin on the detection of common laboratory indicators by different methods. This study might prompt clinical testing of blood from heparinized patients or blood samples mixed with higher concentrations of heparin in which the test results may be affected to some extent. This study also provides solutions to laboratories when dealing with samples containing high concentrations of heparin. When laboratories encounter such samples, the validity of the results obtained by Clauss method should be inquired, and dilution should be considered to weaken the effect of heparin.

5. Conclusion

Heparin affects the detection of fibrinogen by Clauss method, and this effect can be reduced by diluting the sample.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Analysis of Multi-Drug Resistant Organism Surveillance and Antimicrobial Resistance Early Warning in a Hospital in 2022

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Abstract: *Objective:* To determine the clinical distribution of multi-drug resistant organism (MDRO) in Jiangyan Hospital and the monitoring and warning of drug-resistance bacteria to provide an important basis for guiding the application of broad-spectrum antibiotics in clinical treatment and reducing the occurrence of nosocomial infection. *Methods:* Retrospective screening and analysis were conducted on the pathogenic strains of hospitalized patients in our hospital in 2022. *Results:* A total of 2,769 strains of pathogenic bacteria and 390 strains of MDRO were detected and isolated in our hospital in 2022; the detection rate of MDRO was 14.08%. A total of 516 strains (18.64%) *Klebsiella pneumoniae* (KP) and 62 strains (12.02%) of carbapenem-resistant *Klebsiella pneumoniae* (CR-KP) were detected; 436 strains (15.75%) of *Escherichia coli* (ECO) were detected, including 8 strains (1.83%) of CR-ECO; 342 strains (12.35%) of *Pseudomonas aeruginosa* (PA) and 116 strains (33.92%) of CR-PA were detected; there were 194 strains (7.01%) of *Acinetobacter baumannii* (AB), among which 125 strains (64.43%) were CR-AB; there were 291 strains (10.51%) of *Staphylococcus aureus*, among which 79 strains (27.15%) of methicillin-resistant *Staphylococcus aureus* (MRSA) were detected; 78 strains (2.82%) of *Enterococcus faecalis* were detected, and vancomycin-resistant enterococcus (VRE) was not detected. The first five MDROs were CR-AB, CR-PA, MRSA, CR-KP, and CR-ECO. The top five departments with the highest MDRO detection rate in 2022 were the ICU (37.44%), the Pulmonology Department (ward 13; 31.03%), the Department of Rehabilitation (ward 5; 6.67%), the Department of Neurosurgery (ward 11; 4.62%), and the Department of General Surgery (ward 10; 3.59 The resistance rate of antibacterial drugs is divided into four levels for early warning: 30% to 40%, 41% to 50%, 51% to 75%, and 75% or more. *Conclusion:* Our hospital should strengthen the monitoring of antimicrobial resistance warning related to MDRO and the abuse of antimicrobial drugs. Based on the results of drug sensitivity and antimicrobial resistance warning, the use of antibiotics should be standardized in clinical practice to reduce nosocomial infection.

Keywords: Antimicrobial resistance; Antibiotics; Early warning; Multi-drug resistant organism

Online publication: May 30, 2023

1. Introduction

With the widespread use of broad-spectrum antimicrobial drugs in patients, the issue of antimicrobial resistance is worsening, and the detection rate of multi-drug resistant organism (MDRO) has risen sharply. The worsening antimicrobial resistance increases the hospitalization time of drug-resistant patients, the economic burden on patients [1], and the fatality rate [2]. The aim of this study was to evaluate and analyze the MDRO monitoring situation in Jiangyan Hospital of Traditional Chinese Medicine throughout 2022 and the early warning index of antimicrobial resistance in the same year to provide a basis for promoting

the active, effective, and rational use of various conventional broad-spectrum antimicrobial drugs by clinicians in our hospital, so as to reduce antimicrobial resistance in patients and the occurrence of nosocomial infections.

2. Materials and methods

2.1. Strain source

According to the requirements of the National Inspection Technology Operation Guidelines [3], all pathogenic bacteria isolated from clinical specimens submitted for inspection (repeated strains from the same patient and the same site were excluded) were collected for disinfection inoculation and *in vitro* isolation and purification. The hospital's information system was used to collect target data, and WPS Office was used for statistical analysis. In this study, we selected a few common drug-resistant bacteria for analysis, including carbapenem-resistant *Pseudomonas aeruginosa* (CR-PA), carbapenem-resistant *Escherichia coli* (CR-ECO), carbapenem-resistant *Acinetobacter baumannii* (CR-AB), methicillin-resistant *Staphylococcus aureus* (MRSA), and carbapenem-resistant *Klebsiella pneumoniae* (CR-KP) [4]. Ward 4 and Ward 9 belong to the Department of Orthopedics and Traumatology, Ward 5 belongs to the Department of Rehabilitation, Ward 6 belongs to the Department of Orthopedics 1, Ward 7 belongs to the Department of Orthopedics 2, Ward 8 belongs to the Department of Orthopedics 3, Ward 10 belongs to the Department of General Surgery, Ward 11 belongs to the Department of Neurosurgery, Ward 12 belongs to the Department of Thoracic Surgery, Ward 13 belongs to the Pulmonology Department, Ward 14 belongs to the Department of Cardiovascular Disease, Ward 15 belongs to the Oncology Department, Ward 16 belongs to the Department of Encephalopathy, Ward 17 belongs to the Department of Pediatrics, and Ward 18 belongs to the Department of Geriatrics.

2.2. Pathogen identification and drug susceptibility test

For bacteria identification and drug susceptibility test, VITEK 2 COMPACT (bioMerieux, France) bacterial identification card and supporting drug sensitivity card was used. The quality-control strains were *Pseudomonas aeruginosa* ATCC27853, *Escherichia coli* ATCC25922, and *Staphylococcus aureus* ATCC29213, which were purchased from Symerfeld, USA. Drug susceptibility test was performed according to the American Clinical and Laboratory Standards Institute (CLSI) M100-S29 [5] standard operation and result judgment, supplemented by Kirby-Bauer (KB) Paper method. The medium used for blood plate and drug susceptibility test was MH agar plate purchased from Antu Company, and the drug susceptibility reagent disc of KB method agar was imported from the United Kingdom.

3. Results

3.1. Bacterial distribution

Among the bacteria detected in 2022, Gram-negative bacteria were the main ones; 516 strains (18.64%) of KP were detected, of which 62 strains (12.02%) were CR-KP; 436 strains (15.75%) of ECO were detected, of which 8 strains (1.83%) were CR-ECO; 342 strains (12.35%) of PA were detected, of which 116 strains (33.92%) were CR-PA; there were 194 strains (7.01%) of AB, of which 125 strains (64.43%) were CR-AB; there were 291 strains (10.51%) of SA, of which methicillin resistance was detected in 79 strains (27.15%); 78 strains (2.82%) of *Enterococcus faecalis* were detected without VRE. The top five MDROs were CR-AB, CR-PA, MRSA, CR-KP, and CR-ECO. See **Table 1** and **Figure 1** for more details.

Table 1. Detection of pathogenic bacteria and MDROs

Bacteria name	Detected number (strain)	Detection rate (%)	Multidrug-resistant bacteria	Detected number (strain)	Detection rate (%)
Klebsiella pneumoniae	516	18.64	CR-KP	62	12.02
Escherichia coli	436	15.75	CR-ECO	8	1.83
Staphylococcus aureus	291	10.51	MRSA	79	27.15
Pseudomonas aeruginosa	342	12.35	CR-PA	116	33.92
Acinetobacter baumannii	194	7.01	CR-AB	125	64.43
Enterococcus faecalis	78	2.82	VRE	0	0

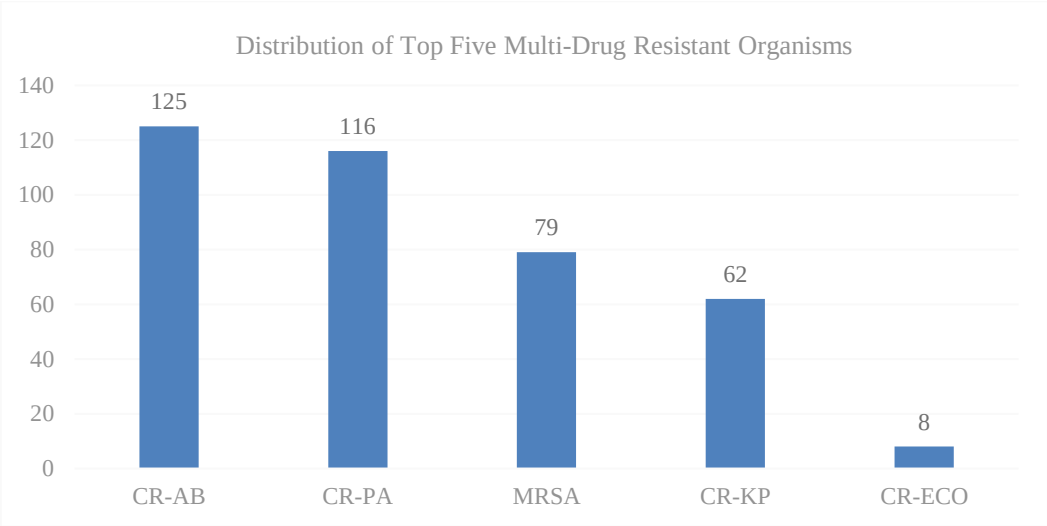

Figure 1. Distribution of the top five MDROs

3.2. Clinical distribution of multi-drug resistant organism

In 2022, CR-AB was mainly distributed in the ICU, CR-PA was mainly distributed in the ICU and 13 other wards, and CR-KP was mainly distributed in 13 wards. The highest number of detected MDRO strains in our hospital was CR-AB, followed by CR-PA, and MRSA.

The top five departments with the highest detection rate of MDRO were the ICU (37.44%), Ward 13 (31.03%), Ward 5 (6.67%), Ward 11 (4.62%), and Ward 10 (3.59%). See **Table 2** and **Figure 2** for detailed results.

Table 2. Distribution of muti-drug resistant organism in each ward

Ward	MRSA	CR-KP	CR-PA	CR-AB	CR-ECO	Total
ICU	6	16	48	76	0	146
Ward 4	4	1	0	0	0	5
Ward 5	7	3	7	8	1	26
Ward 6	4	0	0	0	0	4
Ward 7	6	0	1	0	0	7
Ward 8	7	0	1	3	0	11
Ward 9	7	0	0	0	0	7
Ward 10	9	0	0	3	2	14

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Ward	MRSA	CR-KP	CR-PA	CR-AB	CR-ECO	Total
Ward 11	1	0	5	12	0	18
Ward 12	2	0	0	0	0	2
Ward 13	4	42	48	22	5	121
Ward 14	1	0	0	0	0	1
Ward 15	1	0	1	0	0	2
Ward 16	9	0	0	1	0	10
Ward 17	6	0	0	0	0	6
Ward 18	5	0	5	0	0	10
Total	79	62	116	125	8	390

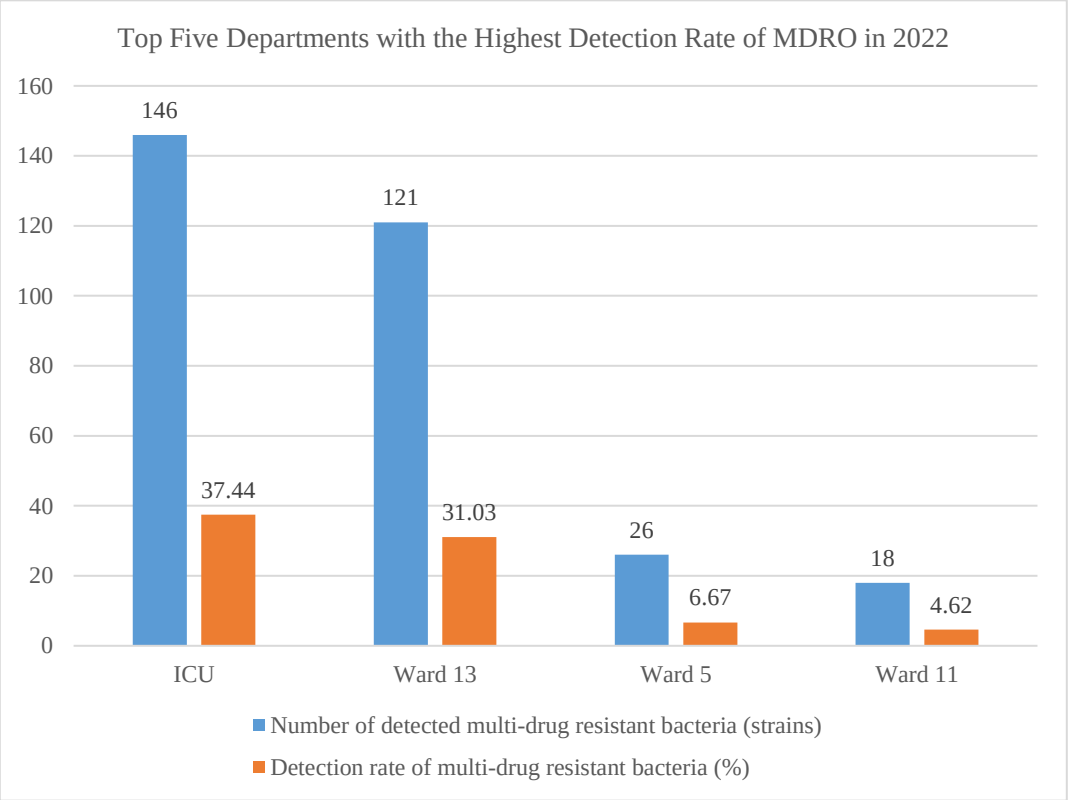

Figure 2. Top five wards with the highest detection rate of MDRO in 2022

3.3. Surveillance and early warning of antimicrobial resistance

When the antimicrobial resistance rate is within 30%–40%, relevant medical institutions and medical staff should be notified; when the antimicrobial resistance rate is 51%–75%, antibiotics should be used with reference to the results of drug sensitivity tests; when the antimicrobial resistance rate of bacteria reaches more than 75%, the clinical application of antimicrobials should be suspended. The decision to resume the clinical application of antimicrobials is based on the results of antimicrobial resistance surveillance [6]. The ranking of the top five bacteria in proportion is as follows: KP, ECO, PA, SA, and AB. The antimicrobial resistance rate is shown in **Figures 3–7**.

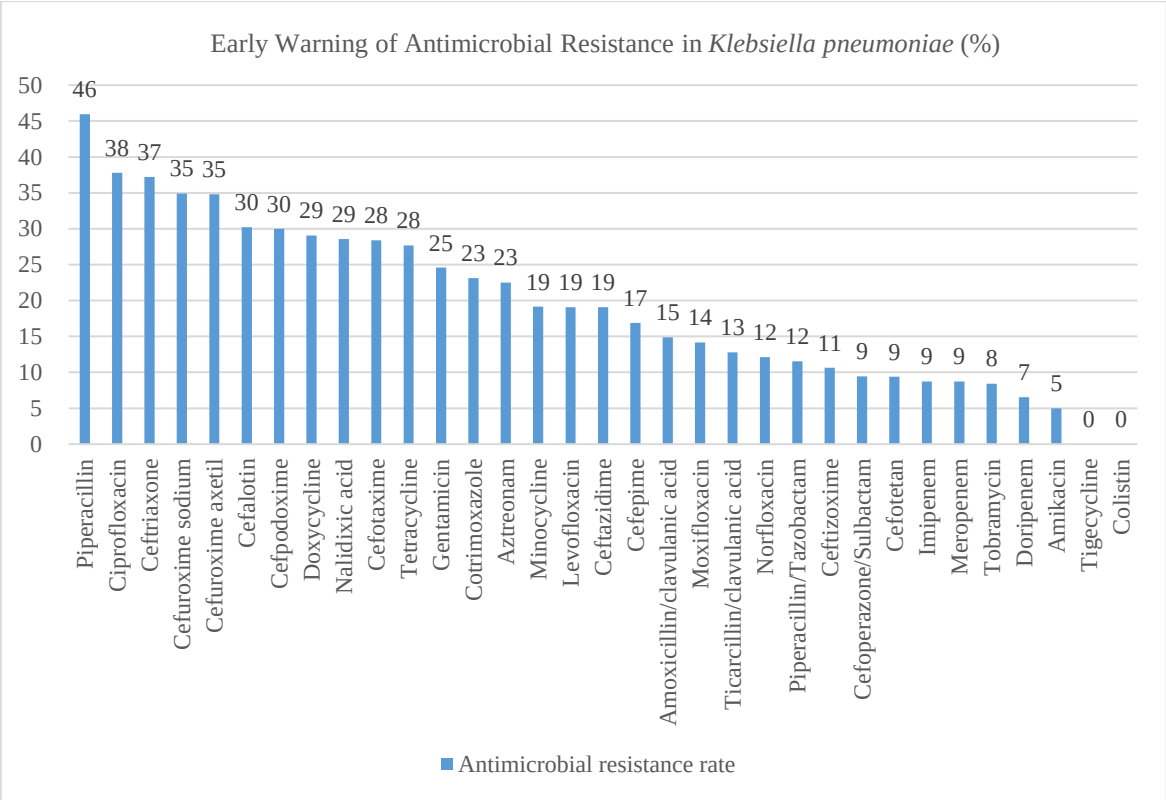

Figure 3. Surveillance and early warning of antimicrobial resistance in *Klebsiella pneumoniae*

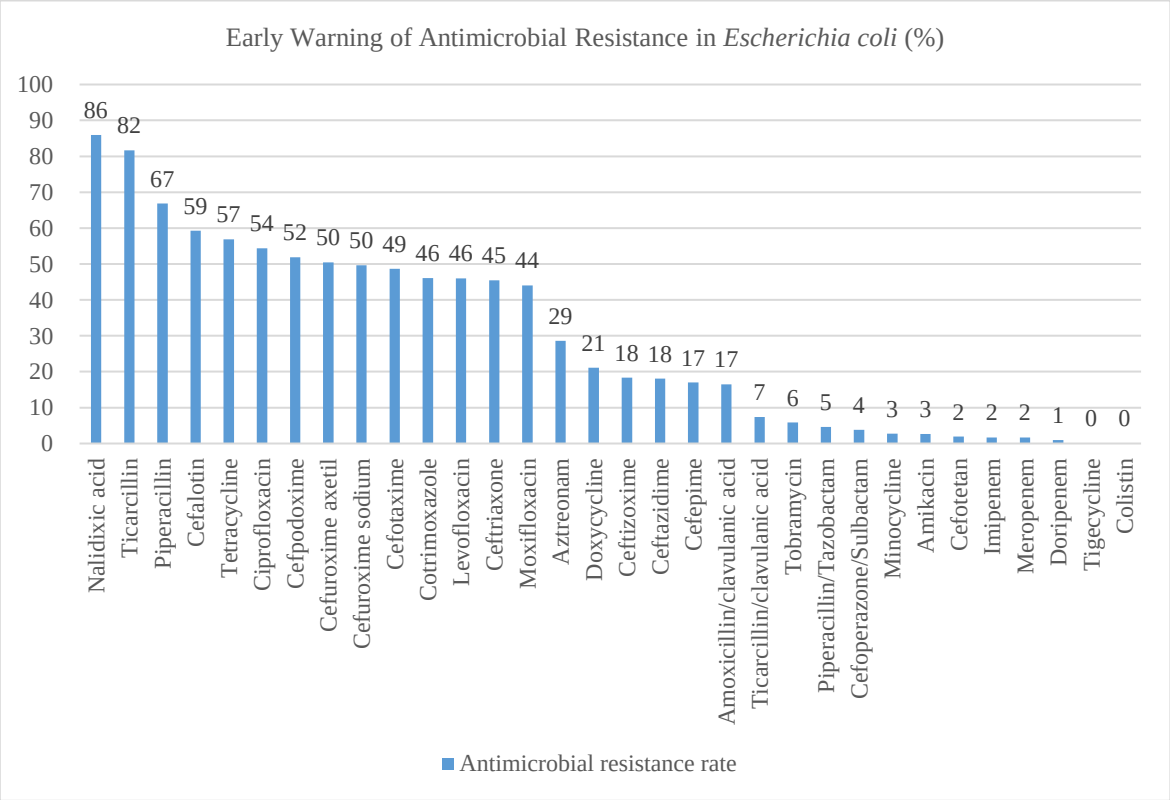

Figure 4. Surveillance and early warning of antimicrobial resistance in *Escherichia coli*

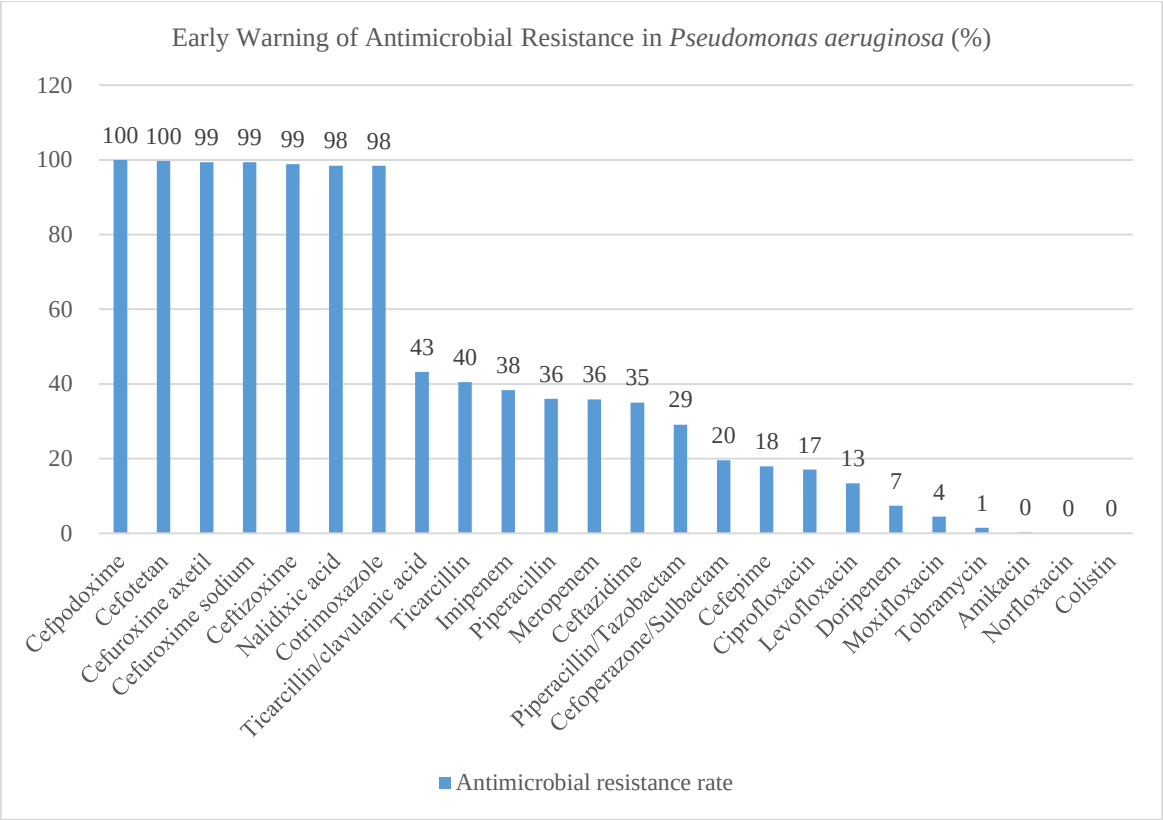

Figure 5. Surveillance and early warning of antimicrobial resistance in *Pseudomonas aeruginosa*

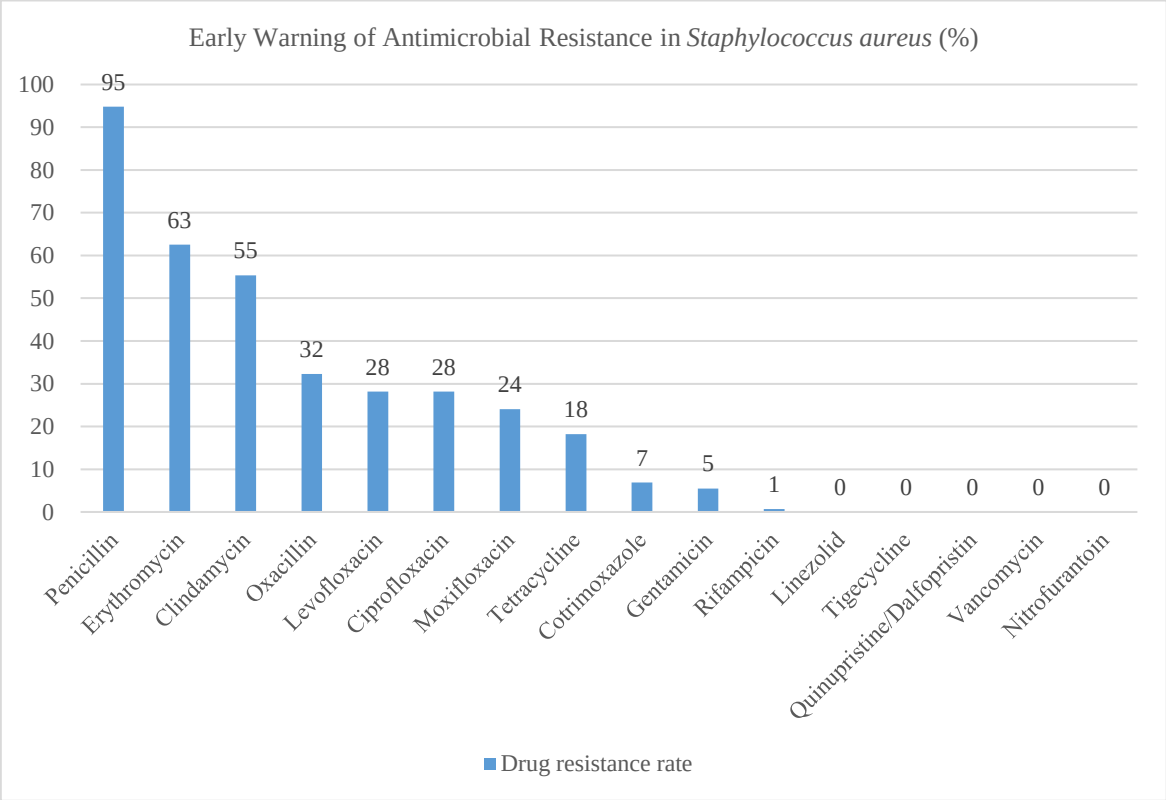

Figure 6. Surveillance and early warning of antimicrobial resistance in *Staphylococcus aureus*

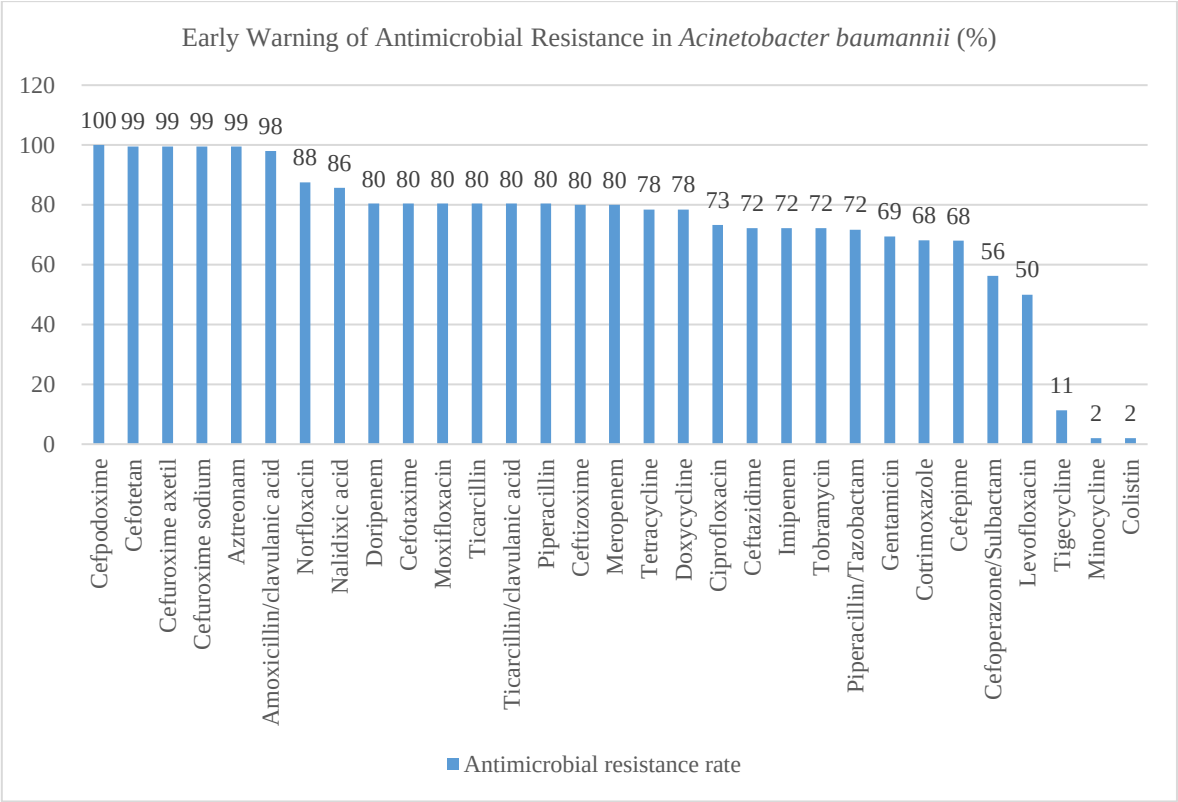

Figure 7. Surveillance and early warning of antimicrobial resistance in *Acinetobacter baumannii*

4. Discussion

With the widespread use of antibiotics, multi-drug resistance has become a major clinical issue, which not only leads to increased treatment costs, but also poses a significant threat to life and health [7]. Since 2018, our hospital has carried out quarterly and annual antimicrobial resistance surveillance and early warning work and published it on the hospital office automation OA to provide a basis for clinicians when choosing antimicrobials [8].

In 2022, our hospital isolated and collected 2,769 strains of pathogenic bacteria and 390 strains of MDRO from hospitalized patients. The detection rate of MDRO was 14.08%, which is lower than the detection rate of MDRO (32.07%) in a study by Zhang [9] but similar to the detection rate of MDRO (16.57%) in a study by Qiang [10]. This may be related to the regional differences in the distribution of MDRO. In our study, the top five MDROs were CR-AB (64.43%), CR-PA (33.92%), MRSA (27.15%), CR-KP (12.02%), and CR-ECO (1.83%), which differed from the study by You [11]. This may be due to the difference in MDRO distribution between traditional Chinese medicine hospitals and general hospitals. The department with the highest detection rate of MDRO in our hospital in 2022 was the ICU (37.44%); this finding is consistent with the finding of Xing [12], whose detection rate of MDRO was 30.3% in the ICU. In our hospital, CR-AB was found to be mainly distributed in the ICU. The reason for this may be that CR-AB is resistant to commonly used disinfectants; thus, it is difficult to eradicate it from the ICU environment and the surface of objects when contaminated. CR-AB is one of the most common pathogenic bacteria yet the most difficult to control in hospitals [13]. In addition, most patients admitted to the ICU have low immunity, are in severe states, had undergone major surgery, and are receiving broad-spectrum antimicrobials [14]. The widespread use of carbapenem has a predisposition for a large number of CR-AB. In our hospital, CR-PA was found to be mainly distributed in Ward 13 and the ICU. This may be due to the fact that patients in these wards generally have severe illness, a long course of disease, and low immunity, with some patients needing long-term broad-spectrum antibiotics [15]. CR-KP was also found to be mainly distributed in Ward

13, followed by the ICU. The majority of patients in Ward 13, under the Pulmonology Department, are elderly patients, and most of them have low immunity; this is the cause of CR-KP infection [16]. Admission to the ICU, endotracheal intubation, mechanical ventilation, and sputum suction are risk factors for CR-KP [17], which easily lead to the growth of CR-KP in these two wards.

The analysis of the surveillance data in this clinical research showed that in 2022, KP, one of the common clinical opportunistic pathogens, ranked first in our hospital and was found to be sensitive to cephalosporins (cefotaxime, ceftazidime, cefepime, and ceftizoxime), cephalosporin antibiotics (cefotetan), tetracyclines (doxycycline, minocycline, tetracycline, and tigecycline), colistin, co-trimoxazole, aztreonam, quinolones (levofloxacin, norfloxacin, and moxifloxacin), carbapenems (imipenem, meropenem, and doripenem), aminoglycosides (tobramycin and amikacin), amoxicillin/clavulanic acid, ticarcillin/ clavulanic acid, piperacillin/tazobactam, cefoperazone/sulbactam, and gentamicin. According to the report, the rate of resistance to cephalosporins (first-generation, cefotaxime and cefazolin; second-generation, cefuroxime; third-generation, ceftriaxone and cefpodoxime) and quinolones (nalidixic acid and cyclic ciprofloxacin) is between 30% and 40%, while the rate of resistance to ampicillin/sulbactam and piperacillin is between 41% and 50%. Medication should be given cautiously. For urinary tract infection, nitrofurantoin should be selected according to the antibiotic susceptibility results instead of empiric antibiotics. ECO ranked second in our hospital in 2022 and was found to be sensitive to aztreonam, gentamicin, tetracyclines (doxycycline, minocycline, and tigecycline), cephalosporin antibiotics (cefixime, ceftazidime, and cefepime), amoxicillin/clavulanic acid, ticarcillin/clavulanic acid, piperacillin/tazobactam, cefoperazone/sulbactam, aminoglycosides (tobramycin and amikacin), cephalosporins, cefotetan, carbapenems (imipenem, meropenem, and doripenem), and peptides. The rate of resistance to norfloxacin reached 36%. The medical staff in our hospital were notified. The resistance rate to antibacterial drugs, such as ampicillin/sulbactam, co-trimoxazole, quinolones (levofloxacin, moxifloxacin), cephalosporins (cefazolin, cefuroxime, cefotaxime, ceftriaxone, and cefpodoxime), etc., is between 41% and 50% thus they can be used with caution. Antimicrobials should be used promptly if they are discovered. The rate of resistance to piperacillin, ciprofloxacin, tetracycline, and cephalothin is between 51% and 75%. When selecting antimicrobials, antibiotic susceptibility test results should be referred to, and they should not be used empirically. The rate of resistance to ticarcillin, ampicillin, and nalidixic acid is more than 75%; hence, clinicians should actively avoid the use of these antimicrobials. At the same time, the drug department should track it before deciding whether to resume medication. Cefoperazone/sulbactam, piperacillin/tazobactam, cefepime, quinolones (norfloxacin, ciprofloxacin, levofloxacin, and moxifloxacin), gentamicin, aminoglycosides (tobramycin and amikacin), colistin, and other antimicrobial-sensitive PA ranked third in our hospital in 2022. These drugs were used to treat PA, and the medical staff were informed of the resistance rate (between 31% and 40%) to ceftazidime, piperacillin, and carbapenem (imipenem and meropenem). Ticarcillin/clavulanic acid should be used with caution considering the 43% resistance rate. Clinicians should not use antimicrobials with a resistance rate of more than 75%. These antimicrobials include nalidixic acid, cefotetan, and cephalosporins (ceftizoxime, cefuroxime, ceftizoxime, and cefazolin). SA ranked fourth in our hospital in 2022, and its rate of resistance to clindamycin and erythromycin reached 51%–75%. The antibiotic sensitivity test results should be referred to when choosing antimicrobials. The rate of resistance to penicillin was found to be 95%. Therefore, clinicians should avoid using penicillin in such cases. When choosing drugs, it is necessary to pay attention to the antimicrobial resistance rate. Although AB ranked fifth, it has the highest antimicrobial resistance and is only sensitive to three drugs (minocycline, tigecycline, and colistin). The rate of resistance to cefoperazone/sulbactam, ampicillin/sulbactam, piperacillin/ tazobactam, ceftazidime, ceftriaxone, cefepime, co-trimoxazole, gentamicin, tobramycin, imipenem, and quinolones (levofloxacin and ciprofloxacin) reached 50%–75%. If these antibiotics are used, the rate of resistance to these antibiotics may increase. On the other hand, the

rate of resistance to tetracyclines (doxycycline), piperacillin, ticarcillin/clavulanic acid, amoxicillin/clavulanic acid, ticarcillin, carbapenem (doripenem and meropenem), cefotetan, quinolones (nalidixic acid, moxifloxacin, and norfloxacin), cephalosporins (cefazolin, cefotaxime, cefuroxime, ceftizoxime, and cefpodoxime) was found to be more than 75%; thus, their use should be avoided. The irrational use of antimicrobials will lead to bacterial resistance.

