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Clinical Neuroscience Research

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Analysis and Discussion on the Effect of Early Rehabilitation on Motor Dysfunction in Patients with Acute Cerebral Infarction

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Abstract: *Objective:* To analyze the effect of early rehabilitation on motor dysfunction in patients with acute cerebral infarction. *Methods:* A total of 70 patients with acute cerebral infarction admitted to Suqian Zhongwu Hospital (our hospital) from January 2020 to December 2021 were selected as research subjects. The participants were divided into two groups through envelopes. The patients of the reference group (n = 35) received conventional treatment whereas the observation group underwent early rehabilitation and conventional treatment (n = 35). The scores of limb motor function (Fugl-Meyer Assessment [FMA]), functional independence (Barthel Scale), and Motor Assessment Scale (MAS) of the two groups were compared. *Results:* There was no significant difference between the scores of the two groups before treatment ($P > 0.05$); after early rehabilitation, the FMA and Barthel scale scores of the observation group were higher than those of the reference group, and the MAS scores of the observation group were also better than the reference group ($P < 0.05$). *Conclusion:* Early rehabilitation treatment on the basis of conventional treatment for patients with acute cerebral infarction can promote the recovery of motor function and improve the ability to perform daily activities of patients, thus it should be popularized.

Keywords: Early rehabilitation therapy; Acute stage of cerebral infarction; Motor dysfunction

Online publication: March 10, 2023

1. Introduction

The lifestyles of Chinese residents changed drastically in recent decades, leading to a trend of diseases that were originally more common in the elderly appearing among youngsters. Cerebral infarction is a type of ischemic cerebrovascular disease. The acute stage of cerebral infarction is characterized by rapid onset and disease progression and poor prognosis, with a high risk of disability or death. In addition, the disease also has a high risk of recurrence, with a rate of recurrence as high as 40% or more [1]. In the acute stage of cerebral infarction, the aorta supplying blood to the brain often has atherosclerosis or is accompanied by thrombus. When the blood supply to the local brain tissue is suddenly interrupted, the patient will experience dizziness, headache, nausea, vomiting, hemiplegia, aphasia, coma, etc. [2]. Even after symptomatic treatment, patients are prone to sequelae, the most common of which is limb motor dysfunction. Rehabilitation medicine believes that rehabilitation therapy can be carried out in the initial stage of the disease [3]. In this study, 70 patients with cerebral infarction admitted to our hospital (January 2020–December 2021) were selected as research subjects, and the 70 patients were grouped and compared to study the effect of early rehabilitation therapy on improving motor dysfunction in patients.

2. Materials and methods

2.1. General information

The study began in January 2020 and ended in December 2021. A total of 70 subjects were included in the study, all of whom were patients with acute cerebral infarction who were diagnosed and treated in our hospital within this time frame, and they were separated into a reference group and an observation by the envelope method. The patients in the reference group (35 patients) received conventional treatment, and the patients in the observation group (35 patients) underwent early rehabilitation on the basis of conventional treatment. The patients in the reference group were 44–68 years old, with an average of 56.29 ± 5.47 years old, and there were 18 male and 17 female patients; the patients in the observation group were 45–70 years old, with an average of 56.94 ± 5.52 years old, and there were 19 male and 16 female patients. There was no significant difference between the baseline data of the two groups ($P > 0.05$). This study was approved by the ethics committee.

Inclusion criteria: (i) Patients who were diagnosed with cerebral infarction based on the Chinese Expert Consensus on Emergency and First Aid of Acute Ischemic Stroke by the Emergency Medicine Branch of the Chinese Geriatrics Society (2018 edition) [4], with an onset of not more than 3 days; (ii) patients who are stable, conscious, and can communicate normally; (iii) patients with muscle strength of the affected side lower than level 4; (iv) Voluntary participation in this research, sign the consent form.

Exclusion criteria: (i) Patients with malignant tumors; (ii) patients with other organ failures; (iii) patients with motor dysfunction before the onset of cerebral infarction; (iv) patients with mental illness.

