Urology Research

Editors-in-Chief

Arnold P. P. Achermann

University of Campinas, Brazil

Yunshan Zhang

Affiliated Hospital of Guangdong Medical University, China

BIO-BYWORD SCIENTIFIC PUBLISHING PTY LTD
(619 649 400)
Level 10
50 Clarence Street
SYDNEY NSW 2000
Copyright © 2024. Bio-Byword Scientific Publishing Pty Ltd.
Complimentary Copy

Urology Research

Focus and Scope

Urology Research publishes peer-reviewed research articles across basic, translational, and clinical Urology medicine. The Journal covers all aspects of Urology medicine (full listing below) with an emphasis on studies that challenge the status quo of treatments and practices in Urology care or facilitate the translation of scientific advances into the clinic as new therapies or diagnostic tools.

About Publisher

Bio-Byword Scientific Publishing is a fast-growing, peer-reviewed and open access journal publisher, which is located in Sydney, Australia. As a dependable and credible corporation, it promotes and serves a broad range of subject areas for the benefit of humanity. By informing and educating a global community of scholars, practitioners, researchers and students, it endeavors to be the world's leading independent academic and professional publisher. To realize it, it keeps creative and innovative to meet the range of the authors' needs and publish the best of their work.

By cooperating with University of Sydney, University of New South Wales and other world-famous universities, Bio-Byword Scientific Publishing has established a huge publishing system based on hundreds of academic programs, and with a variety of journals in the subjects of medicine, construction, education and electronics.

Publisher Headquarter

BIO-BYWORD SCIENTIFIC PUBLISHING PTY LTD
Level 10
50 Clarence Street
Sydney NSW 2000
Website: www.bbwpublisher.com
Email: info@bbwpublisher.com

2024, Volume 2, Issue 1

Table of Contents

Urology Research, 2024, Volume 2, Issue 1
https://ojs.bbwpublisher.com/index.php/UR

A Study on Pain Improvement Using Compound Diclofenac Sodium with Pethidine and Scopolamine in the Treatment of Acute Renal Colic

Weidong Wang*

Foresea Life Insurance Shaoguan Hospital, Shaoguan 512026, Guangdong Province, China

***Corresponding author:** Weidong Wang, werton@126.com

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To analyze the improvement effect of compound diclofenac sodium with pethidine and scopolamine on patients' pain in the treatment of acute renal colic. *Methods:* 360 patients with acute renal colic admitted from January 2022 to December 2023 were selected and divided into the control group and the observation group by double-blind method. The control group applied pethidine with scopolamine treatment and the observation group adopted the same treatment combined with compound diclofenac sodium. Comparison between the two groups was made in terms of pain improvement, the disappearance time of each symptom, as well as the treatment effect and adverse drug reactions. *Results:* The pain score of the observation group after treatment was lower than that of the control group, the disappearance time of each symptom was shorter than that of the control group, the total treatment effectiveness was higher than that of the control group ($P < 0.05$), and the difference in the incidence of adverse reactions between the two groups was not significant ($P > 0.05$). *Conclusion:* In the treatment of acute renal colic, the combined application of compound diclofenac sodium with pethidine and scopolamine can actively improve the pain symptoms and promote the disappearance of each symptom as early as possible, which is effective and has few adverse reactions.

Keywords: Acute renal colic; Compound diclofenac sodium; Pethidine; Scopolamine; Pain

Online publication: March 29, 2024

1. Introduction

Renal colic is a kind of acute abdominal disease with high morbidity, which is usually caused by spasm of ureteral smooth muscle or partial lumen obstruction due to certain diseases, and ureteral colic is the most common, i.e., it is probable that renal colic is triggered by ureteral stones [1]. Clinical treatment of acute renal colic commonly uses antispasmodic drugs, such as scopolamine, but a single drug is usually slower to take effect, and the side effects are more obvious. Thus, it is often combined with other drugs, such as scopolamine combined with pethidine. Pethidine belongs to the phenylpiperidine class of opioid analgesic drugs, a special

class of drugs that may cause drug dependence [2]. In order to maximize the drug efficacy, reduce the dosage, and control adverse effects, better treatment options need to be explored. Compound diclofenac sodium has antipyretic and analgesic effects, commonly used in the treatment of various febrile fevers, as well as acute gout, renal colic, and other painful diseases. In order to analyze the effect of the combination of compound diclofenac sodium with pethidine and scopolamine on the improvement of pain in patients with acute renal colic, a total of 360 cases were selected for evaluation.

2. General information and methods

2.1. General information

360 patients with acute renal colic admitted from January 2022 to December 2023 were selected and grouped into two groups of 180 cases by double-blind method. In the control group, there were 126 males and 54 females, aged 22–63 (48.24 ± 6.17) years old; onset to treatment time was 0.5–4 (1.91 ± 0.36) hours. In the observation group, there were 128 males and 52 females, aged 24–61 (48.45 ± 6.10) years old; onset to treatment time was 0.6–4 (1.89 ± 0.31) hours. The data of the two groups were compared and found no significant difference ($P > 0.05$).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) patients diagnosed with acute renal colic by imaging and other examinations, and it is the first-time onset; (2) patients with a stone of 1.2 cm or less in long diameter and 1.0 cm or less in short diameter; (3) patients meeting the indications for medication and having good medication adherence; (4) patients who cooperate to complete the assessment of the relevant scales; and (5) patients with complete general information.

Exclusion criteria: (1) patients with a combination of other serious somatic diseases, such as malignant tumors, liver and kidney failure, etc.; (2) patients with acute obstructive ureteral problems; (3) patients with a combination of psychiatric disorders, or presence of cognitive disorders; (4) patients who were in pregnancy or breastfeeding; and (5) patients with serious allergic reactions to the drug.

2.3. Methods

On the basis of conventional anti-infection and other treatments, the control group adopted the combined program of pethidine + scopolamine. It included an intramuscular injection of 100 mg of pethidine hydrochloride and an intramuscular injection of 5–10 mg of scopolamine hydrochloride.

Based on the treatment program of the control group, the observation group received an additional compound diclofenac sodium treatment, which was an intramuscular injection of 2 ml of compound diclofenac sodium.

2.4. Observation indicators

The below indicators were observed and compared between the groups:

(1) Improvement of pain symptoms: This was assessed by using the visual analog scale (VAS) [3], with 0–10 points, indicating no pain to most pain.

(2) Disappearance time of symptoms including fever, nausea, and vomiting.

(3) Treatment effect [4]: The symptoms of nausea and vomiting disappeared within one hour after the administration of the drug indicating that the treatment was “effective”; the symptoms were significantly improved within one hour after the administration of the drug, and the pain relief was more than 30%, indicating that the treatment was “highly effective”; the symptoms were improved but

did not completely disappear, and the pain relief was less than 30%, indicating that the treatment was "ineffective." The treatment is "ineffective" if the degree of pain relief is less than 30%. Total effective rate = 100% – Ineffective

(4) Adverse drug reactions including flushing, blurred vision, and so on.

2.5. Statistical methods

SPSS25.0 statistical software was used to analyze the data; measurement data in line with normal distribution used mean ± standard deviation (SD) and *t*-test; [n (%)] indicated the count data, χ^2 test; $P < 0.05$ indicated the data were statistically significant.

3. Results

3.1. Pain improvement

As shown in **Table 1**, the pain scores of the two groups of patients were higher before treatment, $P > 0.05$; and the pain scores of the observation group were lower than those of the control group when comparing the pain scores at 10 minutes, 30 minutes, and 60 minutes after treatment, $P < 0.05$.

Table 1. Pain score (mean ± SD, points)

Group	Cases (n)	Before treatment	10 minutes after treatment	30 minutes after treatment	60 minutes after treatment
Control group	180	7.96 ± 1.10	6.06 ± 1.23	4.15 ± 0.64	3.10 ± 0.26
Observation group	180	7.89 ± 1.17	4.18 ± 1.10	2.23 ± 0.56	1.19 ± 0.29
t	-	0.585	15.285	30.291	65.793
P	-	0.559	0.000	0.000	0.000

3.2. Disappearance time of each symptom

As presented in **Table 2**, the disappearance time of fever, nausea, and vomiting symptoms in the observation group was shorter than that in the control group, $P < 0.05$.

Table 2. The disappearance time of each symptom (mean ± SD, minutes)

Group	Cases (n)	Fever	Nausea	Vomiting
Control group	180	37.15 ± 6.26	21.05 ± 4.19	16.23 ± 3.35
Observation group	180	21.17 ± 5.20	13.34 ± 2.28	10.15 ± 2.27
t	-	26.345	21.685	20.158
P	-	0.000	0.000	0.000

3.3. Treatment effectiveness

As demonstrated in **Table 3**, the total treatment effectiveness of the observation group was higher compared to the control group, $P < 0.05$.

Table 3. Treatment effect [n (%)]

Group	Cases (n)	Ineffective	Effective	Highly effective	Total effective rate
Control group	180	41 (22.78)	43 (23.89)	96 (53.33)	139 (77.22)
Observation group	180	9 (5.00)	43 (23.89)	128 (71.11)	171 (95.00)
χ^2	-	-	-	-	23.783
P	-	-	-	-	0.000

3.4. Adverse reactions

As displayed in **Table 4**, the difference in the incidence of adverse reactions between the two groups was not significant compared to the incidence of adverse reactions in the two groups, $P > 0.05$.