When using antimicrobials, it is imperative to monitor the antimicrobial resistance of bacteria and make timely announcements and notifications, so as to reduce nosocomial infections, while referring to drug sensitivity results.

Our hospital's inpatients were taken as the research subjects in the present study. By analyzing the hospital's surveillance of MDRO and early warning of antimicrobial resistance of the top five bacteria in the hospital, we provide a basis for the rational use of antibiotics in hospitals through this study. With the aim of reducing nosocomial infection, it is necessary to continuously strengthen the surveillance of MDRO and early warning of antimicrobial resistance, as well as effectively prevent the incipient development of diseases and the ineffectiveness of antibiotics.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Prediction of Hypotension During Neuraxial Anesthesia in Patients with Pregnancy-Induced Hypertension Through Subclavian Vein Collapsibility Index

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Abstract: *Objective:* To explore and evaluate the predictive value of subclavian vein collapsibility index (SCV-CI) on hypotension during neuraxial anesthesia in patients with pregnancy-induced hypertension (PIH). *Methods:* Pregnant women with PIH who underwent elective cesarean section in our hospital from January to July 2021 were selected as the research subjects. Patients who experienced hypotension during anesthesia were included into the hypotension group, whereas patients who had a normal blood pressure during anesthesia were included in the normotensive group. The SCV-CI was then calculated for three respiratory cycles, the average value was taken as the base value, and the patient was monitored for another 20 minutes. The blood pressure, heart rate, blood oxygen saturation, and SCV-CI of the patients were measured, and the incidence of maternal nausea and vomiting and cord blood gas were recorded. Then, a correlation analysis was conducted on the relationship between subclavian vein collapsibility index and hypotension. A receiver operating characteristic curve was drawn to seek the threshold value of subclavian vein collapsibility index for post-anesthesia hypotension. *Results:* There was no significant difference in systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) between the two groups before anesthesia ($P > 0.05$). After anesthesia, the above indexes (SBP, 103.25 ± 12.48 mmHg; DBP, 58.94 ± 7.46 mmHg; and HR, 52.96 ± 6.48 beats/min) were significantly lower than those of the normal blood pressure group, and the difference was statistically significant ($P < 0.05$). In comparison, the SCV-CI in the hypotension group was 35.82 ± 4.93% greater than that in the normal blood pressure group (23.85 ± 5.27%), and the incidence of nausea and vomiting in the hypotension group (40.0%) was significantly higher than that in the normotensive group (10.53%), and the difference was statistically significant ($P < 0.05$). The area under the curve of SCV-CI prediction against hypotension in patients with PIH under neuraxial anesthesia was 0.825 (95% CI: 0.762–0.893, $P < 0.001$), the cut-off value was 25.68%, the predictive sensitivity was 92.68%, and the specificity was 81.24%. *Conclusion:* SCV-CI has a good predictive value for the occurrence of hypotension in patients with PIH during neuraxial anesthesia.

Keywords: Subclavian vein collapsibility index; Pregnancy-induced hypertension; Neuraxial anesthesia; Hypotension

Online publication: May 30, 2023

1. Introduction

General anesthesia in obstetrics has been improving, but spinal anesthesia is still the preferred technique in cesarean section. This is because spinal anesthesia avoids some risks of general anesthesia, and patients with pregnancy-induced hypertension (PIH) can stay awake and participate in the childbirth process, which

promotes early bonding with newborns and breastfeeding, and is helpful in postoperative pain control [1]. After spinal anesthesia, the fetus and uterus presses against the inferior vena cava and (or) the abdominal aorta, and the blood returned to the heart decreases drastically, resulting in a decrease in cardiac output, which is the main cause of hypotension or supine position syndrome [2,3]. After spinal anesthesia, blood vessels below the sympathetic nerve block plane dilates, and muscle relaxation aggravates venous dilation, all of which results in reduced cardiac blood return and reduced cardiac displacement [4]. Therefore, an early prediction of hypotension after spinal anesthesia in patients with PIH is important to ensure a smooth delivery [5]. In this research, pregnant women with PIH who underwent elective cesarean section in our hospital from January to July 2021 were selected as the research subjects, and the relationship between subclavian vein collapsibility index SVC-CI on hypotension in PIH patients during neuraxial anesthesia.

2. Materials and methods

2.1. General information

After the study was approved by the ethics committee, 68 pregnant women with pregnancy-induced hypertension who underwent elective cesarean section in our hospital from January to July 2021 were selected as research subjects. The patients with contraindication of intraspinal anesthesia and those who are deemed not suitable for the study were discharged. Cases with intraspinal anesthesia level lower than T6, which meant that the anesthesia was not effective, were excluded. Patients who needed to change the anesthesia method were not included in the statistics.

2.2. Method

All subjects of this research fasted for 6 hours (food) and 2 hours (drink) before the operation. They received sedative and antispasmodic therapy before the operation. After entering the operating room, their blood pressure, electrocardiogram (ECG), and oxygen saturation were monitored. All puerperae involved in this research were treated with combined spinal epidural anesthesia, L3-4 space puncture. They also received subarachnoid injection of 14-15mg 0.5% ropivacaine. A tunneled epidural catheter of 3–4 cm was inserted, and controlled anesthesia was injected into plane T6-T4. At the beginning of anesthesia, the patients were given rapid fluid supplement of 10 mL/kg. 0.3mg atropine were administered to patients with heart rate lower than 50 times/minute, and patients with blood pressure below 20% of the normal value was considered as post-anesthesia hypotension and was included in the hypotension group (n = 30), and norepinephrine was injected to maintain their blood pressure. Patients with blood pressure above 20% of the baseline value without the need for vasopressors were included in the normotensive group (n = 38).

Inspection of subclavian vein collapsibility index: Before anesthesia, a high-frequency linear array probe was placed on the sagittal plane of the right midclavicular line perpendicular to the long axis of the subclavian vein for the best effect. The diameter and cross-sectional area of the right subclavian vein at the end of inspiratory and expiratory processes were then measured. Then, the SCV-CI was measured. The procedure was repeated for three respiratory cycles were recorded and their average values were taken as the basis value, followed by continuous monitoring for 20 minutes.

2.3. Observation indicators

The changes of hemodynamic indexes (systolic blood pressure [SBP], diastolic blood pressure [DBP], and heart rate [HR]), the subclavian vein collapsibility index (SCV-CI) of the patients, and the incidence of nausea and vomiting were recorded. A receiver operating characteristic (ROC) curve was drawn to analyze the relationship between SCV-CI and hypotension.

2.4. Statistical processing

SPSS26.0 was used to perform statistical analysis, and a *t* test was carried out on the measurements, and a chi-square test was also performed on the count data. A receiver operating characteristic (ROC) curve was plotted to determine the cut-off value of SCV-CI for post-anesthesia hypotension.

3. Results

3.1. Comparison of hemodynamic indicators between the two groups

There was no significant difference in systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) between the two groups before anesthesia ($P > 0.05$). During anesthesia, The SBP, DBP, and HR in hypotensive group were significantly lower than those in the normotensive group (SBP, 103.25 ± 12.48 mmHg; DBP, 58.94 ± 7.46 mmHg; HR, 52.96 ± 6.48 beats/min), and the difference was statistically significant ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of hemodynamic indicators between the two groups of patients (mean ± s)

Group	SBP (mmHg)		DBP (mmHg)		HR (times/min)	
	Before anesthesia	After anesthesia	Before anesthesia	After anesthesia	Before anesthesia	After anesthesia
Hypotension group (*n* = 30)	147.92 ± 13.58	103.25 ± 12.48	92.68 ± 8.73	58.94 ± 7.46	78.85 ± 7.43	52.96 ± 6.48
Normotensive group (*n* = 38)	148.04 ± 14.26	121.09 ± 12.35	92.09 ± 9.57	68.47 ± 8.15	78.26 ± 7.68	64.52 ± 6.13
t	2.318	6.792	2.574	7.458	2.907	8.126
P value	> 0.05	0.012	> 0.05	0.006	> 0.05	0.001

3.2. Comparison of SCV-CI and incidence of nausea and vomiting between the two groups

The SCV-CI in the hypotensive group was 35.82 ± 4.93%, which was greater than that in the normotensive group 23.85 ± 5.27%, and the incidence of nausea and vomiting in hypotensive patients (40.0%) was significantly higher than that that of the normotensive group (10.53%), and the difference was statistically significant ($P < 0.05$), as shown **Table 2**.

Table 2. Comparison of subclavian vein collapsibility index and incidence of nausea and vomiting between the two groups

Group	*n*	SCV-CI (%)	Incidence rate of nausea and vomiting (%)
Hypotension group	30	35.82 ± 4.93	12 (40.0)
Normotensive group	38	23.85 ± 5.27	4 (10.53)
χ^2/ *t*		8.219	9.675
P		0.001	0.000

3.3. The predictive value of SCV-CI on hypotension in patients with PIH who underwent neuraxial anesthesia

The area under the ROC curve of SCV-CI in predicting hypotension in patients with PIH under neuraxial anesthesia was 0.825 (95% CI: 0.762–0.893, $P < 0.001$), the cut-off value was 25.68%. Besides, the

predictive sensitivity of SCV-CI against hypotension was 92.68%, and the specificity was 81.24%, as shown in **Figure 1**.

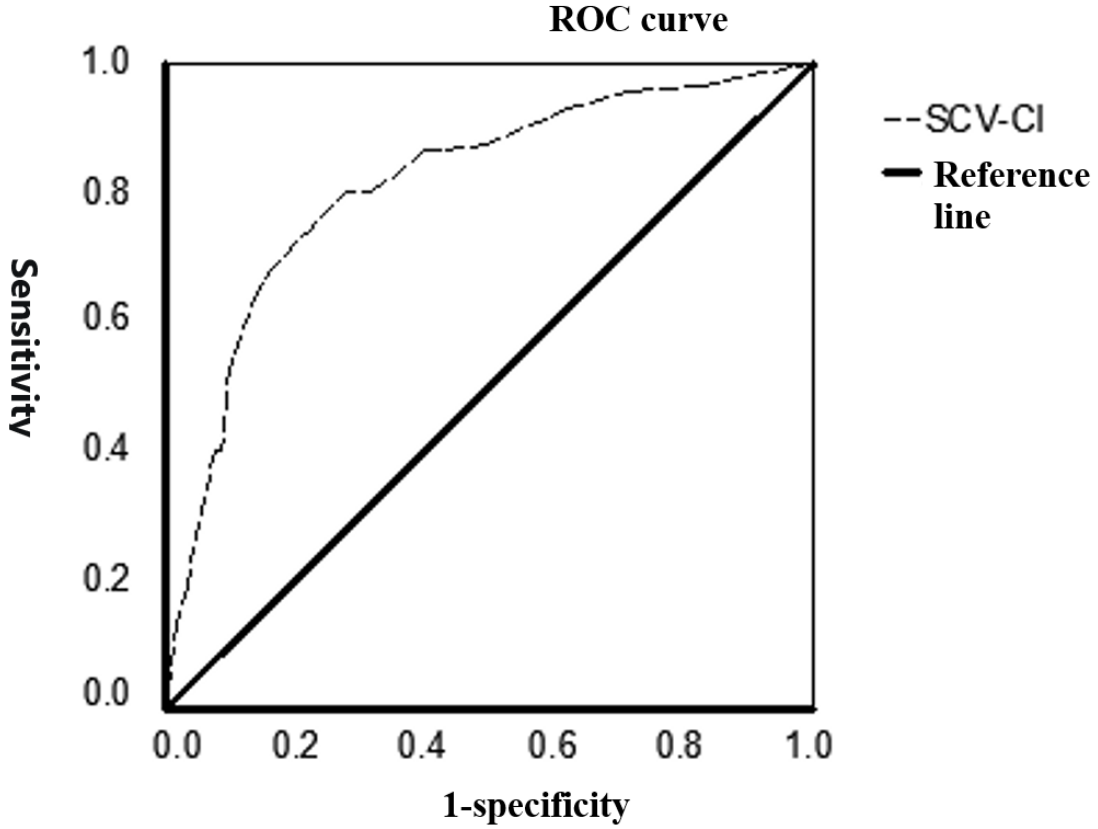

Figure 1. ROC curve of SCV-CI for predicting hypotension after neuraxial anesthesia in patients with PIH

4. Discussion

During spinal anesthesia for cesarean section in patients with PIH, the probability of hypotension is high, and it is harmful to the patients. There are many reasons for intraoperative hypotension, and many of the reasons are unexpected, and there are currently no clear and effective prediction methods. The method and mechanism of hypotension in cesarean section are also unclear., the most common and effective methods for the prevention and treatment of hypotension during neuraxial anesthesia for cesarean section are fluid infusion and vasoactive drugs [6,7].

Ultrasonic measurement of the inferior vena cava (IVC) has been widely recommended as a method for volume assessment. Because of its repeatability and accessibility, ultrasonic measurement of inferior vena cava diameter, maximum diameter at the end of respiration and collapse index in the state of spontaneous respiration is highly recognized by emergency, intensive care and anesthesiologists. In addition to measuring the inferior vena cava, the subclavian vein can also be measured [8]. Measuring collapsibility index is more sensitive than measuring vein width. The subclavian vein collapse index and inferior vena cava collapse index in shock patients were higher than those in non-shock patients [9,10]. The subclavian vein collapse index was positively correlated with the inferior vena cava collapse index [11]. The study [12] reported that for patients at high risk of complications caused by intraoperative hypovolemia and hypotension, the measurement of SCV-CI can provide clinically useful information. Before anesthesia, a high-frequency linear array probe was placed on the sagittal plane of the right midclavicular line perpendicular to the long axis of the subclavicular vein for the best effect. The diameter and cross-sectional area of the right subclavicular vein at the end of inspiratory and expiratory processes were then measured. The results showed that there were no significant differences in SBP, DBP and HR between the two groups

before anesthesia. During anesthesia, the SBP, DBP, and HR in hypotensive group were significantly lower than those in the normotensive group (SBP, 103.25 ± 12.48 mmHg; DBP, 58.94 ± 7.46 mmHg; HR, 52.96 ± 6.48 beats/min), and the difference was statistically significant ($P < 0.05$). The SCV-CI in the hypotensive group was 35.82 ± 4.93% greater than that of the normotensive group 23.85 ± 5.27%, and the incidence of nausea and vomiting in hypotensive patients (40.0%) was significantly higher than that in the normotensive group (10.53%). The area under the curve of SCV-CI predicting hypotension in patients with pregnancy-induced hypertension under neuraxial anesthesia was 0.825 (95% CI: 0.762–0.893, $P < 0.001$), the cut-off value was 25.68%, the predictive sensitivity was 92.68%, and the specificity was 81.24%.

Therefore, SCV-CI has a good predictive value for the occurrence of hypotension in patients with PIH who undergo neuraxial anesthesia. Hence, it can be used to guide the prevention and control measures of hypotension in patients with PIH after caesarean section. However, because this study was single-centered with a small sample size, the conclusions of the study may be biased, and it may be better to combine other indicators to predict the occurrence of hypotension in patients with PIH who undergo neuraxial anesthesia.

Funding

This work was supported by the 2021 Shaoguan City Supporting Scientific Research Workers Project (Project No. 210809174533267)

Disclosure statement

The author declares no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Nursing Management During Public Health Emergencies

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Abstract: Public health emergencies are difficult to predict, have complex causes, and are extremely destructive. In order to reduce the impact of public health emergencies, this paper introduces a refined nursing management method to deal with public health emergencies. By establishing a sound management system, implementing scientific management processes, ensuring the overall quality of nursing, and improving the logistics, etc., the cooperation between the medical staff can be improved, and the safety of personnel can be ensured.

Keywords: Public health emergencies; Nursing management; Refined management

Online publication: May 30, 2023

1. Introduction

Emergencies occur every year all around the world, such as natural disasters, accidents, and pandemics. When these emergencies occur, people will feel nervous and fearful, and these emergencies will also have a significant impact on people's lives and mental states. Among them, public health emergencies have the greatest impact on public health or group health. Public health emergencies are defined as sudden outbreaks of major infectious diseases, group diseases of unknown cause, major food and occupational poisoning, and other events that have a major impact on public health [1]. Issues regarding public health emergencies should be highlighted due to their unpredictability, complexity of causes, and destructiveness. In recent years, there have been large-scale public safety emergencies in the country, which require advanced medical technology and good emergency management by medical staff. By establishing a sound management system and implementing scientific management processes, ensuring the overall quality of nursing care, and improving the level of logistics services, etc., the coordination between the medical staff can be improved, and the safety of personnel can be ensured.

2. Improve the management system and implement scientific management

The medical team is one of the most important forces in a public health emergency, [2]. To establish a sound management system to ensure the safety of medical staff and logistics personnel, professional protective equipment should be provided. Besides, special operating equipment and standard operating rooms should be provided. Systematic training should also be provided to the staff to ensure the implementation of various measures to avoid medical accidents, so that the safety of medical staff and patients can be ensured.

2.1. Perfect protection details, and strict training and assessment

Based on previous experiences in handling health emergencies, in accordance with the relevant instructions

issued by the National Health and Family Planning Commission [3], and the input of experts, a set of procedures on wearable protective clothing can be designed. Each link and requirement should be specified in detail, including the proper method of wearing a protective mask and measures to prevent fogging when using goggles. Tutorials and video recordings of the standard operating procedure can also be used to train medical staff. In addition, a set of emergency treatment procedures should be formulated for medical staff who may experience dizziness and vomiting during the operation, so that occupational hazards in virus-contaminated areas can be prevented and ensure the safety of medical staff. To better respond to emergency public health incidents of infectious diseases, pre-job training should be carried out systematically, so that every medical staff can fully grasp the protection measures and key points and the medical staff and patients can be protected. Training can be carried out in various ways, such as distributing training materials and self-study videos, simulation drills, and assessments, so that every medical staff can fully understand their own responsibilities and priorities. In addition, safety training should also be carried out frequently to enhance the medical staff's safety awareness.

2.2. Setting up supervisory positions

In order to control disease infection among hospital personnel more effectively, a special supervisor post can be set up in the ward. The supervisor is to check the wearing of protective equipment by medical staff when entering and leaving the polluted area, remind and deal with uncivilized behavior, and improve the effectiveness of protective equipment. Besides, the supervisors should conduct regular inspections on the protective equipment of the medical staff. Once the protective equipment is found to be detached or damaged, the personnel should be notified immediately, and the equipment should be repaired or replaced. In addition, any medical staff who experience symptoms such as abnormal body temperature, dizziness, and vomiting, etc., they must immediately report to their superiors and receive timely treatment. Their duties should also be assigned to other staff to ensure smooth workflow in the hospital.

2.3. Reasonable deployment of personnel and scientific and dynamic scheduling

Due to high work intensity, large number of patients, and heavy physical load of medical staff in infectious disease wards, it is important to scientifically manage the medical team, formulate a reasonable scheduling system. In order to ensure a smooth workflow, the areas of the hospital can be divided into clean area, potentially polluted area, and polluted area according to the tasks performed in that area. The location of each tasks should be defined to ensure that the work handover process between medical staff is efficient and smooth [4]. In addition, a 4-hour shift system can also be implemented, where the nurses are divided into different groups according to their working experience and working hours. Besides, relevant experts will be the team leaders, and the nurses are assigned to specific patients, and an accountability system can be created to improve quality of care. In addition, the nurses on duty should be adjusted according to number of patients admitted to the hospital on that day, and a shift system should be implemented to ensure the quality of care while improving work efficiency.

3. Carrying out holistic care and ensure the quality of care

3.1. Formulating nursing procedure and standardizing nursing management

Highly infectious diseases with rapid onset are often accompanied by a series of complications and organ failure [5]. In order to save the patient's life, the patient must be given proper care. Besides, the patient's vital signs and physical condition, including body temperature, respiration, pulse, blood pressure, etc., should be monitored. The nursing plan should be adjusted according to the patient's condition, carry out airway management, basic nursing and other measures should be taken. In addition, it is necessary to focus on the details while observing the patient to prevent adverse reactions and ensure the safety of patients. In

addition, the content and procedure of nursing should be clarified according to the patient's diseases; and the process should be revised and changed according to the characteristics of the disease and the patient's condition [6]. During the process of registration of patients' admission and information transfer, a sound verification system should be established to ensure the authenticity and accuracy of the information, and the personal belongings and nursing supplies of the patients should be checked and listed in detail to ensure the authenticity and accuracy of the information, so that the nursing management process can be standardized.

3.2. Carrying out emergency training and improving professional quality

When faced with new types of diseases, new working environment, and new working system and equipment, nursing staff need to quickly grasp the workflow, nursing routines, and measures that should be taken. Therefore, it is very important to strengthen the training of nursing staff in terms of using different technologies and equipment and psychological adaptability. We have carried out comprehensive research on the key points of nursing critically ill patients with major infectious diseases and constructed a complete set of training curriculum system and formulated a well-organized training plan. The training content includes occupational protection, job responsibilities, equipment operating procedure, and priorities, etc., so that each nursing staff can understand their roles and can respond to emergencies accordingly and ensure the patients' safety. In terms of the teaching staff, we must pay attention to the cultivation of professional nursing talents, so that they can become the backbone of the industry. Lessons are conducted with the combination of on-site demonstrations, online training, and group learning. This system makes full use of the short time between nursing staff's shifts to strengthen targeted operations and make up for weaknesses. Through this teaching system, nurses can quickly improve their emergency handling and practical skills, thus effectively ensuring the safety of patients and the quality and level of nursing. The establishment of a sound training organization and management system, evidence-based and practical training content, the application of diverse training methods, and maximizing the role of teachers can make a significant impact on emergency training [7].

3.3. Improving the quality of nursing care and ensuring the safety of patients

Quality of care has always been an important aspect in nursing management. The head nurse and nursing supervisors strictly control the quality of basic nursing care of critically ill patients with infectious diseases and make detailed requirements for quality management points in airway assessment. During this process, it is also important to pay attention to the basic physiological state of the patient, such as skin care, oral care, etc., to prevent various complications of critically ill patients, such as pressure injury and respiratory tract infection. Nursing staff should be assigned to inspect and supervise the ward every day, so as to find out details and report abnormal situations in time to ensure that the complications can be found and treated immediately [8]. Besides, the infection prevention and control in the intensive care unit should also be improved by improving the environmental sanitation of the intensive care unit, the cleaning and disinfection of surfaces, and other measures. Hand cleaning procedures and the awareness towards infection control should be improved. After the patient is transferred, the ward that the patient was at should be disinfected properly, and eye-catching signs should be pasted in the ward. In addition, the monitoring of vital signs should be strengthened.

3.4. Strengthen teamwork and give full play to multidisciplinary advantages

Through the establishment of a multidisciplinary nurse team and close coordination between medical staff, diversified, individualized, and continuous care of critically ill patients can be achieved, which in turn reduces the probability of complications and improve the quality of life of patients [9]. The nursing team

perform their duties and carry out detailed discussions on difficult and critical patients every day. ICU nurses are the core members of the entire nursing team. While providing patients with professional care such as airway management, respiratory support, and blood purification, they must also do a good job in basic nursing, psychological support, and hospice care. In terms of nursing skills, corresponding measures should be formulated according to specific situations. Through the insertion of venous and peripheral arterial catheters under the guidance of ultrasound, the rate of puncture can be improved the pain of patients can be reduced. At the same time, ultrasound can also be used to evaluate the condition of the stomach, so that timely intervention and adjustment of treatment plans can be made in case of complications. Psychological counseling should be given to patients who are emotionally negative or uncooperative, which includes sharing cases of recovery, so as to improve patients' confidence in the treatment, accelerate their recovery, and relieve their pain [10].

4. Comprehensive management and improving team confidence

4.1. Strict on-site management to reduce the risk of mass infection

In order to reduce the risk of mass infection, the medical team has paid a lot of attention to the management of centralized living quarters. The nursing department should formulate a clear set of residency management plans that includes details on entering and leaving the quarters and countermeasures that should be taken during an emergency. The Nursing Department should adopt a resident grid management method and divide the members into multiple groups. Each group should have an experienced as the team leader who will be in charge of a comprehensive understanding the members' mindset, monitoring and reporting of body temperature, and regular mental health training to ensure the mental health of medical team members.

4.2. Improving the security and protecting the physical and mental health of personnel

In the wards of critically ill patients, medical staff often have frequent shifts due to insufficient staff. Emergency rescue are carried out often due to sudden deterioration of the patient's condition and physical and psychological pressures like infection risks that may be caused by occupational exposure. If there is no psychological counseling, the work efficiency of the staff may reduce [11]. Therefore, it is necessary to ensure that medical team members can maintain an optimistic attitude and a good physical condition, so that they can devote themselves to their work. Hence, it is important to do a good job in all aspects of security work, arrange regular training for relevant mental health counselors, set up a special line for psychological counseling, and help improve the mental health of medical staff. Nurses who have performed well at work should be rewarded, and team-building activities can be organized to increase the teamwork spirit between medical staff. In addition, a good working atmosphere should be created, the sense of pride and responsibility of medical staff and the level of refined management should be improved.

5. Conclusion

Public health emergencies is a huge challenge for both the nursing management system and the problem-solving skills of medical staff. In the process of dealing with major infectious diseases, a scientific and reasonable management system is crucial to ensure the smooth workflow of the medical team. A sound nursing system is an important factor in achieving emergency response and providing high-quality care. In order to improve the emergency rescue capabilities of medical staff, it is necessary to strengthen the handling of public health emergencies and improve the emergency plan, strengthen the training and simulation of infectious disease risk identification and critical treatment. It is also important to pay attention to the attitude of nurses when dealing with emergencies, teamwork spirit, and other aspects of quality training. The rotation training and assessment system for nursing staff should be improved, and the

establishment of a regular training and re-education system for nursing staff should be explored. A complete nursing emergency team should be created to ensure that medical personnel better prevent, control, and treat major infectious diseases.

Disclosure statement

The author declares no conflict of interest.

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Publisher's note

Bio-Byword Scientific Publishing remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Effect and Significance of Comprehensive Training in Infection Prevention and Control on the Psychological Health of Oral Health Staff

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Abstract: *Background:* Oral health staff have close contact with patients in the process of diagnosis and treatment, and it is inevitable for them to come into contact with patients' secretions. Therefore, oral health staff are at greater risk of infectious diseases in their daily work, and their psychological health is also greatly challenged. *Objective:* To study the effect and significance of comprehensive training in infection prevention and control on the psychological health of oral health staff. *Methods:* We selected 400 oral health staff from a tertiary stomatological hospital in Guangzhou, China in this study. The respondents were randomly divided into an intervention group and a control group. After the first round of investigation, the intervention group received comprehensive training in prevention and control of infection for three months, while the control group received no intervention. *Results:* The comprehensive training in infection prevention and control improved the respondents' psychological health and job satisfaction. Further strengthening infection prevention and control training for oral health staff will increase their self-confidence, improve their mental health, and increase their job satisfaction. *Conclusion:* For oral health staff, it is particularly important to formulate an effective and operable preventive and control training program and then implement it in a standardized manner.

Keywords: Oral health staff; Infection prevention; Infection control; Psychological health; Comprehensive training; Job satisfaction

Online publication: May 30, 2023

1. Introduction

Studies have shown that medical workers need to be in close contact with patients of various diseases in the diagnosis and treatment process; thus, they will be at high risk for infection [1]. This situation has a significant impact on the psychological health of medical workers, as they experience varying levels of anxiety and stress due to fears of possible infection or the possibility of transmitting diseases to their family members [2]. In a study, medical staff were invited to participate in a questionnaire survey on the level of anxiety to infectious diseases. The results showed that a large proportion of medical staff expressed significant anxiety and fear of getting infected by infectious diseases [3].

Since secretions act as a transmission medium for certain infectious diseases, and oral health workers are unable to avoid exposure to these substances in their daily work, the risk of infection faced by staff in the department of stomatology, compared with other specialties, is relatively high [4,5]. The droplets formed

by high-speed dental handpieces, air/water guns, ultrasonic dental cleaning, and other oral medical equipment or the droplet nuclei formed by these substances can be suspended in the air in the form of aerosols for more than half an hour [6]. If these substances with the source of infection permeate in the air or splash onto the face or eyes, they can cause infection. Therefore, the psychological health of oral health workers is greatly challenged. In a survey of dentists, it was found that most of respondents were worried about suffering from infectious diseases upon exposure to secretions during oral treatment [7]. Through psychological assessments, it was found that half of the respondents showed some symptoms of anxiety. The most common concern of the respondents was the possibility of them contracting infectious diseases and then passing them on to their family, followed by anxiety about their own risk of infection at work [8]. A survey has found that most nurses in dental clinics were worried about being infected in clinical activities [9].

2. Research model and hypotheses

2.1. Impact of comprehensive training in infection prevention and control on the psychological health of oral health staff

Studies have shown that some oral health workers are unfamiliar with prevention and control measures and lack prevention and control training. Furthermore, there is no guarantee for these high-risk workers in terms of occupational protection. According to a survey on oral health staff's understanding of their protection status [10], a significant proportion of respondents lacked knowledge of prevention and control of nosocomial infection and scored lower than average in terms of awareness of infection transmission pathways, infective fluids, human immunodeficiency virus (HIV) transmission, and unhealthy behaviors. From this, the conclusion was that some practitioners in dental institutions lacked training in nosocomial infection [10]. The risk of infection among medical staff and the predisposition to negative emotions, such as fear and anxiety, increase with the lack of basic knowledge of hospital infection prevention and control, familiarity with the standardized nosocomial infection prevention and control operation procedures, as well as the standardized implementation of prevention and control measures.

2.2. Role and significance of comprehensive training in infection prevention and control

In a survey on dental students, the vast majority of respondents deemed that knowledge training in nosocomial infection prevention and control has a guiding role in personal infectious disease prevention and control [11]. It has also been pointed out that dentists need to have good psychological health as well as scientific and effective knowledge reserves on prevention and control. If they can effectively protect themselves, they may have higher confidence in the diagnosis and treatment of diseases, thus overcoming their fears [12].

2.3. Impact of psychological health of oral health workers on job satisfaction

Studies have shown that the fear and pressure that doctors endure in diagnosis and treatment have a great impact on job satisfaction. A study has found that mental stress can lead to chronic fatigue and unhealthy lifestyles among doctors, thereby being an important factor that affects job satisfaction [13]. A survey on 1,100 medical staff has shown that psychological health status is significantly related to job satisfaction and significant psychological health issues could reduce job satisfaction and affect the quality of service provided to patients [14].

2.4. Research model

Through literature study, we can infer the priori hypothesis linking the three observed variables: "knowledge and norms of infection prevention and control," "degree of psychological impact," and "job

satisfaction of oral health staff." We used these variables as the observed variables in this study and constructed a hypothetical model (**Figure 1**).

Studies have shown that strengthening the training in infection prevention and control plays an important role in improving the psychological health and job satisfaction of oral health workers. Through literature review, previous research on the psychological health of oral health workers predominantly remained in a relatively isolated or static perspective. Recruiting oral health staff in Guangzhou, China as respondents, we conducted two rounds of surveys to evaluate the changes of oral health staff, such as their psychological health and job satisfaction, after receiving intervention (comprehensive knowledge and skills training in infection prevention and control).

Figure 1. Hypothetical model

H1: The degree of comprehensive training in the knowledge and norms of infection prevention and control negatively affects the degree of psychological impact of oral health staff.

H2: The degree of psychological impact of oral health staff negatively affects their job satisfaction.

3. Method

3.1. Respondents and source

The respondents of this study were stomatologists and nurses from a tertiary stomatological hospital in Guangzhou, age ranging from 18 to 60. Guangdong Province occupies a considerable proportion of China's oral healthcare system and is currently one of the three major national medical centers in China. Guangzhou, as the capital of Guangdong Province, has taken on a leading role in China's medical and health development. This hospital is a specialized stomatological hospital with great influence in South China oral industry in terms of its technical level, social benefit, and scale; it is a representative hospital of the industry. This study was reviewed and approved by Medical Ethics Committee of Affiliated Stomatological Hospital of Guangzhou Medical University. The participants provided written informed consent prior to participating in this study.

3.2. Survey design and implementation

The survey was conducted using printed and electronic questionnaires. The data were organized in a database by a specially designated person and checked by two independent people. The first round of survey (R1) was carried out in October 2021, and the samples were selected based on the inclusion criteria. After the end of R1, the researchers analyzed the data to understand the respondents' scores on each subscale as a baseline to verify the hypothesized relationship. Thereafter, the respondents were randomly divided into two groups. One group was selected to receive comprehensive knowledge and skills training in nosocomial infection prevention and control for a period of three months, and this group was named "intervention group"; the other group did not receive training, and was named "control group." After training, the second round of survey (R2) was conducted in March 2022. The questionnaire was the same one used in R1. Differences between the two cross-sections and two groups were assessed by data analysis from both rounds of survey.