2.2. Methods

Both groups received routine treatment, mainly brain protection treatment, anticoagulant treatment, plaque stabilization, and blood vessel expansion. Patients in the observation group underwent early rehabilitation on the basis of conventional treatment. (i) An early rehabilitation treatment team was established, which consisted of experienced doctors and nurses. A targeted early rehabilitation plan was formulated for each patient based on their condition. (ii) Active and passive rehabilitation exercises were performed by the patients on the bed, and the nurses assisted the patients in passive rehabilitation exercises. The main exercises included knee flexion, elbow exercises, ankle joint exercises, shoulder joint exercises, sitting and standing exercises, etc. If the patient was unable to move on his/her own, it was necessary to regularly turn over the patient, move the joints, and massage the muscles; when the patient could move, the patient in performed posture exercises such as kneeling on the bed and four-point kneeling with assistance, and then gradually transitioned to sitting on the bed, standing by the bed, walking, etc. (iii) Acupuncture and moxibustion, rood therapy and other treatments was used to stimulate the recovery of nerve function according to condition of the patient. To avoid muscle stiffness or muscle spasm during treatment, a special muscle relaxation massage was performed on the patient by the nurses. (iv) The patients were protected when they changed position. For example, when the patient took a sitting position, a cushion was used to support the affected side to prevent him/her from slipping to the side. Besides, it can also avoid joint deformation of the patient due to improper position; when the patient had just started standing training, he/she could use the electric upright bed for assistance. (v) When the patient could get out of bed, he/she was required to practice daily activities such as standing, walking, dressing, washing, and so on with the company of the nursing staff. (vi) A scientific diet was formulated for each patient based on his/her condition. The patient's diet was comprehensive in nutrition and easy to digest, with lesser oil, salt, sugar, and low fat. (vii) The intensity of the exercise progressed from low to high based on the ability of the patient, so that it will be tolerable for the patient and avoid straining them. (viii) The patients were affirmed of their progress so that they could be more confident. Patients with slow recovery were also encouraged, and they were comforted so that they felt better.

2.3. Observation indicators

2.3.1. Limb movement function scores

The Fugel-Meyer (FMA) Rating Scale [5] was used to evaluate the limb motor function of the patients. Two dimensions of upper limbs and lower limbs were included. There were 10 items in the upper limb dimension, with a score range of 0–66 points; and 7 items in the lower limb dimension, with a score range of 0–34 points. The higher the score, the better the patient's limb motor function.

2.3.2. Functional independence

Before and after the intervention, the functional independence [5] of the patients were evaluated using the Barthel Scale. The scale ranges from 0 to 100 points. The higher the score, the better the patient's functional independence.

2.3.3. Motor Assessment Scale (MAS)

MAS was used to evaluate the occurrence time and strength of the resistance of the passively moving joints to stretch the spastic muscles [5]. No increase in muscle tone was classified as grade 0, mild increase in muscle tone was classified as grade 1 and grade 1+, markedly increased muscle tension was classified as grade 2, significantly increased muscle tone and difficulty in passive movement was classified grade 3, and stiffness when flexing or extending the affected part was classified as grade 4.

2.4. Statistical methods

The data obtained in the research were sorted out by Microsoft Excel and processed by SPSS 24.0. The count data were described as *n* (%), and the measurement data were described as mean ± standard deviation (SD). The differences between groups were analyzed by a *t*-test and χ^2-test, where a difference with $P < 0.05$ was considered significant.

3. Results

3.1. Limb movement function scores

There was no significant difference between the motor function scores of the upper and lower limbs in the FMA scale of the two groups before treatment ($P > 0.05$). After treatment, the motor function scores of the upper and lower limbs in the FMA scale of the observation group were higher than those of the reference group ($P < 0.05$), as shown in **Table 1**.

Table 1. Comparison of limb movement function scores between the two groups [(mean ± SD), points]

Group	Number of patients	Upper body		Lower body	
		Before treatment	After treatment	Before treatment	After treatment
Reference group	35	42.08 ± 2.45	53.37 ± 3.26 △	24.75 ± 1.32	27.36 ± 2.15 △
Observation group	35	41.79 ± 2.36	61.84 ± 3.56 △	24.54 ± 1.27	30.39 ± 1.43 △
t		0.504	10.453	0.678	6.942
P		0.615	< 0.001	0.499	< 0.001

Note: △ means there is a significant difference between the score before and after treatment ($P < 0.05$).