Table 4. Adverse reactions [n (%)]

Group	Cases (n)	Flushing	Blurred vision	Drowsiness	Dry mouth	Total
Control group	180	2 (1.11)	1 (0.56)	2 (1.11)	1 (0.56)	6 (3.33)
Observation group	180	2 (1.11)	1 (0.56)	2 (1.11)	2 (1.11)	7 (3.89)
χ^2	-	-	-	-	-	0.080
P	-	-	-	-	-	0.778

4. Discussion

Acute renal colic is the onset of urinary tract obstruction due to urinary stones. Due to acute urinary tract obstruction, the pressure of the renal pelvis and ureter rises, leading to spasms of ureteral smooth muscle and then renal colic. The condition involves an increase in the amount of synthesis and release of prostaglandins in the kidneys, a decrease in renal vascular resistance, a decrease in the secretion of antidiuretic hormone, and a change in the volume of urine, which aggravates the degree of renal colic, and the renal pelvis and the ureter are compressed by the stones. Edema of the renal pelvis or ureter wall may occur, as well as smooth muscle ischemia problems, elevating inflammatory mediators and gradually increasing pain [5]. Acute renal colic requires prompt treatment to control pain symptoms, reduce smooth muscle spasms, and improve disease symptoms.

There are several methods in the clinical treatment of acute renal colic, such as intramuscular injection of pethidine hydrochloride, belonging to the opioid receptor agonist and categorized as a narcotic analgesic, which can activate the opioid system of the central nervous system, and then exert the analgesic effect. However, there is a risk of drug dependence, and due to the special type of drug, the actual use of the drug is more inconvenient. Intramuscular injection of scopolamine hydrochloride is also a common method of treating acute renal colic, the drug is more convenient to use, with a lower price and high clinical application rate [6], but the onset of its effect is slower and the effect of single-use is poor. Morphine offers a better analgesic effect and a rapid onset of action, but easily leads to respiratory depression, dizziness, and other adverse reactions. Additionally, because of its effect on sphincter contraction [7], it may lead to aggravated tubal or renal pelvic spasm, and urine and stone discharge is thus impeded, limiting its clinical application. Compound diclofenac sodium injection includes 25 mg diclofenac sodium and 0.15 g acetaminophen, of which diclofenac sodium belongs to a kind of phenylacetic acid derivatives, which is antipyretic and analgesic, with a more ideal anti-

inflammatory effect [8]. Compared with aspirin, the analgesic effect of diclofenac sodium is 26–50 times higher [9], with strong efficacy, fewer side effects, smaller individual variability, and no addiction. This component can competitively inhibit the cyclooxygenase in the metabolic pathway of arachidonic acid and control the conversion of arachidonic acid to prostaglandins, which decreases the body's nociceptive receptor sensitivity to inflammatory stimuli and increases the threshold of nociception [10], exerting the analgesic effect; and the other component, acetaminophen, also has a better analgesic effect. The result data in the article showed that the pain score of the observation group after treatment was lower than that of the control group, and the disappearance time of each symptom was shorter than that of the control group, indicating that the combined medication has a faster and better effect in improving the symptoms; and the observation group had a higher total treatment effective rate (95.00%) than the control group (77.22%), but there was not much difference in the adverse reactions of the two groups, which further proves that the combined treatment program has better effectiveness without affecting the safety of the medication.

5. Conclusion

In conclusion, the treatment of acute renal colic using compound diclofenac sodium with pethidine and scopolamine can positively improve pain symptoms with precise effects and few adverse effects.

Disclosure statement

The author declares no conflict of interest.

References

[1] Liu H, 2023, Effect of Compound Diclofenac Sodium Combined with Pethidine and Scopolamine in the Treatment of Patients with Acute Stone Renal Colic. Medical Journal of Chinese People's Health, 35(16): 21–23.

[2] Shen L, Li J, Shen Y, 2023, Clinical Efficacy Observation of Acupoint Injection of Compound Diclofenac Sodium Injection Combined with Auricular Pressure Bean in the Treatment of Ureteral Stone Renal Colic. Primary Medical Forum, 27(35): 126–129.

[3] Weltings S, Buddingh KT, Van Diepen DC, et al., 2021, The BUSCOPAN Study: A Randomized-Controlled Non-Inferiority Trial of a Continuous Butylscopolamine Infusion Versus Placebo in Patients with A Renal Colic Not Responding to Oral Non-Steroidal Anti-Inflammatory Drugs. World Journal of Urology, 39(7): 2747–2752.

[4] Ji K, Yuan C, Qi J, 2023, The Efficacy of Tonglong Dashi Dishi Fang Combined with Acupuncture on Sanyinjiao in Treating Urinary Stone Renal Colic and its Effect on Patients' Serum Pain-Causing Substances, Urinary Calcium, and Urinary Bone Coelomocyte Protein Levels. Shaanxi Traditional Chinese Medicine, 44(9): 1241–1244.

[5] Johnson BA, Sorokin I, Antonelli J, et al., 2022, Efficacy of Intramuscular Ketorolac for Preventing Renal Colic Post Stent Removal. Randomized Controlled Trial. The Journal of Urology, 208(3): 650–656.

[6] Zhang J, Yu T, Liao Z, et al., 2020, A Prospective, Multicenter, Randomized Controlled Clinical Study of Physical Vibration Lithotripter in Different Positions for the Treatment of Ureteral Stone Renal Colic. Chinese Journal of Urology, 41(1): 46–50.

[7] He X, 2020, Comparison of the Effects of Different Administration Modes of Scopolamine Butylbromide Combined with Diclofenac in the Treatment of Stone Renal Colic. China Primary Medicine, 27(11): 1286–1289.

[8] Liu Y, Zhang H, Chen H, et al., 2022, A Study of Ureteral Wall Thickness to Predict the Likelihood of Ureteral Stone Self-Discharge After Renal Colic. Journal of Clinical Urology, 37(3): 172–174, 179.

[9] Li F, Xu X, Zhou Z, et al., 2021, Clinical Efficacy Observation on the Treatment of Moderate-To-Severe Osteoarthritis by External Application of Traditional Chinese Medicine Combined with Compound Diclofenac Sodium. Journal of Hubei University of Traditional Chinese Medicine, 23(1): 92–94.

[10] Luo X, Zhang Y, Yu Z, et al., 2022, Clinical Study and Analysis of the Efficacy and Safety of Resorcinol and Scopoletin in the Treatment of Renal Colic. Chinese Journal of Clinical Pharmacology, 38(8): 832–836.

Publisher's note

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

Urology Research, 2024, Volume 2, Issue 1
https://ojs.bbwpublisher.com/index.php/UR

The Usefulness of Positron Emission Tomography/Computed Tomography in the Diagnosis of Metastasis in Patients with Urothelial Carcinoma — A Secondary Publication

Akio Takayanagi[1]*, Atsushi Takahashi[1], Wakako Yorozuya[1], Kou Okabe[1], Tomohito Kaji[2], Yoshio Takagi[1]

[1]Department of Urology, Hakodate Goryoukaku Hospital, Hokkaido, Japan
[2]Division of Radiology, Hakodate Goryoukaku Hospital, Hokkaido, Japan

***Corresponding author:** Akio Takayanagi, aktakaya@sapmed.ac.jp

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Purpose:* This study examined the usefulness of positron emission tomography (PET)/computed tomography (CT) in the diagnosis of metastasis in patients with urothelial carcinoma. *Materials and methods:* The subjects were patients who were newly diagnosed with urothelial carcinoma in our department on whom we performed CT and PET/CT to search for metastasis. *Results:* The median age of the 92 subjects was 71 years, and bladder and upper tract urothelial cancer were underlying diseases in 41 (46%) and 51 (54%) patients, respectively. In 66 (72%) of the 92 cases, no metastasis was observed by CT, while PET/CT revealed metastasis in 9 (14%). The 57 (86%) patients in whom both CT and PET/CT showed no metastasis underwent radical surgery, while 2 patients (4%) exhibited pathological lymph node metastasis. Of the 26 patients in whom CT revealed metastasis, PET/CT showed no metastasis in 3 (12%), and the absence of pathological metastasis was confirmed in all patients. Of the 23 patients found to have metastasis in both CT and PET/CT, metastasis that could not be identified by CT was discovered by performing PET/CT in 10 (43%) patients. PET/CT showed significantly higher diagnostic accuracy than CT alone ($P < 0.01$), with sensitivities of 94.1% and 67.6%, specificities of 100% and 94.8%, and accuracy rates of 97.8% and 84.7%, respectively. *Conclusions:* PET/CT of patients with urothelial cancer revealed that metastases that cannot be diagnosed by CT alone are found at a significant frequency. Since these metastases can affect treatment choices in patients with urothelial cancer, PET/CT is considered to be useful in diagnosing metastases in patients with urothelial cancer.

Keywords: Urothelial cancer; PET/CT; Diagnosis

Online publication: March 29, 2024

1. Introduction

For patients with localized urothelial carcinoma, radical cystectomy and radical nephroureterectomy are well-established treatments [1,2]. However, complications occur with a certain frequency during surgery, and postoperative quality of life (QOL) is decreased after surgery [3]. In order to avoid ineffective radical surgery in

patients who cannot be cured and unnecessary anticancer drug treatment in patients who have not undergone metastasis, accurate staging is considered important when planning treatment [4-6].

Fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) is a diagnostic imaging method that observes the accumulation of ^{18}F-FDG (fluorodeoxyglucose), an analog of glucose, in tissues. Since glucose uptake is increased in many malignant tumors, it is used as an imaging evaluation method for various types of cancer [7]. ^{18}F-FDG is unsuitable for the diagnosis of primary urothelial carcinoma because it is excreted in the urine. However, its usefulness in the diagnosis of regional lymph node metastasis and distant metastasis has been reported [6,8]. On the other hand, compared to CT and MRI (magnetic resonance imaging), some reports suggest that PET/CT is not highly useful [4,5], and the significance of PET/CT in the diagnosis of urothelial carcinoma metastasis is controversial. In this study, we investigated the usefulness of PET/CT in the diagnosis of metastasis in patients with urothelial carcinoma.