3.3. Comprehensive knowledge and skills training in nosocomial infection prevention and control for the intervention group

3.3.1. Establish a training group

The training group was made up of experts who were infection control management professionals from both inside and outside the hospital and had participated in systematic, standardized, and comprehensive knowledge and skills training in nosocomial infection as well as obtained appropriate certification of competency.

3.3.2. Professional theoretical training

Relevant knowledge of infectious disease prevention and disinfection as well as quarantine was explained by the experts. They demonstrated the standard procedure of putting on and taking off protective clothing. The oral health staff were required to put on and take off their protective clothing on site. The issues found in the current operation of each team member in wearing and taking off their protective clothing were corrected to enhance the staff's ability and awareness of emergency protection against infectious diseases as well as improve the basic skills of the trained staffs in putting on and taking off personal protective equipment.

3.3.3. Skills training

(i) With reference to corresponding international and national norms and guidelines, the staff were trained to specify the types of personal protective equipment (PPE) and gain proficiency in the methods and procedures of wearing and taking off PPE. The standard PPE includes masks, medical protective clothing, and gloves.

(ii) The staff were trained in hand hygiene, encouraged to implement the five hand hygiene indicators of the World Health Organization (WHO) in accordance with the requirements of standard prevention, and learned the seven-step hand washing method.

3.4. Instrumentation

Based on the research model and literature review, we developed a measurement system on the basis of the mature scales applied in related research. Subscales based on three major variables were established, so were the corresponding measurement dimensions of each variable. The research framework based on literature review is shown in **Table 1**.

(i) Knowledge and norms of infection prevention and control: standard diagnosis and treatment (SDT), hand hygiene (HH), and personal protection (PP).

(ii) Degree of psychological impact: psychological impact of work (PIW) and psychological impact of life (PIL).

(iii) Job satisfaction: general feeling (GF), management style (MS), and work autonomy (WA).

Table 1. Research framework

Variables	Dimensions	Sources
Knowledge and norms of infection prevention and control	SDT, HH, PP	[15]
Degree of psychological impact	PIW, PIL	[16,17]
Job satisfaction	GF, MS, WA	[18]

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

3.5. Scale construction

3.5.1. Delphi method

On the basis of the established dimensions and index system and in line with literature review, we integrated the items that meet the research design goals and used Excel to build an item pool. Two experts with good nosocomial infection knowledge and familiarity with the diagnosis and treatment process were commissioned to classify and sort the items according to the research design using the Q-sort technique. Through three rounds of sorting, the experts had basically the same opinions on sorting and classification. In combination with the results, we screened out items with relatively good validity to formulate the initial scale.

3.5.2. Preliminary investigation

We randomly selected eight oral health staff from the hospital who met the inclusion criteria and invited them to fill in the initial scale. Based on their feedback, some items were inappropriately expressed. Therefore, we made further modifications and identified the official version of the formal questionnaire. The questionnaire mainly consisted of closed-ended questions in seven-point Likert scale (1 = strongly disagree; 7 = strongly agree).

3.5.3. Encoding and translation

We coded the measurement items of each dimension accordingly. The coding principle was as follows: English initial abbreviation of the dimension corresponding to the item + item serial number." Taking the subscale corresponding to SDT as an example, the item codes are as follows: SDT1, SDT2, …SDT7. Part of the measurement items were taken from literatures in English, so the preliminary questionnaire was compiled in English (the questionnaire can be obtained from https://www.scidb.cn/s/7jeUn2). However, since the survey was conducted in China, we invited a bilingual translator who is familiar with both Mandarin and English to translate the preliminary English-version questionnaire into Chinese and then invited another bilingual translator to translate the Chinese-version questionnaire into English, so as to make sure that both the English and the Chinese versions are accurate.

3.5.4. Statistical analysis

SPSS 24.0 and Amos 21 were used for statistical processing.

(i) SPSS 24.0 was used for the following processing: data entry, reliability analysis, validity analysis (exploratory factor analysis), statistical description, correlation analysis, and difference analysis.

(ii) Amos 21 was used for the following analyses: confirmatory factor analysis and establishment of structural equation model.

4. Results

4.1. Descriptive statistics

A total of 413 questionnaires were distributed in R1, and 405 questionnaires were collected, with a collection rate of 98.1%. There were 400 valid questionnaires, with an overall effective rate of 98.8%. Among the respondents, 210 (52.5%) were male, and 190 (47.5%) were female; 317 (79.3%) had a master's degree or above, while 83 (20.8%) had a bachelor's degree or below; 193 were doctors (48.3%), while 207 were nurses (51.8%); 360 (90%) were married, while 40 (10%) were single or divorced; 311 (77.8%) had children, while 89 (22.3%) were childless; 208 (52%) did not live alone, while 192 (48%) lived alone.

4.2. Reliability and validity analysis

Through adaptive test of each subscale, the Kaiser-Meyer-Olkin (KMO) value of each subscale was greater

than 0.9, and Bartlett's test of sphericity showed that $P < 0.001$. Therefore, principal component factor analysis could be performed on each subscale. We used the varimax method to orthogonally rotate the factors, analyzed the results of 25 iterations of convergence, and extracted principal components with eigenvalues greater than 1 as common factors. The factor load value of all measurement items was more than 0.6. The items included in the eight common factors were all consistent with the original questionnaire design dimensions. The questionnaire had good validity.

4.3. Differences in the scores of different individual characteristics in each dimension

In order to compare the differences in scores of the corresponding items in each dimension among respondents with different gender, age, educational background, marital and childbirth status, and occupation, we used an independent sample *t*-test to analyze the results. The results showed that the difference in scores of respondents with different gender were not statistically significant ($P > 0.05$). Compared with the respondents in the "40–59" age group, those in the "18–39" age group had lower mean scores in PIW and PIL, but their mean scores in PP, GF, and MS were higher, and the difference was statistically significant ($P < 0.05$). See **Table 2** for details.

Table 2. Difference tests of ages and variables

Index	Age	Mean	Standard deviation	*t*	*P*
PIW	18–39	2.826	1.019	-3.804	0.000
	40–59	3.293	1.016		
PIL	18–39	2.844	1.003	-2.777	0.006
	40–59	3.183	1.042		
SDT	18–39	3.142	1.057	1.840	0.067
	40–59	2.911	0.993		
HH	18–39	2.992	1.068	1.930	0.054
	40–59	2.741	1.108		
PP	18–39	3.000	0.993	2.258	0.024
	40–59	2.727	1.022		
GF	18–39	3.046	1.028	2.940	0.003
	40–59	2.682	1.018		
MS	18–39	3.049	1.042	3.047	0.002
	40–59	2.662	1.088		
WA	18–39	3.004	1.053	1.273	0.204
	40–59	2.841	1.093		

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

As shown in **Table 3**, compared with respondents with "bachelor's degree or below," those with "master's degree or above" had lower mean in PIW and PIL, and the difference was statistically significant ($P < 0.05$). There were no significant differences in the scores of the remaining dimensions.

Table 3. Difference tests of education background and variables

Index	Educational background	Mean	Standard deviation	*t*	*P*
PIW	Master's degree or above	2.863	0.998	-2.301	0.023
	Bachelor's degree or below	3.178	1.139		
PIL	Master's degree or above	2.814	0.996	-4.106	0.000
	Bachelor's degree or below	3.320	1.017		
SDT	Master's degree or above	3.097	1.042	0.204	0.839
	Bachelor's degree or below	3.071	1.068		
HH	Master's degree or above	2.978	1.090	1.528	0.127
	Bachelor's degree or below	2.775	1.036		
PP	Master's degree or above	2.974	0.982	1.279	0.203
	Bachelor's degree or below	2.807	1.079		
GF	Master's degree or above	2.996	1.030	1.149	0.251
	Bachelor's degree or below	2.849	1.053		
MS	Master's degree or above	2.995	1.055	1.159	0.247
	Bachelor's degree or below	2.843	1.090		
WA	Master's degree or above	2.968	1.073	-0.017	0.987
	Bachelor's degree or below	2.970	1.029		

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

In terms of marital and childbearing factors, compared with "single or divorced" respondents, "married" respondents had higher mean in PIW and PIL, but lower mean in SDT, HH, PP, GF, MS, and WA. All differences were statistically significant ($P < 0.05$), as shown in **Table 4**. Compared with respondents "without children," those "with children" had higher mean in PIW and PIL, and the difference was statistically significant ($P < 0.05$). There was no significant difference in the scores of other dimensions (see **Table 5**).

Table 4. Difference tests of marital status and variables

Index	Marital status	Mean	Standard deviation	*t*	*P*
PIW	Married	2.992	1.034	4.283	0.000
	Single or divorced	2.358	0.871		
PIL	Married	2.958	1.033	2.825	0.007
	Single or divorced	2.561	0.820		
SDT	Married	3.049	1.039	-2.436	0.015
	Single or divorced	3.471	1.052		
HH	Married	2.885	1.092	-3.460	0.001
	Single or divorced	3.396	0.860		
PP	Married	2.877	1.010	-4.876	0.000
	Single or divorced	3.507	0.745		
GF	Married	2.921	1.044	-3.058	0.003
	Single or divorced	3.369	0.859		

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Index	Marital status	Mean	Standard deviation	t	*P*
MS	Married	2.894	1.058	-4.573	0.000
	Single or divorced	3.594	0.902		
WA	Married	2.929	1.070	-2.457	0.017
	Single or divorced	3.319	0.937		

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

Table 5. Difference tests of procreation status and variables

Index	Procreation status	Mean	Standard deviation	*t*	*P*
PIW	With children	3.001	1.037	2.624	0.009
	Without children	2.676	0.995		
PIL	With children	2.983	1.028	2.382	0.018
	Without children	2.693	0.963		
SDT	With children	3.056	1.041	-1.265	0.207
	Without children	3.215	1.063		
HH	With children	2.920	1.099	-0.581	0.562
	Without children	2.993	1.017		
PP	With children	2.919	1.002	-0.762	0.446
	Without children	3.011	1.014		
GF	With children	2.934	1.046	-1.140	0.255
	Without children	3.076	0.994		
MS	With children	2.910	1.071	-1.897	0.058
	Without children	3.152	1.018		
WA	With children	2.973	1.081	0.160	0.873
	Without children	2.952	1.001		

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

Compared with nurses, doctors had higher mean in PIW, but lower mean in SDT, HH, PP, GF, MS, and WA, and the difference was statistically significant ($P < 0.05$). There was no significant difference in PIL between doctors and nurses (see **Table 6**).

Table 6. Difference tests of occupation and variables

Index	Occupation	Mean	Standard deviation	*t*	*P*
PIW	Doctor	3.131	1.017	3.843	0.000
	Nurse	2.740	1.019		
PIL	Doctor	3.007	1.014	1.676	0.095
	Nurse	2.836	1.021		
SDT	Doctor	2.884	1.040	-3.899	0.000
	Nurse	3.285	1.017		

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Index	Occupation	Mean	Standard deviation	*t*	*P*
HH	Doctor	2.727	1.049	-3.799	0.000
	Nurse	3.131	1.076		
PP	Doctor	2.753	0.979	-3.649	0.000
	Nurse	3.114	0.999		
GF	Doctor	2.808	1.028	-2.964	0.003
	Nurse	3.112	1.023		
MS	Doctor	2.773	1.055	-3.508	0.001
	Nurse	3.141	1.043		
WA	Doctor	2.772	1.021	-3.618	0.000
	Nurse	3.151	1.071		

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

4.4. Building a structural equation model

We built a structural equation model in this study to verify the research hypothesis. First, Amos 21 was used to establish a structural equation model based on the hypothesis, as shown in **Figure 2**. Each fitting index of the model reached the ideal value, indicating that the model fits well (minimum discrepancy function by degrees of freedom divided [CMIN/DF] = 1.357; root mean square error of approximation [RMSEA] = 0.03; normed fit index [NFI] = 0.903; incremental fit index [IFI] = 0.973; Tucker-Lewis index [TLI] = 0.971; comparative fit index [CFI] = 0.972; root mean square residual [RMR] = 0.065).

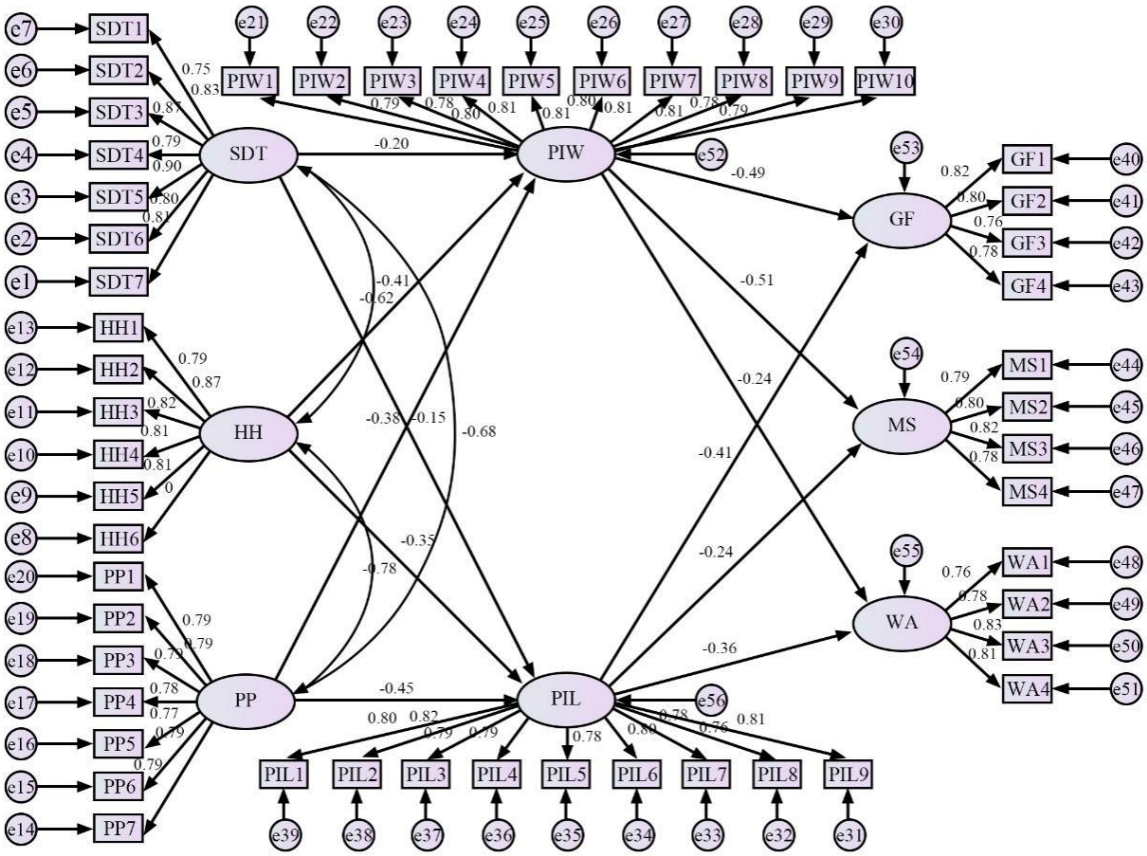

Figure 2. Structural equation model

According to **Table 7**, in the full sample, SDT (β = -0.196, *P* = 0.000), HH (β = -0.405, *P* = 0.000), and PP (β = -0.379, *P* = 0.000) had significant direct negative effect on PIW; SDT (β = -0.149, *P* = 0.000), HH (β = -0.352, *P* = 0.000), and PP (β = -0.454, *P* = 0.000) had significant direct negative effect on PIL. Therefore, each dimension (SDT, HH, and PP) under the variable "knowledge and norms of infection prevention and control" in the research hypothesis model had significant negative effect on each dimension (PIW and PIL) of the variable "degree of psychological impact" (H1 supported). We also learned through analysis that PIW (β = -0.491, *P* = 0.000) and PIL (β = -0.412, *P* = 0.000) had significant direct negative effect on GF; PIW (β = -0.512, *P* = 0.000) and PIL (β = -0.236, *P* = 0.001) had significant direct negative effect on MS; PIW (β = -0.240, *P* = 0.003) and PIL (β = -0.360, *P* = 0.000) had significant direct negative effect on WA. Therefore, each dimension under the variable "degree of psychological impact" in the research hypothesis model had significant negative effect on each dimension (GF, MS, and WA) of the variable "job satisfaction" (H2 supported).

Table 7. Model analysis results

Path	SE	Estimate	S.E.	C.R.	*P*
SDT→PIW	-0.196	-0.196	0.042	-4.679	0.000
SDT→PIL	-0.149	-0.149	0.044	-3.392	0.000
HH→PIW	-0.405	-0.412	0.057	-7.289	0.000
HH→PIL	-0.352	-0.359	0.058	-6.135	0.000
PP→PIW	-0.379	-0.387	0.061	-6.367	0.000
PP→PIL	-0.454	-0.465	0.065	-7.103	0.000
PIW→GF	-0.491	-0.509	0.066	-7.764	0.000
PIW→MS	-0.512	-0.501	0.074	-6.773	0.000
PIW→WA	-0.240	-0.214	0.072	-2.962	0.003
PIL→GF	-0.412	-0.426	0.064	-6.681	0.000
PIL→MS	-0.236	-0.230	0.070	-3.288	0.001
PIL→WA	-0.360	-0.321	0.074	-4.362	0.000

Abbreviations: SE, standardized effect; C.R., critical ratio; GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; S.E., standard error; WA, work autonomy.

5. Comparison of results of the two rounds of survey

5.1. Comparison of scores between groups before and after R2

The 400 respondents who participated in R1 were randomly divided into an intervention group and a control group, with 200 individuals in each group. In order to ensure the reliability of the verification, a pre-test was carried out on the two groups before R2 to evaluate the differences in scores of the two groups in each dimension. Through analysis, no significant difference was observed between the two groups in their scoring (PIW: *t* = 0.096, *P* = 0.923; PIL: *t* = 0.082, *P* = 0.935; SDT: *t* = -0.314, *P* = 0.754; HH: *t* = -0.485, *P* = 0.628; PP: *t* = -0.121, *P* = 0.904; GF: *t* = -0.398, *P* = 0.691; MS: *t* = 0.023, *P* = 0.981; WA: *t* = -1.212, *P* = 0.226).

After the intervention group completed the training as planned, the second round of survey was carried out. A post-test was carried out for both the groups, and *t*-test was used to compare and analyze the differences in scores of each dimension between the two groups in the second round of survey. According to **Table 8**, it can be seen that the mean scores of the intervention group in PIW and PIL, compared with the control group, were lower, but the mean scores in other dimensions were higher, and the difference was

statistically significant ($P < 0.05$).

Table 8. Post-test difference analysis

Index	Group	Mean	Standard deviation	*t*	*P*
PIW	Intervention group	2.608	0.892	-3.267	0.001
	Control group	2.918	1.000		
PIL	Intervention group	2.584	0.841	-4.014	0.000
	Control group	2.933	0.897		
SDT	Intervention group	3.404	0.931	3.298	0.001
	Control group	3.086	0.999		
HH	Intervention group	3.251	0.992	2.655	0.008
	Control group	2.983	1.023		
PP	Intervention group	3.345	0.916	4.114	0.000
	Control group	2.966	0.928		
GF	Intervention group	3.414	0.963	3.994	0.000
	Control group	3.025	0.983		
MS	Intervention group	3.309	0.933	3.561	0.000
	Control group	2.958	1.036		
WA	Intervention group	3.305	0.999	3.206	0.001
	Control group	2.978	1.044		

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

5.2. Difference in scores between groups in the two rounds of survey

We compared and analyzed the scores of the control group for each dimension in the two rounds of survey, and the results showed that the difference in the mean scores of the control group in the two rounds of survey was not statistically significant ($P > 0.05$). According to **Table 9**, the mean scores of the intervention group in the second round of survey were lower compared with those in the first round of survey in terms of PIW and PIL but higher in other dimensions. The differences were statistically significant ($P < 0.05$).

Table 9. Difference tests of the intervention group in R1 and R2

Index	Survey	Mean	Standard deviation	*t*	*P*
PIW	R1	2.934	1.034	13.135	0.000
	R2	2.608	0.892		
PIL	R1	2.923	1.025	12.487	0.000
	R2	2.584	0.841		
SDT	R1	3.075	1.045	-11.368	0.000
	R2	3.404	0.931		
HH	R1	2.910	1.086	-11.934	0.000
	R2	3.251	0.992		
PP	R1	2.934	1.010	-15.021	0.000
	R2	3.345	0.916		

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Index	Survey	Mean	Standard deviation	t	*P*
GF	R1	2.945	1.042	-12.954	0.000
	R2	3.414	0.963		
MS	R1	2.965	1.054	-8.328	0.000
	R2	3.309	0.933		
WA	R1	2.904	1.066	-10.592	0.000
	R2	3.305	0.999		

Abbreviations: GF, general feeling; HH, hand hygiene; MS, management style; PIL, psychological impact of life; PIW, psychological impact of work; PP, personal protection; SDT, standard diagnosis and treatment; WA, work autonomy.

6. Discussion

6.1. Relationship between variables and dimensions

Based on our results, our hypothesis is supported. The more inferior their prevention and control capabilities, the more pronounce the negative impact on the psychological health and job satisfaction of oral health staff, and vice versa. Through group test and comparison of results of the two rounds of survey, no significant difference was observed between groups in R1. After the intervention, the scores of the intervention group in terms of "degree of psychological impact" (PIW and PIL) were significantly lower than those of the control group, and the scores of the former in terms of "knowledge and norms of infection prevention and control" (SDT, HH, and PP) and "job satisfaction" (GF, MS, and WA) were significantly higher than those of the latter. In R2, the scores of the intervention group in terms of "degree of psychological impact" significantly decreased, but the scores in "knowledge and norms of infection prevention and control" and "job satisfaction" significantly increased. The difference between scores of the control group in the two rounds of survey was insignificant. Thus, we can see that by receiving comprehensive knowledge and skills training in nosocomial infection prevention and control, the infection prevention and control capability, psychological status, and job satisfaction of the intervention group were significantly better than their own performance in R1 and that of the control group. Therefore, comprehensive training in nosocomial infection prevention and control plays a positive role in enhancing the psychological quality of oral health staff and improving their job satisfaction.

6.2. Influence of different individual attributes on various variables and dimensions

Through analysis, it was observed that the prevention and control capability of young respondents are not as good as that of older respondents. It is believed that this is related to the fact that senior oral health staff have undergone more training in the past and have a relatively solid business foundation. Concerning the relationship between age and job satisfaction, previous studies have revealed different findings. It has been proven that senior professionals bring about stronger job adaptability and higher satisfaction [19]. However, there are also research results suggesting that senior professionals are discriminated against due to the decline of knowledge and skills, thereby reducing job satisfaction [20]. The results of the present study suggested that the satisfaction of young oral health staff is higher than that of older staff. We reason that since senior oral health staff have different career goals, life experiences, living conditions, and demands on working conditions and environment from back when they were younger, their threshold of job satisfaction is higher. In addition, it has also been found that dentists aged 35–55 are more concerned and anxious about their career prospects. Perhaps, this is also one of the causes of their low job satisfaction [21]. In terms of the degree of psychological impact, the impact on those with higher education levels is lesser than those with lower education levels. Education background has a positive effect on individual psychological accomplishment. Medical personnel with higher education levels have advantage in coping

with stress and handling psychological issues since they tend to experience different challenges in learning and academic research. Our results showed that married respondents had poor prevention and control capability but were less psychologically affected and satisfied with their jobs. Dentistry is a high-intensity but high-income occupation, and family ties do affect the investment of oral health staff in medical learning. Also, due to changes in living conditions and levels of demand, they have higher expectations for work, which may cause psychological discrepancy. In addition, research has shown that marriage and family are protective factors of individual psychological health. Individuals who are married and have families are more able to cope with stress and negative emotions, with their spouses acting as an alternative support [22]. The results of the present study are consistent with this conclusion. In our study, the degree of psychological impact was higher in respondents with children. Considering that dental work has a high risk of infection, out of concern for the health of their children, those with children are affected to a certain extent in terms of their psychological status.

7. Conclusion

Greater risk of infection from infectious diseases has brought great challenges to the psychological health of oral health staff engaged in oral diagnosis and treatment. Through this study, we showed that the knowledge and skills of oral health staff in infection prevention and control are closely related to their psychological health and job satisfaction. It is particularly important to formulate an effective and operable protection training program and implement it in a comprehensive and standardized manner for those engaged in high-risk diagnosis and treatment. In addition, due to the particularity of the occupation, differences in their demographics, including education background, age, marital status, and procreation status, have different effects on their professional literacy, psychological quality, and job satisfaction. These factors should be taken into account by hospital managers. In the present study, only one case in China was selected for research. In the future, multiple representative survey cases can be used to carry out further extended research. Qualitative methods such as in-depth interviews and grounded theory can be adopted to further verify or explore the relationship among the variables.

Acknowledgments

The authors wish to thank Professor Virginia Trigo from University Institute of Lisbon for providing part of the materials to support the research.

Funding

This article is based on the 2021 co-construction project of the “14th Five-Year Plan” for the development of philosophy and social sciences in Guangzhou, China (Project number: 2021GZGJ219), and it is the research result of this project.

Disclosure statement

The authors declare no conflict of interest.

Author Contributions

Data curation: Z.W.

Methodology: Z.W.

Supervision: M.Z.

Validation: M.Z.

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Writing– review and editing: M.Z.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

An Interpretable Prediction Model for Stroke Based on XGBoost and SHAP

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Abstract: *Objective:* To establish a stroke prediction and feature analysis model integrating XGBoost and SHAP to aid the clinical diagnosis and prevention of stroke. *Methods:* Based on the open data set on Kaggle, with the help of data preprocessing and grid parameter optimization, an interpretable stroke risk prediction model was established by integrating XGBoost and SHAP and an explanatory analysis of risk factors was performed. *Results:* The XGBoost model's accuracy, sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve (AUC) were 96.71%, 93.83%, 99.59%, and 99.19%, respectively. Our explanatory analysis showed that age, type of residence, and history of hypertension were key factors affecting the incidence of stroke. *Conclusion:* Based on the data set, our analysis showed that the established model can be used to identify stroke, and our explanatory analysis based on SHAP increases the transparency of the model and facilitates medical practitioners to analyze the reliability of the model.

Keywords: Stroke risk prediction; XGBoost algorithm; SHAP model; Risk factor analysis

Online publication: May 30, 2023

1. Introduction

Stroke can be classified as ischemic stroke or hemorrhagic stroke. Due to its high morbidity and mortality, the health and safety of our citizens are at risk. According to the Global Burden of Disease (GBD), the cerebrovascular mortality rate of Chinese residents in 2018 was 149/100,000 (the death toll was 1.57 million), an increase in 41% compared with that in 1990; it is the third cause of death among urban residents and the second cause of death among rural residents [1]. However, among the more than 90% of the stroke burden caused by potentially modifiable risk factors, more than 75% of the stroke burden can be reduced by controlling metabolic and behavioral risk factors [2]. Therefore, it is of great significance to establish an accurate stroke risk prediction model and mine the key risk factors of stroke from the data.

The early stroke risk assessment focused on influencing factors, and statistical methods such as systematic review, meta-analysis, Cox proportional hazards regression model, and logistic regression model were used to identify key risk factors [3]. In recent years, machine learning algorithms have played an important role in the field of disease prediction. Through the establishment of a machine learning risk prediction model to identify stroke accurately and scientifically as well as provide an explanation for the model based on the inherent laws of the data, medical practitioners will be able to make better decisions.

2. Literature review

As the incidence of stroke continues to rise, along with the economic burden of treatment, the scientific identification of risk factors and the early and accurate prediction of individual incidence have become the top priorities of stroke prevention and treatment. Researchers in the field have applied statistics, machine learning, and deep learning methods to their research work (**Table 1**) in order to identify and analyze stroke-related risk factors as well as provide support for the primordial prevention and primary prevention of stroke. Barra *et al*. [4] modified the R-CHA2DS2VASc score, verified its predictive performance on 1,711 patients with myocardial infarction, and obtained the improved R-CHA2DS2VASc score to predict the area under the ROC curve (AUC; 0.717) of ischemic stroke. Based on three different 10-year cohort follow-ups of random population samples from three regions in Finland, Vartiainen *et al*. [5] proposed the FINRISK calculator, which is now widely used to predict the risk of coronary heart disease, stroke incidence, and its combination. Hou *et al*. [6] applied logistic regression to extract feature variables, divided 1,288 effective samples into two sets (a training set and a test set) in an 8:2 ratio, and trained with support vector machine algorithm to obtain a complex clinical-level model with an accuracy rate of 91.09% on the test set. Luo *et al*. [7] used the current parameters of their patients and those of the regression prediction one year later as input data, as well as adopted the bidirectional long-short term memory (BiLSTM) model with Attention mechanism. After training on a data set containing 983 samples, the accuracy rate of the test set was 86%. Chen *et al*. [8] proposed a novel stroke risk prediction framework based on deep transfer learning for data imbalance and small amount of data dispersion, Hybrid Deep Transfer Learning-based Stroke Risk Prediction (HDTL-SRP), which has been extensively tested in synthetic and real-world scenarios.

Table 1. Comparison of existing studies

Researchers	Year	Risk factors	Research methods
Barra *et al*. [4]	2013	Age, gender, acute myocardial infarction, diabetes, history of stroke, hypertension, coronary artery disease, peripheral arterial disease, glomerular filtration rate, blood urea nitrogen, and mean $CHADS_2$ score	Modified R-CHA_2DS_sVASc score
Vartiainen *et al*. [5]	2016	History of smoking, systolic blood pressure, total cholesterol, high-density lipoprotein, diabetes, and family history of stroke	FINRISK calculator
Hou *et al*. [6]	2019	Gender, occupation, and history of heart disease, hypertension, diabetes, smoking, hyperhomocysteinemia, hyperlipidemia, hyperuricemia, atherosclerosis, and carotid artery stenosis	Support vector machines
Luo *et al*. [7]	2021	Gender, age, history of hypertension, C-reactive protein, total cholesterol, LPA, arterial plaque, degree of stenosis, and intima-media thickness	BiLSTM model with Attention mechanism
Chen et al. [8]	2022	Age, neutrophil count, lymphocyte count, eosinophil count, basophil count, total protein, albumin, globulin, total bilirubin, direct bilirubin, blood urea nitrogen, *etc*.	Deep transfer learning

Most of the studies above are based on small data sample training models [4,6,7], and the accuracy of the test sets is also average [6,7,]. Foreign research mainly focused on American and European populations [5], which may not be applicable to our country. Although the model based on deep transfer learning [8] can solve the overfitting problem of small data sets, the interpretability of the model is poor. In this study, we used the public data set on Kaggle, which contains a total of 5,110 valid clinical samples, and XGBoost (eXtreme Gradient Boosting) early stroke risk prediction model to assess individual stroke risk. The algorithm has good application advantages, as it excludes complex test indicators and uses only common

demographic data, clinical history, and lifestyle factors related to stroke. At the same time, it integrates SHAP (SHapley Additive exPlanations), a unified framework for explaining predictions. SHAP analyzes the contribution of different risk factors to stroke risk, so that clinicians can further conduct comprehensive analyses of stroke risk prediction models.

3. Methods

The process of constructing the interpretable stroke prediction model combined with XGBoost and SHAP is shown in **Figure 1**. First, data preprocessing such as outlier processing, feature variable coding, and data imbalance processing was performed on the original data; second, the XGBoost risk prediction model was constructed, and its hyperparameters were optimized; third, performance comparison analysis was carried out with the models constructed by different algorithms to verify the prediction effect of the model; lastly, an explanatory analysis of the risk factors in the prediction model was carried out by integrating the introduced SHAP framework.

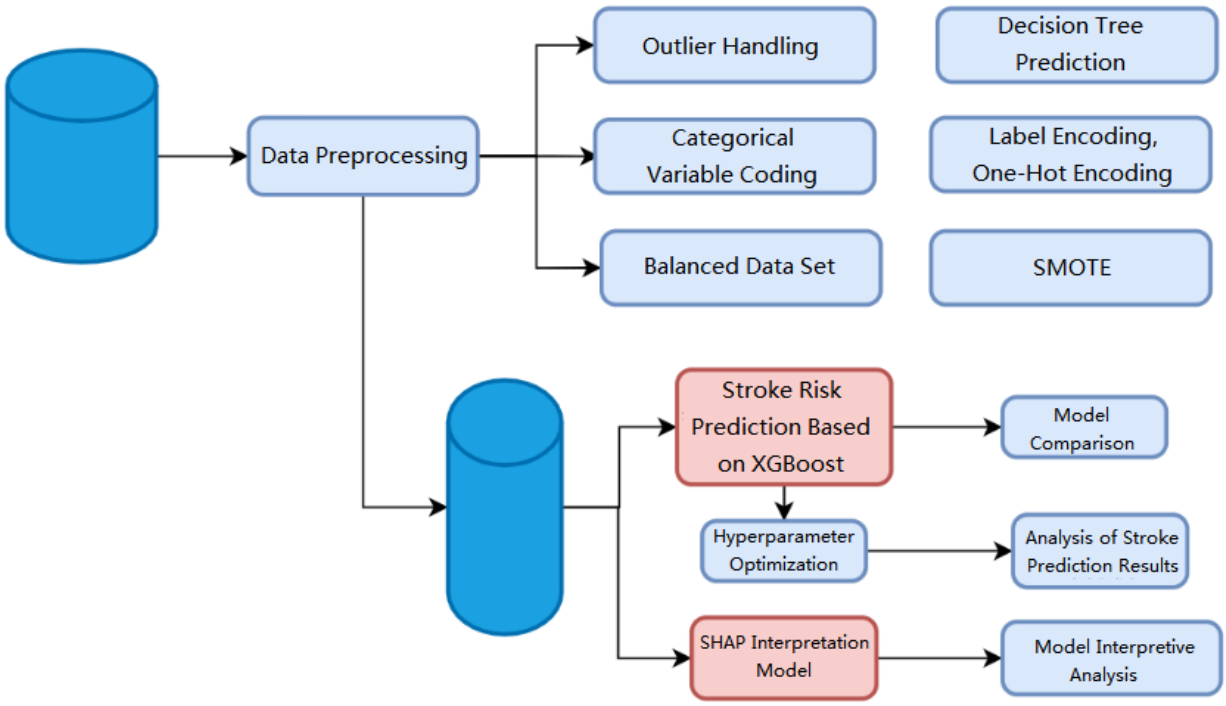

Figure 1. Process of constructing the interpretable stroke prediction model

3.1. Data source

Kaggle is a data science competition platform that involves data analysis, machine learning, deep learning, and many other fields. It contains massive data sets. The stroke prediction data set on this platform contains a total of 5,110 valid clinical samples, including 249 cases of stroke patients and 4,861 cases of non-stroke patients. The recorded variables include gender, age, history of hypertension, history of heart disease, marital status, occupation, type of residence, average blood glucose level, body mass index (BMI), and smoking history.