3.2. Functional independence

Before treatment, there was no significant difference between the scores of the Barthel scale of the two groups ($P > 0.05$). After treatment, the scores of the observation group were higher than those of the

reference group ($P < 0.05$), as shown in **Table 2**.

Table 2. Comparison of activities of daily living between the two groups of patients [(mean ± SD), points]

Group	Number of patients	Before treatment	After treatment	*t*	*P*
Reference group	35	66.24 ± 3.61	72.56 ± 4.15	6.797	< 0.001
Observation group	35	65.69 ± 3.53	84.78 ± 3.59	22.431	< 0.001
t		0.644	13.174	--	--
P		0.521	< 0.001	--	--

3.3. Motor Assessment Scale (MAS)

Before treatment, there was no significant difference between MAS score of the two groups ($P > 0.05$). After treatment, the MAS score of the observation group was significantly better than that of the reference group ($P < 0.05$), as shown in **Table 3**.

Table 3. Comparison of MAS score between the two groups

Group	Number of patients	Period	Grade 1	Grade 1+	Grade 2	Grade 3
Reference group	35	Before treatment	5	10	13	7
		After treatment	6	11	12	6
Observation group	35	Before treatment	3	10	14	8
		After treatment	8	15	9	3

4. Discussion

In recent years, the number of cerebral infarction patients in our country has increased significantly. On one hand, this is due to the continuous acceleration of aging in our country; on the other hand, it is also related to the development trend of the disease in younger age. Atherosclerosis is a major cause of this disease. After cerebral infarction, the blood supply and oxygen supply to the brain tissue of the patient becomes insufficient, which in turn causes the corresponding nerve function to be damaged to varying degrees. As a result, the nervous tissues of the brain are destroyed, while the motor nerves remain normal. The conduction of impulse is impaired, which leads to the impairment of limb motor function [6]. With the continuous advancement of medical technology, the mortality rate of this disease has declined, but there is still a high disability rate. Some researchers believe that the degree of recovery of brain function in patients with acute cerebral infarction is closely related to the time of medical intervention [7]. Therefore, early rehabilitation can be performed based on the theory of brain function reorganization and plasticity, in which the nerves motor pathway can be stimulated accordingly through passive and active rehabilitation exercises, and the damaged nerves' function can be restored [8]. Moreover, the excitability of the nerves can also be regulated, which will be helpful in improving limb dysfunction and restoring muscle contractility [9].

For early rehabilitation of patients with acute cerebral infarction, moderate exercise and other therapies can improve the enthusiasm of patients [10]. When performing motor function exercises, various rehabilitation techniques can be used to improve the muscle spasm of the affected limb as soon as possible. However, the purpose of rehabilitation should not only be to improve muscle strength, but also to improve the patient's functional independence. Through diversified rehabilitation exercises, patients can return to their normal lives as soon as possible [11]. Patients should be reminded to maintain aa correct posture during bed rest to reduce the risk of joint deformation, while passive and active training can promote blood circulation to maintain the basic functions of articular cartilage and traction and massage of muscles can

prevent muscle atrophy and degeneration. In addition, early rehabilitation also focuses on the reconstruction of brain tissue function. Repeated exercises can restore the lost motor function of the patient and help the patient return to normal lives. The results of this study showed their limb motor function and the functional independence of the patients in the observation group, who underwent rehabilitation on the basis of conventional treatment, were significantly improved. Moreover, the observation group also showed a greater improvement in all parameters compared to the reference group. These results are consistent with Zhang's research results in the article "Early Rehabilitation Therapy for Patients with Motor Dysfunction in the Acute Stage of Cerebral Infarction" [12], further confirming that the effectiveness and feasibility of early rehabilitation for patients with acute cerebral infarction on the basis of conventional treatment.