2. Research subjects and methods

Patients diagnosed with urothelial carcinoma who underwent CT and PET-CT between January 2012 and December 2017 in our department were included in the study. The patients were pathologically diagnosed as having newly diagnosed invasive bladder carcinoma or carcinoma of the renal pelvis or ureter. In order to verify the accuracy of the CT and PET/CT diagnoses, we performed surgery on patients with pathologically proven metastatic disease. The diagnosis of metastasis should be verified in patients who have undergone surgery and have pathologically proven the presence of metastasis, or in patients who have undergone regular examinations for at least 6 months after the examination. The patients with metastases were included in the study. In addition, because of the anticancer treatment, it was not possible to determine the accuracy of the image evaluation, these cases were excluded. In this study, the clinical stage was determined only by CT and PET/CT results.

CT was performed with simple CT of the chest and contrast-enhanced CT of the abdomen. The PET/CT machine was a GE Healthcare Discovery ST Elite. The fasting time was 5 hours, and imaging was performed 1 hour after the administration of ^{18}F-FDG 3.0 MBq/kg. The imaging time was 21 minutes, and reconstruction was performed by the 3D OSEM method. FDG accumulation in comparison with other sites or background tissue metastasis was assessed by PET/CT. The standardized uptake value (SUV), which is a semi-quantitative measure of FDG accumulation, was not used as a reference value for determining metastasis.

In this study, we evaluated the reading results of radiologists who performed CT and PET/CT at the time of the study. The results were evaluated retrospectively. The sensitivity and specificity of the positive diagnosis of metastasis were evaluated on a case-by-case basis.

Statistical analysis was performed using EZR, and $P < 0.05$ was considered a significant difference. The difference in diagnostic accuracy by test method was analyzed using the McNemar test [9]. In conducting this study, approval was obtained from the ethics committee of Hakodate Goryoukaku Hospital (Approval number: 2020-015).

3. Results

A total of 134 patients were examined, of which 108 patients had newly diagnosed invasive bladder cancer and ureteral carcinoma of the renal pelvis. 8 patients could not be evaluated by diagnostic imaging because they were treated with anticancer drugs and 8 patients could not be evaluated by diagnostic imaging because they did not undergo periodic examinations for a sufficient period of time, after excluding them, the study included 92 patients. The 92 patients had a median age of 71 years, 73 (79%) were male, and 41 (46%) had bladder cancer

as the primary disease (**Table 1**).

Table 1. Information of 92 patients

Patient information		Cases
Age (years)		71 (46–89)
Gender	Male	73 cases (79%)
	Female	19 cases (21%)
Primary illness	Bladder cancer	41 cases (46%)
	Cancer of the renal pelvis and ureter	51 cases (54%)
Local clinical stage	cT1	11 cases (12%)
	cT2	33 cases (36%)
	cT3	37 cases (40%)
	cT4	11 cases (12%)
Example of primary site excision		69 cases (75%)

The clinical diagnoses when CT and PET/CT were performed are shown in **Table 2**. The number of cases with no metastasis, lymph node metastasis only, and distant metastasis on CT were 66 (72%), 15 (16%), and 11 (12%) cases, respectively; while the results of PET/CT were 60 (65%), 19 (21%), and 13 (14%), respectively.

Table 2. Clinical stage and metastases-positive site when performing CT and PET/CT

Method of examination	CT	PET/CT
cTanyN0M0	66 (72%)	60 (65%)
cT1N0M0	11 (12%)	10 (11%)
cT2N0M0	26 (29%)	27 (31%)
cT3N0M0	25 (27%)	21 (23%)
cT4N0M0	4 (4%)	2 (2%)
cTanyN + M0	15 (16%)	19 (21%)
cTanyNanyM+	11 (12%)	13 (14%)
Site of metastasis		
Lymph node metastasis	24 (26%)	29 (32%)
(Extra-regional lymph node metastasis)	15 (16%)	16 (18%)
Liver metastasis	3 (3%)	4 (4%)
Lung metastasis	3 (3%)	2 (2%)
Bone metastasis	1 (1%)	6 (7%)
Peritoneal dissemination		2 (2%)
Pleural metastasis		2 (2%)
Accidental cancer case		Colorectal cancer 2 (2%)

PET/CT showed metastasis in 9 (14%) of the 66 patients who did not show metastasis on CT (**Figure 1**), there were lymph node metastases in 6 cases (67%), and extra-regional lymph node metastases in 2 cases (**Figure**

2). In addition, two patients (22%) had bone metastasis and one (11%) had peritoneal dissemination. On the other hand, 57 patients (86%) who had no metastasis on PET/CT underwent radical surgery. Two patients (4%) had pathological lymph node metastases.

Of the 26 patients with metastases on CT, 23 (88%) had metastases on PET/CT, while 3 (12%) had no metastases on PET/CT. In all three cases, CT revealed lymph node involvement. However, PET/CT showed no FDG accumulation in the lymph nodes, indicating the absence of metastasis. In all three cases, lymph node dissection was performed at the time of radical surgery and pathologically confirmed that there were no metastases. On the other hand, of the 23 patients who had metastases on PET/CT, new metastasis was discovered in 10 (43%) by performing PET/CT. Of these patients, 5 (19%) had bone metastases, 2 (9%) pleural metastases, and 1 (4%) each had liver metastases, peritoneal dissemination, and abdominal wall metastases. Two patients (9%) had more extensive lymph node metastases compared to CT, and two patients (9%) were found to have colorectal cancer.

The diagnostic accuracy of using CT only and CT and PET/CT for the diagnosis of metastasis respectively, were sensitivity of 67.6% and 94.1%, specificity of 94.8% and 100%, and accuracy rate of 84.7% and 97.8%. The McNemar test was performed for diagnostic accuracy. The results of the McNemar test showed that CT and PET/CT were significantly more accurate than CT alone ($P < 0.01$).

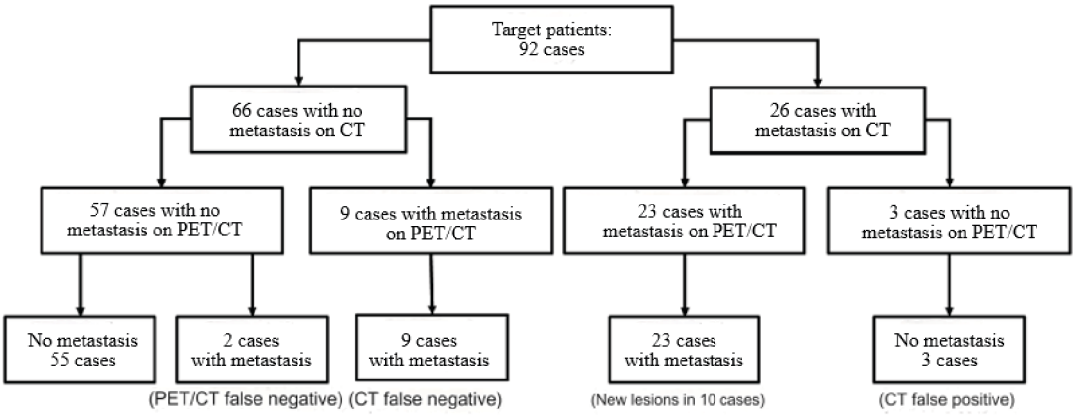


Figure 1. Diagnosis results of 92 cases of urothelial carcinoma performed by CT and PET/CT

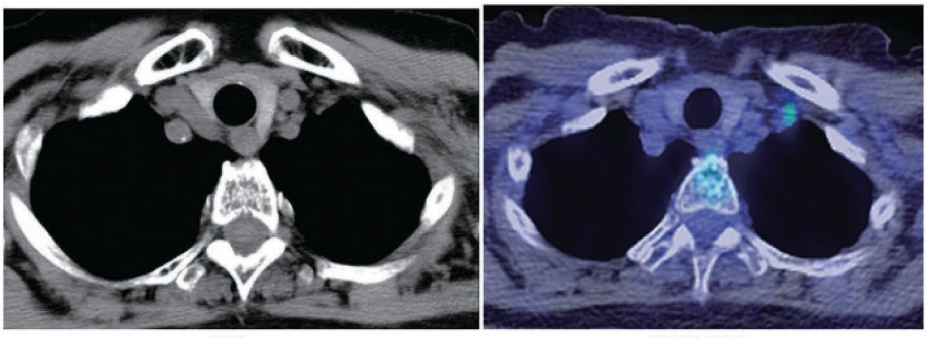


Figure 2. A case in which no metastasis was found on CT, but metastasis was found in the left supraclavicular lymph node by PET/CT. This case underwent lymph node biopsy and was pathologically diagnosed as metastasis of urothelial carcinoma.

4. Discussion

CT and MRI are often used to diagnose lymph node metastases and distant metastases, but the sensitivity of these tests alone is low. Therefore, it may influence the optimal treatment decision [5,10]. FDG-PET/CT has been reported to be useful in the diagnosis of bladder cancer metastasis. In this study, we investigated the usefulness of FDG-PET/CT in the diagnosis of metastasis of urothelial carcinoma.

The present study included patients with newly diagnosed invasive bladder cancer and renal pelvis ureteral cancer who underwent both CT and PET/CT for metastasis detection. PET/CT has been used to detect metastases that were not seen on CT in 9 (12%) patients. The results of this study were as follows. The results suggest that PET/CT was useful in the diagnosis of metastasis, and that in these cases, ineffective curative treatment could be avoided. On the other hand, PET/CT could not identify lymph node metastasis in two patients (4%), which is a limitation of PET/CT in the diagnosis of metastasis. Tanaka *et al.* performed PET/CT on patients with urothelial carcinoma and showed that 20% of patients with urothelial carcinoma had new metastases, which necessitated a change in treatment [11]. PET/CT may change the treatment strategy for a certain number of patients with urothelial carcinoma and may be useful in the diagnosis of metastasis of urothelial carcinoma.