3.2. Data preprocessing

The categorical variables were encoded and converted into numerical variables. **Table 2** lists the relevant information of the variables after the data were encoded. For the 201 cases (4.0%) in which the BMI variable is missing, a decision tree was used to predict and fill, thus avoiding random noise. At the same

time, the garbage data whose age is not an integer were replaced and rounded by filling missing values. The ratio of the number of cases of stroke patients (249) to that of non-stroke patients (4,861) is close to 1:20, indicating that the categorical distribution of this data set is extremely unbalanced. Synthetic Minority Oversampling Technique (SMOTE) [9], an improvement over random sampling methods, can improve the class distribution of samples, while reducing the risk of overfitting. SMOTE was used on the stroke data set to alleviate the data imbalance problem, making the ratio of stroke patients to non-stroke patients close to 1:1.

Table 2. Relevant information of encoded variables

Variable	Type	Code/data value range
Demographics		
Gender	Unordered three categories	One-hot encoding
Age	Value type	[1,82]
Body mass index (kg/m^2)	Value type	[10.3,97.6]
Clinical history		
History of high blood pressure	Unordered binary classification	Yes = 1; No = 0
History of heart disease	Unordered binary classification	Yes = 1; No = 0
Average blood glucose level (mg/dL)	Continuous	[55.12,271.74]
Lifestyle		
Occupation	Unordered five categories	One-hot encoding
Smoking history	Unordered four categories	One-hot encoding
Type of residence	Unordered binary classification	City = 1; Country = 0
Marital status	Unordered binary classification	Married = 1; Single = 0

3.3. Prediction model

Ensemble learning completes learning tasks by constructing and combining multiple learners and achieves significantly superior generalization performance than a single learner [10].

The XGBoost algorithm is a boosting-based ensemble learning algorithm proposed by Chen *et al.* [11] in 2016. It is widely used in many machine learning and data mining problems owing to its fast execution speed and ability to guarantee model performance. In addition to the loss of prediction, the loss function of the XGBoost algorithm also adds a regularization part, which can prevent overfitting and has a stronger generalization ability. For each weak learner, such as the decision tree, parallel selection was made during the establishment process to find appropriate subtree node split features and eigenvalues, thereby improving operating efficiency. In this study, we established an XGBoost model to complete the stroke risk prediction analysis. In order to verify its performance, we compared it with several common machine learning algorithms, such as support vector machine (SVM), logistic regression (LR), decision tree (DT) and adaptive boosting (AdaBoost).

3.4. Parameter adjustment

In order to maximize the predictive ability of the model, it is necessary to adjust the parameters of the algorithm. Grid search is a commonly used hyperparameter adjustment technique. Following the arrangement and combination of parameters to generate a “grid,” each set of parameters was used for algorithm training, and the prediction effect of the model was verified. Through grid search, the set of parameters with the best effect was selected. In order to avoid the influence of prediction randomness, the results of cross-validation are frequently used as the judging criteria in this process. Therefore, using

GridSearchCV in the machine learning library scikit-learn to perform hyperparameter optimization, the optimal parameter values of the XGBoost classifier were obtained as follows:

learning_rate = 0.01, max_depth = 6, n_estimators = 700, min_child_weight = 1, gamma = 0.5, colsample_bytree = 0.7, subsample = 0.8, reg_alpha = 0.05, reg_lambda = 0.5.

The experimental part of this study is in Kaggle Notebooks.

3.5. Model evaluation

The data set balanced by SMOTE were divided into two sets (training set and test set) in a 4:1 ratio. The training set was further divided into 10 parts, 9 parts of which were used for training the model each time, and the remaining part was used for evaluating the performance of the model. In this process, each sampling result was guaranteed to be different, and the performance index of the model under ten-fold cross-validation can be obtained by repeating 10 times. Although this method increases the amount of calculation, it greatly reduces the statistical uncertainty in model evaluation, which is conducive to the selection of models with excellent performance. Subsequently, we evaluated the model's predictions on the test set.
In this study, the four indicators accuracy (Acc), sensitivity (Sen), specificity (Spe), and area under the receiver operating characteristic (ROC) curve, namely AUC, were used to evaluate the predictive effect of the model on unseen data. The relevant indicators were calculated as follows:

$$Acc = \frac{TP + TN}{TP + FN + FP + TN} \tag{1}$$

$$Sen = \frac{TP}{TP + FN} \tag{2}$$

$$Spe = \frac{TN}{FP + TN} \tag{3}$$

where TP, FN, FP, and TN represent true positive cases, false negative cases, false positive cases, and true negative cases, respectively. The ROC curve can be used to evaluate the quality of the model; the abscissa is the false positive rate (FPR), and the ordinate is the true positive rate (TPR). The calculation formulas for both are as follows:

$$TPR = \frac{TP}{TP + FN} \tag{4}$$

$$FPR = \frac{FP}{FP + TN} \tag{5}$$

AUC corresponds to the area under the ROC curve, which considers the sorting quality of the sample prediction; the larger the value, the better the prediction performance of the model.

3.6. Model interpretation

In order to enhance their ability to solve problems, data scientists have proposed various algorithms to build complex models. However, the reasons behind the decisions made by these complex models are not known. Model interpretability aims to help interested parties understand the characteristics of the model and the reasons for decisions, thereby making the process more transparent. There is a large body of research work

devoted to exploring interpretability in the medical field. Gomolin *et al*. [12] pointed out that artificial intelligence, as a black box, is a "powerful limitation" of interpretability applications in dermatology, as it cannot be customized for evaluation by board-certified dermatologists to interpret clinical evidence. SHAP, as proposed by Lundberg *et al*. [13], is a unified framework for explaining forecasts. Its main idea comes from Shapley value in combinatorial game theory [14]. SHAP attributes the predicted value of the model to the Shapley value of each feature. Assuming that the *j* th feature of the *i* th sample is x_{ij}, the predicted value of the model for the *i* th sample is y_i, and the predicted mean of all samples is y_0, the formula is as follows:

$$y_i = y_0 + \sum_{j=1}^{m} f(x_{ij}) \tag{6}$$

where *m* is the number of features, with $f(x_{ij})$ representing x_{ij} the Shapley value. To determine the overall influence of a feature on the predicted value, the Shapley values of all samples corresponding to the feature can be averaged. In this study, we analyzed the results of the prediction model by drawing a SHAP-risk factor value scatter diagram.

4. Results

4.1. XGBoost model prediction

For the training set, a stroke risk prediction model was established with the XGBoost algorithm, and its performance was evaluated on the test set. In order to verify the superiority of the model's performance, the XGBoost model was compared with models constructed by four mainstream algorithms AdaBoost, DT, LR, and SVM. **Figure 2** is a boxplot of ten-fold cross-validation evaluation indicators based on accuracy on the training set. Among them, the average ten-fold cross-validation accuracy on the XGBoost model training set was the highest (97.2%), and the performance was stable (standard deviation [SD] = 0.0039); followed by the AdaBoost model in which the average ten-fold cross-validation accuracy on the training set was 96.2%; however, the fluctuation was larger (SD = 0.0068) compared to XGBoost; DT came in third in terms of performance, while LR and SVM had the worst performance. The results verified the performance of the XGBoost model.

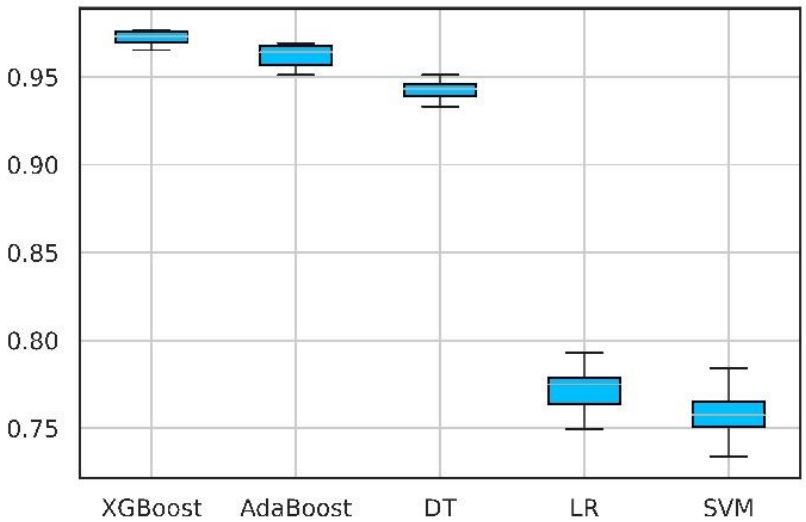

Figure 2. Box plot of cross-validation accuracy on training set

Figure 3 is the ROC curve that can reflect the prediction performance of different models. It can be seen that the ROC curve of the XGBoost model completely "wraps" the ROC curve of other mainstream models (SVM, LR, DT, and AdaBoost), suggesting that the overall prediction effect of the XGBoost model on the test set is the best.

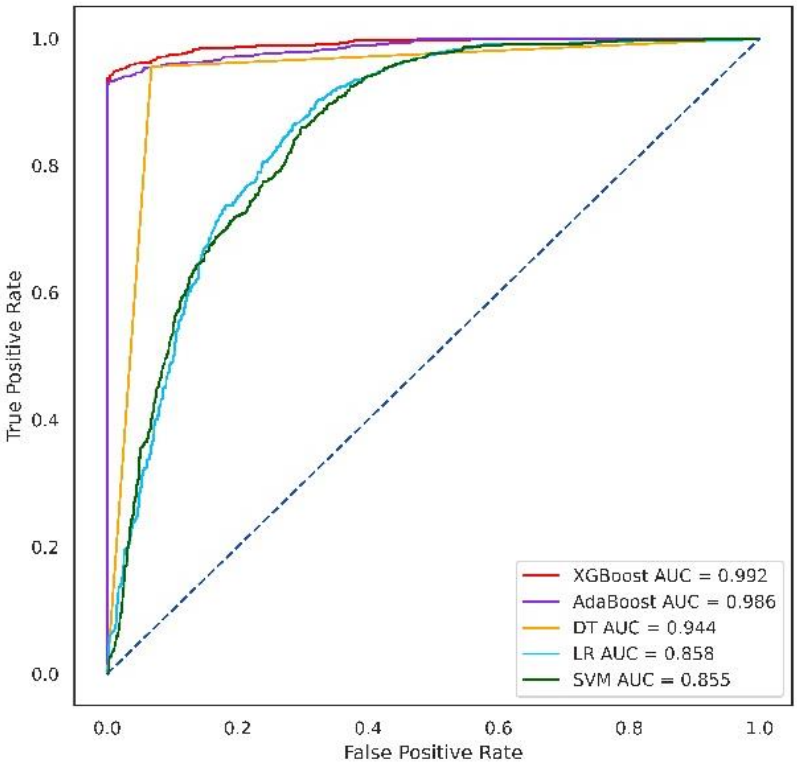

Figure 3. Receiver operating characteristic curves of different models on test set

Table 3 shows the results of performance comparison of different indicators among the five stroke risk prediction models on the test set. The overall prediction accuracy of the XGBoost model was 96.71%; its sensitivity, specificity, and AUC were 93.83%, 99.59%, and 99.19%, respectively (see the first row in **Table 4**). Among them, the overall accuracy and AUC were the highest among the five models, while its sensitivity and specificity were the second highest. In terms of overall performance, the XGBoost model performed the best. Comparing with existing research [6] (accuracy rate, 91.47%; sensitivity, 86.44%; specificity, 95.71%) and literature [15] (sensitivity, 89.7%; specificity, 72.7%; AUC, 87.8%), these indicators were higher, indicating that the model in our study can better predict the risk of stroke.

Table 3. Performance comparison of different models on test set

Model algorithm	Acc	Sen	Spe	AUC
XGBoost	**0.9671**	0.9383	0.9959	**0.9919**
AdaBoost	0.9635	0.9300	**0.9970**	0.9862
DT	0.9440	**0.9558**	0.9322	0.9440
LR	0.7820	0.8148	0.7492	0.8583
SVM	0.7722	0.8282	0.7163	0.8551

Abbreviations: AdaBoost, adaptive boosting; Acc, accuracy; AUC, area under the receiver operating characteristic curve; DT, decision tree; LR, logistic regression; Sen, sensitivity; Spe, specificity; SVM, support vector machine; XGBoost, extreme gradient boosting.

4.2. Model explanatory analysis based on SHAP

It can be seen that the stroke risk prediction model based on XGBoost has good predictive ability, but the contributing relationship between risk factors and risks can provide better support for auxiliary diagnosis analysis. In order to further analyze the positive/negative relationship between risk factors and output results, the integration of SHAP in this study can aid the explanatory analysis of the stroke risk prediction model based on XGBoost and demonstrate the SHAP-risk factor value distribution of the prediction model on the data set. The dot plot, as shown in **Figure 4**, directly reflects the impact of different risk factors of the sample and their values on the prediction results. Each point corresponds to the risk factor value of a sample. The color of the point is reminiscent of red when the value is larger. The abscissa represents the SHAP value of the point, *i.e.*, the impact on the output result. The vertical axis represents different risk factors; the higher the position of the risk factor, the greater the potential of the risk factor affecting the model output. It can be seen from the figure that among all risk factors, age affects the prediction results the most. This indicates that as age increases, the probability of stroke increases. The second is the type of residence; when other risk factors are kept constant, the risk of stroke is lower in rural residents. The likelihood of stroke is also higher with underlying heart disease or higher blood glucose level. All these are reflected in the high-risk groups of stroke in the stroke prevention report [1], which verifies the risk factor prediction analysis results of the model in this study. In addition, the figure also shows that non-smokers have a lower probability of stroke than those with a history of smoking, as mutually verified by Pandian *et al*. [2]. Thus, controlling tobacco should be made a priority as a primary stroke prevention strategy.

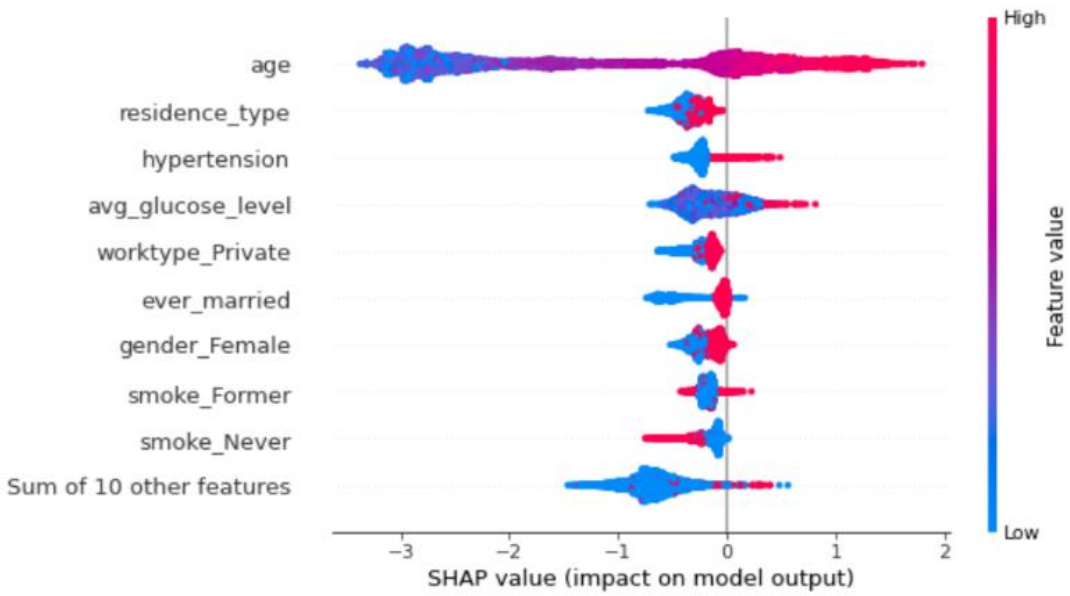

Figure 4. SHAP-risk factor distribution

Through the explanatory framework, we can further analyze how a single risk factor affects the model output and the interaction between different risk factors. Taking age, which has the most significant impact on the model output, as an example, a SHAP-risk factor dependency diagram was drawn, as shown in **Figure 5**. It can be seen that before the age of 40, aging hardly affects the risk of stroke, but after that, the risk of stroke increases linearly with age. High blood glucose level accounts for less in the lower age group, reducing the SHAP value at this time, but the opposite is true in the higher age group.

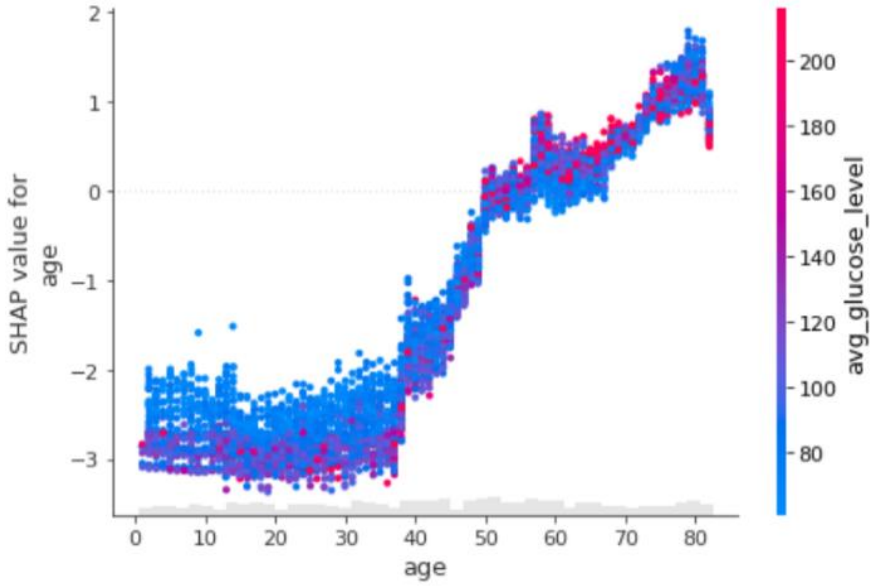

Figure 5. SHAP-risk factor (age) dependency diagram

Through the explanatory framework, we can also analyze the prediction results of the model for a single sample. **Figures 6** and **7** are interpretations for the prediction of stroke patients and non-stroke patients, respectively. The red part represents the contribution of risk factor values to the prediction of stroke, while the blue part represents the contribution of risk factor values to the prediction of non-stroke. **Figure 6** shows that high body mass index, high blood glucose level, old age, and heart disease are the main factors contributing to the prediction of stroke. **Figure 7** shows that the reasons for the prediction of non-stroke include the absence of heart disease, freelancing, and no history of hypertension.

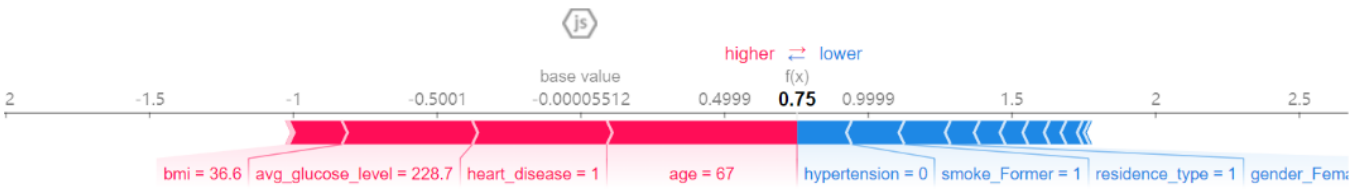

Figure 6. Example of SHAP interpretation predicted as stroke

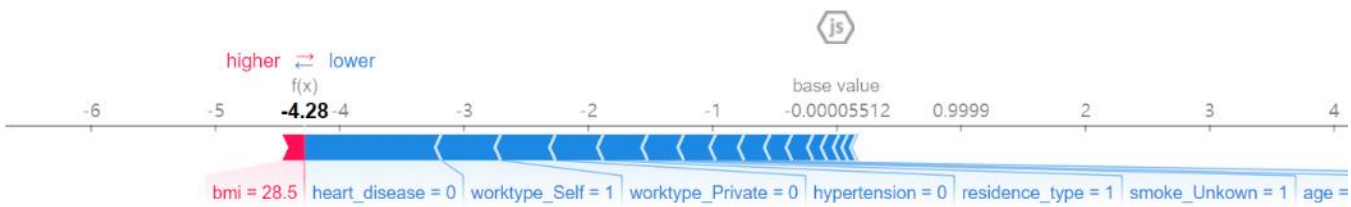

Figure 7. Example of SHAP interpretation predicted as non-stroke

Figure 8 presents the average SHAP values of different risk factors and their sorting results. For the XGBoost model, age is the most important factor affecting individuals suffering from stroke, followed by the type of residence, history of hypertension, and average blood glucose level. These important risk factors observed based on SHAP are consistent with the results demonstrated by existing studies [16]. It is worth noting that marital status is also an important factor in the prediction model of this study, thus suggesting that this component should be taken into consideration as a risk factor in research.

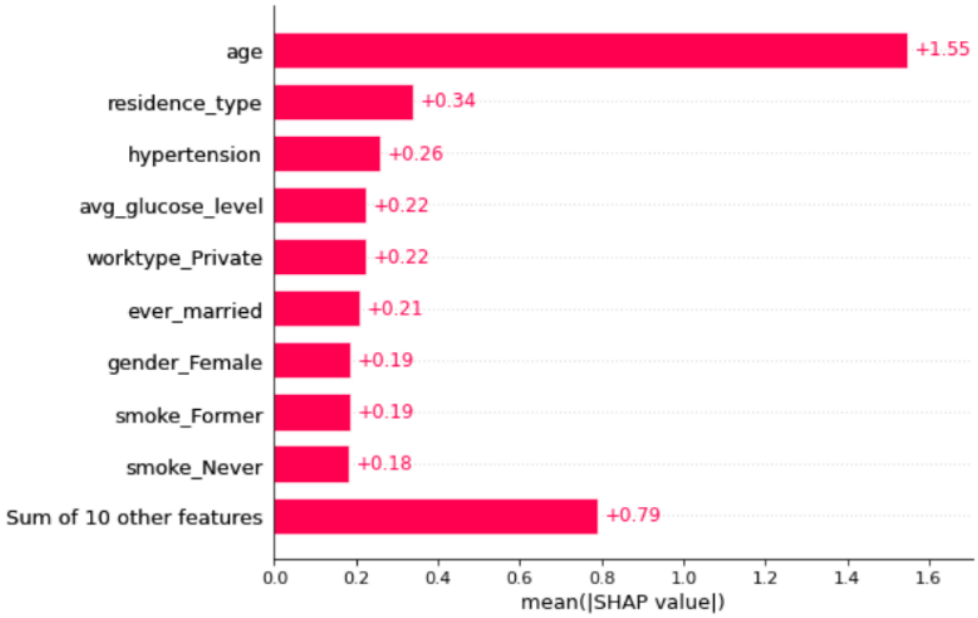

Figure 8. Ranking of risk factor based on SHAP

5. Conclusion

In recent years, stroke has become the second leading cause of death and disability worldwide [17]. In order to screen out risk factors more scientifically and actualize risk prediction and early warning to carry out early prevention work, we propose an integrated model that uses the XGBoost algorithm to establish a risk prediction model and the SHAP explanatory framework for model prediction analysis.

(i) Through outlier processing, feature variable coding, data category balance, and other data preprocessing and grid search parameter optimization, we established the XGBoost risk prediction model and compared it with four mainstream algorithm models. The performance of the model in predicting stroke risk was verified in this study.

(ii) By constructing an explanatory analysis model based on the integration of the XGBoost risk prediction model with SHAP, an explanatory analysis of the contribution of risk factors to risk prediction was performed. It can further assist medical workers in further diagnostic analysis. The results of this study showed that age, type of residence, history of hypertension, *etc*., are important factors affecting the incidence of stroke.

In future practice, we shall incorporate more risk factors to explore the prediction of stroke risk and the contribution of risk factors to stroke risk, as well as use clinical data to conduct more in-depth model research to better assist medical workers in realizing early warning and prevention of stroke risk.

Funding

This work was supported the National Natural Science Foundation Project (Grant No. 61863027), the Special Research Project on High Quality Development of Innovation and Entrepreneurship Education of the Chinese Society of Higher Education (Grant No. 21CXD01), and the Key R&D Plan of Jiangxi Province (Grant No. 20202BBGL73057).

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Relationship Between the Efficacy of Low-Dose Glucocorticoids Combined with Tacrolimus in the Treatment of Adult Idiopathic Membranous Nephropathy and the Level of Serum Anti-PLA2R Antibodies

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Abstract: *Objective:* To further evaluate the efficacy and safety of low-dose glucocorticoids combined with tacrolimus in the treatment of adult idiopathic membranous nephropathy (IMN) in a clinical setting. *Methods:* We carried out a single-center prospective study of 88 patients with IMN who were admitted into the Affiliated Hospital of Hebei University from January 2019 to December 2021, and the participants were divided into two groups based on their serum anti-PLA2R antibody levels: the negative group and the positive group. 46 patients were positive for anti-PLA2R antibodies and 42 were negative. *Results:* After 6 months of treatment, the serum albumin, cholesterol, and 24h urine protein quantification in the anti-PLA2R negative group improved more significantly compared to the positive group ($P < 0.05$); after 6 months of treatment, the remission rate of the positive group was significantly lower than that of the negative group, and ($P < 0.05$); *Conclusion:* After treatment with tacrolimus combined with low-dose glucocorticoids, patients with idiopathic membranous nephropathy who were tested positive for anti-PLA2R antibodies had a higher overall remission rate compared those who were tested negative for serum anti-PLA2R antibodies.

Keywords: Tacrolimus; Idiopathic membranous nephropathy; PLA2R antibody

Online publication: May 30, 2023

1. Introduction

Membranous nephropathy (MN) is a glomerular disease characterized by the deposition of immune complexes on the outer glomerular basement membrane (GBM), subepithelial cells with GBM thickening, which can involve the whole kidney, and its diagnostic criteria are mainly based on renal histopathology, and clinical treatment is more difficult. idiopathic membranous nephropathy (IMN) is the most common type of MN and the most common renal cause of massive proteinuria in adults in China. Recent domestic and international research have shown that IMN shows a diversity of natural course, with about 30% of patients in spontaneous complete remission, about 30% in partial remission, and the remaining 30% to 40% of IMN patients with progressive decompensation of renal function, which then progresses to end-stage renal disease [1-4]. Thus, IMN is not a benign disease, and early diagnosis, prognosis, and effective treatment are major tasks clinical practice. Glucocorticoid (GC) is the main drug for the treatment of MN, but its clinical application is limited due to its severe adverse effects, unclear efficacy, and difficulty in long-term

use. Tacrolimus (FK506) is a novel calcium-regulated phosphatase inhibitor that inhibits the gene transcription of various cytokines (gamma interferon, interleukin-2, etc.) by inhibiting calcium-dependent signaling pathways in T cells and suppressing T cell activation and proliferation, thus suppressing abnormal immune responses to reduce proteinuria. The side effects of FK506 are low, and several studies have shown that low-dose GCs combined with FK506 are effective in MN. The aim of this study is to evaluate the relationship between the efficacy of low-dose GCs combined with tacrolimus in the treatment of adult IMN and the level of serum anti-phospholipase A2 receptor (anti-PLA2R) antibodies, and to provide a basis for the clinical treatment of IMN.

2. Information and methods

2.1. General information

A single-center prospective study was performed using the clinical data of 88 patients with IMN who were admitted into our hospital from January 2019 to December 2021. All 88 patients enrolled in this study were diagnosed with IMN by renal biopsy, and this study complied with the Guidelines for the Treatment of MN and the Guidelines for the Reporting of Kidney Biopsy Pathology by the Ethics Committee of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences.

Among the 88 patients, there were 42 males and 46 females, aged 65.3 ± 14.7 years old. All the 88 patients had different levels of urinary protein at 24h > 3.5g/d, with an average of 6.74 ± 0.15 g/d. The patients were divided according to their serum anti-PLA2R antibody levels: negative and positive. 46 of 88 patients (52.27%) were positive for anti-PLA2R antibodies and 42 (47.73%) were negative for anti-PLA2R antibodies.

Inclusion criteria: (i) meeting the diagnostic criteria of IMN and hospitalized in our hospital and treated with FK506 for at least 6 months; (ii) blood creatinine (Scr) < 132.6 μmol/L; (iii) renal biopsy pathology showed membranous nephropathy and the stage of illness was determined.

Exclusion criteria: (i) secondary membranous nephropathy caused by drugs, infection, hepatitis, systemic lupus erythematosus, etc.; (ii) patients with other serious renal diseases or combined with diseases affecting renal function; (iii) patients with combined oncological diseases; (iv) patients with other systemic diseases, such as leukemia, dry syndrome, etc.; (v) patients with combined active infection; (vi) patients with severe cardiac, pulmonary, hepatic, renal, and other major organ deficiencies.

2.2. Methods

All patients were treated with angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) analogues for blood pressure control and received anticoagulants and statins. The initial dose of tacrolimus was 0.05 mg/kg per day, which was taken after breakfast and 2 h after dinner. The daily dose of tacrolimus was adjusted according to the tacrolimus trough concentration. During the first month of treatment, patients were seen every 2 weeks and their dose was adjusted according to the tacrolimus serum concentration (5–10 ng/ml); a daily dose of 0.5 mg/kg of prednisone acetate was also given.

2.3. Observation indicators

Patients were treated with low-dose glucocorticoids in combination with tacrolimus for at least 6 months. The primary endpoints were 24 h urine protein quantification, serum albumin, cholesterol, and serum anti-PLA2R antibody levels. The secondary endpoint was the overall remission rate.

2.4. Statistical methods

SPSS 20.0 software was used for statistical analysis. The measurement data were expressed as mean ± standard deviation, and *t*-test was used for comparison between groups. Differences were considered

statistically significant at $P < 0.05$.

3. Results

3.1. Comparison of clinical indicators between the two groups of patients

After 6 months of treatment, serum albumin, cholesterol, and 24h urine protein quantification improved more significantly in the anti-PLA2R negative group than in the positive group ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of clinical indicators between the two groups of patients

Group	Negative group (*n* = 42)			Positive group (*n* = 46)		
	Before treatment	3 months of treatment	6 months of treatment	Before treatment	3 months of treatment	6 months of treatment
Serum albumin (g/L)	20.14 ± 3.45	24.69 ± 3.12	30.11 ± 3.88	20.24 ± 3.05	24.29 ± 3.02	28.11 ± 3.88
Serum ALT (U/L)	30.12 ± 3.21	38.71 ± 4.01	36.12 ± 3.44	30.02 ± 3.41	38.41 ± 4.11	32.12 ± 3.44
Serum creatinine (μmol/L)	76.21 ± 5.69	81.12 ± 4.98	80.11 ± 3.66	76.01 ± 5.49	81.32 ± 4.48	78.11 ± 3.66
Cholesterol (mmol/L)	7.22 ± 0.36	6.24 ± 0.78	4.12 ± 0.69	7.42 ± 0.26	6.34 ± 0.58	5.12 ± 0.69
Urine protein quantification (g/24h)	6.87 ± 0.11	4.69 ± 0.44	1.11 ± 0.24	6.67 ± 0.21	4.19 ± 0.34	2.91 ± 0.24
Tacrolimus (ng/ml)	0	5.41 ± 0.24	7.78 ± 0.21	0	5.11 ± 0.14	6.78 ± 0.21
Hemoglobin (g/L)	124.11 ± 8.01	131.29 ± 8.36	136.11 ± 8.12	124.61 ± 8.11	131.29 ± 8.36	130.11 ± 8.12

Note: $P < 0.05$ compared to the negative group

3.2. Therapeutic efficacy analysis

After 6 months of treatment, the remission rate in the positive group was significantly lower than that in the negative group, and $P < 0.05$ was considered a statistically significant difference, as shown in **Table 2**.

Table 2. Efficacy analysis

Group	Negative group (*n* = 42)		Positive group (*n* = 46)	
	3 months of treatment	6 months of treatment	3 months of treatment	6 months of treatment
Complete relief	5	16	4	10
Partial relief	10	18	11	14
No relief	27	8	31	22
Remission rate (%)	35.71	76.19	32.61	52.17

Note: $P < 0.05$ compared to the negative group

4. Discussion

IMN is a common cause of primary glomerular disease in adults, with an incidence of 1/100,000 in China. Its pathogenesis is unclear, and is generally thought to be related to genetic factors, infection, immune system factors, etc. The main treatment for IMN is GCs combined with immunosuppressants, but the adverse effects of GCs are severe, and their long-term effect is unclear. Tacrolimus is a new type of immunosuppressant invented by Professor Satoshi Hirata in Japan in 1975 [5]. It inhibits the production of complement and cytokines, thus achieving anti-inflammatory, antioxidant, and immunomodulatory effects [6]. Tacrolimus can significantly improve the clinical and immunological prognosis of IMN patients.

In this study, we analyzed the relationship between the efficacy of low-dose glucocorticoids combined with tacrolimus in the treatment of adult IMN and the level of serum anti-PLA2R antibodies. The results showed that the overall efficiency of the treatment in serum anti-PLA2R antibody-positive patients was significantly lower than that of serum anti-PLA2R antibody-negative patients ($P < 0.05$). The results of this study suggest that low-dose GCs combined with tacrolimus for the treatment of adult IMN can improve the clinical and immunological prognosis of patients, but there is a correlation between the efficacy and serum anti-PLA2R antibody levels, which may be due to the adverse effects of low-dose GCs combined with tacrolimus for the treatment of IMN in most patients due to the presence of immunosuppression, especially to hormone and tacrolimus allergic individuals [7,8].

In this study, all patients enrolled were examined monthly after starting treatment with low-dose glucocorticoids in combination with tacrolimus. Parameters like routine blood, urine, 24-hour urine protein quantification, liver function, kidney function, blood lipids, and tacrolimus concentration were tested 3 and 6 months after the treatment was initiated. During the course of tacrolimus treatment, the glomerular filtration rate (GFR) was found to have decreased to below 30 ml/min-1.73m^2 in 3 patients (mean decrease of 1.22 ml/min-1.73m^2) during the renal function examination 3 months into the tacrolimus treatment.

There are some limitations to this study, such as the small sample size and the uncertainty of the continuity of tacrolimus treatment for patients with negative serum anti-PLA2R antibodies. However, this study provides a basis for clinical practice in the treatment of IMN and can be used as a first- line treatment option. The feasibility of conducting single-center, large-sample, multicenter clinical trials in patients with IMN can be further explored in the future.