5. Conclusion

In conclusion, it can be seen that early rehabilitation for patients with acute cerebral infarction is conducive to promoting the recovery of lost motor function as soon as possible and is conducive to improving functional independence of patients.

Disclosure statement

The author declares no conflict of interest.

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Is C-Reactive Protein an Indicator of Periodontal Risk?

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Abstract: Periodontitis is a chronic, multifactorial, inflammatory disease caused by microorganisms and characterized by the progressive destruction of tooth-supporting tissue. In recent years, studies have shown a correlation and association between periodontitis and atherosclerotic cardiovascular disease, because both the disease has some similar risk factors and they produce an increase in plasma C-reactive protein (CRP) level. This protein has been attributed favorable characteristics as an inflammatory marker. This study was aimed to identify if there is any relationship between periodontitis and CRP values before starting periodontal treatment in a group of patients from the Faculty of Dentistry of the University of Costa Rica. Periodontal examinations were performed on 30 patients, and a blood sample was obtained from each patient to determine the P-CR concentration. The average P-CR was found to be 3.72mg/L (95%CI: 2.06–5.38), which is a moderate to severe risk marker. Fifty-four percent of the total patients had chronic generalized periodontal disease, with no significant difference between the different periodontal disease with gender (p=0.416) or age (p=0.477). Meanwhile, forty-three and three percent of the total patients had localized chronic periodontal disease, and gingivitis respectively. It was observed that the female gender showed a relatively higher cardiovascular risk compared to the opposite gender (p=0.640). In contrast, no statistically significant difference was found in the P-CR value by gender, age or the presence of other diseases, although it was higher in those with metabolic diseases (5.5mg/L) compared to those without (2.7mg/L).

Keywords: Periodontitis; C-reactive protein; Cardiovascular disease

Online publication: April 20, 2023

1. Introduction

Periodontitis is a chronic, inflammatory disease caused by multiple factors, mainly caused by dental biofilm. The mechanism which caused the damage is the production of pro-inflammatory cells that can damage the bone matrix, which are elevated in the bloodstream [1,2]. Bacteria can invade into the tissues that forms the periodontium, thereby generating an immune response by the host body against the bacteria, however, this response could cause damage to the healthy tissue [1]. Among the established risk factors for periodontal disease, there are some risk factors which are modifiable and related to an individual lifestyle, such as smoking, obesity, type II diabetes, stress, and diet. In addition, the incident of overweight and obesity are increasing in recent years, and become a global public health problem. Several studies have shown a higher prevalence or severity of periodontitis incident in the overweight or obese individuals compared to non-overweight individuals [3]. The difference in the internal environment between these two groups may contribute to this observation, for example, there are some differences in the oral microbiota content

between the overweight or obese individuals and non- non-overweight individuals [4]. More research is conducted with the aim to find the link between individuals with obesity and increased level of inflammatory response. Further, the increase in inflammatory mediators is thought to be produced by the adipose tissues [5].

In addition, some studies have linked some clinical manifestations of cardiovascular disease (such as myocardial infarction, stroke, angina or sudden death) to the inflammatory alterations produced by periodontitis [6,7].

The inflammatory aspect of these two conditions can be justified by the similarity in the pathogenic, clinical, and pathophysiological features [8]. Both the conditions are linked to the systemic effects of bacterial lipopolysaccharides released at the site of periodontal infection, subsequently travel through the bloodstream and can anchor in the sub-endothelium of the intima, leading to overexposure of adhesion molecules by the endothelial cells. This binding leads to the detection of proinflammatory proteins such as proinflammatory cytokines or some other substances such as C-reactive protein found in plasma [9]. C-reactive protein is an accurate biomarker used in the inflammatory and infectious processes, interestingly, the American Heart Association included the increase in the C-reactive protein level as a cardiovascular risk factor.

C-reactive protein is a plasma protein involved in the acute phase response, a phenomenon involving non-specific biochemical changes in response to inflammatory and infectious processes, malignancies or tissue damage [10]. Further, the liver is the major site for the synthesis and secretion of this protein, and its production is increased in response to interleukin stimulus [11].