Vind-Kezunovic *et al.* reported that performing PET/CT in patients with urothelial carcinoma allows more accurate diagnosis of lymph node metastasis. They concluded that PET/CT is useful for treatment selection [6]. Mertens *et al.* also reported that PET/CT can be used to identify the metastatic sites of urothelial carcinoma and that PET/CT is useful for predicting the prognosis of patients with urothelial carcinoma [8]. On the other hand, Goodfellow *et al.* found that PET/CT increased sensitivity by 22% compared to CT alone, and new metastases could be diagnosed in 5.6% of cases. However, the study concluded that PET/CT is not meaningful as a routine procedure because of its low diagnostic accuracy and high medical cost [4].

In the present study, the presence of FDG accumulation was considered positive for metastasis. There is no established opinion on how to judge metastasis positivity. Vind-Kezunovic *et al.* defined metastasis positivity as an SUVmax of 2 or greater [6]; Girard *et al.* judged positive for metastasis by combining SUVmax and the size of the lesion [12]; while Mertens *et al.*, on the other hand, did not define SUVmax as they did, but considered the presence of FDG accumulation to be positive for metastasis [4,5,8]. When defining SUVmax for metastasis diagnosis, a higher reference value is considered to decrease sensitivity and increase specificity. The specificity of the diagnosis is increased by increasing the standard value. At present, there are no fixed criteria for judging metastasis positivity and it is assumed that it should be evaluated comprehensively based on the degree of FDG accumulation, comparison with other sites, size of the lesion, and other factors.

The present study was a retrospective study and there was a patient selection bias in the included patients. In other words, some patients who could not be evaluated by CT or PET/CT were excluded from the study. Specifically, in cases where the success or failure of the image test was not pathologically diagnosed, only those cases for which follow-up could be performed for six months or more were included, so eight cases for which sufficient follow-up could not be performed were not excluded from the study. In addition, among the cases in which preoperative anticancer drug treatment was performed, eight cases in which a discrepancy was observed between the imaging test and the pathological test were excluded because it was not possible to evaluate whether the anticancer drug treatment was successful or whether the image diagnosis was incorrect. Furthermore, routine bone scintigraphy was not performed because there were no bone-related symptoms. Bone metastases were identified in 6 patients (7%) by PET/CT, suggesting that PET/CT may be able to identify asymptomatic bone metastases.

5. Conclusion

Performing PET/CT in patients with urothelial carcinoma reveals a certain number of metastases that cannot be diagnosed by CT alone. Since these metastases can influence the choice of treatment for patients with urothelial carcinoma, PET/CT was considered useful for the diagnosis of patients with urothelial carcinoma.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Stein JP, Lieskovsky G, Cote R, et al., 2001, Radical Cystectomy in the Treatment of Invasive Bladder Cancer: Long-Term Results in 1,054 Patients. J Clin Oncol, 2001(19): 666–675.

[2] Margulis V, Shariat SF, Matin SF, et al., 2009, The Upper Tract Urothelial Carcinoma C: Outcomes of Radical Nephroureterectomy: A Series from the Upper Tract Urothelial Carcinoma Collaboration. Cancer, 2009(115): 1224–1233.

[3] Hirobe M, Tanaka T, Shindo T, et al., 2018, Complications Within 90 Days After Radical Cystectomy for Bladder Cancer: Results of a Multicenter Prospective Study in Japan. Int J Clin Oncol, 2018(23): 734–741.

[4] Goodfellow H, Viney Z, Hughes P, et al., 2014, Role of Fluorodeoxyglucose Positron Emission Tomography (FDG PET) -Computed Tomography (CT) in the Staging of Bladder Cancer. BJU Int, 2014(114): 389–395.

[5] Swinnen G, Maes A, Pottel H, et al., 2010, FDG-PET/CT for the Preoperative Lymph Node Staging of Invasive Bladder Cancer. Eur Urol, 2010(57): 641–647.

[6] Vind-Kezunovic S, Bouchelouche K, Ipsen P, et al., 2019, Detection of Lymph Node Metastasis in Patients with Bladder Cancer Using Maximum Standardised Uptake Value and (18)F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography: Results from a High-Volume Centre Including Long-Term Follow-Up. Eur Urol Focus, 2019(5): 90–96.

[7] Minamoto R, Tateishi T, Inoue T, 2010, Uroepithelial Carcinoma and PET Surgery. Clinical Urology, 2010(64): 1009–1015.

[8] Mertens LS, Fioole-Bruining A, Vegt E, et al., 2013, Impact of (18)F-Fluorodeoxyglucose (FDG) -Positron-Emission Tomography/Computed Tomography (PET/CT) on Management of Patients with Carcinoma Invading Bladder Muscle. BJU Int, 2013(112): 729–734.

[9] Kanda Y, 2012, Investigation of the Freely Available Easy-to-Use Software 'EZR' for Medical Statistics. Bone Marrow Transplantation, 2012(48): 452–458.

[10] Scolieri MJ, Paik ML, Brown SL, et al., 2000, Limitations of Computed Tomography in the Preoperative Staging of Upper Tract Urothelial Carcinoma. Urology, 2000(56): 930–934.

[11] Tanaka H, Yoshida S, Komai Y, et al., 2016, Clinical Value of 18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Upper Tract Urothelial Carcinoma: Impact on Detection of Metastases and Patient Management. Urol Int, 2016(96): 65–72.

[12] Girard A, Rouanne M, Taconet S, et al., 2019, Integrated Analysis of (18)F-FDG PET/CT Improves Preoperative Lymph Node Staging for Patients with Invasive Bladder Cancer. Eur Radiol, 2019(29): 4286–4293.

Publisher's note

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

Urology Research, 2024, Volume 2, Issue 1
https://ojs.bbwpublisher.com/index.php/UR

Study of Urine Treatment After BCG Intravesical Instillation Therapy — A Secondary Publication

Yoshimasa Kondo[1,2]*, Tatsuya Takayama[1]

[1]The Department of Urology, Haga Red Cross Hospital, Moka, Tochigi 321-4308, Japan
[2]Tochigi Public Health Service Association, Tochigi 320-0065, Japan

***Corresponding author:** Yoshimasa Kondo, y.kondo@tochigi-health.or.jp

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Background and methods:* Bacillus Calmette-Guérin (BCG) intravesical instillation therapy is used to treat non-muscle invasive bladder cancer. Instilled BCG is typically collected at the time of initial urination and disposed of after sterilization with 10% sodium hypochlorite or household bleach, however, these methods can have unpleasant effects, such as pungent odor, rapid foaming, and fever. We investigated whether isopropanol can be used to sterilize and dispose of urine after BCG intravesical instillation therapy since isopropanol at a concentration of 33% or higher (70% isopropanol was used in this study) has the same disinfectant and bactericidal effects against *Mycobacterium tuberculosis* as 10% sodium hypochlorite or household bleach. *Results:* The use of isopropanol eliminated the unpleasant effects experienced with sodium hypochlorite and no growth of *Mycobacterium tuberculosis* was observed in culture tests. *Conclusion:* Isopropanol is safer than sodium hypochlorite, and should be considered for sterilizing and disposing of urine after BCG intravesical instillation therapy in the future. However, fire and ventilation precautions are required.

Keywords: BCG intravesical instillation therapy; Urine treatment; Isopropanol

Online publication: March 29, 2024

1. Introduction

Bacillus Calmette-Guérin (BCG) is an intravesical injection of a live attenuated bovine tuberculosis vaccine originally intended to prevent tuberculosis. When BCG suspension is injected into the bladder, the urine contains a large amount of *Mycobacterium tuberculosis*. It is generally recommended that urine be collected in an appropriate container (e.g., urine storage container) and disinfected before disposal at the first voiding after BCG intravesical injection therapy [1,2]. According to the "Guidelines for Infection Control in Urology" [3] (hereafter referred to as the "Guidelines"), the recommended disinfection method is to add half the volume of urine to a 10% sodium hypochlorite solution or household bleach and allow it to stand for 15 minutes. However, when 10% sodium hypochlorite is added to urine, the urine may foam violently or the temperature of the solution may rise rapidly. In addition, the odor of chlorine may waft into the room, making medical personnel uncomfortable. Coughing fits and respiratory distress may occur in some healthcare workers who treat the urine. Therefore, since isopropanol with a commercial concentration of 33% or higher is effective as an alternative to sodium

hypochlorite with an action time of 15 minutes [3,4], this study investigated the use of 70% isopropanol (hereinafter referred to as "Isopro"), which is commonly used as a disinfectant for external use in the medical field, for the safe treatment of urine after BCG injection.

2. Methods

We used a household bleach, Purelox® (6% sodium hypochlorite) (n = 6), and added half the amount of Isopro (n = 8) to the urine after BCG injection, and (1) observed the state of urine immediately after injection, at 5, 10, and 15 minutes, and submitted the urine at each observation time for *Mycobacterium tuberculosis* culture test. The same sample was used for each of the three *Mycobacterium tuberculosis* culture tests. (2) At each observation time, the concentrations of chlorine and isopropanol directly above the container were measured using a detector tube gas measuring device (hereinafter referred to as "detector tube"). (3) The temperature of the urine in the container was measured at each observation time.

This study was conducted with the approval of the hospital ethics committee (Approval number: R3-9). Statistical analysis was performed by repeated measures analysis of variance using EZR (Easy R) software.

3. Results

Immediately after the addition of Purelox, bubbles appeared and bubbled violently (**Figure 1**), and a strong chlorine odor was observed, while the temperature rose (35–42°C). The chlorine concentration immediately above the container was measured using a detector tube, and the maximum concentration was 10 ppm. When Isopro was used, a characteristic odor was observed, but no bubbles were generated. The concentration of isopropanol measured directly above the container using a detector tube was below the sensitivity of the measurement. No sudden temperature increase was observed. A significant difference ($P = 7.52 \times 10^{-15}$) was observed between the temperature change over time after the addition of Purelox and that of Isopro (**Figures 2** and **3**). *Mycobacterium tuberculosis* cultures 15 minutes after the addition of Purelox and Isopro were negative in all three culture tests (**Figure 4**).