In conclusion, low-dose glucocorticoids combined with tacrolimus have a higher overall remission rate in the treatment of patients with IMN who are serum anti-PLA2R antibody-negative compared to patients who are serum anti-PLA2R antibody-positive.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Analysis of the Efficacy of Humidified High-Flow Nasal Oxygen Therapy Combined with Alveolar Lavage in the Treatment of Patients with Severe Pneumonia Complicated with Respiratory Failure

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Abstract: *Objective:* To analyze the curative effect of humidified high-flow nasal oxygen therapy combined with alveolar lavage in patients with severe pneumonia and respiratory failure. *Methods:* 120 patients with severe pneumonia complicated with respiratory failure admitted to the Third People's Hospital of Xining from July 2021 to December 2022 were randomly divided into two groups: group A and group B. The patients in group A were given humidified high-flow nasal oxygen therapy combined with alveolar lavage, whereas those in group B were given humidified high-flow nasal oxygen therapy. The treatment efficacy, blood gas analysis results, and differences in inflammatory mediators were compared between the two groups. *Results:* The curative effect in group A (96.67%) was significantly higher than that in group B (81.67%), $P < 0.05$; the partial pressure of carbon dioxide ($PaCO_2$), partial pressure of oxygen (PaO_2), oxygen saturation (SpO_2), and Horowitz index (P/F) of group A were significantly better than group B, $P < 0.05$; the interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α), and C-reactive protein (CRP) levels, white blood cell (WBC) count, serum procalcitonin (PCT), and neutrophil (N) percentage of group A were significantly lower than those of group B, $P < 0.05$. *Conclusion:* For patients with severe pneumonia complicated with respiratory failure, alveolar lavage, on the basis of humidified high-flow oxygen therapy, can inhibit local inflammation, improve blood gas analysis results, promote disease recovery, and improve the clinical treatment effect.

Keywords: Alveolar lavage; High-flow oxygen therapy; Humidified nasal oxygen therapy; Severe pneumonia; Respiratory failure

Online publication: May 31, 2023

1. Introduction

Severe pneumonia is related to infection caused by bacteria or viruses. It reduces immunity and may cause serious complications, such as respiratory failure. Severe pneumonia needs to be treated as soon as possible to prevent mortality. The conventional treatment for severe pneumonia complicated with respiratory failure includes correcting acid-base balance, supplementing with oxygen, and administrating anti-inflammatory drugs. Although it can alleviate the symptoms of respiratory failure and delay the progression of pneumonia, the overall curative effect is limited [1]. In recent years, bronchoalveolar lavage, a safe and efficient method, has taken precedence in the early treatment of respiratory diseases. Drugs are directly injected into the diseased area, completely removing airway secretions and restoring the patient's respiratory function [2]. In this study, 120 patients with severe pneumonia complicated with respiratory failure treated from July 2021

to December 2022 were included to explore the therapeutic effect of humidified high-flow nasal oxygen therapy combined with alveolar lavage.

2. Materials and methods

2.1. Patient information

A sample of 120 patients with severe pneumonia and respiratory failure treated from July 2021 to December 2022 was randomly divided into two groups. In group A, the ratio of male to female was 37:23, and the mean age was 62.43 ± 1.94; in group B, the ratio of male to female was 38:22, and the mean age was 62.51 ± 1.99. There was no significant difference in baseline data between group A and group B ($P > 0.05$).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (i) patients who met the diagnostic criteria for severe pneumonia in *Guidelines for the Diagnosis and Treatment of Community-Acquired Pneumonia* [3], and with respiratory failure; (ii) patients who voluntarily participated in this study and had given informed consent; (iii) patients with clear awareness and good compliance; (iv) patients with normal coagulation function.

Exclusion criteria: (i) patients with pulmonary fibrosis, lung tumor, pulmonary tuberculosis, pneumoconiosis, or upper airway obstruction; (ii) patients with immune dysfunction; (iii) patients with severe heart, liver, and kidney dysfunction.

During admission, the two groups of patients received conventional treatment for infection, cough, phlegm, and obstructive symptoms; maintenance of electrolyte balance; correction of acid-base balance; and other treatments.

2.3 Treatment methods

Group A received humidified high-flow nasal oxygen therapy combined with alveolar lavage.

(i) Humidified high-flow nasal oxygen therapy

The humidified high-flow nasal oxygen therapy system was used. The device was fixed in front of the patient's nose, and the oxygen therapy parameters were adjusted based on the patient's tolerance and arterial blood gas analysis results. The oxygen flow rate was adjusted to 40–60 L/min, temperature was maintained at 31–37°C, and the oxygen volume fraction, blood oxygen saturation, and oxygen partial pressure were adjusted to 35%–60%, 90%–98%, and 80–100 mmHg, respectively.

(ii) Alveolar lavage

Each patient in group A was required to fast for 2 h before treatment. Atomized lidocaine (2%, 5 mL) was administered, and after the anesthesia had taken effect, the patient was placed on electrocardiogram (ECG) monitoring, a fiberoptic bronchoscope was inserted through the patient's oral cavity or nasal cavity, and the patient was observed for airway lesions. After removing stagnant sputum in the airway, the bronchoscope was placed at the target lung segment, and 20 mL of normal saline at 37°C was prepared to lavage the infected area of the lung lobe for 4 times, with each lavage lasting about 30 s. During the lavage, the patient's vital signs were monitored, and if the saturation of oxygen was found to be < 85%, the lavage was stopped immediately and oxygen was given. All operations were performed by the same group of medical staff. The patients were treated for 1 week.

Group B received humidified high-flow nasal oxygen therapy, and the operation was the same as that of group A. The patients in group B were also treated for 1 week.

2.4. Observation indicators

(i) Curative effect: "significantly effective" was denoted as improvement in clinical symptoms (cough, dyspnea, and hypoxia), normalization of blood gas analysis results, and resolved inflammation

(absorbed exudation) on chest radiograph; "effective" was denoted as improvement in clinical symptoms (cough, dyspnea, and hypoxia) and arterial blood gas analysis results, as well as less lung shadow on chest radiograph; "ineffective" was denoted as aggravation or no improvement in clinical symptoms and blood gas analysis results [4].

(ii) Blood gas analysis: arterial blood samples were collected from the patients, and a blood gas analyzer was used to detect partial pressure of carbon dioxide ($PaCO_2$), partial pressure of oxygen (PaO_2), oxygen saturation (SpO_2), and Horowitz index (P/F).

(iii) Inflammatory indicators: interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α), C-reactive protein (CRP), white blood cell (WBC) count, serum procalcitonin (PCT), and neutrophil (N) percentage were detected by enzyme-linked immunosorbent assay.

2.5. Statistical analysis

SPSS 21.0 was used for data processing. The count and measurement data were recorded in percentage (%) and mean ± standard deviation, respectively, and tested by chi-square test (χ^2) and *t*-test. $P < 0.05$ indicates statistical significance.

3. Results

3.1. Curative effect

As shown in **Table 1**, the curative effect in group A (96.67%) was significantly higher than that in group B (81.67%), $P < 0.05$.

Table 1. Comparison of curative effects

Group	Significantly effective	Effective	Ineffective	Efficacy
Group A (n = 60)	43 (71.67%)	15 (25.00%)	2 (3.33%)	96.67%
Group B (n = 60)	26 (43.33%)	23 (38.33%)	11 (18.33%)	81.67%
χ^2	–	–	–	6.9878
P	–	–	–	0.0082

3.2. Blood gas analysis

Before treatment, there was no significant difference in $PaCO_2$, PaO_2, SpO_2, and P/F ratio between group A and group B, $P > 0.05$; after treatment, the $PaCO_2$, PaO_2, SpO_2, and P/F ratio of group A were significantly better than those of group B, $P < 0.05$. See **Table 2** for details.

Table 2. Comparison of blood gas analysis results

Group	$PaCO_2$ (mmHg)		PaO_2 (mmHg)		SpO_2 (%)		P/F	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 60)	52.87 ± 4.81	35.77 ± 2.73	54.17 ± 4.25	84.11 ± 8.25	90.14 ± 1.85	98.41 ± 2.71	212.84 ± 18.43	328.41 ± 21.43
Group B (n = 60)	52.91 ± 4.83	41.26 ± 3.86	54.21 ± 4.27	77.69 ± 7.43	90.12 ± 1.87	94.36 ± 2.52	212.91 ± 18.39	298.67 ± 19.62
t	0.0376	7.4353	0.0425	3.7026	0.0487	7.0077	0.0208	7.9286
P	0.9701	0.0000	0.9662	0.0004	0.9613	0.0000	0.9834	0.0000

3.3. Inflammatory mediators

Before treatment, there was no significant difference in IL-6, TNF-α, CRP, WBC, PCT, and N percentage between group A and group B, $P > 0.05$; after treatment, the IL-6, TNF-α, CRP, WBC, PCT, and N percentage of group A were lower than those of group B, $P < 0.05$. See **Table 3** for details.

Table 3. Comparison of inflammatory mediators

Group	IL-6 (pg/mL)		TNF-α (μg/mL)		CRP (mg/L)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 60)	30.98 ± 2.42	10.48 ± 1.38	9.64 ± 1.52	2.74 ± 0.78	124.11 ± 15.25	46.11 ± 5.15
Group B (n = 60)	30.87 ± 2.48	17.96 ± 1.87	9.68 ± 1.49	5.39 ± 1.15	124.25 ± 15.31	61.38 ± 6.36
t	0.2033	20.6084	0.1203	12.2112	0.0502	14.4533
P	0.8394	0.0000	0.9045	0.0000	0.9601	0.0000
Group	**WBC (× 10^9/L)**		**Serum PCT (ng/mL)**		**N percentage (%)**	
	Before treatment	**After treatment**	**Before treatment**	**After treatment**	**Before treatment**	**After treatment**
Group A (n = 60)	16.14 ± 1.28	4.51 ± 0.48	36.18 ± 2.25	0.21 ± 0.08	86.11 ± 2.15	72.89 ± 1.87
Group B (n = 60)	16.17 ± 1.31	9.38 ± 0.51	36.21 ± 2.27	0.49 ± 0.19	86.14 ± 2.19	80.41 ± 1.96
t	0.1269	53.8623	0.0727	10.5206	0.0757	21.5025
P	0.8993	0.0000	0.9422	0.0000	0.9398	0.0000

4. Discussion

Patients with severe pneumonia often have concomitant pulmonary ventilation disorder, resulting in impaired gas exchange and secondary respiratory failure; thus increases the mortality of patients [5]. Conventional comprehensive plans such as expectorant, anti-infective, and oxygen administration are used in the treatment of severe pneumonia complicated with respiratory failure, but the curative effect is limited. In order to restore the ventilatory function and increase the blood oxygen concentration in patients with severe pneumonia, humidified high-flow nasal oxygen therapy can be used to improve effective alveolar ventilation and end-expiratory lung volume, thereby improving the physiological comfort of patients [6]. However, it is difficult to achieve the desired effect with oxygen therapy alone. Therefore, the use of oxygen therapy in combination with alveolar lavage has been suggested. Repeated washing of airway secretions and removal of stagnant sputum, inflammatory mediators, toxins, pathogens, and other substances can improve atelectasis and restore pulmonary ventilation function [7].

According to our study, the curative effect in group A (96.67%) was higher than that in group B (81.67%), $P < 0.05$, indicating that humidified high-flow oxygen therapy combined with alveolar lavage can enhance the curative effect. High-flow oxygen humidifiers can constantly and continuously supply oxygen to patients, which is beneficial to improving oxygen saturation, while preventing the re-inhalation of carbon dioxide, thereby reducing $PaCO_2$ content and optimizing the oxygenation function. During the treatment, oxygen is heated and humidified, which can dilute sputum, promote sputum expulsion, and enhance the airway's cilia cleaning function. All these are beneficial to reducing the risk of lung infection [8]. This oxygen therapy, along with bronchial lavage under fiberoptic bronchoscopy, promotes the discharge of airway secretions, allows the sampling of the lesion area, and guides the later antibacterial treatment through bacteriological examination, which is beneficial to alleviating respiratory failure [9]. Another set of data showed that the $PaCO_2$ (35.77 ± 2.73 mmHg), PaO_2 (84.11 ± 8.25 mmHg), SpO_2 (98.41 ± 2.71 %), and P/F ratio (328.41 ± 21.43) in group A were significantly better than those in group

B, $P < 0.05$; moreover, the IL-6 (10.48 ± 1.38 pg/mL), TNF-α (2.74 ± 0.78 μg/mL), CRP (46.11 ± 5.15 mg/L), WBC (4.51 ± 0.48 × 10^9/L), PCT (0.21 ± 0.08 ng/mL), and N percentage (72.89 ± 1.87%) of group A were lower than those of group B, $P < 0.05$. Our findings suggest that high-flow humidified oxygen therapy combined with alveolar lavage can improve patients' blood gas analysis results and inhibit the progress of inflammation. At present, the role of inflammatory mediators such as IL-6 and TNF-α is unclear, and the levels of CRP, a non-specific inflammatory factor, vary in different autoimmune diseases and infectious diseases. On the basis of conventional inflammatory factors, WBC, PCT, and N percentage in clarifying the therapeutic effect of humidified high-flow nasal oxygen therapy combined with alveolar lavage, this treatment not only provides continuous and stable oxygen supply to meet the body's metabolic needs, but also improves the oxygenation state of the body, promotes the discharge of carbon dioxide, and relieves the ventilation barrier, while diluting airway secretions and reducing airway damage. In addition, repeated alveolar lavage can stimulate the airway mucosa and produce cough reflexes, thereby stimulating the body to remove inflammatory secretions and, at the same time, promote the absorption of edema caused by inflammation. This is conducive to the resolution of inflammation [10].

In conclusion, humidified high-flow nasal oxygen therapy combined with alveolar lavage has clinical value, as its use in patients with severe pneumonia complicated with respiratory failure can inhibit local inflammation, improve blood gas indicators, and relieve symptoms of respiratory failure.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Mechanism of Action and Therapeutic Effect of Modified Qiwei Baishu Powder in Diabetes

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Abstract: *Objective:* To study the mechanism of action and therapeutic effect of modified Qiwei Baishu powder in diabetic patients. *Methods:* From January 2021 to January 2022, 80 diabetic patients were recruited in our study and divided into two groups by the random number table method. Group A was treated with modified Qiwei Baishu powder, whereas group B was treated with western medicine. The therapeutic effect, traditional Chinese medicine (TCM) syndrome score, blood sugar level, and incidence of adverse reaction were compared between the two groups. *Result:* The therapeutic effect in group A was significantly higher than that in group B ($P < 0.05$); the TCM syndrome scores of group A were significantly lower than those of group B ($P < 0.05$); the fasting blood glucose (FBG), 2 hour-postprandial blood glucose (PBG), and glycosylated hemoglobin (HbA1c) levels of group A were significantly lower than those of group B ($P < 0.05$); the incidence of adverse reaction in group A was significantly lower than that in group B ($P < 0.05$). *Conclusion:* On the basis of western medicine, the addition of modified Qiwei Baishu powder can maintain stable blood sugar levels in patients and alleviate diabetic symptoms; thus, it is not only effective, but also safe for clinical use in diabetes.

Keywords: Diabetes; Modified Qiwei Baishu powder; Therapeutic effect; Mechanism of action

Online publication: May 30, 2023

1. Introduction

Diabetes belongs to the category of "diabetes" in traditional Chinese medicine (TCM), and it is related to various factors such as fatigue, emotional disorders, and improper diet. The typical symptoms of diabetes are polyuria, polyphagia, and polydipsia [1]. TCM practitioners believe that the loss of yin and fluid is the main pathogenesis of diabetes, which falls under the syndrome of deficiency in origin and excess in superficiality. In western medicine, drugs such as metformin are used for treatment. These drugs limit the overall effect and only delay the progression of the disease [2]. In recent years, TCM has been used in the treatment of diabetes. Modified Qiwei Baishu powder is useful in nourishing the kidney, strengthening the spleen, and replenishing qi, as well as lowering blood sugar and preventing diabetic complications [3]. In this study, 80 diabetic patients admitted from January 2021 to January 2022 were studied to explore the therapeutic effect of modified Qiwei Baishu powder.

2. Materials and methods

2.1. Patient information

A sample of 80 diabetic patients admitted from January 2021 to January 2022 was grouped by the random

number table method. In group A, the male to female ratio was 24:16, and the mean age was 52.17 ± 8.41 (36–72 years old); in group B, the male to female ratio was 25:15, and the mean age was 52.21 ± 8.33 (37–73 years old). There was no significant difference in baseline data between group A and group B ($P > 0.05$).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (i) patients who met the diagnostic criteria for diabetes in *Guidelines for the Prevention and Treatment of Diabetes in China* [4] and whose fasting blood glucose/postprandial blood glucose ≥ 7.0/11.1 mmol/L; (ii) patients with symptoms of polyphagia, polyuria, and polydipsia; (iii) patients who had given informed consent; (iv) patients whose body mass index (BMI) ≥ 28.0 kg/m^2.

Exclusion criteria: (i) patients who had taken drugs for weight loss and hyperglycemia before enrollment; (ii) patients with infectious diseases; (iii) patients with malignant tumor; (iv) patients with allergies.

2.3. Treatment methods

The western medicine regimen used for patients in group A was the same as that in group B. The prescription of Qiwei Baishu powder used was as follows: *Rehmannia glutinosa* 20 g; *Poria cocos*, Kudzu root, ginseng, and fried *Atractylodes macrocephala*, each 15 g; *Ligusticum wallichii*, sealwort, and corni fructus, each 12 g; *Schisandra* 10 g; licorice and patchouli leaves, each 9 g. The addition and subtraction formulas used were as follows: (i) for those with dry and hot lungs, add corni fructus, common *Anemarrhena* rhizome, and Chinese wolfberry root-bark for lung-clearing effect; *Rehmannia* and *Trichosanthes* to promote body fluid and nourish yin; (ii) for those with abdominal distension and reduced appetite, add *gallinacea* and *Amomum* to invigorate the spleen and aid transportation. After decoction, the patients were required to take one dose in the morning and evening. Each patient had to undergo three courses of treatment in which a single course extended till 15 days after administration.

The western medicine treatment used in group B included metformin (Liaoning Meida Kang Huabang Pharmaceutical Co., Ltd.), 0.5 g orally after meals, 3 times a day; and acarbose (Zhejiang Hisun Pharmaceutical Co., Ltd.), single oral dose 50–100 g, 3 times a day. The treatment lasted for 45 days.

2.4. Observation indicators

(i) Therapeutic effect

"Markedly effective" was denoted by a reduction in traditional Chinese medicine (TCM) syndrome score by more than 90% and normal blood sugar; "effective" was denoted by a reduction in TCM syndrome score by more than 30% and lowered blood sugar level; "ineffective" was denoted by a reduction in TCM syndrome score by less than 30% and no reduction in blood sugar level.

(ii) TCM syndrome score

A 3-point method was used to evaluate diabetic symptoms, including body ache, polydipsia, fatigue, and pain and numbness.

(iii) Blood glucose

Changes in fasting blood glucose (FBG), postprandial blood glucose (PBG), and glycosylated hemoglobin (HbA1c) were detected.

(iv) Adverse reaction

Incidence of abdominal pain, nausea and vomiting, as well as indigestion among the patients was recorded.

2.5. Statistical analysis

SPSS 21.0 was used for data processing. Count data were recorded in percentage (%) and tested by chi-

square (χ^2) test; measurement data were recorded in mean ± standard deviation and tested by *t*-test. $P < 0.05$ indicates statistical significance.

3. Results

3.1. Therapeutic effect

The therapeutic effect in group A (97.5%) was higher than that in group B (85.0%), $P < 0.05$ (**Table 1**).

Table 1. Comparison of therapeutic effect between group A and group B

Group	Markedly effective	Effective	Ineffective	Efficacy
Group A (n = 40)	32 (80.0%)	7 (17.5%)	1 (2.5%)	97.5%
Group B (n = 40)	26 (65.0%)	8 (20.0%)	6 (15.0%)	85.0%
χ^2	-	-	-	3.9139
P	-	-	-	0.0479

3.2. TCM syndrome score

Before treatment, the TCM syndrome scores of group A were not different from those of group B, ($P > 0.05$). After treatment, the TCM syndrome scores of group A were significantly lower than those of group B ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of TCM syndrome scores between group A and group B

Group	Body ache		Polydipsia		Fatigue		Pain and numbness	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 40)	2.64 ± 0.84	0.75 ± 0.35	2.59 ± 0.79	0.72 ± 0.37	2.55 ± 0.79	0.79 ± 0.33	2.43 ± 0.78	0.83 ± 0.36
Group B (n = 40)	2.62 ± 0.86	1.41 ± 0.47	2.61 ± 0.83	1.43 ± 0.49	2.57 ± 0.83	1.43 ± 0.42	2.44 ± 0.76	1.52 ± 0.45
t	0.1052	7.1232	0.1104	7.3134	0.1104	7.5781	0.0581	7.5726
P	0.9165	0.0000	0.9124	0.0000	0.9124	0.0000	0.9538	0.0000

3.3. Blood glucose indicators

As shown in **Table 3**, there was no significant difference in FBG, PBG, and HbA1c between group A and group B ($P > 0.05$) before treatment; however, the FBG, PBG, and HbA1c of group A were lower than those of group B after treatment ($P < 0.05$).

Table 3. Comparison of blood sugar indicators between group A and group B

Group	FBG (mmol/L)		PBG (mmol/L)		HbA1c (%)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 40)	8.08 ± 1.11	5.13 ± 0.61	12.62 ± 1.58	8.99 ± 0.57	10.21 ± 1.25	6.09 ± 0.74
Group B (n = 40)	8.09 ± 1.09	6.87 ± 0.89	12.65 ± 1.56	11.38 ± 0.68	10.27 ± 1.34	8.21 ± 0.85
t	0.0407	10.1992	0.0855	17.0356	0.2071	11.8973
P	0.9677	0.0000	0.9321	0.0000	0.8365	0.0000

3.4. Incidence of adverse reaction

The incidence of adverse reaction in group A was significantly lower than that in group B ($P < 0.05$), as shown in **Table 4**.

Table 4. Comparison of incidence of adverse reaction between group A and group B

Group	Abdominal pain	Nausea and vomiting	Indigestion	Incidence rate
Group A (n = 40)	1 (2.5%)	0 (0.0%)	0 (0.0%)	2.5%
Group B (n = 40)	2 (5.0%)	3 (7.5%)	1 (2.5%)	15.0%
χ^2	-	-	-	3.9139
P	-	-	-	0.0479

4. Discussion

The hallmark of diabetes is insulin resistance, which progressively worsens over time. When pancreatic beta cells can no longer compensate for insulin resistance, symptoms of hyperglycemia will develop, thus increasing glycosylation products in the body and the risk of microvascular disease. Therefore, diabetic patients often have blood stasis syndrome, and attention should be paid to regulating the meridians during treatment [5,6]. In TCM, diabetes belongs to the category of "wasting-thirst," which is related to the patient's preference for fatty and sweet food, poor dietary habits, *etc*., resulting in deficiency of both qi and yin; thus, the condition should be treated with the formula of blood circulation and blood stasis, nourishing qi and nourishing yin [7]. When treating diabetic patients, TCM practitioners emphasize on treating not only the symptoms, but also the root causes, which include restoring visceral functions on the basis of lowering blood sugar and choosing drugs based on the principle of "invigorating the spleen, promoting body fluid, and nourishing qi." In the present study, we used Qiwei Baishu powder, a famous prescription in TCM, which is suitable for body fluid internal consumption. In the treatment of patients with spleen and stomach deficiency syndrome, this prescription has the effect of nourishing yin and replenishing qi, and the dialectical addition and subtraction of the basic prescription have the effect of regulating blood lipid and lowering blood sugar [8].

According to our results, the therapeutic effect in group A (97.5%) was significantly higher than that in group B ($P < 0.05$); the TCM syndrome scores of group A were significantly lower than those of group B ($P < 0.05$); moreover, group A had significantly lower FBG, PBG, and HbA1c compared to group B ($P < 0.05$); the incidence of adverse reaction in group A was also significantly lower than that in group B ($P < 0.05$). Our findings suggest that modified Qiwei Baishu powder can effectively control the progression of diabetes.

Ginseng, which is a component in Qiwei Baishu powder, can produce body fluid, quench thirst, nourish vitality, promote the recovery of heart function, and stabilize blood pressure in patients; *Poria cocos* can harmonize the stomach, strengthen the spleen, act as a diuretic, and relieve symptoms such as edema and fullness; fried *Atractylodes macrocephala* can promote drainage, generate blood, replenish qi, dry dampness, as well as restore the biochemical function of qi and blood; Kudzu root can produce fluid, quench thirst, stop diarrhea, and relieve thirst; *Rehmannia glutinosa* can produce fluid, nourish yin, cool blood, clear away heat, and relieve knee and hip weakness; *Schisandra* can produce body fluid, replenish qi, solidify astringency, calm the heart, and nourish the kidney; corni fructus can nourish both the liver and the kidney; sealwort can moisten the lungs, invigorate the spleen, and promote body fluid; patchouli leaves can invigorate the spleen, stop vomiting, eliminate belching, and harmonize the stomach; *Ligusticum wallichii* can promote qi, promote blood circulation, relieve pain, and dispel wind; licorice can regulate various medicines and also relieve cough, eliminate phlegm, and clear away heat [9].

By combining Qiwei Baishu powder with various TCMs, it is possible to promote blood circulation, remove blood stasis, nourish yin, and replenish qi. Based on the analysis of modern pharmacological effects, Qiwei Baishu powder contains rich xylene lactones in the woody fragrance, which can reduce insulin resistance; *Poria cocos*, which can strengthen the body's immune function and relax the smooth muscle of the digestive tract, rendering a hypoglycemic effect; ginseng, *Schisandra*, *etc*., which can regulate lipid metabolism, increase myocardial oxygen supply, stimulate myocardial contraction, and lower blood lipid levels; *Ligusticum wallichii*, which can inhibit the synthesis of collagen, stimulate local microcirculation, enhance the body's immune function, and delay the progression of diabetes. The application of modified Qiwei Baishu powder and subtracted prescriptions have better therapeutic effect [10].

In conclusion, the addition of modified Qiwei Baishu powder for diabetic patients can alleviate diabetic symptoms and stabilize blood sugar levels. This TCM prescription is mild in nature and has high safety profile; thus, it has some promotional value.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Clinical Distribution and Drug Resistance of *Acinetobacter baumannii* in a Hospital from 2019 to 2021

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Abstract: *Objective:* To analyze the clinical distribution and drug resistance of *Acinetobacter baumannii* (AB) and provide reference for the treatment of AB infection. *Methods:* AB isolated from clinical specimens of Huaihua First People's Hospital from 2019 to 2021 were collected and identified by VITEK 2 Compact, an automated microbial identification and susceptibility testing system, in which drug sensitivity test was also performed. Excel was used for statistical analysis. *Results:* Among the 1,311 AB strains, 81.16% (1,064 strains) were from sputum samples, and the departments with the highest detections rates of AB were neurosurgery (24.33%), intensive care (15.48%) and infectious disease (11.44%). The drug sensitivity test showed that the resistance rate of 1,311 AB strains to compound sulfamethoxazole and amikacin was 28.38% and 20.54%, respectively, and the resistance rate to 10 other kinds of common antibiotics was more than 40%. *Conclusion:* The 1,311 AB strains isolated were widely distributed in clinical settings and had strong resistance to commonly used antibiotics. Therefore, it is necessary to strengthen the monitoring of pathogens and drug resistance, formulate reasonable and effective infection control measures, and ensure that antibiotics are used in a reasonable manner.

Keywords: *Acinetobacter baumannii*; Drug resistance; Drug sensitivity test

Online publication: May 30, 2023

1. Introduction

Acinetobacter baumannii (AB) is a common opportunistic pathogen found in nature, hospitals, and various parts of the human body [1]. It has become one of the most serious pathogens of iatrogenic infection in view of its strong environmental adaptability and ability to acquire exogenous drug resistance genes [2]. In recent years, with the increasing severity of AB drug resistance, we see an increase in length of hospital stay, incidence and mortality, as well as cost of healthcare; moreover, there are now limited selections of effective antibiotics, and many other hazards are becoming increasingly significant [3]. In order to understand the distribution of AB in hospitals and its drug resistance to provide reference for reasonable and effective infection control measures, we collected data of AB isolated from inpatients in Huaihua First People's Hospital from 2019 to 2021 and analyzed the clinical distribution and drug resistance status of infected patients.

2. Materials and methods

2.1. Strain sources

A total of 1,311 AB strains were collected from clinical isolates of Huaihua First People's Hospital from 2019 to 2021. The repeated isolates from the same part of the same patient were excluded. The quality control strain was the standard strain ATCC25922.

2.2. Research design

We used the VITEK-2 Compact, an automatic microbial identification system, and supporting reagents (bioMérieux, France) for bacterial identification and drug sensitivity test *in vitro*. We referred to the Clinical & Laboratory Standards Institute (CLSI) M100S document (2019) to interpret the drug sensitivity results [4].

2.3. Statistical analysis

Excel was used for statistical analysis.

3. Results

3.1. Source and distribution of specimens

A total of 1,311 strains of *Acinetobacter baumannii* were detected in Huaihua First People's Hospital from 2019 to 2021, of which sputum samples had the highest detection rate, accounting for 81.16%, followed by pus samples and urine samples, accounting for 4.20% each. See **Table 1** for details.

Table 1. Source and composition ratio of specimens

Specimen	N (strain)	Constituent ratio (%)
Sputum	1,064	81.16
Urine	55	4.2
Pus	55	4.2
Blood	46	3.51
Bronchoalveolar lavage fluid	32	2.44
Cerebrospinal fluid	19	1.45
Wound secretion	12	0.92
Ascites	12	0.92
Bile	8	0.61
Pleural fluid	4	0.31
Venous catheter	2	0.15
Lung tissue	1	0.08
Drainage	1	0.08

3.2. Clinical distribution of specimens

Among the 1,311 AB specimens, neurosurgery accounted for the highest proportion (24.33%), followed by intensive care unit and infection department, accounting for 15.48% and 11.44%, respectively. See **Table 2** for details.

Table 2. Clinical distribution and composition ratio of *Acinetobacter baumannii* specimens

Department	N (strain)	Constituent ratio (%)
Neurosurgery	319	24.33
Intensive care unit	203	15.48
Infectious disease	150	11.44
Neurology	102	7.78
Outpatient	87	6.64
Emergency	80	6.10
Neonatology	69	5.26
Orthopedics	42	3.20
Internal medicine	40	3.05
Respiratory medicine	34	2.59
Nephrology	25	1.91
Rehabilitation medicine	22	1.68
Urology	21	1.60
Pediatrics	20	1.53
Thoracic surgery	18	1.37
Obstetrics and gynecology	13	0.99
Geriatric medicine	11	0.84
Hematology	11	0.84
Plastic and burn	10	0.76
Cardiology	8	0.61
Oncology	6	0.46
Endocrinology	5	0.38
General surgery	5	0.38
Rheumatology and immunology	4	0.31
Gastroenterology	3	0.23
Otorhinolaryngology	2	0.15
Ophthalmology	1	0.08

3.3. *Acinetobacter baumannii* antibiotic resistance

The sensitivity rate of AB to amikacin and cotrimoxazole was 76.35% and 71.62%, respectively. AB showed high resistance to other commonly used antibiotics, especially ceftriaxone, with a resistance rate of 63.25%. See **Table 3** for specific results.

Table 3. Drug resistance of *Acinetobacter baumannii* to commonly used antibiotics

Antibiotic	Drug resistance (%)	Intermediary (%)	Sensitivity (%)
Ceftriaxone	63.25	26.26	10.49
Cefepime	60.03	1	38.97
Gentamicin	59.01	2.52	38.47
Ciprofloxacin	58.27	1.84	39.89
Imipenem	57.55	0.92	41.53
Piperacillin/tazobactam	54.88	4.29	40.83

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Antibiotic	Drug resistance (%)	Intermediary (%)	Sensitivity (%)
Levofloxacin	52.18	5.58	42.23
Cefoperazone/sulbactam	51.73	10.13	38.15
Tobramycin	50.47	5.81	43.72
Tigecycline	41.81	0	58.19
Compound sulfamethoxazole	28.38	0	71.62
Amikacin	20.54	3.12	76.35

3.4. Trends of *Acinetobacter baumannii* resistance to commonly used antibiotics

From 2019 to 2021, the drug resistance and sensitivity of AB to 12 commonly used antibiotics fluctuated slightly but remained stable. See **Table 4** for details.

Table 4. Trends of *Acinetobacter baumannii* resistance to commonly used antibiotics

Antibiotic	2019			2020			2021		
	DR (%)	I (%)	S (%)	DR (%)	I (%)	S (%)	DR (%)	I (%)	S (%)
Ceftriaxone	64.64	26.03	9.33	62.5	26.72	10.78	62.47	26.09	11.44
Cefepime	61.74	0.43	37.83	57.95	1.47	40.59	60.18	1.14	38.67
Gentamicin	61.26	2.38	36.36	59.61	2.19	38.2	56.06	2.97	40.96
Imipenem	59.04	0.87	40.09	54.63	1.22	44.15	58.72	0.69	40.6
Ciprofloxacin	58.91	1.74	39.35	56.72	2.44	40.83	59.04	1.37	39.59
Piperacillin/tazobactam	54.5	4.95	40.54	54.7	3.71	41.58	55.43	4.16	40.42
Cefoperazone/sulbactam	53.61	10.94	35.45	50	9.69	40.31	51.26	9.66	39.08
Tobramycin	53.42	4.86	41.72	50.5	5.69	43.81	47.34	6.93	45.73
Levofloxacin	52.16	6.06	41.77	49.88	6.11	44.01	54.36	4.59	41.06
Tigecycline	42.6	0	57.4	39.7	0	60.3	42.96	0	57.04
Amikacin	32.94	4.71	62.35	20.78	3.91	75.31	17.89	2.06	80.05
Compound sulfamethoxazole	24.19	0	75.81	33.82	0	66.18	27.69	0	72.31

Abbreviations: DR, drug resistance; I, intermediary; S, sensitivity.

4. Discussion

In this study, 1,311 AB strains isolated from clinic specimens of Huaihua First People's Hospital from 2019 to 2021 were analyzed. The results showed that the specimen sources and clinical distribution were consistent with several reports [1,2,5,6]. The departments with the highest detection rates mostly comprised of elderly patients, critically ill patients, or patients who had received invasive treatment. These patients generally have low immunity; thus, they have a higher risk of AB infection [7].

In recent years, due to the extensive use of antibiotics, the resistance rate of AB has shown an upward trend. The results of this study showed that the 1,311 AB strains generally had high resistance to commonly used antibiotics. The resistance rate of AB to 9 kinds of antibiotics, including ceftriaxone, was more than 50%, but the resistance rate of AB to compound sulfamethoxazole and amikacin was low (28.38% and 20.54%, respectively). The results are similar to those of local and foreign studies [8,9].