In most countries, the prevalence of periodontitis is estimated to be greater than 50% [12]. Meanwhile, in a study conducted in Costa Rica, the prevalence of periodontal disease was found to be 35%, with a prevalence of 59.10% and 40.64% in the age group 20-45 years and age group 64 years and older respectively [13].

Globally, cardiovascular diseases are the leading cause of death, and in Costa Rica the figures are very similar. According to the National Institute of Statistics and Censuses (NISC) report, of the 11,000 deaths registered in the first half of 2020, 573 death cases were due to acute myocardial infarction, while more than 1, 200 death cases are reported due to heart-related and cerebrovascular diseases.

Given the high incidence of patients suffering from both the diseases and there is a correlation between both the diseases, therefore this study was conducted with the aim of finding the concentration of C-reactive protein in a group of patients who come for periodontal treatment to the Preclinic of Periodontology of the University of Costa Rica. Knowledge of these values will relate the blood findings to the extent of periodontal disease and whether there are other inflammatory diseases that may be associated.

2. Materials and methods

This study was conducted in 30 patients who attended the Faculty of Dentistry of the University of Costa Rica to receive the periodontal treatment. The informed consent form was approved by the Scientific Ethical Committee of the University of Costa Rica in session No.260 on October 9, 2013, and the form was signed by the patients prior to participation in this study. Participants were selected based on the following inclusion and exclusion criteria.

Inclusion criteria:

(1) Individuals over 18 years of age.
(2) Individuals with clinical diagnosis of chronic periodontitis.
(3) Individuals with at least 20 teeth in the mouth

Exclusion criteria:

(1) Individuals who have started the periodontal treatment within the last 6 months.
(2) Individuals who have received antibiotic therapy 6 months before starting the treatment
(3) Women who are pregnant or breastfeeding

All patients underwent a health questionnaire and were asked if they suffered from any chronic diseases such as diabetes or hypertension. A periapical radiographic examination was performed with a parallel technique, periodontal probing was performed in six sites per tooth, the degree of mobility, and the indices of bleeding and dental plaque were established. All this test was performed in the Periodontics Preclinic, reviewed, and endorsed by the section instructors. With the information obtained, a periodontal diagnosis was made for each patient.

Before starting the treatment, a blood sample was obtained from each participant. The collected blood samples were analyzed using the quantitative determination of hs-CRP (high-sensitivity C-reactive protein) in serum on the Roche/Hitachi cobas c111 systems. Measurements of P-CR concentrations were performed at the Centre for Research in Cellular and Molecular Biology of the UCR (CRCMB).

3. Results

The medical, dental, and periodontal condition of 30 patients was analyzed. A convenience coding was established for each variable; categorizing gender as 0 for men and 1 for women; periodontal diagnosis as 0 for gingivitis, 1 for localized chronic periodontitis and 2 for generalized chronic periodontitis; associated metabolic diseases as 0 for those without systemic involvement, 1 for diabetes mellitus, 2 for arterial hypertension, 3 for rheumatoid arthritis and 4 for other pathologies. In addition, the age in years of each patient and the P-CR value (mg/L) obtained from the laboratory examination was included. A summary of the findings is presented in **Table 1**.

Table 1. Coded data of the subjects participating in the study, according to gender, age, periodontal diagnosis, C–reactive protein (CRP) value and the presence of associated metabolic diseases (UCR, J. Castillo).

No.	Gender	Age (Years)	Periodontal diagnosis	P–CR value (mg/L)	Associated diseases
1	0	43	1	7.81	0
2	1	57	2	5.35	1
3	1	47	2	12.55	4
4	0	55	1	20.35	4
5	1	29	2	5.33	0
6	1	51	2	3.63	0
7	1	66	1	5.2	3
8	1	58	1	1.18	2
9	0	42	2	2.07	0
10	0	63	2	0.84	0
11	0	33	2	0.57	0
12	0	34	1	1.89	0
13	0	47	2	0.95	0
14	0	40	2	0.71	4
15	0	21	2	0.43	0
16	1	32	0	0.60	0