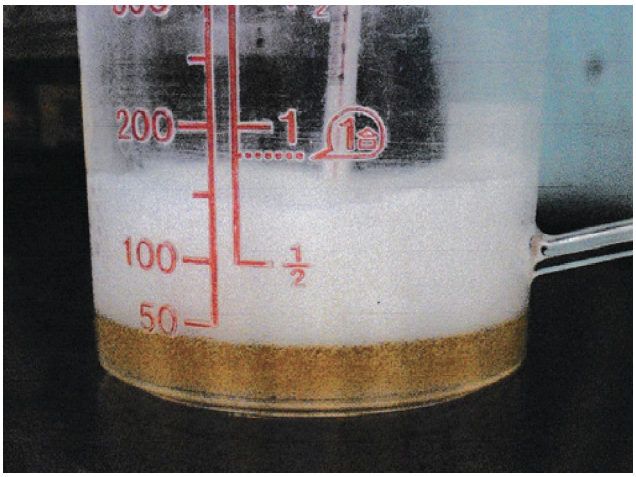


Figure 1. Condition immediately after adding Purelox to urine after BCG intravesical injection

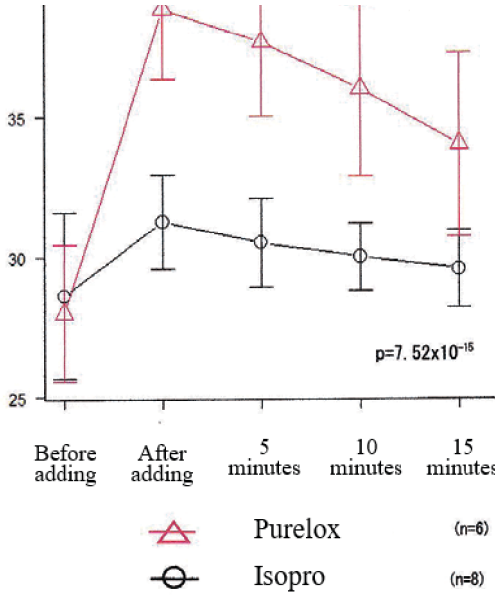


Figure 2. Temperature change over time with Purelox and Isopro ($P = 7.52 \times 10^{-15}$)

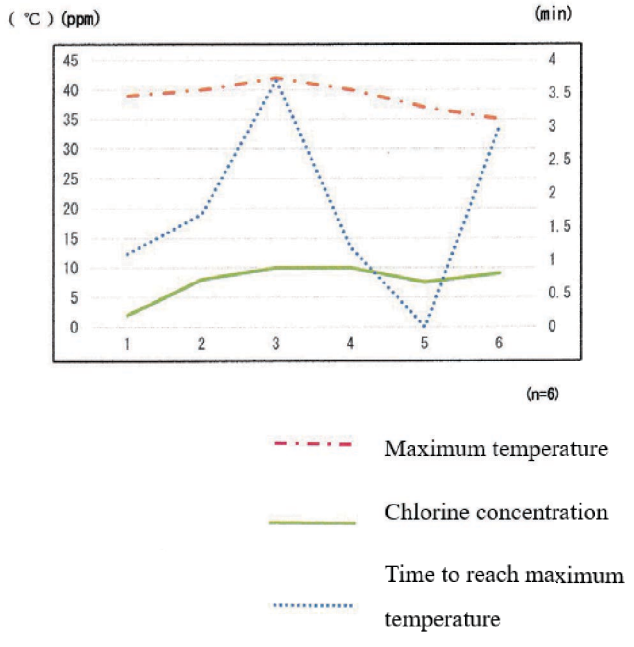


Figure 3. Maximum temperature, time to reach maximum temperature, and chlorine concentration directly above the container when Purelox is injected

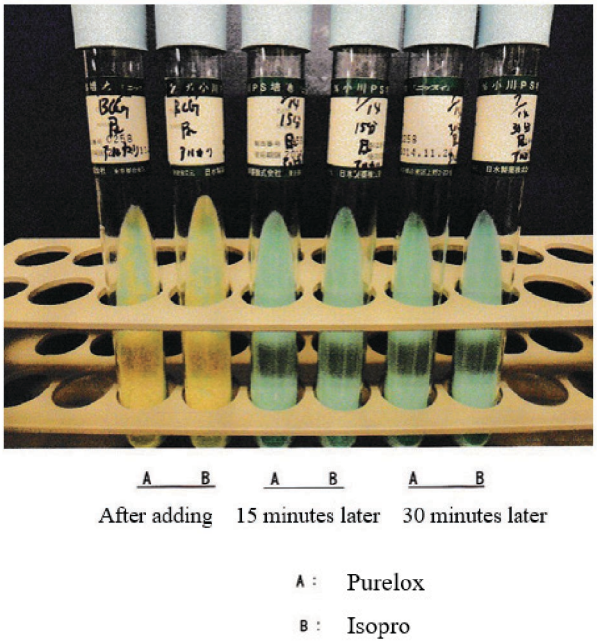


Figure 4. *Mycobacterium tuberculosis* culture after treatment with Purelox and Isopro (immediately, 15 minutes, and 30 minutes after application)

4. Discussion

The "Guideline" states that "urine after intravesical BCG injection should be disinfected and discarded to prevent infection. It is recommended that half the volume of 10% sodium hypochlorite or household bleach be added to the urine, allowed to stand for 15 minutes, and then discarded." The report states that "isopropanol is effective at a commercial concentration of 33% or more with a 15-minute action time," but because "isopropanol is flammable," "treatment with 10% sodium hypochlorite may be appropriate from the standpoint of versatility and safety." Kobayashi *et al.* [5] stated that "sodium hypochlorite generates a large amount of chlorine gas when mixed with acidic substances (e.g., acidic cleaning agents)." The chemical reaction between sodium hypochlorite and urine generates chlorine gas and bubbles, which may cause health problems for healthcare workers who treat urine. In this study, the maximum chlorine concentration measured by the detector tube directly above the container was 10 ppm. The maximum allowable concentration of chlorine is 0.5 ppm [6], and the maximum allowable concentration (the concentration at which no adverse health effects are observed in almost all workers if the exposure concentration is below this value at any time during the workday) is 0.5 ppm [7]. According to the information on poisoning for physicians published by the Japan Poisoning Information Center, chlorine concentrations of 5 to 15 ppm are considered to be moderately irritating to the upper respiratory tract. There is concern that this may have adverse effects not only on medical personnel but also on patients in daily medical practice. On the other hand, isopropanol is one of the substances classified as Volatile Organic Compounds (VOC) under the Air Pollution Control Law and is considered a cause of photochemical oxidants (a generic term for oxidizing substances in the air that cause photochemical smog). The emission standard is 400 ppmC (133 ppm) [8]. It is classified as a Class 2 Organic Solvent in the Ordinance on Prevention of Organic Solvent Poisoning under the Industrial Safety and Health Law, with a controlled concentration of 200 ppm [6] and a maximum allowable concentration of 400 ppm [7]. In this study, the concentration of isopropanol

immediately above the container was below the measurement sensitivity and was clearly lower than the emission standard, controlled concentration, and maximum allowable concentration. However, isopropanol is volatile and can be flammable. Although isopropanol has a characteristic odor, we did not use an odor meter to compare the odor in this study. The commercial price of Purelox is approximately 500 yen for 600 mL (approximately 10 yen per 10 mL), and the price of Isopro is 4.5 yen per 10 mL, making Isopro less expensive.

5. Conclusion

Isopro is safer than Purelox in the indoor environment, including medical personnel and patients, and should be considered for use in the future.

Acknowledgments

The authors would like to thank Dr. Masato Ito, Professor of the Department of Otorhinolaryngology, Jichi Medical University, for his advice in writing this paper.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Japan Hospital Pharmacists Association, 2006, Drug Interview Form “Immucyst® for Bladder,” Revision 2.

[2] Japan Hospital Pharmacists Association, 2015, Drug Interview Form “Immunobladder® Intravesical 40 mg,” Revision 3.

[3] Japan Urological Association Infection Control Guideline Development Committee in Urology, 2009, Guidelines for Infection Control in Urology, 18–19.

[4] Iwama K, Kadozawa M, Matsumoto H, et al., 1998, Disinfection Efficacy of Various Disinfectants Against Urinary BCG. BCG-BRM Therapy Journal, 1998(22): 65–71.

[5] Kobayashi K, (ed.), 2002, Supplemented Guidelines for Disinfection and Sterilization, 1st edition, Herusu Publishing, Tokyo, 83.

[6] Ministry of Health, Labour and Welfare, 2010, List of Controlled and Allowable Concentrations of Substances to be Measured in the Working Environment, 2, 5.

[7] Japan Society for Occupational Health, 2016, Recommendations on Allowable Concentrations, etc. (FY2016). Journal of the Japan Society for Occupational Health, 2016(58): 181–212.

[8] Director of the Environmental Management Bureau, Ministry of the Environment, 2004, Enforcement of the Law Partially Amending the Air Pollution Control Law (Notice): Kankan Daihatsu No. 05067001.