From 2019 to 2021, the resistance and sensitivity of AB to 12 kinds of commonly used antibiotics fluctuated slightly. Among them, the resistance of AB strains to 7 kinds of antibiotics decreased; the resistance to amikacin decreased significantly, from 32.94% to 17.89%, while the resistance to other drugs

decreased by only 1%–5%. There was a slight increase, ranging between 1% and 3%, in AB resistance to 5 kinds of antibiotics. This may be related to the implementation of various measures, such as strengthening the management of antibiotics, paying attention to the monitoring of hospital infection, strengthening hand hygiene and environmental cleaning, and reducing invasive procedures in recent years [10].

In conclusion, the dynamic monitoring of AB drug resistance and its trends can provide a basis for the rational use of antibiotics in clinical practice. The key to treating AB is to select appropriate antibiotics strictly according to the drug sensitivity test. At the same time, it is also important to strengthen the management of hospital infection, implement the hand hygiene compliance and disinfection work, and reduce invasive procedures.

Funding

This work was supported by the Scientific Research Project of Hunan Provincial Department of Education (19C1328) and the Research-Based Learning and Innovative Experimental Program for College Students in Hunan Province (S202012214040).

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Clinical Observation of Non-Staining Circular Capsulorhexis for Hypermature Cataract

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Abstract: *Objective:* To explore the circular capsulorhexis method and its clinical effect in phacoemulsification of hypermature cataract without staining. *Methods:* In this prospective randomized case-control study, 22 patients (22 eyes) with hypermature cataract were randomly divided into a staining agent group (10 cases, 10 eyes) and a non-staining agent group (12 cases, 12 eyes). Both groups underwent phacoemulsification with foldable intraocular lens implantation under topical anesthesia. In the staining agent group, 0.5% indocyanine green was used to stain the anterior lens capsule to assist in circular capsulorhexis; in the non-staining agent group, after puncturing the anterior lens capsule and aspirating the liquefied cortical material, the capsular bag was filled with viscoelastic agent to increase the contrast prior to circular capsulorhexis. The operability of the anterior capsule without staining in capsulorhexis was observed, and the effect of capsulorhexis, diameter of capsulorhexis opening, and operative time were compared and analyzed between the two groups. *Results:* Both groups successfully underwent circular capsulorhexis, with a success rate of 100%. The diameters of capsulorhexis opening in the staining agent group and non-staining agent group were 5.68 ± 0.15 mm and 5.54 ± 0.16 mm, respectively, without any statistical difference between the groups ($P > 0.05$); the operative time of the staining agent group (40.40 ± 5.42 s) was shorter than that of the non-staining agent group (50.92 ± 3.97 s), and the difference was statistically significant ($P < 0.001$). In both groups, phacoemulsification was successful, and intraocular lens were implanted into the capsular bags; their visual acuity showed significant improvement during the 1-month follow-up period after surgery, without any surgical complications. *Conclusion:* In hypermature cataract, injecting viscoelastic agent into the capsular bag for volume replacement, given a lack of capsule staining agent, can increase the contrast for capsulorhexis and reduce the risk of large capsular bag collapse on the zonular ligament. Thus, it is considered safe and effective. Circular capsulorhexis is conducive to a smooth phacoemulsification procedure.

Keywords: Hypermature cataract; Capsulorhexis; Phacoemulsification

Online publication: May 31, 2023

1. Introduction

With the improvement of people's living standards and health awareness, many cataract cases in the early and mid-stages can be cured by surgery. However, hypermature cataract remains a problem in remote and underdeveloped areas. Hypermature cataracts can lead to a number of complications, including phacogenic uveitis [1], secondary glaucoma [2], and dislocation of the lens or lens nucleus [3,4]. Surgical extirpation is currently the only effective means of treating such cataracts. However, due to the liquefaction of fibers in the lens cortex and the fragility of suspensory ligaments in hypermature cataracts, it is often difficult to

perform circular capsulorhexis [5-7], and the radial tear of the anterior capsule may extend to the equator part, which would increase the risk of dropped nucleus. Therefore, the surgery for hypermature cataract is a relatively complicated one. A successful continous circular capsulorhexis and the treatment of exposed hard nuclei are the challenges in hypermature cataract surgery [8,9]. The use of stains (such as indocyanine green or trypan blue) for the anterior capsule can significantly improve the visibility of the anterior capsule under the operating microscope, which would help surgeons accurately determine the extent and effect of capsule tearing [7-11]. However, knowing how to increase the success rate of circular capsulorhexis and reduce the difficulty of surgery when there is a lack of staining agent or when the staining effect is poor has become an issue that perplexes grassroots ophthalmologists to carry out hypermature cataract surgery smoothly. In view of this, we introduce a non-staining circular capsulorhexis method in this study. We compared it clinically with the indocyanine green staining-assisted circular capsulorhexis method and determined its effect on the success rate and efficiency of hypermature cataract surgery in hope to provide reference for the clinical application of this method.

2. Data and methods

2.1.General information

Twenty-two patients (22 eyes) with hypermature cataract admitted to Xi'an Savaid Ophthalmic Hospital from January 2021 to January 2023 were included in this prospective randomized case-control study. Among the 22 patients, 8 were male and 14 were female, with an average age of 75.8 (68–92 years old). **Table 1** shows the baseline data of the patients.

Inclusion criteria: hypermature cataract (cloudy-white lens, liquefied cortex, reddish and sinking nucleus, and absent red reflex). Exclusion criteria: (i) non-hypermature cataract; (ii) concurrent phacolytic glaucoma or lens-induced uveitis; (iii) concurrent corneal disease, glaucoma, fundus disease, and other eye diseases that affect vision; (iv) local and systemic contraindications to cataract surgery, such as severe hypertension, coronary heart disease, diabetic patients with poor blood sugar control, *etc*. This study was approved by the hospital ethics committee, informed consent was obtained from the patients, and all patients included in the study signed the informed consent form before the surgery.

Table 1. Comparison of preoperative baseline data of patients in the staining agent group and non-staining agent group

Group	Number of cases (eyes)	Age	Gender (number of cases)	Intraocular pressure (mmHg)	Visual acuity before surgery
Staining agent group	12	77 ± 7.2	Male 6: Female 6	16.10 ± 2.18	Light perception/hand movement
Non-staining agent group	10	74 ± 3.3	Male 4: Female 6	16.75 ± 2.68	Light perception/hand movement
P	–	0.2502	–	0.7185	–

2.2. Surgical methods

All 22 patients received topical anesthesia (0.4% oxybuprocaine hydrochloride eye drops [Benuoxi, Japan Santen Pharmaceutical]) before surgery. A 2.4-mm dual plane limbal incision was made, and phacoemulsification was performed on the affected eye using a phacoemulsification device (Alcon, Centurion, USA). After capsulorhexis, the patients in both groups did not undergo hydrodissection, the cataracts were removed through the same operative steps, and foldable intraocular lens were implanted. All the surgeries were performed by the same physician.

2.2.1. Capsulorhexis in staining agent group

After injecting sterile air into the anterior chamber, 0.2 mL of 0.5% indocyanine green (Dandong Yichuang Pharmaceutical Co., Ltd.) was injected and left for 5–6 s. Circular capsulorhexis was completed by pulling the flap, during which viscoelastic agent was injected in the anterior chamber as appropriate to flatten the anterior capsule.

2.2.2. Capsulorhexis in non-staining agent group

An appropriate amount of viscoelastic agent (Alcon, USA) was injected into the anterior chamber. The anterior capsule of the central area was punctured with a 1-mL syringe needle, which was extended into the capsular bag to aspirate the liquefied cortex, and an appropriate amount of viscoelastic agent was injected into the capsular bag through the puncture port to maintain the shape of the capsular bag. The anterior capsule was flattened, and a capsulorhexis forcep was used to gently pick up the anterior capsule. Continuous circular capsulorhexis was then performed against the background of the transparent viscoelastic agent (**Figure 1**), during which the viscoelastic agent was supplemented as appropriate.

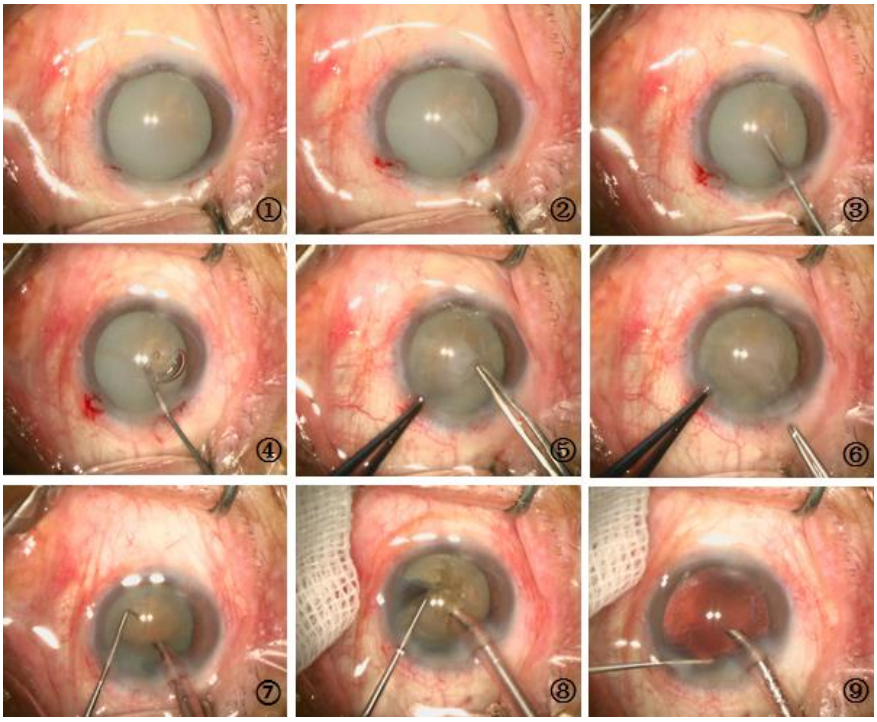

Figure 1. Capsulorhexis for hypermature cataract without staining. ① Hypermature cataract under the operating microscope (milky white and turbid lens, liquefied cortex, reddish and slightly sunken nucleus, and absent red reflex). ② Liquefied cortex overflows after anterior capsule puncture with a 1-mL syringe needle. ③ Aspiration of liquefied cortex in the capsular bag with a flat needle. ④ Appropriate amount of viscoelastic agent injected into the capsular bag to maintain the shape of the capsular bag. ⑤ Flap opened from the puncture port for capsulorhexis, and viscoelastic agent added to flatten the anterior capsule. ⑥ Complete circular capsulorhexis. ⑦ and ⑧ Phacoemulsification to remove the lens nucleus. ⑨ Lens nucleus cleaned, with presence of red reflex and complete anterior capsule ring.

2.3. Criteria for capsulorhexis success

The anterior capsule tearing diameter was controlled at 5–6 mm. Successful capsulorhexis: continuous capsulorhexis; round or slightly oval in shape; both ends are completely connected. Capsulorhexis failure: anterior capsulorhexis splits toward the equator during capsulorhexis; capsulorhexis opening is seriously off-centre; or capsulorhexis cannot be completed and converted into capsulotomy.

2.4. Observation indicators

The entire procedure was recorded on video. The success rate of circular capsulorhexis, capsulorhexis time (time record: three times of video playback, stopwatch record), and capsulorhexis diameter were compared between the two groups. Complications such as capsular tear (a tear at one site is counted as 1 site) and posterior capsular rupture (number of cases) were observed. The start time of capsulorhexis in the staining agent group was the injection of the staining agent into the anterior chamber; whereas the start time of capsulorhexis in the non-staining agent group was when the 1 mL syringe needle punctured the anterior capsule. Calculation of capsulorhexis diameter: after closing the corneal incision and the normalization of intraocular pressure, we took a screenshot of the orthotopic surgery video (**Figure 2**); the short axis of the annular capsulorhexis and the diameter of the optical zone of the intraocular lens implanted during the operation (6 mm) were taken as reference, along with the long-axis mean.

Visual acuity, intraocular pressure, and corneal edema were recorded on the first day and one month after surgery.

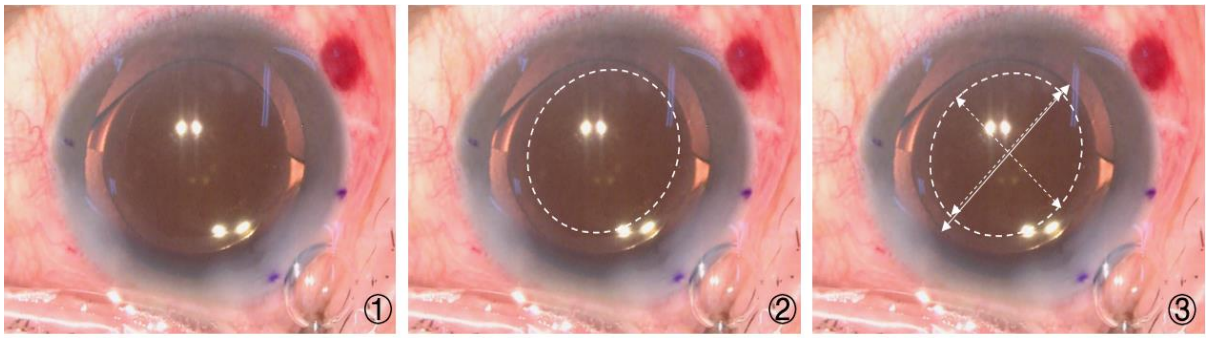

Figure 2. Measurement of capsulorhexis diameter. ① Completion of water-tight incision, with moderate intraocular pressure; and screenshot taken; ② Marking of capsulorhexis range. ③Average diameter of annular capsulorhexis (the mean value of the short axis and the long axis; showing the range of capsulorhexis; showing the short and long axis diameters of the anterior capsular ring; indicating the diameter of the optical zone of the intraocular lens).

2.5. Statistical analysis

Measurement data were expressed as mean ± standard deviation (s), and SPSS 25.0 was used to perform paired t-test of independent samples for data analysis. $P < 0.05$ indicates statistically significant difference.

3. Results

3.1. Intraoperative circular capsulorhexis

Circular capsulorhexis was successfully completed in the two groups of patients, although the direction of capsulorhexis had to be adjusted several times during the surgery according to situations. No complications were observed, such as anterior capsular tear and posterior capsular rupture. One case (1 eye) in the staining agent group had a small capsulorhexis, and in order to prevent postoperative capsular bag shrinkage, the capsulorhexis was enlarged after implantation of the intraocular lens. In the non-staining agent group, under the background of the transparent viscoelastic agent, the edge of the torn anterior capsule was clearly visible, and viscoelastic was added 1 or 2 times during the surgery to flatten the anterior capsule as needed; the capsulorhexis went smoothly, with a success rate of 100%.

Capsulorhexis time: the capsulorhexis time in the staining agent group and non-staining agent group was 30–50 s and 47–58 s, respectively. The capsulorhexis time in the non-staining agent group was significantly longer than that in the staining agent group ($P = 0.00002$). The capsulorhexis diameter pf the staining agent group and the non-staining agent group was 5.4–5.9 mm and 5.2–5.8 mm, respectively, and the difference was not statistically significant ($P = 0.07528$), as shown in **Table 2**.

Table 2. Comparison of intraoperative data between the staining agent group and the non-staining agent group

Group	Number of eyes	Anterior capsule tear (site)	Posterior capsule rupture (example)	Capsulorhexis time (s)	Capsulorhexis diameter (mm)
Staining agent group	10	0	0	40.40 ± 5.42	5.68 ± 0.15
Non-staining agent group	12	0	0	50.92 ± 3.97	5.54 ± 0.16
P	–	–		0.00002	0.07528

3.2. Postoperative effect

On day 1 after surgery, the uncorrected visual acuity of both groups improved significantly. The visual acuity and intraocular pressure of the staining agent group were 0.8–0.2, and 12.2–18.7 mmHg, respectively, while the visual acuity and intraocular pressure of the non-staining agent group were 0.7–0.2 and 11.4–19.8 mmHg, respectively; there was no significant difference in the postoperative visual acuity and intraocular pressure between the two groups ($P > 0.05$), as shown in **Table 3**. On postoperative day 1, 3 patients (3 eyes) had mild corneal edema in the central region of the cornea in each of the two groups. Local hypertonic agent was given, and it resolved in all 6 patients after 2 days.

At the re-examination 1 month after surgery, the visual acuity of the two groups was stable, with LogMAR 0.5–0.2 in the staining agent group and LogMAR 0.5–0.1 in the non-staining agent group; there was no significant difference in visual acuity and intraocular pressure between the two groups 1 month after surgery ($P > 0.05$), as shown in **Table 4**.

Table 3. Visual acuity, intraocular pressure, and corneal edema in the staining agent group and non-staining agent group on postoperative day 1

Group	Number of cases	Visual acuity (LogMAR)	Intraocular pressure (mmHg)	Corneal edema (number of eyes)
Staining agent group	10	0.49 ± 0.20	15.30 ± 2.20	3 (25%)
Non-staining agent group	12	0.45 ± 0.17	15.83 ± 3.46	3 (30%)
P	–	0.7247	0.8506	–

Table 4. Visual acuity, intraocular pressure, and corneal edema in the staining agent group and non-staining agent group 1 month after surgery

Group	Number of cases	Visual acuity (LogMAR)	Intraocular pressure (mmHg)	Corneal edema (number of eyes)
Staining agent group	10	0.36 ± 0.11	15.70 ± 2.00	0
Non-staining agent group	12	0.36 ± 0.10	16.08 ± 2.41	0
P	–	0.6960	0.4893	–

4. Discussion

Cataract is one of the leading causes of blindness worldwide, and although drug reversal may become a potential treatment for cataract, surgery remains the only viable treatment at this stage [12]. With the continuous improvement of ophthalmic surgical instruments and techniques, hypermature cataract is no

longer a contraindication for phacoemulsification [9, 13-14]. Continuous circular capsulorhexis is the key to completing phacoemulsification for hypermature cataract [10]. The main features of hypermature cataract include the liquefaction of lens cortex and hard and floating lens nucleus. In this case, even if femtosecond laser-assisted capsulorhexis is used, it is not easy. Furthermore, femtosecond laser, minimally invasive vitrectomy, electric capsulorhexis, *etc*., are not widely used in our country, especially in remote areas at present [5-7, 15]. Manual capsulorhexis has certain flexibility and is still the most basic capsulorhexis method in cataract surgery. When dealing with hypermature cataract, other than the poor contrast of the lens, the anterior capsule is often loose and inelastic, and the suspensory ligament is also fragile. Therefore, the edge of capsulorhexis is not easily controlled by conventional capsulorhexis flap, and the anterior capsular tear is prone to crack, thus increasing the risk of surgery [15,16].

The anterior capsule staining technique is often used to improve the success rate of circular capsulorhexis in hypermature cataracts. The common staining agents are 0.1% trypan blue and 0.5% indocyanine green [7,11,16]. However, at times, there is a shortage of staining agents or poor staining of the anterior capsule. In addition, during capsulorhexis, the liquefied cortex may overflow, causing the field of view to be obscured. Therefore, during the surgery, the operator must use various capsulorhexis techniques flexibly based on the situation to complete circular capsulorhexis and subsequent lens nucleus processing. The non-staining method of "volume replacement" with viscoelastic filling of the capsular bag that was used in this study has the following characteristics: (i) aspiration of the liquefied cortex reduces pressure in the capsular bag; when the anterior capsule is punctured, it can be seen that the liquefied cortex overflows in the form of "smoking", causing an instant decrease in tension of the capsular bag; further suctioning the anterior chamber and the liquefied cortex from the capsular bag can reduce the interference of the overflow on subsequent capsulorhexis; (ii) the filling restores capsular bag volume and increases anterior capsule contrast; injecting an appropriate amount of cohesive viscoelastic into the capsular bag through the puncture of the anterior capsule pushes the exposed lens nucleus and other interfering cortex away from the anterior capsule and restores the intracapsular volume (volume replacement); this step not only increases the contrast between the anterior capsule and the subcapsular material, but also helps reduce the interference of the excessive collapse of the capsular bag on the zonule; (iii) the filling maintains a certain tension in the anterior capsule; after injecting the viscoelastic agent into the capsular bag, adding a little cohesive viscoelastic agent on the surface of the anterior capsule further flattens the capsular membrane to avoid excessive pressure in the capsular bag and rupture the capsulorhexis opening; (iv) different types of viscoelastic agents; mixed viscoelastics can be used during surgery; both cohesive and diffuse types can be used together according to situations to form a "soft shell technology" [9] to protect the corneal endothelium, stabilize the anterior capsule, and improve viscoelasticity; capsulorhexis can be well-achieved by shearing force, and the ideal shape of capsulorhexis can be maintained.

Among the patients in the present study, the success rate of circular capsulorhexis in the non-staining agent group was 100%, the capsulorhexis time was slightly longer than that in the staining agent group, and there was no significant difference in capsulorhexis diameter and postoperative vision recovery between the two groups. At the same time, when dealing with the nucleus, since the capsular bag is filled with viscoelastic agent, the phacoemulsification needle can enter the anterior chamber without perfusion and directly "pile" into the interior of the nucleus to complete the interception and chopping of the nucleus, which is beneficial to retaining the inside of the capsular bag. The viscoelastic agent stabilizes the posterior capsule and the exposed nucleus, prevents large-scale rotation or stabbing and scratching of the capsular bag, and improves the safety in surgery.

In non-staining circular capsulorhexis for hypermature cataract, viscoelastic agent is used to replace the volume in the capsular bag, which not only maintains the shape and tension of the anterior capsule as well as increases the contrast, but also forms a soft shell to stabilize the nucleus. This simple and practical

method increases the success rate of capsulorhexis and guarantees the completion of the surgery. The method we propose benefits patients with hypermature cataract for vision restoration surgery through phacoemulsification and also provides a choice of high-end intraocular lenses to meet the requirements for higher visual quality; thus, it is worthy of clinical application. However, this study has several limitations, including the small sample size. A multicenter clinical study with a larger sample size is needed to observe the possible surgical complications of non-staining circular capsulorhexis. Treatment with circular capsulorhexis for hypermature cataracts is still difficult, regardless of whether staining capsulorhexis or "volume displacement" capsulorhexis is used. We advise against its use in novices as much as possible.

Funding

This work was supported by the First Affiliated Hospital of Xi'an Medical College (XYFYPT-2023-01) and Medical Research Project of Xi'an Science and Technology Bureau (21YXYJ0127).

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Analysis of the Implementation of Integrated Healthcare Management in Preoperative Preparation

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Abstract: *Objective:* To strengthen preoperative preparation management and reduce preoperative preparation defects. *Methods:* We set up a special medical care management team to investigate the preoperative preparation in surgical departments, analyze the causes of the shortcomings in preoperative preparation, and propose countermeasures. The medical staff jointly formulated plans related to preoperative preparation management including clear outline of responsibilities, strengthening of training, integrated medical care, timely feedback, and continuous improvement. Besides, the preoperative preparation of patients before and after the improvement measures were compared using statistical analysis. *Results:* The rate of inadequate preoperative preparation was 11.14 per thousand before the integrated management model was implemented. After the implementation of the integrated management model, the rate of inadequate preoperative preparation decreased to 2.99 per thousand, and the difference was statistically ($P < 0.05$). *Conclusion:* The integrated management of preoperative preparation can help reduce the rate of preoperative complications and ensure the safety of surgery.

Keywords: Integrated healthcare; Preoperative preparation; Rate of inadequate preoperative preparation

Online publication: May 31, 2023

1. Introduction

Preoperative preparation is one of the important parts of the perioperative period, and the quality of the perioperative preparation very much depends on the preoperative preparation, which will also affect the effect of the surgical treatment [1]. For surgical patients, preoperative anxiety, panic, and inadequate preoperative preparation will increase the risks and affect the quality of surgery, causing serious physical, psychological and financial burdens, which can easily cause medical disputes [2]. For the safety of the patients and staff of the surgical department, an integrated management of the preoperative preparation is crucial, so that the preoperative preparation process can be more refined.

2. Information and methods

2.1. General information

A total of 12970 patients who underwent surgery in the large operating room between January 1, 2020, and December 30, 2020, in The First Affiliated Hospital of Jinan University were selected and divided into two groups according to the time of operation. The control group consisted of 5296 patients who underwent surgery between January 1 and June 30, 2020. On July 1, 2020, the integrated management of preoperative preparation was initiated, so 7674 patients who underwent surgery between July 1 and December 30, 2020,

were included in the observation group. Inadequate preoperative preparation meant the nurses in the operating room did not complete their tasks when the patient was sent to the operating room from the ward, . The preoperative preparation items included wrist straps, surgical consent forms, safety checklists, risk assessment forms, and preoperative checklists of 5 categories of defects, covering a total of 22 items. Preoperative preparation defect rate (per thousand) was defined as follows: Number of cases of inadequate preoperative preparation /Total number of patients × 1000 (only patients who were operated in the large operating room).

2.2. Method

The preoperative preparation management team was led by the Director of Surgery and the Chief of Surgical Nursing and consisted of a chief nurse and a head surgical nurse. The Director of Surgery was responsible for supervising the implementation of preoperative preparations and surgical care. The members of the team were responsible for refining the preoperative preparation and implementing relevant countermeasures. The surgical nurse was responsible for supervising the registration and feedback of patients that experienced inadequate preoperative preparation, and the surgical caregiver was responsible for supervising each patient associated with inadequate preoperative preparation for cause analysis and propose improvement measures.

2.3. Status survey

Through a retrospective analysis of 5296 items involved in preoperative preparation for patients who were operated in the main operating room between January 1 and June 30, 2020, it was found that 59 patients were affected by inadequate preoperative preparation, with 7 cases related to wristband, 20 cases related to surgical consent forms, 9 cases related to safety checklists, 9 cases related to risk assessment forms, 14 cases of preoperative checking of unilateral defects. The rate of inadequate preoperative preparation was 11.14 per thousand.

2.4. Causal analysis

Through brainstorming and drawing a fishbone diagram, the team members identified the main reasons for the inadequate preoperative preparation: (1) insufficient understanding of preoperative safety management.

2.5. Improvement measures

(1) The Director of Surgery urged the medical staff to implement the integrated management system and reaffirmed the need for clear communication regarding the person responsible for signing, the time of signing, and other related requirements. (2) The Director of Surgery reiterated that the surgical site must be indicated by the main surgeon or other relevant doctors before surgery by marking the surgical site on the patient with a “plus” sign for identification. (3) The operating room immediately provided feedback on inadequate preoperative preparation to the section director who is responsible for rectification. (4) Steps were taken to refine the preoperative inspection process, where the time and site inspection, person in charge, and the content and order of inspection were defined. (5) Further steps were taken to standardize the procedure of inspection and establish the sequence of medical record keeping regarding patient information to ensure that the inspection was done well.

In addition to the above measures, there was a consensus that patients could not undergo surgery without a doctor’s signature, surgical site identification, or a wristband.

2.6. Statistical analysis

In this study, SPSS 22.0 software was used to analyze and process each set of data, counting the number of

cases of inadequate postoperative preparation. Items of inadequate preoperative preparation included wrist straps, surgical, safety checklist, risk assessment form, preoperative check unilateral defects, a χ^2 test was performed, with $P < 0.05$ indicating differences that are statistically significant.

3. Results

The rate of inadequate preoperative preparation of the observation group was 2.99 per thousand (23/7674), which was significantly lower than the control group, which was 11.14 per thousand (59/5296), and the difference was statistically significant ($P < 0.05$) as shown in **Table 1**.

Table 1. Comparison of preoperative preparation defect rates between the two groups of patients

Group	Number of patients	Number of inadequate preoperative preparation	Rate of inadequate preoperative preparation
Control group	5296	59	11.14
Observation group	7674	23	2.99
P			< 0.05

The incidence of inadequate preoperative preparation of the two groups of patients were compared based on the five categories mentioned. The rate of incidence of preoperative preparation of observation group was significantly lower than that of the control group, and the differences were statistically significant ($P < 0.05$, as shown in **Table 2**.

Table 2. Comparison of the incidence of preoperative preparation defect categories in the two groups of patients

Group	The number of cases	Wrist strap	Surgical consent form	Security checklist	Risk assessment forms	Preoperative checklist
Control group	5296	7 (1.32)	20 (3.78)	9 (1.70)	9 (1.70)	14 (2.64)
Observation group	7674	1 (0.13)	1 (0.13)	2 (0.26)	2 (0.26)	8 (1.04)
P		0.007	0.0000003	0.006	0.006	0.029

4. Discussion

Healthcare integration is a kind of interpersonal relationship between physicians and nurses. It is not simply a matter of doctors and nurses working together, it is also about effective communication, where each party contributes their own strength to enhance medical security [3]. Preoperative preparation is not only the work of nurses, but also all medical and healthcare staff [4]. In this study an integrated medical care management model was implemented. Although the implementation of improvement measures only lasted for 6 months, the results of the study show that the rate of inadequate preoperative preparation significantly decreased, indicating that the management model is applicable to the management of surgical preparation.

Surgery is an important method of treatment, and good preoperative preparation is an important part ensuing a successful surgery [5].

The preparation of surgery is performed in the treatment of various diseases, and it involves not only technical aspects but also management due to its complexity and the number of medical personnel involved [6]. Only by strengthening the preoperative preparation can the rate of inadequate preoperative preparation be reduced. An orderly medical system requires adequate preoperative preparation, and this study reaffirmed use of medical instruments and surgical identification. The director of the section was

responsible for supervising the implementation of the medical system. The occurrence of inadequate preoperative preparation was recorded by the nurses in the operating room and sent back to the relevant department in time for immediate rectification to avoid the recurrence of similar situations, and the rate of inadequate preoperative preparation after the implementation of this model was reduced to 6.07 per thousand (8/1319).

Patient safety is the priority of hospital management. In this study, preoperative preparation management was effectively implemented, and the feasibility of the preoperative preparation process was assessed [7]. In this study, the preoperative preparation process was refined from the procedure of preoperative inspection to the language used in preoperative inspection so that the preoperative process can smoother. According to the statistical report released by Joint Commission on Accreditation of Healthcare Organizations (JCAHO), sending patients to the wrong surgical department ranks second in in the causes of serious medical accidents. Therefore, it is important to correctly identify the surgical to prevent performing the wrong surgery on the wrong patient [8]. The logo of the operating room is a crucial detail. In addition, there was a lack of coordination and cooperation between the medical staff, and there was also an imbalance of power between physicians and nurses, where nurses are like subordinates. Physicians direct the work of nurses, and nurses only carry out what they are told to do. Therefore, it is difficult for nurses to communicate with physicians effectively, develop a consensus on medical care, and draw out the responsibilities and rights of nurses in the preoperative process. Besides, it is also important to come up with comprehensive preoperative inspection content that includes both the roles of doctors and nurses. Preoperative preparations, whether by doctors or nurses, may or may not be complete, and inspection nurses have the right to request perfect work before sending patients into the operating room for surgery. After the implementation of this consensus, surgical site identification rate in patients reached 100%, and mistakes in medical documents also decreased sharply.

5. Conclusion

Integrated healthcare management promotes the cooperation between healthcare and medical staff so that preoperative preparation can be more standardized and institutionalized. In this way, the goal “correct patient, correct operating part, and correct surgery” can be achieved and the patient’s safety can be ensured.

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

The Role and Mechanism of LncRNA-p21 in Regulating Gastric Cancer Metastasis by Mediating Wnt/β-Catenin Signaling Pathway

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Abstract: *Objective:* To study the mechanism of lncRNA p21 inhibiting the growth and metastasis of human gastric cancer SGC7901/GES-1 cells by mediating the Wnt/β-catenin signaling pathway. *Methods:* Lentiviral overexpression of lncRNA-p21 in human gastric cancer SGC7901/GES-1 cell transfections was observed and analyzed for *in vitro* migration, invasion, cell morphology and proliferation. Besides. Wnt/β-catenin signaling pathway was tested for direct involvement in lncRNA-p21-mediated inhibition of gastric cancer cell growth and proliferation. Wnt/β-catenin signaling pathway was validated using Li-C1. *Results:* Gastric cancer SGC7901/GES-1 cells in the overexpression of lncRNA-p21 showed changes in stellate morphology, low invasion, or spindle-shaped morphology. LncRNA-p21 inhibited the growth and proliferation of gastric cancer SGC7901/GES-1 cells both *in vivo* and *in vitro*, and Wnt/β-catenin signaling pathway mediated the proliferation, invasion, and migration of lncRNA-p21 on gastric cancer SGC7901/GES-1 cells. *Conclusion:* LncRNA-p21 can inhibit the growth and metastasis of gastric cancer SGC7901/GES-1 cells *in vitro* and *in vivo*, and the inhibition of lncRNA p21 is mainly mediated by inhibiting the Wnt/β-catenin signaling pathway.

Keywords: LncRNA-p21; Wnt/beta-catenin signaling pathway; Gastric cancer

Online publication: May 31, 2023

1. Introduction

Stomach cancer is a common malignant tumor, which is the second cause of malignant tumor- and cancer-related death in China. Metastasis occurs in gastric cancer, and metastasis and invasion are important factors for the low overall survival rate and poor prognosis of gastric cancer patients. Therefore, clarifying the molecular mechanism of gastric cancer occurrence and metastasis is of great significance for improving the prognosis of gastric cancer patients and developing new clinical treatments. The current research on gastric cancer metastasis mainly focuses on cytokines, glucose metabolism, and signaling pathways. LncRNA is closely related to tumor development and metastasis, and there have been many studies on the mechanism of lncRNA in tumor metastasis. LncRNA-p21 has a regulatory effect, in which it interacts with the downstream target gene *TCF4* through binding proteins and promotes its accumulation in the cytoplasm to increase the expression of β-catenin protein, thereby mediating the Wnt/β-catenin signaling pathway.