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No.	Gender	Age (Years)	Periodontal diagnosis	P–CR value (mg/L)	Associated diseases
17	1	31	1	1.28	0
18	0	23	1	0.51	0
19	0	35	2	1.05	0
20	0	59	2	1.49	4
21	0	29	1	2.1	0
22	1	42	2	2.02	0
23	0	54	2	0.63	0
24	1	23	1	1.25	0
25	1	55	2	2.37	4
26	0	51	1	1.05	4
27	0	40	2	9.50	0
28	0	37	1	9.25	0
29	1	27	1	4.29	4
30	0	46	1	5.42	4

Based on **Table 1**, the mean age was 42.7 years (95%CI: 38.2-42.7), of which 40% were female. Although no statistically significant difference was found in the mean age of females compared to males, it was observed that the female gender had a higher P-CR concentration value compared to the male gender.

Table 2 summarizes the results of the age groups with the highest cardiovascular risk according to P-CR levels. The range with the highest cardiovascular risk ranged from 40-49 years.

Table 2. Patients were classified according to a ten-year age group by cardiovascular disease risk (UCR, J. Castillo)

Ten-year age groups	Low Risk		Medium Risk		High Risk	
(years)	#	%	#	%	#	%
20–29	2	40%	2	40%	1	20%
30–39	2	28.5%	3	42.8%	2	28.5%
40–49	2	25%	2	25%	4	50%
50–59	1	12.5%	4	50%	3	37.5%
60 and above	1	50%	0	0%	1	50%

Figure 1 presents the percentage of distribution of the participants' metabolic conditions. 36% of the patients had chronic metabolic diseases, such as type 2 diabetes mellitus, hypertension or rheumatoid arthritis.

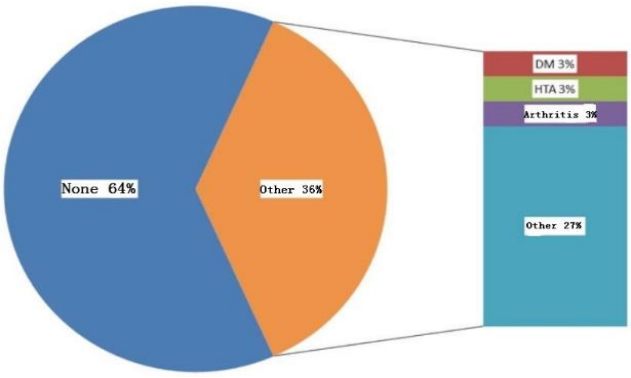

Figure 1. Distribution of patients according to disease prevalence (UCR J. Castillo)

Regarding periodontal diseases, 3% of the patients had gingivitis, 43% had localized chronic periodontal disease, and 54% had generalized chronic periodontal disease, with no statistically significant difference by gender (p=0.416) or age (p=0.477).

Regarding the P-CR value, the average was found to be 3.72mg/L (95%CI: 2.06–5.38) (MODERATE TO HIGH RISK). Although no statistically significant difference was found in P-CR values by sex, age or the presence of other metabolic diseases, the average was higher for those with disease (5.5mg/L) compared to those without (2.7mg/L). These data are shown in **Figure 2**.