Publisher’s note

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

Urology Research, 2024, Volume 2, Issue 1
https://ojs.bbwpublisher.com/index.php/UR

Comparison of Clinical Effects of Sacubitril Valsartan Sodium Tablets and Nifedipine Controlled-Release Tablets in the Treatment of Chronic Renal Insufficiency Complicated with Hypertension

Meijuan Ma[1], Fen Yang[2]*

[1]Department of Cadre Physical Examination Center, Shaanxi Provincial People's Hospital , Xi'an 710068, Shaanxi Province, China
[2]Department of Respiratory and Critical Care Medicine, Shaanxi Provincial People's Hospital (Xixian), Xi'an 710068, Shaanxi Province, China

***Corresponding author:** Fen Yang, 13227822115@126.com

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To compare the clinical effects of using sacubitril valsartan sodium tablets with nifedipine controlled-release tablets in patients with chronic renal insufficiency combined with hypertension. *Methods:* 110 patients with chronic renal insufficiency combined with hypertension treated in our hospital from April 2023 to February 2024 were taken as the study subjects. They were divided into the test group (n = 55) and the comparison group (n = 55) by randomized numerical table method. The test group was provided with sacubitril valsartan sodium tablets and the comparison group was treated with nifedipine controlled-release tablets. The urine excretion rate of albumin and blood urea nitrogen levels as well as adverse effects were compared before and after treatment in both groups. *Results:* In the test group, the urinary albumin excretion rate was 101.77 ± 7.42 μg/min and the blood urea nitrogen level was 15.81 ± 1.76 mmol/L, which was much lower than that of the comparison group; the total rate of adverse reactions in the test group was 1.82%, which was significantly lower than that of the comparison group, the difference between the data of the test group and the comparison group after treatment is statistically significant ($P < 0.05$). *Conclusion:* By providing treatment with sacubitril valsartan sodium tablets for patients with chronic renal insufficiency combined with hypertension, their urinary albumin excretion rate and blood urea nitrogen level are significantly improved, and the total occurrence rate of adverse reactions is low.

Keywords: Sacubitril valsartan sodium tablets; Nifedipine controlled-release tablets; Chronic renal insufficiency; Hypertension

Online publication: May 9, 2024

1. Introduction

Patients suffering from chronic renal insufficiency, due to the metabolites in the body cannot be normally

discharged to the outside of the body, usually have abnormal blood pressure, complicating hypertension, which in turn will lead to the aggravation of chronic renal insufficiency. The control of blood pressure in patients with chronic renal insufficiency is difficult compared to ordinary hypertension. Sacubitril valsartan sodium tablets and nifedipine controlled-release tablets are both commonly used medication to lower blood pressure, and their therapeutic effects differ. One hundred and ten patients with chronic renal insufficiency combined with hypertension treated in our hospital between April 2023 and February 2024 were taken as the study subjects, and are reported as follows.

2. General information and methods

2.1. General information

110 patients with chronic renal insufficiency combined with hypertension treated in our hospital between April 2023 and February 2024 were selected for the study and their general information is shown in **Table 1**. Consent was obtained from the patients and their families for this study. There was no statistically significant difference between the general information of the two groups ($P > 0.05$).

Table 1. Basic data of patients with chronic renal insufficiency combined with hypertension

Groups	Male patients	Female patients	Age	Average age
Test group (55 cases)	27 cases	28 cases	42–81 years	57.3 ± 8.1 years
Comparison group (55 cases)	26 cases	29 cases	44–78 years	59.2 ± 6.9 years

2.2. Methods

Nifedipine controlled-release tablets were provided for the patients in the comparison group, they were taken once a day, each time taking 30 mg, and the dose was maintained for 4 weeks [1]. The patients' blood pressure and renal function indexes were tested regularly, and the dosage was adjusted based on the test results.

For the test group, sacubitril valsartan sodium tablets were taken twice a day, 100 mg each time, and the dosage was maintained for 4 weeks [2,3]. The patients' blood pressure and renal function indexes were tested regularly, and the dosage was adjusted based on the test results.

2.3. Observation indexes

The urinary albumin excretion rate and blood urea nitrogen of patients in the test group and comparison group before and after treatment were compared. Statistics on the occurrence of adverse reactions in patients with chronic renal insufficiency combined with hypertension after treatment, including hyperkalemia, nausea and vomiting, and edema were recorded. The formula for calculating the total occurrence rate is as follows. Total occurrence rate = Number of cases of adverse reactions/Total number of cases × 100%.

2.4. Statistical analysis

SPSS22.0 statistical software was applied, *t*-test was used for the measurement data (mean ± standard deviation [SD]), and χ^2 test was used for the count data [n (%)], and $P < 0.05$ indicated a statistically significant difference.

3. Results

3.1. Comparison of urinary albumin excretion rate and blood urea nitrogen before and after treatment in two groups of patients

The urinary albumin excretion rate and blood urea nitrogen values of the 55 patients in the test group who were

treated with sacubitril valsartan sodium tablets were significantly better than those of the comparison group, and $P = 0.000$ (**Table 2**).

Table 2. Comparison of urinary albumin excretion rate and blood urea nitrogen before and after treatment in the two groups (mean ± SD)

Groups	Before treatment		After treatment	
	Urinary albumin excretion rate (μg/min)	Blood urea nitrogen (mmol/L)	Urinary albumin excretion rate (μg/min)	Blood urea nitrogen (mmol/L)
Test group (55 cases)	139.82 ± 11.59	19.68 ± 1.04	101.77 ± 7.42	15.81 ± 1.76
Comparison group (55 cases)	139.87 ± 11.56	19.53 ± 1.12	126.66 ± 10.56	17.25 ± 2.03
t	0.023	0.728	14.302	3.975
P	0.982	0.468	0.000	0.000

3.2. Comparison of adverse reactions in two groups of patients with chronic renal insufficiency combined with hypertension

Only one case of nausea and vomiting was found in 55 patients with chronic renal insufficiency combined with hypertension in the test group, and the total rate of adverse reactions was 1.82%, which was significantly lower than that of the comparison group, and the P value was calculated to be 0.015 (**Table 3**).

Table 3. Comparison of adverse reactions in patients with chronic renal insufficiency combined with hypertension in the two groups [n (%)]

Groups	Hyperkalemia	Nausea and vomiting	Edema	Overall incidence
Test group (55 cases)	0 (0.00)	1 (1.82)	0 (0.00)	1 (1.82)
Comparison group (55 cases)	2 (3.64)	3 (5.45)	3 (5.45)	8 (14.55)
χ^2	-	-	-	5.930
P	-	-	-	0.015

4. Discussion

Chronic renal insufficiency is usually accompanied by hypertension, which is a major risk factor for exacerbation of the disease. If the blood pressure is uncontrolled, the condition will be aggravated gradually, thus the blood pressure is controlled with appropriate drugs to promote the recovery of the disease [4-7].

The antihypertensive mechanism of nifedipine controlled-release tablets is relatively single, resulting in the urinary albumin excretion rate and blood urea nitrogen in some patients not improving after a period of time, while the antihypertensive mechanism of sacubitril valsartan sodium tablets is more comprehensive, with a protective effect on the kidneys and a more satisfactory therapeutic effect. During the implementation of treatment for the two groups of patients, once adverse reactions occurred, the use of drugs should be stopped immediately [8-10].

In this study, after treatment with sacubitril valsartan sodium tablets, the urinary albumin excretion rate in the test group was 101.77 ± 7.42 μg/min and blood urea nitrogen was 15.81 ± 1.76 mmol/L, which was significantly lower than that of the comparison group; there was only one case of adverse reactions, and the total rate of adverse reactions was 1.82%, which was significantly lower than that of the comparison group. The difference between the data of the test group and the comparison group after treatment was statistically

significance ($P < 0.05$).

Practice has shown that in the treatment of patients with chronic renal insufficiency combined with hypertension using sacubitril valsartan sodium tablets, the therapeutic effect is more satisfactory with a lower occurrence of adverse reactions.

5. Conclusion

In conclusion, patients with renal insufficiency combined with hypertension can be treated using sacubitril valsartan sodium tablets under the guidance of doctors, so as to promote the early recovery of the disease.

Disclosure statement

The authors declare no conflict of interest.

References

[1] Zhang CS, Chen LC, Zhou WS, et al., 2024, Clinical Observation on 50 Cases of Chronic Renal Insufficiency Treated by Adding and Subtracting Gui Shao San Qi Di Huang Tang. Hunan Journal of Traditional Chinese Medicine, 40(03): 1–4.

[2] Shi SH, Zhang Y, Lin CD, 2024, Efficacy of Sacubitril Valsartan in the Treatment of Chronic Heart Failure Combined with Renal Insufficiency and Its Effect on Microinflammatory Response. Clinical rational drug use, 17(07): 8–11.

[3] Jiang S, 2023, Observation on the Efficacy of Sacubitril Valsartan Sodium in the Treatment of Heart Failure Combined with Chronic Renal Insufficiency. China Metallurgical Industry Medical Journal, 40(06): 678–679.

[4] Zhang Y, Lu Y, Li C, 2023, Influence of Sevelamer Carbonate on Serum Calcium and Phosphorus Levels and Effects in Patients with Chronic Renal Insufficiency Combined with Hyperphosphatemia. Medical Theory and Practice, 36(21): 3679–3681.

[5] Tian Y, Wu Q, 2023, Observation on the Effect of Tolvaptan Combined with Sacubitril Valsartan Sodium in the Treatment of Patients with Acute Heart Failure with Chronic Renal Insufficiency. Guizhou Medicine, 47(06): 905–906.

[6] Chu Y, 2023, Analysis of the Effect of Sacubitril Valsartan Sodium Tablets and Metoprolol Succinate in the Treatment of Coronary Heart Disease Combined with Chronic Heart Failure. China Medical Guide, 21(24): 53–56.

[7] Liu W, Wei H, 2022, Clinical Effect of Sacubitril Valsartan Sodium Tablets in the Treatment of Coronary Heart Disease Combined with Chronic Heart Failure. Chinese Contemporary Medicine, 29(1): 68–71.

[8] Li J, Ye Q, Zhang S, et al., 2023, Exploring the Clinical Efficacy and Safety of Sacubitril Valsartan Sodium Tablets Combined with Bisoprolol in the Treatment of Chronic Diastolic Heart Failure. North Pharmacology, 20(7): 125–127.