Through *in vivo* and *in vitro* experiments, this study further confirmed that inhibiting lncRNA-p21 can inhibit the invasion and metastasis of gastric cancer cells and increase the expression of β-catenin protein, thereby improving the sensitivity and survival of gastric cancer cells to chemotherapy drugs. About 10% of the DNA in the human genome is RNA, a ratio that may be linked to many diseases. The expression of these molecules is influenced by many factors — genetic mutations, environmental or intrinsic factors and genetic traits, and many more. The expression of these molecules is influenced by many factors — genetic mutations, environmental or personal factors, and genetic characteristics. In addition, in epigenetics, RNA production is regulated by mechanisms such as specific chromatin modifications, demethylation, or changes in RNA splicing resulting from gene expression. Therefore, epigenetics is complex and confusing. There is currently no complete system that comprehensively and systematically describes how various genetic alterations are discovered and characterizes the molecular mechanisms involved in biological processes. Although the human genome contains approximately 3 billion base pairs, they are extremely fragmented, randomly distributed, and difficult to understand and analyze. In fact, DNA methylation is a phenomenon produced by gene encoding proteins such as DNA methyltransferase, demethylase, and histone acetylase through catalyzing a series of biochemical reactions. Many types of epigenetic regulatory functions have been discovered and characterized in the human genome. Epigenetic regulation, as an important and widespread process in life systems, can regulate a series of life activities such as cell cycle, apoptosis, and differentiation and development in tissues and organs by affecting gene expressions. In some tumors, this regulation occurs through changes in DNA methylation. Many tumors, including lung cancer, breast cancer, and colon cancer, are associated with mutations in DNA methylation sites, for example: (1) DNA methylation changes appearing in cancer tissues or cancer patients; (2) the decrease of expression in normal tissues or even absence; (3) tumor growth due to gene mutation or loss; (4) abnormal gene mutation leading to abnormal cell function; (5) disease caused by tumor treatment-related gene mutation and deletion, and many more. RNA-binding protein (RBP) is a molecular RNA complex related to gene post-transcriptional regulation, which can bind to target molecules to regulate gene expression; RBP can regulate gene expression related to cell proliferation and migration. Studies have shown that RBP plays an important role in human diseases and cancers, especially in processes such as DNA methylation, demethylation, and RNA splicing. At the cellular level, RBP regulates the expression of cytokines, receptors, and inflammatory mediators, growth factors, or apoptosis molecules by interacting with proteins. In addition, at the tissue level, RNA-binding proteins can regulate the expression of related signaling pathways and key proteins such as Wnt/ β-catenin signaling pathways in a variety of tumor cells to regulate the complex interactions between various cell types and pathway processes during tumorigenesis and development. In addition, RBPs can also regulate various molecular signaling systems such as endoplasmic reticulum stress and autophagy, mitochondrial inner membrane-dependent pathways, membrane homeostasis and cell cycle, and other biophysical processes such as DNA damage repair. RBP is a common molecular network in tumors, and it plays an important role (including a variety of biological functions such as post-transcriptional expression regulation, protein interaction, chromatin-binding protein, post-translational modification, protein degradation, etc.) and regulates the specific role of various proteins such as NDRG1, RBP2, and PAPE1 in the occurrence and development of gastric cancer. The method and its involvement in the regulation of key signaling pathways and key proteins such as Wnt/β-catenin signaling pathway and the expression regulation mechanism of various downstream cancer factors such as VEGF and PDGF should be further studied. Therefore, the purpose of this paper is to explore the mechanism of gastric cancer development by exploring RBP and its upstream non-coding RNA. Besides the specific role and mechanism of RBP in regulating gastric cancer cell proliferation, migration and invasion are also explored, so as to further understand the role of RBP in gastric cancer. This paper is important for understanding the occurrence and development of tumor cells, and deeply studies and elucidates the molecular mechanism

and the interaction relationship between genes that may be involved, as well as the possible regulatory pathways and molecular basis, and explores the regulatory process involved in tumor cell migration, invasion, etc. [1-6].

2. Materials and methods

2.1. Materials

RPMI1640 was purchased from Invitrogen; nude mice were purchased from Beijing Experimental Animal Co., Ltd.; fetal bovine serum, paraformaldehyde, streptomycin, β-actin antibody, basement membrane, and Transwell chamber were all selected from Corning; coating matrix, TritonX-100 and rabbit anti-β-cate-nin were purchased from CST; CCK-8 reagent and RIPA lysis buffer were purchased from Beijing Suolaibao.

2.2. Method

(1) *In vitro* cell experiment

Human gastric cancer cell lines SGC7901/GES-1 were cultured in an incubator at 37℃ and 5% CO_2. Cell growth was observed under an inverted microscope containing 20% FBS at a cell density of 4×10^6, and cell proliferation was detected by CCK-8.

(2) *In vivo* experiment:

The human gastric cancer cell lines SGC7901/GES-1 were cultured and randomly divided into two groups. The cells in the two groups were subcutaneously inoculated into mice at 4×10^6, and they were sacrificed on the 3rd and 7th day (the body weight decreased by 10%). Then, the tumor tissues were taken for immunohistochemical analysis.

3. Results

3.1. Effect of overexpression of lncRNA-p21 on the morphology of gastric cancer SGC7901/GES-1 cells

Compared to the control group, the star shape or spindle of SGC7901/GES-1 cells in the lncRNAp21-overexpression (lncRNA-p21-OE) group changed to a rounder and less invasive state, as shown in **Figure 1**.

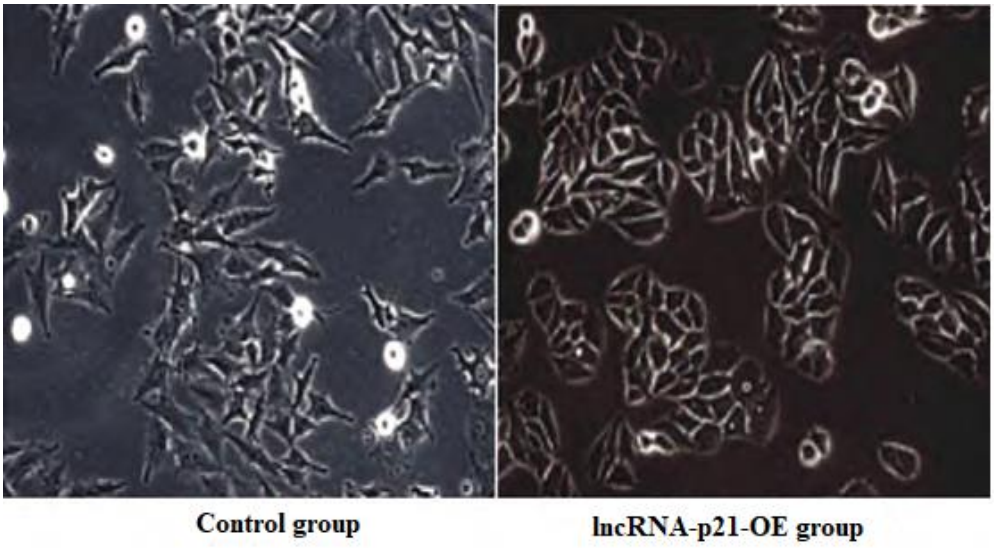

Figure 1. Overexpression of lncRNA-p21 changes the morphological characteristics of SGC7901/GES-1 cells (×400)

3.2. Effect of overexpression of lncRNA-p21 on the invasion and migration of gastric cancer SGC7901/GES-1 cells

Compared to the control group, the migration and invasiveness of SGC7901/GES-1 cells in the lncRNAp21-OE group were significantly reduced ($P < 0.05$), as shown in **Table 1**.

Table 1. The effect of overexpression of lncRNAp21 on the invasion and migration of SGC7901/GES-1 cells (mean ± SD, individual, $n = 3$)

Group	Migration	Invasiveness
Control group	461.62 ± 51.37	367.89 ± 42.52
LncRNAp21-OE group	104.54 ± 27.05	85.9 ± 12.17

3.3. Overexpression of lncRNA p21 inhibits gastric cancer cells *in vitro* and *in vivo*

The differences in cell proliferation between the lncRNAp21-OE group and the control group on the 3rd and 4th day was statistically significant ($P < 0.05$). The lncRNAp21-OE group significantly inhibited the transplanted tumor volume on the 10th day, 20th day, and 30th day ($P < 0.05$) compared to the control group, as shown in **Table 2**.

Table 2. Effects of overexpression of lncRNA p21 on gastric cancer cells *in vivo* and *in vitro*

Group	1d	2d	3d	4d
Control group	0.26 ± 0.02	0.38 ± 0.01	0.63 ± 0.05	0.89 ± 0.04
LncRNAp21-OE group	0.28 ± 0.03	0.30 ± 0.02	0.42 ± 0.01	0.47 ± 0.02

3.4. Inhibition of Wnt/β-catenin signaling pathway activity by overexpression of lncRNA p21

Immunofluorescence staining showed that the lncRNAp21-OE group significantly the accumulation of β-catenin in SGC7901/GES-1 cells was significantly inhibited compared to the control group ($P < 0.05$). Western blotting showed that the expression of β-catenin protein in the lncRNAp21-OE group was significantly reduced compared to the control group, ($P < 0.05$), as shown in **Table 3**.

Table 3. Inhibition of Wnt/β-catenin signaling pathway activity by overexpression of Lnc RNA p21

Group	β-catenin fluorescence	β-catenin protein
Control group	161.62 ± 21.37	97.89 ± 12.52
Lnc RNA p21-OE group	34.54 ± 7.05	25.9 ± 6.17

4. Discussion

Gastric cancer is one of the common malignant tumors in China and it has poor prognosis. Due to the lack of effective diagnostic and treatment methods, most gastric cancer patients are already in the middle and advanced stages when they are diagnosed and have lost the chance of radical surgery and long-term survival, and the prognosis is poor. The mechanism of action of lncRNA-p21 in malignant tumors is still unclear. This study found that lncRNA-p21 is related to the malignant degree of gastric cancer through gene expression profiling analysis; using *in vitro* cell experiments and *in vivo* animal models, it was found that lncRNA-p21 can promote the invasion, migration and clone formation ability of gastric cancer cells and their metastasis *in vivo*. In addition, this study also revealed that lncRNA-p21 can regulate the Wnt/β-catenin signaling pathway by down-regulating the expression of β-catenin protein. Although there is no

drug that directly acts on β-catenin protein, the accumulation of β-catenin protein in cells can activate its downstream target gene transcription factors, thereby promoting the proliferation, migration, and invasion of cancer cells. LncRNA-p21 can inhibit the expression of β-catenin protein in gastric cancer cells by regulating this pathway. On the other hand, there is a certain correlation between lncRNA-p21 and the activation of Wnt/β-catenin signaling pathway in gastric cancer tissues, so this study provides a basis for the clinical diagnosis of gastric cancer. It is a new target and provides a theoretical basis for clinical chemotherapy [7-9].

LncRNA-p21 is highly expressed in gastric cancer tissues and cells, and its expression is correlated with the malignancy of gastric cancer. Through gene expression profiling analysis, it was found that the expression of lncRNA-p21 was closely related to invasion and metastasis and was highly expressed in gastric cancer tissues and cells. LncRNA-p21 plays an important role in tumor development and metastasis. Inhibiting the expression of lncRNA-p21 in gastric cancer cells can promote the invasion and metastasis of cells, and down-regulate the protein expression of β-catenin in cells [10-15]. LncRNA-p21-binding protein is a gene located on chromosome 1q12.2-12.4 discovered by TCGA database analysis. LncRNA-p21 can inhibit β-catenin protein binding enzyme, so that β-catenin accumulates in the cytoplasm to promote the combination of β-catenin and *TCF4* to regulate the increase of β-catenin protein expression. After knocking down lncRNA-p21 with siRNA, we found that downregulation of lncRNA-p21 inhibited the formation of GSK3/GSK4α complex, decreased the functional activity of GSK3/β-Catenin complex, and decreased the expression of transcription factors. Finally, we found that knocking down lncRNA-p21 inhibited the accumulation of *TCF4* in the cytoplasm and promoted β-catenin into the nucleus to increase protein expression. This study shows that lncRNA-p21 can affect the invasion, metastasis, chemosensitivity, and survival of gastric cancer tissues and cells by regulating its downstream target gene *TCF4*, providing a theoretical basis for clinical molecular targeted therapy of gastric cancer.

We found that knocking down lncRNA-p21 can down-regulate the protein expression of β-catenin in cells, while overexpressing lncRNA-p21 can up-regulate the protein expression level of β-catenin in cells. lncRNA-p21 has a unique tissue distribution feature, suggesting that it may function in a variety of tumors. Knockdown of lncRNA-p21 promoted the invasion and metastasis of gastric cancer cells and down-regulated the protein expression level of its downstream target gene *TCF4* in cells after knockdown. Knockdown of lncRNA-p21 can up-regulate the phosphorylation level of β-catenin and down-regulation of cyclinD1 and Rac1.

In conclusion, (1) lncRNA-p21 can affect the invasion and metastasis of gastric cancer by regulating the Wnt/β-catenin signaling pathway, and silencing lncRNA-p21 can down-regulate the expression of *TCF4*, RAC1, etc. in the downstream target genes of Wnt/β-catenin signaling pathway. (2) LncRNA-p21 can inhibit the formation of GSK3/β-catenin complex by binding to its binding protein, thereby down-regulating the accumulation of *TCF4* in the cytoplasm and then regulating the increase of β-catenin protein expression. Knocking down the expression of TCF4 can significantly reduce the expression of β-catenin protein expression. (3) Both lncRNA-p21 and *TCF4* were found to be highly expressed in gastric cancer cell lines and clinical tissue specimens and were correlated with the degree of malignancy of tumors, suggesting that they contribute to the formation of gastric cancer tissue, overall survival of patients, tumor recurrence and metastasis, and chemotherapy sensitivity. (4) LncRNA-p21 regulates the activation of Wnt/β-catenin signaling pathway through binding proteins to promote the development and metastasis of gastric cancer, which may serve as a new target for the diagnosis and treatment of gastric cancer and a potential target for new drug development.

Disclosure statement

The authors declare no conflict of interest.

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Publisher's note

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Nano-Sustained CO-Releasing Molecules Alleviates Cyclosporin-A-Induced Nephrotoxicity and Renal Fibrosis by Inhibiting *NLRP3* Inflammasome-Mediated TGF-β/Smad Signaling Pathway

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Abstract: *Objective:* To investigate the effect nano-sustained CO-releasing molecules on cyclosporin-A (CsA)-induced nephrotoxicity by inhibiting the *NLRP3* inflammasome-mediated TGF-β/Smad signaling pathway. *Methods:* 3×10^5 cell/mL human renal tubular epithelial cells (HK-2) and mouse primary cultured renal tubular epithelial cells (RTECs) were cultured under an inverted microscope and incubated with 10% DMEM and 0.25% β2M in NaCl solution for 3 h. HK-2 and RTECs were divided into 5 complex numbers. MTT assay was used to detect the relative proliferation level of one of the HK-2 cells and calculate the multiplication ratio. *Results:* The nano-sustained CO-releasing molecules CS-CO had a strong protective effect on the kidney. HK-2 and RTECs cells were treated with siRNA, inhibitors, and *NLRP3* knockout mice, and the changes in cell activity and expression of intracellular inflammatory factors were studied. The expression of TGF-β1/Smad signaling pathway related proteins in HK-2 and RTECs was detected by ELISA, western blot, immunofluorescence, and other techniques. *Conclusion:* SMA/CORM2 alleviates CsA-induced renal fibrosis by inhibiting *NLRP3* inflammasome-mediated TGF-β/Smad signaling pathway.

Keywords: *NLRP3*; TGF-beta; Smad; Renal fibrosis

Online publication: May 31, 2023

1. Introduction

NLRP3 inflammasome activation is a major cause of renal inflammatory response in rat models of cyclosporine A (CsA)-induced renal fibrosis. Therefore, inhibition of *NLRP3* inflammasome activation is of great significance in alleviating CsA-induced renal fibrosis. Nano-sustained CO-releasing molecules (CS-CO) is a novel drug-carrying CO-releasing molecule, which plays an anti-inflammatory role *in vivo*. Our previous studies have shown that CS-CO can effectively inhibit the activation of *NLRP3* inflammasome in rat renal tissue, and blocking the activation of *NLRP3* inflammasome can alleviate CsA-induced renal fibrosis. In this study, rat renal tubular epithelial cells (RTECs) and human renal tubular epithelial cells (HK-2) were cultured to obtain renal tubular epithelial cells, renal tubule interstitium, and renal fibrosis models. siRNA, and *NLRP3* knockout mice were used, and then the changes in cell activity were detected. The activation of *NLRP3* inflammasome and the expression of inflammatory factors in HK-2 cells and

RTECs were observed by fluorescence staining. The plasma protein levels of HK-2 cells and RTECs were detected by western blotting. Fibroblast culture was treated with siRNA in *NLRP3* knockout mice, respectively, and the expression of TGF-β1/Smad signaling pathway related proteins was detected. A mouse model of renal fibrosis with *NLRP3* gene knockout was constructed, which confirmed that inhibition of *NLRP3* gene knockout can effectively alleviate the progression of CsA-induced renal fibrosis [1-5].

2. Information and methods

2.1. Materials

Non-stress responsive male rats of ≥ 1000g were used as lab rats. The main instruments and equipment are biochemical analyzer, cell culture kit (ViralSystems, USA). The cell lysis solution was purchased from Beijing Dinghao Biotechnology Co Ltd. The petri dishes with were rinsed with sterile water at least 3 times to remove white blood cells and then with 0.1% benzyl ammonium chloride solution 2 times to remove dead cells. 10% HNO_3 (2mL/L) was used to prepare the buffer solution and 5% HNO_3 (2mL/L) was used to prepare PBS solution.

2.2. Main reagents

MTT kit (Shanghai Boosays Biotechnology Co., Ltd.), SDS-PAGE gel electrophoresis instrument (JC16Y1, USA) was for quantitative detection of protein expression.

Other reagents: 5% PBS buffer solution (pH 6.8), DAPI reagent, SDS gel preparation kit (Beijing Bosyes Company), CCK-8 solution (10 × cell adhesion method/PBS solution), Transwell cell culture medium and Transwell agarose gel column, BSA solution, 5% fetal bovine serum and 10×PBS buffer solution, and cytokines (human interleukin-2, type 1, IL-10,IL-1,IL-12 and IL-6 [ELISA method], etc.) were prepared.

2.3. Methods

(1) HK-2 and RTECs cell cultures: 3×10^5 cell/mL Human renal tubular epithelial cells (HK-2) with and primary cultured mouse renal tubular epithelial cells (RTECs) were cultured under an inverted microscope and incubated with 10% DMEM and 0.25% β2M in NaCl solution for 3h.
(2) Experimental grouping: The ratio of the experimental groups and control groups were 1:1
(3) Cell count: 1 mL human kidney tissue specimens were collected and stored in 1 mmol/L chloroform epoxide at the concentration of 1×10^5 cells/mL.
(4) Cell activity detection: HK-2 and RTECs cells were divided into 5 complex numbers. MTT assay was used to detect the relative proliferation level of one of the cells and calculate the multiplication factor.
(5) Fluorescence staining (0.1 MPBS): Fibroblasts were divided into three complex numbers: blank control group, experimental group, and model group, and cultured for 1 hour in 1 mmol/L chloroform.
(6) Western blotting: The proteins were detected by the western blot method.
(7) Serum sample treatment: Serum samples were collected from animals in each group at different time points.
(8) Statistical analysis: *NLRP3* protein expression in renal tubule epithelial cells was determined by immunohistochemical methods.
(9) Calculation of the degree of renal fibrosis: Luminex kit was used to detect the degree of renal fibrosis of rats in each group, and Microsoft Excel was used for statistical processing (including curve plotting and analysis).

3. Results

3.1. SMA/CORM2 alleviated CsA-induced renal pathological and histological changes

In order to investigate the effect of SMA/CORM2 on renal fibrosis, a CsA-induced renal fibrosis model and a SMA/CORM2 intervention model were first established (**Figure 1A**). Subsequently, we found that different doses of SMA/CORM2 improved CsA-induced renal weight loss and renal coefficient decrease, increased serum creatinine (Cr), and increased blood urea nitrogen (Bun) in male rats (**Figure. 1B-E**). It should be noted that 1 mg/kg SMA/CORM2 showed the most significant protective effect. Therefore, we will select 1 mg/kg SMA/CORM2 as the intervention dose in the following study.

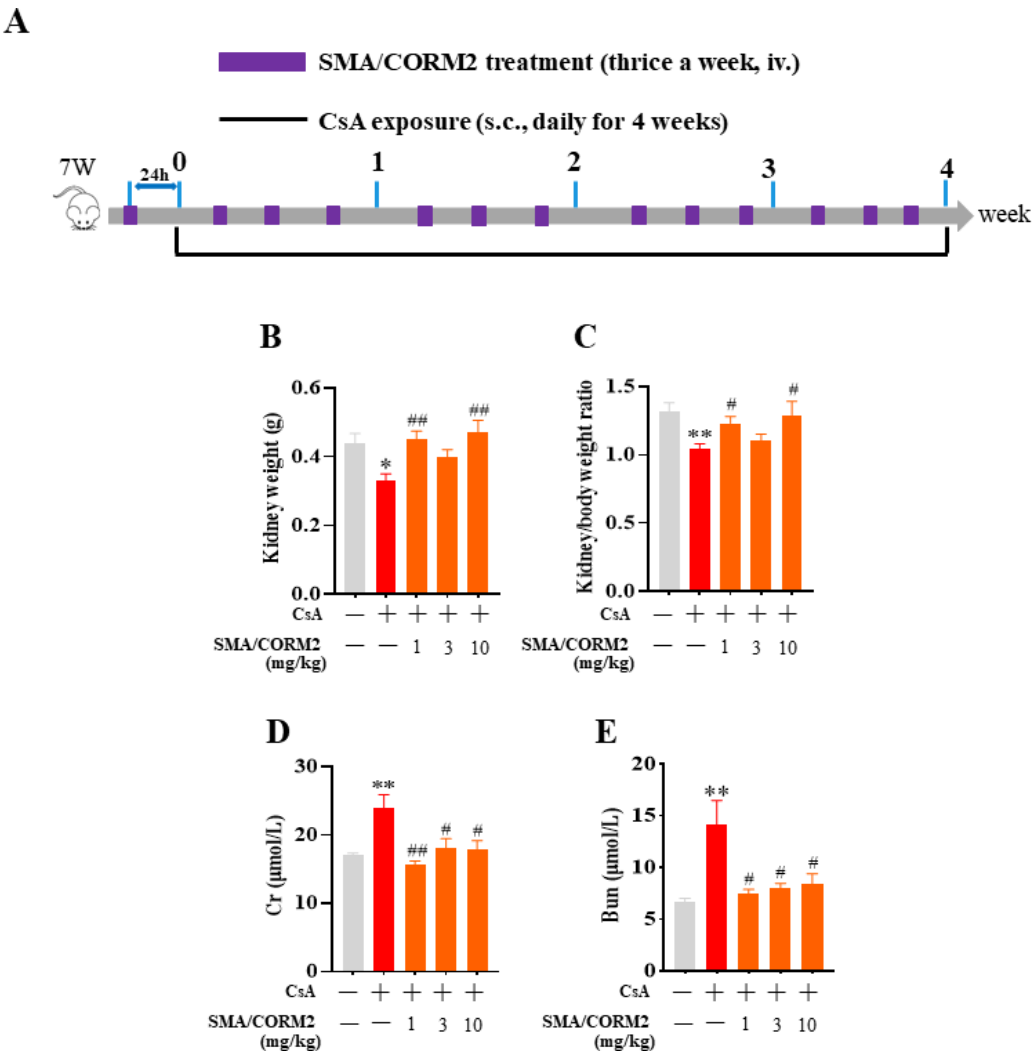

Figure 1. Effect of SMA/CORM2 on CsA- induced nephrotoxicity. (A) Experimental design; Mice were injected subcutaneously with CsA every day for 4 weeks, during which SMA/CORM2 was injected three times a week through the caudal vein. 24 hours after the last CsA injection, the mice were killed, and their renal weights were weighed. (B) Kidney weight. (C) Kidney/body weight ratio. (D) Serum creatinine. (E) blood urea nitrogen. *P < 0.05, **P <0.01 vs control group; #P < 0.05, ##P < 0.01 vs CsA group. The results were expressed by mean ± standard error, n ≥4.

As shown in **Figure 2E-F**, H&E staining showed that CsA significantly damaged the tubular structure and aggravated the renal injury, which was manifested as increased necrotizing debris in the tubular, blurred tubular boundary and inflammatory cell infiltration, and increased tubular injury score. However, SMA/CORM2 significantly reversed this phenomenon. At the same time, we also evaluated the intervention effect of CORM2, as shown in **Figures 2A-D**. Although CORM2 can improve the decrease of

kidney weight, renal coefficient, serum creatinine (Cr) and blood urea nitrogen (Bun) induced by CsA in male rats, it was less effective than SMA/CORM2. As shown in **Figures 2E-F,** CORM2 also had a lower protective effect than SMA/CORM2 on tubular structure.

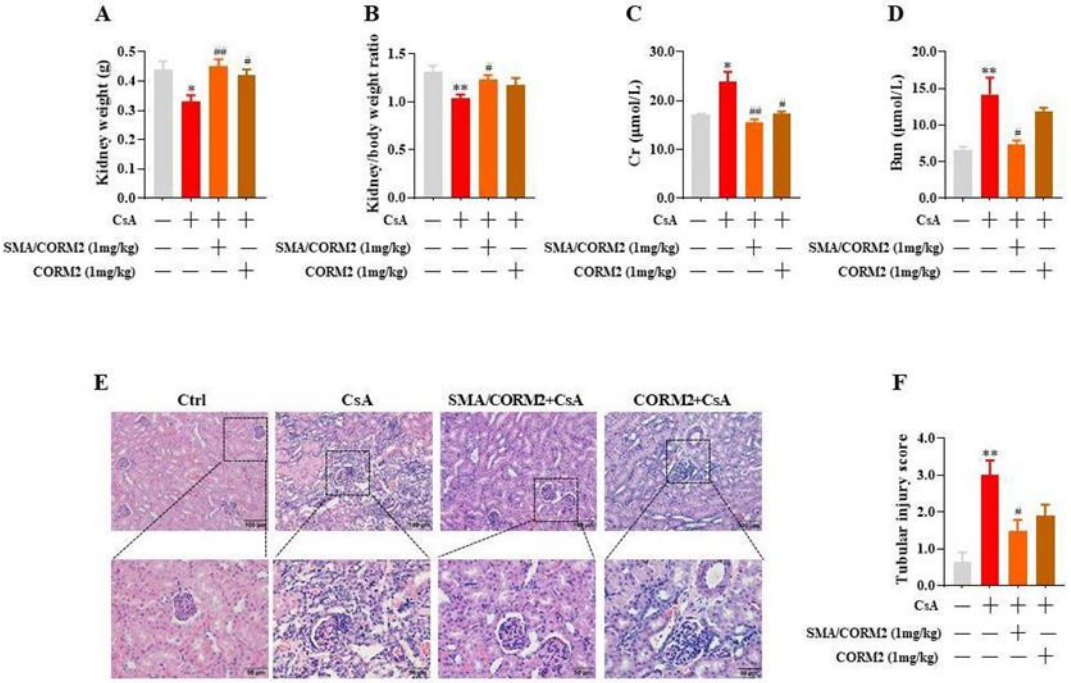

Figure 2. Renal pathological and histological changes after CsA treatment and the protective effect of SMA/CORM2 on renal injury. (A) Kidney weight 24 h after the last infusion of CSA, (B) Kidney/body weight ratio, (C) Serum creatinine, (D) blood urea nitrogen, (E) H&E staining for histological evaluation of the kidneys, (F) tubular injury score to evaluate the pathological changes of the kidneys. *P<0.05, **P<0.01 vs control group; #P<0.05, ##P<0.01 vs CsA group. The results were expressed by mean ± standard error, $n \geq 4$.

3.2. CO content in different tissues after SMA/CORM2 treatment

To further confirm whether the protective effect of SMA/CORM2 is caused by CO and to verify its slow release and high bioavailability, we examined the rate of release of CO of SMA/CORM2 in different solvents under different conditions. As shown in **Figure 3A**, when SMA/CORM2 was dissolved in PBS with DMSO as the solvent, less than 10% of CO was released at 48 h. Within 2h after the 48 h, SMA/CORM2 had released more than 80% of CO. When SMA/CORM2 was dissolved in tissue homogenates or serum, the release of CO increased slightly (~20%) within 24 h. The release of CO within 48 h reached 60%–80%, which was consistent with our previous studies. This confirmed that the formation of SMA/CORM2 micelles can ensure the slow and stable release of CO. Next, we examined the distribution of CO *in vivo* after SMA/CORM2 intervention in a CsA-induced renal fibrosis model. As shown in **Figure 6B**, the amount of CO in the CsA-treated mice was slightly higher than that in the control group, which was due to the upregulation of HO-1 during validation. In addition, SMA/CORM2 treatment increased the concentration of CO in serum in vivo, and increased CO was also found in kidney tissues and increased CO in liver tissues, but no significant difference was found (FIG. 3B). In summary, SMA/CORM2 can target the accumulation of CO in inflammatory tissues and release CO, thus playing a protective role in injured tissues.

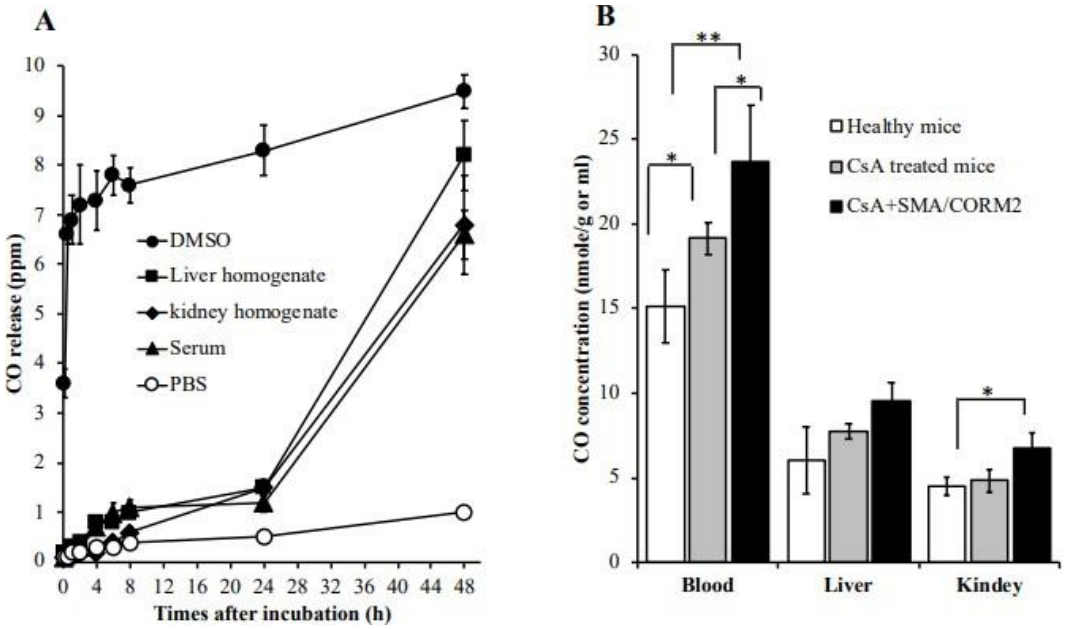

Figure 3. The amount of CO in different tissues after SMA/CORM2 treatment. (A) CO release; SMA/CORM2 was dissolved in different solvents and CO release was measured using gas chromatograph. (B) CO concentration; CsA-induced renal fibrosis model mice were killed 24h after the last injection of CsA. Blood and liver and kidney tissues were collected, 0.4ml PBS was added to every 100 mg of tissue, homogenized by a homogenizer, 0.5ml homogenated tissue and 0.2ml saponin were taken, incubated at room temperature for 24h, and then detected by gas chromatography for quantitative analysis. The control group was the content of CO in normal healthy mouse tissues. SMA/CORM2 alleviates CSA- induced renal fibrosis by inhibiting TGF-β/Smad signaling pathway. *$P < 0.05$, **$P < 0.01$ vs control group; #$P < 0.05$, ##$P < 0.01$ vs CsA group. The results were expressed by mean ± standard error, $n \geq 4$.

Based on the relief of renal toxicity and kidney injury caused by CsA by SMA/CORM2, we will focus on the influence of SMA/CORM2 on CSA-induced renal fibrosis and its mechanism in the following studies. As shown in **Figure 4A-B**, the results of Masson staining showed significant deposition of collagen fibers in the kidney of mice treated with CsA, while SMA/CORM2 intervention significantly reduced the area of renal fibrosis. The protein levels of α-SMA and Col, typical markers of renal fibrosis, were significantly increased after CsA treatment, while SMA/CORM2 almost completely suppressed this trend (**Figures 4C, 4G, and 7H**), which were consistent with the results of Masson staining. In terms of its mechanism, we focused on the TGF-β/Smad signaling pathway and detected the protein levels of TGF-β1, p-Smad2/3, and Smad2/3 in the renal tissue. The results showed that TGF-β1 and p-Smad2/3 protein levels significantly increased after CsA treatment, while SMA/CORM2 intervention significantly inhibited this trend (**Figure 4C-F**). These results suggest that the TGF-β/Smad pathway is a potential mechanism by which SMA/CORM2 inhibits CsA-induced renal fibrosis.

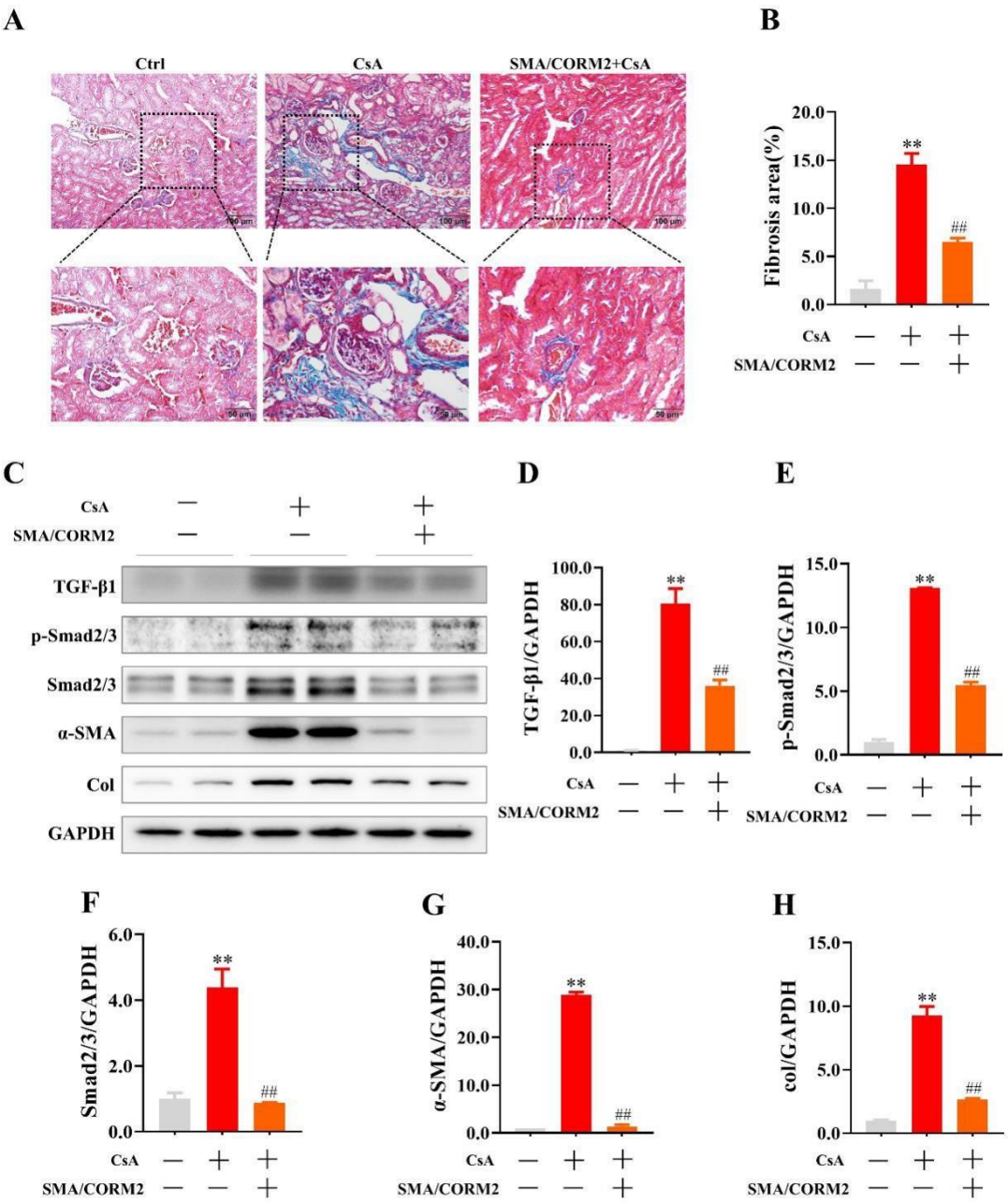

Figure 4. SMA/CORM2 alleviates CsA-induced renal fibrosis by inhibiting TGF-β/Smad signaling pathway. (A) Collagen fiber deposition was observed by Masson staining of renal tissue to assess the degree of renal fibrosis, (B) Quantification of renal fibrosis area, (C) TGF-β/Smad signaling pathway and fibrosis-related protein expression, such as TGF-β1, p-Smad2/3, Smad2/3, α-SMA and Col, (D–H) quantitative analysis results. **P* < 0.05, **P < 0.01 vs control group; #*P* < 0.05, ##*P* < 0.01 vs CsA group. The results were expressed by mean ± standard error, $n \geq 4$.