[9] Ye T, 2022, Comparison of the Effects of Sacubitril Valsartan Sodium and Perindopril in the Treatment of Chronic Heart Failure Combined with Renal Insufficiency in the Elderly. Jilin Medicine, 43(10): 2701–2703.

[10] Hu J, 2023, Clinical Efficacy Study of Sacubitril Valsartan Sodium Tablets Combined with Enalapril in the Treatment of Chronic Heart Failure. Sichuan Journal of Physiological Sciences, 45(2): 330–332.

Publisher's note

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

Urology Research, 2024, Volume 2, Issue 1
https://ojs.bbwpublisher.com/index.php/UR

The Value of Liquid Chromatography-Mass Spectrometry in the Detection of Chemical Constituents of Kidney Tonic and Aphrodisiac Chinese Herbal Preparations

Geng Weng*

Fujian Institute for Food and Drug Quality Control, Fuzhou 350000, Fujian Province, China

***Corresponding author:** Geng Weng, wenggeng@126.com

Copyright: © 2024 Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0), permitting distribution and reproduction in any medium, provided the original work is cited.

Abstract: *Objective:* To investigate the application of liquid chromatography-mass spectrometry (LC-MS) in the determination of chemical constituents of kidney tonic and aphrodisiac Chinese herbal preparations. *Methods:* In this study, 30 kidney tonic and aphrodisiac Chinese herbal preparations were selected as experimental materials, and chromatography and LC-MS were used to detect their chemical compositions in the control group and the experimental group, respectively. The excellent rate of detection method, identification time, and accuracy of the two methods were compared. *Results:* The excellent rate of the detection method in the experimental group (93.33%) was significantly higher than that in the control group (73.33%), and the difference was statistically significant ($P < 0.05$); compared with the control group, the detection time and retention time error in the experimental group were shorter, and the difference showed highly significant correlation ($P < 0.001$). *Conclusion:* LC-MS is of high value in the detection of chemical constituents of kidney tonic and aphrodisiac Chinese herbal preparations, which can significantly improve the excellent rate of the detection method and the success rate, shorten the detection time, and reduce the retention time error, and is worth to be popularized.

Keywords: Liquid chromatography-mass spectrometry; Kidney tonic and aphrodisiac Chinese herbal preparations; Chemical composition determination

Online publication: May 9, 2024

1. Introduction

Kidney tonic and aphrodisiac herbal preparations are a class of herbal formulas for male sexual function problems, usually treating symptoms such as impotence, premature ejaculation, and weakness of the waist and knees. Common herbs include ginseng, wolfberry, epimedium, and dulcimer herb, etc. These herbs are believed to be able to nourish the kidney and yang, benefit the essence and strengthen the body, and improve male sexual function. However, the manufacturing process of these drugs by certain manufacturers is substandard, and the illegally added ingredients vary greatly, resulting in serious overloading of chemical compositions in

many medicines, which poses serious health hazards [1]. Therefore, the use of efficient detection methods can improve the efficiency and accuracy of the detection of the chemical composition of drugs, so as to ensure the safety of medication [2]. Due to the relative complexity of the chemical system of traditional Chinese medicines, there is a wide variety of components and complex pharmacological structures, while there is a high degree of similarity among many traditional Chinese medicines [3,4]. Conventional chemical analysis methods can be limited by sample complexity and low concentration of components, whereas liquid-mass spectrometry can overcome these difficulties and provide highly sensitive, selective, and attributable chemical analysis results. Liquid chromatography-mass spectrometry (LC-MS) combines chromatographic separation and mass spectrometry detection technologies to achieve accurate identification and quantitative analysis of multiple chemical components in complex samples, with the advantages of high sensitivity, accuracy, and throughput [5]. In kidney tonic and aphrodisiac herbal preparations, LC-MS can help identify and quantify various active ingredients, such as phytosterols, alkaloids, flavonoids, polysaccharides, and peptides. Meanwhile, this method can also explore the metabolic pathways and metabolites of Chinese herbal preparations, providing important information for further studies on the pharmacodynamic mechanisms and drug-drug interactions of Chinese herbal medicines.

2. Materials and methods

2.1. Materials

2.1.1. Chinese herbal preparations

Kidney tonic and aphrodisiac Chinese herbal preparations were made from Chinese herbs with the effect of tonifying the kidney and aphrodisiac as the main raw materials, which were processed, extracted, and other processes. The Chinese medicinal preparations used in this experiment included the oral liquid of *Lysimachia nummularia*, oral liquid of antler velvet, oral liquid of Wuzi Yanzong prescription, oral liquid of saffron, Gongxiaoling oral liquid, and ginseng pill.

2.1.2. Experimental equipment

In the process of chemical composition determination of kidney tonic and aphrodisiac herbal preparations, the experimental equipment to be used included, but was not limited to, the following:

(1) Liquid chromatography-mass spectrometry (LC-MS): Used for separating and detecting the chemical compositions in the medicines.

(2) Chromatographic column: An important part of the liquid chromatography-mass spectrometry instrument, which is used to separate the chemical components in the sample.

(3) Weighing instrument: Used for accurate weighing of samples and reagents.

(4) Centrifuge: Used for centrifugal separation of solid particles and liquids in drugs and samples.

(5) Oven: Used to dry the samples or reagents.

(6) pH meter: Used to determine the acid-base properties of drugs or reagents.

(7) Thermometer: Used to measure the temperature of the laboratory.

(8) Ultraviolet-visible (UV) spectrophotometer: Used to determine the absorption spectrum, absorbance, etc. of drugs or reagents.

(9) High-speed centrifuge: Used for rapid centrifugation of drugs or samples.

(10) Magnetic stirrer: Used to stir the reagents or samples well.

2.2. Research methodology

2.2.1. Detection steps

(1) Sample pretreatment: The composition and plant source of the herbal preparation were determined, and the relevant chemical composition structure, UV data, and mass spectrometry data were collected. The samples were crushed and screened to obtain uniform sample powder and extracted by adding appropriate amounts of methanol and other solvents according to certain ratios, so that the chemical components in the samples could be dissolved in the solvent.

(2) Experimental group separation detection method: The extracted sample liquid was injected into a liquid chromatography-mass spectrometer and separated using a chromatographic column. Through mass spectrometry detection, the molecular weight and ion fragment of each component were determined, thus obtaining detailed information about the chemical components in the sample. Further mass spectrometry detection clarified the fragments present in the molecule by cleavage of the fragments and compared them with the molecular weight and the raw source for compound attribution analysis. Additional high-resolution mass spectrometry assays were performed to accurately record the molecular formula. Finally, stereoisomers were identified using reaction mass spectrometry in combination with standards.

(3) Control group separation detection method: Chromatography was used for the chemical composition detection of the herbal preparations. The compounds in the samples were identified by separation and characterization, including separation using a chromatographic column and identification based on retention time. Meanwhile, data such as infrared spectra, miscibility points, and molecular weight were used for further confirmation and identification. Finally, the results were statistically and analytically analyzed to obtain the content and characteristics of the chemical components in the herbal preparations.

(4) Data analysis: The mass spectra obtained were processed and analyzed using mass spectrometry data analysis software. Through processing and analysis, a mass spectrometry spectrum library was established for subsequent chemical composition identification and quantitative analysis.

2.2.2. Configuration of sample solution

The sample solution was configured to ensure that the solubility was appropriate; the solution type was methanol, which can make the chemical components in the sample fully dissolved and separated by liquid chromatography-mass spectrometry, it was chosen to configure the dosage unit of 1 g/L. In addition, there may be some impurities in the sample, which will interfere with the separation and detection of the results. To avoid this effect, appropriate pretreatment steps, such as sample screening, filtration, or dilution, were taken when configuring the sample solution to minimize the presence of impurities.

2.2.3. Establishment of a mass spectral library

The establishment of a mass spectral library was for comparing the mass spectra obtained from the assay with an existing database to determine the chemical composition of the sample. By analyzing the mass spectral profile of the pure product, the molecular weight and ionic fragments of each chemical component were determined and the corresponding mass spectra were established. First, a standard column was selected to accurately collect the plots of each standard, and the retention time and mass spectral information of each standard was extracted. Then the corresponding mode was used to build a standard mass spectral library, which was finally adjusted to the positive and negative ion mode to collect the standards separately for library building.

2.2.4. Identification of sample composition

The chemical components in the two groups of samples were separated and detected one by one, and the mass concentration and content of each chemical component in the samples were determined by comparing them with the mass spectra in the mass spectrometry library, so as to identify and determine the composition of the Chinese herbal preparations.

2.3. Observation indicators

2.3.1. Excellent rate of detection method

(1) Excellent: The accuracy rate of chemical components of traditional Chinese medicine is significantly improved, the operation time is significantly shortened, the precision rate of purification operation is high, and the adaptive range of detection methods is significantly expanded.

(2) Good: The accuracy of chemical components of traditional Chinese medicine is improved, the operation time is slightly shortened, the precision rate of purification operation is good, and the adaptive range of the detection method is expanded.

(3) Poor: The accuracy of the chemical composition of each traditional Chinese medicine has decreased, the operation time has been extended, the precision rate of the purification operation has been reduced, and the adaptive range of the detection method has been narrowed.

Excellent rate = 100% × (excellent + good) / total number of cases.

2.3.2. Detection duration and retention time error

The detection time length and retention time error of the two groups were recorded, compared, and analyzed.

2.4. Statistical methods

This study used SPSS20.0 statistical software for data analysis. Measurement data were expressed as mean ± standard deviation (SD), and *t*-test was used; count data were expressed as number of cases (n) and rate (%), and χ^2 test was used. The difference was considered statistically significant at $P < 0.05$.

3. Results

3.1. Comparison of the excellent rate of detection method between the two groups

As shown in **Table 1**, the excellent rate of detection method in the experimental group (28/30, 93.33%) was significantly higher compared with that in the control group (22/30, 73.33%), and the difference was statistically significant ($P < 0.05$).