4. Discussion

Renal fibrosis is the destruction of renal structure and function caused by various reasons, which leads to the instability of renal structure, abnormal accumulation of extracellular matrix, and the production of a large amount of fibrotic protein, and ultimately leads to the loss of renal function and irreversible end-stage renal failure. The *NLRP3* inflammasome is a pattern recognition receptor whose membrane receptors are activated by the intracellular serine protease. Serine protease activator 1 can promote the expression of serine protease activator 3 in the nucleus, thereby inhibiting its activity and thus playing an anti-inflammatory role. Mas1 also binds to the serine protease activator 1 receptor to play an anti-inflammatory role. Therefore, activation of *NLRP3* inflammasome is an important cause of renal inflammatory response

and renal fibrosis, which means that blocking the activation of *NLRP3* inflammasome can effectively relieve the CsA-induced renal fibrosis.

One of the key issues in drug development is the targeted delivery of the active ingredient of the drug to the diseased tissue (API). In many targeted studies, nanomaterials based on the enhanced permeability and retention effect (EPR effect) in the inflammatory tissue have received much attention and are considered as a valuable research method [6,7]. EPR effect is a common phenomenon in tumor and inflammatory tissues. Compared to normal blood vessels, the blood vessels in tumors and inflammatory tissues have higher vascular permeability. Therefore, macromolecules with molecular weight greater than 40–50 kDa or nanomaterials larger than 5–10 nm cannot pass through normal tissues but can accumulate in the blood vessels of tumors and inflammatory tissues. This phenomenon is called "passive targeting." So far, the EPR effect has been demonstrated not only in animal tumors, but also in human tumors. Based on this property of EPR effect, many nanodrugs, especially anti-cancer nanodrugs targeting tumors, have been developed, some of which have been approved and applied clinically, while others are still undergoing clinical trials. Although most studies based on the EPR effect are focused on cancer, we should also note that inflammatory tissue has similar properties to tumor blood vessels. In fact, the EPR effect was discovered by studying bacterial infections, so targeted nanomaterials using the EPR effect could also be applied to inflammatory diseases [8-10]. In our previous studies, we found the therapeutic potential of nano-designed drugs in inflammatory diseases, including colitis induced by sodium glucoside sulfate (DSS) in mice, repeated perfusion loss in liver ischemia, hypertension, and acetaminophen (APAP) induced liver injury [10-15].

5. Conclusion

This study found that the nano-sustained-CO releasing molecule (CS-CO) has a strong protective effect on the kidney; HK-2 cells and RTECs were treated with siRNA and inhibitors in *NLRP3* knockout mice, and the changes in cell activity and expression of intracellular inflammatory factors were detected. The expression of TGF-β1/Smad signaling pathway related proteins in HK-2 cells and RTECs were detected by ELISA, western blot, immunofluorescence, and other techniques.

Funding

This project was funded by Health Commission of Hebei Province Chuanxiong: Extract Improves Inflammatory Response in Rats with Pyelonephritis through IL-6/STAT3 Signaling Pathway (Project number: 20231486)

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

Risk Factors of Neonatal Medical Adhesive-Related Skin Injury and Management of High-Risk Nodes

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Abstract: *Objective:* To analyze the risk factors of neonatal medical adhesive-related skin injury and put forward targeted preventive measures, so as to provide reference for the care and prevention of neonatal medical adhesive-related skin injuries. *Methods:* Using the convenience sampling method, 262 neonates admitted to the neonatal intensive care unit (NICU) of a tertiary general hospital in Wenzhou from April 2021 to May 2022 were selected as the study subjects. The incidence of medical adhesive-related skin injuries in these neonates was retrospectively analyzed. *Results:* Among the 262 children, 43 cases had skin injuries, with an incidence rate of 16.4%. Single factor analysis showed that the occurrence of medical adhesive-related skin injury was related to gestational age, weight, electrocardiogram (ECG) monitoring, venous access, ambient temperature, and mechanical ventilation ($P < 0.05$). Multivariate logistic regression showed that gestational age, ECG monitoring, and ambient temperature were independent risk factors of medical adhesive-related skin injury (OR values were 0.700, 0.431, and 6.365, respectively). *Conclusion:* The high incidence of neonatal medical adhesive-related skin injury may be caused by one or more factors. Clinical measures should be taken, such as selecting the appropriate type of adhesive according to gestational age and using skin-protecting membrane, minimizing ECG monitoring, *etc*., to prevent the occurrence of neonatal medical adhesive-related skin injury.

Keywords: Newborn; Medical adhesive; Skin injury; Risk factor

Online publication: May 31, 2023

1. Introduction

Medical adhesive-related skin injury (MARSI) refers to skin abnormalities, such as persistent erythema lasting for more than 30 minutes, with or without blisters, erosion, or tearing, that occur after the removal of medical adhesives [1]. Newborns, especially premature infants, are at high risk of skin injury due to their thin skin and weak adherence between the epidermis and dermis. Currently, adhesive products are widely used in neonatal clinical care. Studies have shown that MARSI is the main cause of skin injury in neonatal intensive care units (NICUs), with a prevalence rate of approximately 8%–17% [2,3]. MARSI not only causes pain to the infants, but also prolongs hospitalization. Consequently, the prevention and reduction of MARSI in neonates, as clinical challenges, have become the focus of attention. The aim of this study was to examine the factors that contribute to MARSI in newborns and suggest specific measures for effective management in hope to provide some reference for the prevention and management of MARSI in neonatal care settings.

2. Materials and methods

2.1. General information

A total of 262 newborns admitted to our department from April 2021 to May 2022, including 150 male infants and 112 female infants, were included in this study.

Inclusion criteria: (i) currently or previously using medical adhesives; (ii) age ≤ 28 days; (iii) no skin injury on admission; (iv) good rapport between the healthcare team and the family and no unresolved medical disputes. The family members were informed and willing to participate voluntarily.

Exclusion criteria: congenital skin diseases, such as epidermolysis bullosa.

2.2. Methods

2.2.1. Survey and statistical methods

(i) Based on literature review [5-10], a standardized questionnaire (gender, gestational age, weight, length of hospital stay, skin edema, gastric tube placement, electrocardiogram [ECG] monitoring, blue light therapy, ambient temperature, type of adhesive, mechanical ventilation, and intravenous access) was developed. (ii) Using the retrospective case study method, two trained members of the research team reviewed the cases, recorded the data obtained from the standardized questionnaire, and entered the relevant data into a computer. Statistical analysis was conducted using SPSS. (iii) Depending on the occurrence of MARSI, the subjects were divided into two groups: an observation group and a control group. MARSI occurred in 43 cases, while the remaining 219 cases had no MARSI. Comparison of baseline data between the two groups showed no significant difference ($P > 0.05$). (iv) Univariate analysis was first performed on the observation group, followed by binary logistic regression analysis to determine the significant risk factors.

2.2.2. Diagnosis of MARSI

MARSI was diagnosed when the skin showed abnormalities, such as persistent erythema for at least 30 minutes after the removal of medical adhesives, with or without blisters, erosion, or tearing. It can be classified into four types: erythema, blisters, erosion, and tearing.

2.3. Statistical analysis

SPSS 21.0 was used for statistical analysis. Count data were analyzed using chi-square test, and measurement data were analyzed using t-test. Multivariate logistic regression analysis was performed to analyze the significant factors identified by univariate analysis. $P < 0.05$ indicates statistically significant difference.

3. Results

3.1. Incidence of MARSI

Among the 262 newborns, 43 had skin injuries, with a total of 84 occurrences, and the overall incidence rate was 16.4%. The types of injuries were mechanical injuries in 71 cases (84.52%), contact dermatitis in 9 cases (10.71%), skin infiltration in 3 cases (3.57%), and folliculitis in 1 case (1.19%). Among them, epidermal abrasions were the most common type of mechanical injury, accounting for 59.15% (42 occurrences), while tension injuries and skin laceration injuries accounted for 23.94% (17 occurrences) and 16.90% (12 occurrences), respectively. The types of adhesives that caused skin injuries were electrode pads in 14 cases (16.67%), transparent dressings in 34 cases (40.47%), elastic foam tapes in 20 cases (23.81%), 3M pressure-sensitive tapes in 11 cases (13.10%), ConvaTec patches in 5 cases (5.95%), and silicone tapes in 0 cases (0%).

3.2. Univariate analysis of MARSI in newborns

Table 1 shows the univariate analysis of MARSI in newborns. The results showed significant differences ($P < 0.05$) between the two groups of newborns in terms of gestational age, weight, intravenous access, ECG monitoring, ambient temperature, and mechanical ventilation.

Table 1. Univariate analysis of neonatal medical adhesive-related skin injury in NICU (n = 262)

Item	MARSI		Test statistics	*P*
	Yes (n = 43)	No (n = 219)		
Gender (n/%)			1.488[1]	0.222
Male	21 (48.84)	129 (58.90)		
Female	22 (51.16)	90 (41.10)		
Gestational age (w)	36.86 ± 2.848	35.30 ± 3.872	2.494[2]	0.013
Weight (g)	3,484.09 ± 494.631	3,033.96 ± 935.495	3.054[2]	0.002
Length of hospital stay	22 (10, 46)	34 (18,60)	1.946[3]	0.052
Ambient temperature	28 (27,29)	30 (29,32)	6.343[3]	＜0.01
Edema (n/%)			3.391[1]	0.066
Yes	16 (37.21)	52 (23.74)		
No	27 (62.79)	167 (76.26)		
Blue light therapy (n/%)			1.637[1]	0.201
Yes	13 (30.23)	89 (40.64)		
No	30 (69.77)	130 (59.36)		
Mechanical ventilation			10.982[4]	0.012
None	19 (44.19)	120 (54.79)		
Non-invasive ventilation	13 (30.23)	65 (29.68)		
Tracheal intubation	7 (16.28)	8 (3.65)		
High-flow nasal cannula	4 (9.30)	26 (11.88)		
Indwelling gastric tube			1.566[1]	0.211
Yes	13 (30.23)	47 (21.46)		
No	30 (69.77)	172 (78.54)		
Dry skin			1.194[1]	0.660
Yes	5 (11.63)	31 (14.16)		
No	38 (88.37)	188 (85.84)		
Intravenous access			14.786[1]	0.002
None	12 (27.91)	103 (47.03)		
Peripherally inserted central catheter	9 (20.93)	12 (5.48)		
Umbilical vein catheter	5 (11.63)	15 (6.85)		
Peripheral intravenous line	17 (39.53)	89 (40.64)		
Electrocardiogram monitoring			4.846[1]	0.028
Yes	14 (32.56)	39 (17.81)		
No	29 (67.44)	180 (82.19)		

Notes: [1]Chi-square value; [2]t-value; [3]Z-value; [4]Corrected chi-square test

3.3. Multivariate logistic regression analysis of MARSI

3.3.1. Variable assignment

Binary logistic regression analysis was performed, with the occurrence of neonatal medical adhesive-

related skin injury as the dependent variable and the suspected risk factors derived from univariate analysis as the independent variables. The values of the respective variables are shown in **Table 2**.

Table 2. Assignment of independent variables

Influencing factors	Variable	Assignment
MARSI	Y	No MARSI = 0, MARSI occurred = 1
Gestational age	X1	Input of original values
Body weight	X2	Input of original values
Ambient temperature	X3	Input of original values
Intravenous access	X4	None = 0, PICC = 1, Umbilical vein catheter = 2, Peripheral intravenous catheter = 3
ECG monitoring	X5	No = 0, Yes = 1
Mechanical ventilation	X6	None = 0, Non-invasive ventilation = 1, Endotracheal intubation = 2, High-flow nasal cannula = 3

3.3.2. Multivariate regression analysis

The results of multivariate regression analysis showed that gestational age, ambient temperature, and ECG monitoring were independent risk factors of MARSI in newborns, as shown in **Table 3**. The predictive accuracy of the three factors was 87% (> 60%), indicating that the analysis has high accuracy and practical value. This is shown in **Table 4**.

Table 3. Logistic regression analysis of neonatal MARSI

Variables	Regression coefficient	Standard error	Waldχ2 value	*P*-value	Odds ratio	95% confidence interval
Constant	0.422	6.939	0.004	0.951	1.525	
Gestational age	-0.356	0.123	8.382	0.004	0.700	0.550–0.891
Ambient temperature	0.359	0.145	6.106	0.013	1.431	1.077–1.902
Electrocardiogram monitoring	1.851	0.517	12.818	< 0.01	6.365	2.311–17.531

Table 4. Multivariable logistic regression analysis

Actual		Prediction		Percentage of correct predictions (%)
		MARSI		
		None	Occurred	
MARSI	None	209	10	95.4
	Occurred	24	19	44.2
Overall percentage				87.0

4. Discussion

4.1. Analysis of risk factors of MARSI in newborns

4.1.1. Effects of gestational age on MARSI in newborns

The results showed that gestational age is an independent but protective factor of MARSI in newborns (regression coefficient = -0.356, < 0). The larger the gestational age, the lower the risk of MARSI in newborns. The stratum corneum of fetuses matures at 30–32 weeks, and premature infants, especially those born before 30 weeks, have a thinner stratum corneum and weaker skin barrier, making them more

susceptible to skin injuries from tension or friction [3,11]. Therefore, it is necessary to be cautious when using adhesives in premature infants. Silicone tapes can be considered as an alternative to reduce skin injuries.

4.1.2. Effects of electrocardiogram monitoring on MARSI in newborns

The results showed that the probability of MARSI in newborns without ECG monitoring is only 15.7%, indicating a 6.37 times higher risk for newborns with ECG monitoring. Hydrogel is the type of adhesive type used in ECGs. It increases in adhesiveness over time and is prone to cause skin injuries in newborns. Therefore, we recommend to minimize ECG monitoring and use skin protective sprays to reduce skin injuries caused by hydrogel adhesives. In addition, regular replacement of adhesives could prevent prolonged adhesive contact with the skin in a specific area.

4.1.3. Effects of ambient temperature on MARSI in newborns

The results showed that ambient temperature is an independent factor of MARSI in newborns, where an increase in ambient temperature by 1°C could increase the incidence of MARSI by 1.43 times. This finding is consistent with the research of Wang *et al*. [12]. The adhesiveness of adhesive increases with temperature, possibly due to the softening of the adhesive and the filling of gaps between the adhesive and skin surface in high temperature. Additionally, higher ambient temperature leads to increased water loss and decreased skin elasticity, thereby increasing the risk of skin injuries. Therefore, it is recommended to keep newborns in a lower ambient temperature while maintaining their body temperature to reduce the effects of temperature on adhesives.

4.2. Characteristics and preventive measures of MARSI in neonates

4.2.1. Characteristics of MARSI in neonates

According to the findings of this study, the incidence of MARSI in neonates was 16.4%, which is consistent with previous local and foreign research [2, 11-12]. Mechanical injury is the primary cause of MARSI in neonates, accounting for 76.74% of cases. Epidermal stripping, in particular, is the most common form of injury, which may be attributed to the unique characteristics of neonatal skin. The connection between the epidermis and dermal layer primarily relies on fiber connections, and since neonates possess fewer fibers, the connection is not as tight. Hence, the binding strength between the adhesive and the epidermis is much greater than that between the epidermis and the dermis, making neonatal skin particularly vulnerable. In addition, neonates, especially premature infants, are known to have weak skin barrier, characterized by immature stratum corneum, greater exposure of the epidermis, increased loss of moisture, reduced elastic fibers, and heightened tendency toward edema. Poor techniques while removing adhesives are highly likely to cause epidermal stripping. Therefore, in clinical practice, it is crucial to apply high-risk node management based on the intrinsic skin characteristics of neonates and the factors that contribute to the occurrence of MARSI.

4.2.2. Management of high-risk nodes

4.2.2.1. Management of high-risk populations

Our research findings revealed that the smaller the gestational age, the higher the incidence of MARSI. Therefore, there is a need to strengthen the management of high-risk nodes for premature infants. For neonates with gestational age of less than 30 weeks, appropriate temperature and humidity-controlled warmers as well as transparent adhesive dressings should be used to reduce heat loss and water evaporation. Applying moisturizers can also reduce surface dryness of the skin and improve skin barrier. Prior to the use of adhesive products, skin protectants without alcohol are recommended for protection [13]. Applying a mixture of 0.9% sodium chloride injection and antibacterial aloe vera gel to the adhesive tape or a special

adhesive remover can reduce the incidence of MARSI in premature infants [14,15].

4.2.2.2. Management of product nodes

In this study, we found that the most common type of adhesive causing skin injury is transparent dressing, followed by elastic, soft, and wide tape. The adhesives used in these two types of products, as well as pressure-sensitive tape, are acrylic resins [16]. They have good initial adhesion, strong skin adhesion, and strong water resistance, rendering them suitable for fixing catheters and needles. However, their repeated use may cause skin injury. The results showed that the incidence of MARSI in neonates caused by pressure-sensitive tape was lower. This may be due to the fact that pressure-sensitive tape is commonly used for auxiliary fixation of blood oxygen saturation probes, skin temperature probes, and indwelling needles in clinical practice, all of which have a short duration of use. On the other hand, transparent dressings are commonly used to fix intravenous lines, while elastic, soft, and wide tapes are commonly used for tracheal intubation and to fix gastric tubes, all of which the duration of use is longer, thus increasing the adhesiveness over time. The results also showed that the use of silicone tape does not lead to MARSI. Silicone tape has mild and long-lasting adhesion, does not stick to hair, and can be reused. Its emphasis is in the gel itself, which can minimize skin damage [17]. However, it is less resistant to moisture than acrylic resins and rubber. Considering that it has lower adhesion and is expensive, its use is not recommended for the fixation of important lines [18]. The selection of appropriate medical adhesive products in clinical settings should be based on individual needs and the scenario for which the adhesive will be used.

4.2.2.3. Management of training nodes

Zhang *et al*. [15] emphasized the importance of providing training and education to healthcare workers on neonatal MARSI. Several studies have shown that the theoretical and operational knowledge of nurses regarding MARSI are at a relatively low level [19-21]. Most nurses have not received relevant training on skin care, are unaware of the importance of preventing MARSI, and have different methods for handling MARSI. Therefore, it is necessary to strengthen the theoretical and operational training of healthcare workers in neonatal departments, improve their ability to identify high-risk infants with MARSI, and standardize the methods for applying and removing adhesive tapes. For instance, before using adhesive products, appropriate skin protectants should be used; during application, the aseptic principle should be adhered to, with local skin kept clean and dry and the tape applied without tension and properly molded. When removing adhesive products, the tape should be removed at 0° or 180° in the direction of hair growth, using gentle movements, and if necessary, an adhesive remover [22].

5. Conclusion

In conclusion, the incidence of MARSI in newborns is high, and gestational age, ambient temperature, and ECG monitoring are independent factors that affect MARSI. Clinical training on MARSI-related knowledge and awareness in preventing MARSI in newborns should be strengthened for healthcare workers. Suitable medical adhesive tapes should be selected based on gestational age, and appropriate ambient temperature should be maintained. Learning the correct techniques of applying and removing adhesive tapes is also important, so as to reduce the incidence of MARSI in newborns.

In short, it is necessary to strengthen clinical measures to prevent and reduce the incidence of MARSI in newborns, so as to improve their quality of life and health status.

Funding

This work was supported by the Basic Medical and Health Technology Project of Wenzhou Science and Technology Bureau (Y20190308).

Disclosure statement

The authors declare no conflict of interest.

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Journal of Clinical and Nursing Research, 2023, Volume 7, Issue 3
http://ojs.bbwpublisher.com/index.php/JCNR
ISSN Online: 2208-3693
ISSN Print: 2208-3685

The Clinical Value of Detecting the Level of Exfoliated Cells in Pleural Effusion by Flow Cytometry in the Differential Diagnosis of Non-Small Cell Lung Cancer and Benign Lung Diseases

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Abstract: *Objective:* To explore the value of flow cytometry (FCM) in detecting the level of exfoliated cells in pleural effusion in the differential diagnosis of non-small cell lung cancer and benign lung diseases. *Methods:* Clinical data of patients with non-small cell lung cancer who were hospitalized in Hebei hospital from June 2019 to March 2022 were collected. A total of 98 patients were included, and 63 patients with alveolar lung disease were screened during the same period, and the two groups of patients were analyzed. *Results:* Compared with alveolar lung disease group, FCM detection and analysis showed that the level of exfoliated cells in the pleural effusion of non-small cell lung cancer (NSCLC) patients was 99 (3-969)/100,000, and patients with alveolar lung disease was 4 (0 ~ 19)/100,000. Additionally, compared with the alveolar lung disease group, the level of exfoliated cells in the pleural effusion of patients with non-small cell lung cancer (NSCLC) was significantly increased (P<0.001). The diagnostic efficacy of FCM for detecting pleural fluid exfoliated cells in non-small cell lung cancer was assessed using ROC curves and using 95% CI (-11.1, -13.2) with a sensitivity of 0.75 and specificity of 0.94, and the diagnostic efficacy of FCM for detecting pleural fluid exfoliated cells in alveolar lung disease was assessed using 95% CI (-11.1, -13.2) with a sensitivity of 0.71 and specificity of 0.87. *Conclusion:* Flow cytometry has a wider range of clinical applications, simple operation, low cost, and high sensitivity, which makes it of great significance in disease diagnosis.

Keywords: Flow cytometry detection; Non-small cell lung cancer; Benign lung disease

Online publication: May 31, 2023

1. Introduction

Lung cancer is a disease with highest morbidity and mortality rates among malignant tumors in the world. Because lung cancer has no obvious symptoms in the early stage, it is easy to be misdiagnosed as pneumonia or other lung diseases. Therefore, early and accurate diagnosis has a great impact on the prognosis of patients. As a routine inspection item for lung cancer patients, the examination of pleural effusion exfoliated cells is great significance. The detection of pleural effusion exfoliated cells is an important diagnostic index in the diagnosis and treatment of lung cancer, especially in patients with non-small cell lung cancer (NSCLC). When the cells are negative for tumor markers, their diagnostic value is greater. Although the level of pleural fluid exfoliated cells is low in lung cancer, it may become continuously elevated as the tumor progresses. As one of the main differentiating markers between malignant and non-malignant tumors, it is important for postoperative efficacy assessment, recurrence monitoring, and prognosis judgment of NSCLC patients. However, currently the most commonly used clinical detection methods are pleural

effusion cytology examination, chest CT examination, etc., but they have certain limitations. In recent years, flow cytometry (FCM) has become a research hotspot in disease diagnosis. It has the advantages of high cell count, rapidity and high sensitivity, and has good application value. In lung cancer, FCM can show the cellular differences between NSCLC and alveolar lung disease (Pulmonary bullous disease), but the diagnostic value is still unclear for the identification of NSCLC and alveolar lung. This study retrospectively analyzed the level of exfoliated cells in pleural effusion of patients with NSCLC, explored its value in the differential diagnosis of NSCLC and benign lung diseases, and provide new information for clinicians in the diagnosis and treatment of lung cancer and benign lung diseases. The ideas and methods have a certain guiding significance.

2. Materials and methods

2.1. Study subjects

Clinical data of patients with NSCLC who were hospitalized in Hebai hospital from June 2019 to March 2022 were collected. The age range of the patients was 35-80 years old, and the median age was 59 years old. A total of 98 patients were included, including 63 males and 35 females, and all cases were diagnosed as NSCLC by histopathology. A total of 63 patients with concurrent alveolar lung disease were screened, including 39 males and 24 females.

2.2. Methods

Immunohistochemical staining was used to detect exfoliated cells in pleural effusion in lung cancer tissues. FCM reagent was provided by Sigma Company in the United States. The concentration of the antibody was fixed at 1:100, washed with 10% neutral buffer, and the target cells was detected by FCM. The optical density of tumor cells was detected using DAPI chromogenic kit.

2.3. Statistical method

All the data in this study were processed by SPSS 22.0 statistical software. The measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), expressed by t test, and the adoption rate (%) of enumeration data was expressed by chi-square (χ^2) test.

3. Results

3.1. Analysis of FCM test results

FCM detection and analysis showed that compared with the alveolar lung disease group, the level of exfoliated cells in the pleural fluid of patients with NSCLC was 99(3-969)/100,000, while the level of exfoliated cells in the pleural fluid of the alveolar lung disease group is 4(0-19)/100,000. Compared with the alveolar lung disease group, the level of exfoliated cells in the pleural effusion of patients with NSCLC was significantly increased. The independent sample t-test was used to compare the level of exfoliated cells in the pleural fluid of NSCLC and alveolar lung disease, $P<0.001$, as shown in **Table 1.**

3.2. Efficiency of FCM in detecting exfoliated cells in pleural effusion

The diagnostic efficacy of FCM for detecting pleural fluid exfoliated cells in NSCLC was assessed using ROC curves and using 95% CI (-11.1, -13.2) with a sensitivity of 0.75 and specificity of 0.94, and the diagnostic efficacy of FCM for detecting pleural fluid exfoliated cells in alveolar lung disease was assessed using 95% CI (-11.1, -13.2) with a sensitivity of 0.71 and specificity of 0.87 (**Table 1**).

Table 1. Efficiency of FCM in detecting exfoliated cells in pleural effusion

Group	Sensitivity	Specificity	95% CI
NSCLC	0.75	0.94	(-11.1, -13.2)
Alveolar lung disease	0.71	0.87	(-11.1, -13.2)

4. Discussion

Lung cancer is a disease with highest incidence rate among malignant tumors. About 400,000 people die due to lung cancer every year world-wide, and more than 500,000 people are diagnosed with lung cancer every year. In China, there are about 300,000 new cases of lung cancer reported every year, and it has the highest incident rate of lung cancer world-wide. At present, NSCLC accounts for about 50% of all malignant tumors, and has high degree of malignancy with poor prognosis. Due to the lack of specificity in clinical manifestations and the high invasiveness of NSCLC, it is easy to misdiagnose this disease, therefore early diagnosis is the key to improve the efficacy and prognosis. Exfoliated cytology of pleural effusion is currently a commonly used diagnostic method in clinical practice, but this method is easily affected by other diseases such as pleura, pleural effusion, and other factors. Therefore, it is necessary to improve the diagnostic rate clinically by combining clinical and other examinations methods [1-6]. Single or smaller alveoli will show no signs, chest tightness, shortness of breath, and dyspnea mainly in larger volumes or multiple large pulmonary alveoli. If there is shortness of breath, cough, dyspnea, cyanosis, movement of the trachea and mediastinum, and sensation of tinnitus, it should be a spontaneous pneumothorax. Lung holes of different sizes can be seen under X-ray, and transparent holes of different degrees can be seen, but it is different with lung sac and spontaneous pneumothorax. CT scan is a significance method for the identification of these two. In addition, in an epidemiological study of lung cancer, 0.19% of men with emphysema did not develop overly large emphysema, while 6.1% of patients had large air bubbles.

Pleural effusion exfoliated cells are one of the common cell components in lung cancer, and their content in lung cancer is very low, about $2\sim5\times10^9$ /mL. Although a large number of studies have shown that exfoliated cells in pleural effusion can reflect changes in lung tissue cells, their differential diagnosis value for lung cancer and benign lung diseases is still unclear. The sensitivity of pleural effusion exfoliated cells in the diagnosis of lung cancer is 75% to 90%, and the specificity is 98% to 100%, but the sensitivity and specificity are both low. Therefore, it is essential to improve the detection value of exfoliated cells in pleural effusion to improve the detection rate of lung cancer. FCM is currently the most widely used cytological detection technique, which can simultaneously display the characteristics and status of various malignant tumor cells [7-9]. Pulmonary cyst is a common benign lesion, which mostly occurs in infants and adolescents, and with the highest incidence in children. Cystic lesions are composed of different fluids and commonly found in parabronchial cysts, followed by endobronchial cysts. Cystic lesions can be divided into various types according to the liquid composition in the cyst, such as hydration cystic cyst, fat cystic cyst, etc. However, these types of diagnosis depend on the fluid composition in the cyst, such as cells, lipid particles, and various tissue fragments in the cyst fluid, therefore it is difficult for diagnosis. The results of detecting exfoliated cells in pleural effusion by FCM showed that FCM has high sensitivity and specificity in detecting cystic lesions, and the detected patients were consistent with the pathological results. Therefore, we applied FCM to detect the level of exfoliated cells in the patient's pleural fluid, and by combining the clinical and pathological findings, it can provide an accurate diagnosis of pulmonary cysts. It plays an important role in the diagnosis of lung cysts.

Pleural effusion exfoliated cells are the most important cell components in lung cancer, which can reflect the postoperative curative effect of patients with NSCLC, especially play an important role in the judgment of pulmonary metastases. The results of this study showed that the level of exfoliated cells in

pleural effusion in the NSCLC group was significantly higher than in the alveolar lung disease group (P<0.05), and the level of exfoliated cells in the pleural effusion in the NSCLC group was higher than in the alveolar lung disease group (P<0.05). With the progression of the tumor, the exfoliated cells in the pleural effusion may continue to increase, suggesting that it has a certain value in the diagnosis and monitoring of NSCLC. The level of exfoliated cells in pleural effusion after lung cancer treatment can be used as one of the variables for clinical evaluation to determine the treatment effect, and it is essential for the selection of postoperative adjuvant therapy, prognosis judgment, and recurrence monitoring of lung cancer. This study showed that in the NSCLC group, the level of exfoliated cells in pleural effusion had no significant correlation with tumor stage, lymph node metastasis, TNM stage, and degree of differentiation; while in the alveolar lung disease group, the level of exfoliated cells in pleural effusion had no significant correlation with tumor stage and TNM stage (P>0.05).

In patients with NSCLC, the detection rate of pleural effusion exfoliated cells is low, and the positive rate is differed in different pathological types of lung cancer. At present, the detection of pleural effusion exfoliated cells is mainly based on the pleural effusion exfoliated cell detection card to determine whether the patient has pleural effusion. Although this examination can provide a certain reference value for clinical practice, it cannot be used as the only parameter for the diagnosis of NSCLC because it cannot fully reflect the cause, type, and source of pleural effusion. In addition, the detection of exfoliated cells in pleural effusion has certain limitations on the source of pleural effusion. If only relying on FCM to determine the source of pleural effusion exfoliated cells in patients with NSCLC, there will be a certain degree of missed diagnosis, so further research is needed to determine its accuracy in diagnosis [10-15].

FCM plays an important role in the clinical diagnosis of lung cancer, postoperative curative effect evaluation and prognosis judgment, but because it needs to use the advantages of optical microscopy, it also has certain limitations, therefore FCM has its limitations in clinical application, such as not directly reflecting the actual level and distribution of cells, having certain false positives or false negatives, having large differences in different testing sites for the same patient, only showing the distribution of cells, but not directly reflecting their proliferation and apoptosis status, etc. In addition, there are some limitations in the study: i. Different tumor pathological types and stages have different effects on the level of exfoliated cells in patients' pleural effusion; ii. Currently, there are false positive or false negative phenomena in the detection of pleural effusion exfoliated cells, which may be related to the staining protocol during the detection; iii. Different analytical methods used by different laboratories may lead to discrepancies in the results; and iv. Could not obtain enough sample from some patients, so the study should be conducted after expanding the sample size.

In conclusion, the advantages of wide range of clinical applications, ease of operation, low cost, and high sensitivity of FMC make it as an important tool in disease diagnosis.

Disclosure statement

The authors declare no conflict of interest.

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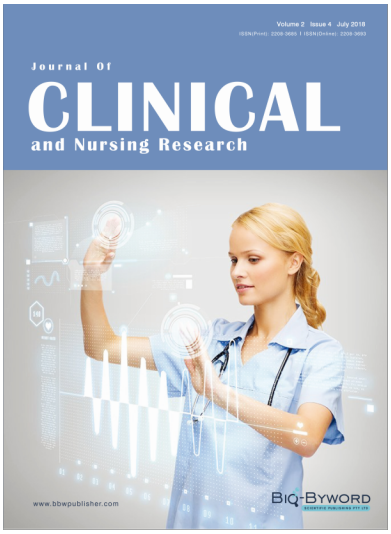

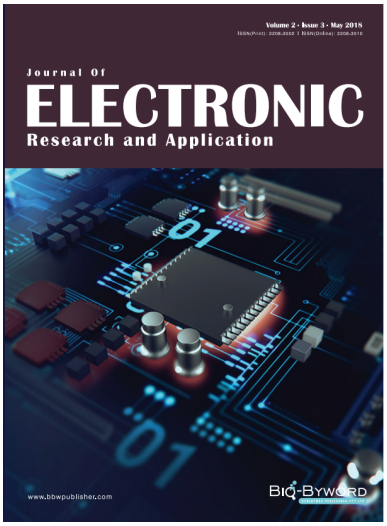

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- Electronic Materials
- Electronics and Communications Engineering
- Power Systems and Power Electronics
- Signal Processing
- Telecommunications Engineering
- Wireless and Mobile Communication