Table 1. Comparison of the excellence rate of detection method in the two groups [n (%)]

Groups	Number of cases	Excellent	Good	Poor	Excellent rate
Control group	30	13 (43.33%)	9 (30.00%)	8 (26.67%)	22 (73.33%)
Experimental group	30	18 (60.00%)	10 (33.33%)	2 (6.67%)	28 (93.33%)
χ^2 value	-	-	-	-	4.320
P value	-	-	-	-	0.038

3.2. Comparison of detection time and retention time error of the two groups' detection methods

As shown in **Table 2**, compared with the control group, the detection time and retention time error of the experimental group were significantly shorter, and the differences showed a highly significant correlation ($P < 0.001$).

Table 2. Comparison of detection time and retention time error between the two groups (mean ± SD, min)

Groups	Number of cases	Detection time	Retention time error
Control group	30	98.46 ± 7.37	0.21 ± 0.01
Experimental group	30	81.37 ± 6.91	0.10 ± 0.01
t value	-	9.265	42.603
P value	-	0.000	0.000

4. Discussion

Liquid chromatography-mass spectrometry (LC-MS) uses liquid chromatography as the separation system and mass spectrometry as the detection system. This technique combines the high separation ability of chromatography for complex samples with the high selectivity and sensitivity of mass spectrometry, as well as the ability to provide relative molecular mass and structural information. This study suggests that the LC-MS method demonstrates significant value in the detection of chemical constituents of kidney tonic and aphrodisiac Chinese herbal preparations, which is reflected in the following aspects:

(1) High detection rate: Compared with the traditional chromatographic method, the LC-MS method has a higher detection rate of chemical components in Chinese herbal preparations.

(2) High detection success rate: The success rate of the LC-MS method is significantly higher than that of the traditional chromatographic method in the detection of chemical constituents in Chinese herbal preparations for tonic kidney and aphrodisiac.

(3) Short detection time: The detection time of the LC-MS method is significantly shorter than that of the chromatographic method, which makes the detection process more efficient.

(4) Low retention time error: In the detection process, the retention time error generated by the LC-MS method is significantly lower than that of the chromatographic method, which further improves the accuracy of the detection.

Compared with the traditional chromatographic method, the LC-MS method usually has a higher rate of excellence in the determination of the chemical constituents of kidney tonic and aphrodisiac herbal preparations. Specifically, this method can provide higher sensitivity and selectivity, and reduce interfering substances in the sample, thus improving the accuracy and reliability of the detection results. Additionally, LC-MS is capable of efficient multi-component analysis, allowing for the simultaneous detection of multiple chemical components, improving analytical efficiency and cost-effectiveness. LC-MS can usually complete the separation and detection of samples in a shorter time, which is faster than traditional chromatographic methods. This is due to the fact that the liquid chromatography part allows for good separation of molecules using different columns and optimized methods as needed. The mass spectrometry (MS) part enables fast acquisition of mass spectrometry data for rapid identification and quantitative analysis. Therefore, LC-MS can save the experiment time and improve the analysis efficiency. In addition, the retention time error of the LC-MS method, i.e., the error in the retention time of separated peaks, is smaller. This helps to accurately determine the peak

shapes and peak heights of chemical components and improves the accuracy and reproducibility of the test results. Therefore, the LC-MS method is of high value in the determination of chemical constituents of kidney tonic and aphrodisiac Chinese herbal preparations, which can improve the accuracy, reliability, and analytical efficiency of the assay.

In addition to the application of LC-MS in the detection of the chemical composition of Chinese medicinal preparations, it is also widely used in other fields. For example, LC-MS technology can be used in vaccine research to analyze the composition, purity, impurities, and residues in vaccines, providing a powerful analytical tool for vaccine regulatory agencies to ensure the safety and reliability of vaccine products [6]. In food testing, the LC-MS method can be utilized to detect veterinary drug residues in food of animal origin to ensure food safety and compliance with regulatory requirements [7]. In clinical applications, tumor markers can be accurately measured by LC-MS, which can be used to study cancer biomarkers, monitor disease progression, assess treatment effects, and develop individualized medical treatment plans [8].

5. Conclusion

In summary, LC-MS has high value in the detection of the chemical composition of kidney tonic and aphrodisiac herbal preparations, which can significantly improve the excellent rate of detection method and detection success rate, shorten the detection time, and reduce the retention time error.

Disclosure statement

The author declares no conflict of interest.

References

[1] Xie R, Zhu Lg, Yu J, et al., 2020, A Study on the Mechanism of Action of Kidney Tonifying and Blood Activating Traditional Chinese Medicine in the Treatment of Degenerative Lumbar Spine Instability Based on Network Pharmacology. World Journal of Integrative Medicine, 15(11): 1992–1997 + 2006.

[2] Meng X, Zhang W, Zhao C, et al., 2020, A Preliminary Study on the Network Molecular Mechanism of Kidney-Yang Tonifying Traditional Chinese Medicine in Treating Gonadotropin-Deficient Male Infertility. Global Chinese Medicine, 13(01): 29–34.

[3] Wu C, Wei J, Chen H, et al., 2020, Prediction and Validation of the Biological Material Basis and Mechanism of Action of Kidney Tonifying and Essence Benefiting Traditional Chinese Medicines for Treating Diseases Related to Kidney Essence Deficiency Syndrome. Journal of Pharmacy, 55(03): 463–472.

[4] Wu C, Zhang J, Liu Y, et al., 2017, Study on the Intervention Effect of Kidney Tonifying and Liver Cleansing Chinese Herbal Medicine Pairing on p38MAPK/NF-κB Signaling Pathway in an Intermittent Hypoxia-Induced Human Umbilical Vein Endothelial Cell Injury Model. Chinese Journal of Traditional Chinese Medicine, 42(23): 4661–4664.

[5] Lu QY, He XS, Fang J, et al., 2022, Simultaneous Determination of Linezolid and Voriconazole Serum Concentrations Using Liquid Chromatography-Tandem Mass Spectrometry. J Pharm Biomed Anal, 2022(212): 114659.

[6] Li Y, Song Y, Wang WT, et al., 2023, Application of Liquid Chromatography-Mass Spectrometry in Vaccine Analysis. China Food and Drug Regulation, 2023(07): 30–43 + 143–144.

[7] Ji B, Yang L, Han Y, et al., 2023, Progress of Matrix Cleanup and Liquid Chromatography-Mass Spectrometry for

Multi-Residue Detection of Veterinary Drugs in Foods of Animal Origin. Journal of Light Industry, 38(05): 8–16.

[8] Fan X, Zhai R, Chu Z, et al., 2022, Progress in Quantification of Protein-Based Tumor Markers Based on Liquid Chromatography-Mass Spectrometry. Journal of Mass Spectrometry, 43(03): 263–277.

Publisher's note

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

Integrated Services Platform of International Scientific Cooperation

Innoscience Research (Malaysia), which is global market oriented, was founded in 2016.Innoscience Research focuses on services based on scientific research. By cooperating with universities and scientific institutes all over the world, it performs medical researches to benefit human beings and promotes the interdisciplinary and international exchanges among researchers.

Innoscience Research covers biology, chemistry, physics and many other disciplines. It mainly focuses on the improvement of human health. It aims to promote the cooperation, exploration and exchange among researchers from different countries. By establishing platforms, Innoscience integrates the demands from different fields to realize the combination of clinical research and basic research and to accelerate and deepen the international scientific cooperation.

Cooperation Mode

Clinical Workers

In-service Doctors

Foreign Researchers

China Collaborators

Oversea Collaborators

Hospital

University

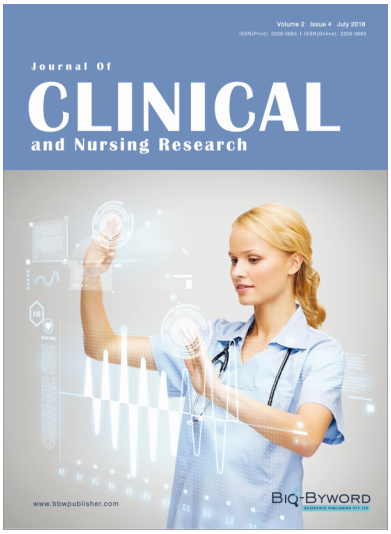
Scientific institutions

Our Journals

The *Journal of Architectural Research and Development* is an international peer-reviewed and open access journal which is devoted to establish a bridge between theory and practice in the fields of architectural and design research, urban planning and built environment research.

Topics covered but not limited to:

- Architectural design
- Architectural technology, including new technologies and energy saving technologies
- Architectural practice
- Urban planning
- Impacts of architecture on environment



Journal of Clinical and Nursing Research (JCNR) is an international, peer reviewed and open access journal that seeks to promote the development and exchange of knowledge which is directly relevant to all clinical and nursing research and practice. Articles which explore the meaning, prevention, treatment, outcome and impact of a high standard clinical and nursing practice and discipline are encouraged to be submitted as original article, review, case report, short communication and letters.

Topics covered by not limited to:

- Development of clinical and nursing research, evaluation, evidence-based practice and scientific enquiry
- Patients and family experiences of health care
- Clinical and nursing research to enhance patient safety and reduce harm to patients
- Ethics
- Clinical and Nursing history
- Medicine

Journal of Electronic Research and Application is an international, peer-reviewed and open access journal which publishes original articles, reviews, short communications, case studies and letters in the field of electronic research and application.

Topics covered but not limited to:

- Automation
- Circuit Analysis and Application
- Electric and Electronic Measurement Systems
- Electrical Engineering
- Electronic Materials
- Electronics and Communications Engineering
- Power Systems and Power Electronics
- Signal Processing
- Telecommunications Engineering
- Wireless and Mobile Communication