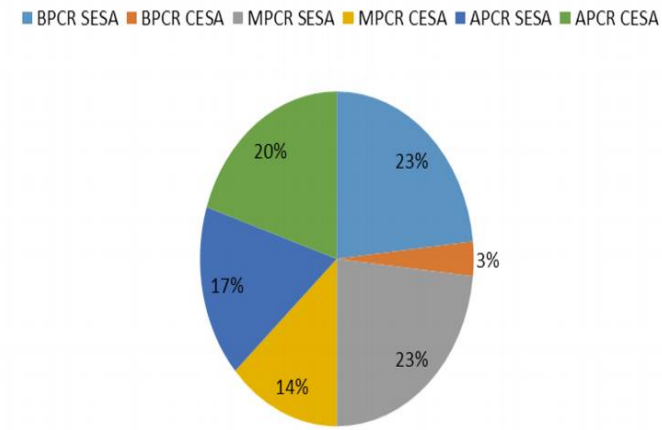

Figure 2. Percentage distribution of patients, according to P-CR content and the existence of associated systemic diseases (UCR, J. Castillo). Note: BPCR SESA=Low P–CR content (<1mg/L) and no associated systemic disease; BPCR CESA=Low content of P–CR content (<of 1mg/L) and with the existence of associated systemic disease; MPCR SESA=Medium content of P–CR (from 1 to 3mg/L) and no associated systemic disease; MPCR CESA=Medium content of P–CR content (from 1 to 3mg/L) and with the existence of associated systemic disease; APCR SESA=High P–CR content (≥ 3mg/L) and no associated systemic disease. APCR CESA=High P–CR content (≥ 3mg/L) and with associated systemic disease.

Although no statistically significant differences were found by periodontal diagnosis, gender, age or the presence of other comorbidities, those who reported having chronic diseases had higher P-CR values. Of all the patients, 26% showed low levels (less than 1mg/L), 37% showed medium levels (1–3mg/L) and 37% showed higher levels (more than 3mg/L). These values are related to patients who did not report any metabolic condition.

4. Discussion

Differences related to gender and age were not significant. According to published research [10], serum

levels have been found to be slightly higher in women than in men, which is consistent with the results obtained in the present study.

The age range with the highest cardiovascular risk was 40-49 years. A linear behavior is observed with respect to the age range and cardiovascular risk, according to the observed P-CR values. Some studies have shown that the average concentration of P-CR in healthy blood donors is 0.8mg/L, but when stimulated the level of P-CR can increase its production more than ten thousand times [10]. The same researchers concluded that the serum levels of P-CR tend to increase with age with an increase in the frequency of subclinical inflammatory processes and the number of apoptotic phenomena.

With respect to systemic condition and gender, this study showed no relevant differences, this may also be affected by the small sample size. Despite the above, the results showed that 50% of all female subjects had associated systemic diseases such as hypertension, diabetes mellitus, rheumatoid arthritis or asthma. Of the male subjects, the percentage of patients with associated systemic diseases was lower (33%) compared to the opposite gender.

In the case of cardiovascular disease, especially atherosclerotic disease, its impacts differ according to sex, regardless of whether individuals have the same prevalence of coronary risk factors [14]. The deleterious effect manifests itself later in women as seen in acute myocardial infarction, whose average age of presentation is 10 years later than in men. Therefore, the male gender is more prone to present cardiovascular alterations and to manifest them at a younger age compared to the female gender. This characteristic is shared by cerebrovascular disease (CVD) and periodontal disease.

With regard to P-CR levels, a mean of 3.72mg/L was obtained, which is within the high-risk range for cardiovascular disease. According to the sources consulted, high-sensitivity P-CR (hs-CRP) is cited as an accepted inflammatory marker as a predictor of cardiovascular risk [15]. The same authors suggested that, based on the publication of the American Heart Association and the Center for Disease Control, (USA, since 2003), plasma hs-CRP concentrations below 1mg/L is considered a low CVD risk, whereas, concentrations fluctuating between 1–3mg/L is considered a medium risk. On the other hand, concentrations above 3mg/L are associated with an increased risk of developing cardiovascular disease and values above 3mg/L are used to define individuals at high cardiovascular risk.

The P-CR values found were not significant in respect to age, sex or periodontal diagnosis. However, the behavior of P-CR in relation to the presence of systemic involvement shows that P-CR levels increase more in these patients in particular.

According, to **Figure 2** on the percentage distribution of P-CR level and the existence of associated diseases, the differences between the high, medium and low risk groups, as mentioned above, were not significant.

According to the same figure, the total sample with both low and medium levels of P-CR, the highest percentage of the sample was represented by patients without associated systemic diseases. This situation varied in the group with high P-CR levels, where out of the total of 37%, a higher percentage of patients with high P-CR levels (above 3mg/L) and associated systemic diseases (20%) was observed, compared to the group of patients with high P-CR levels without associated systemic diseases.

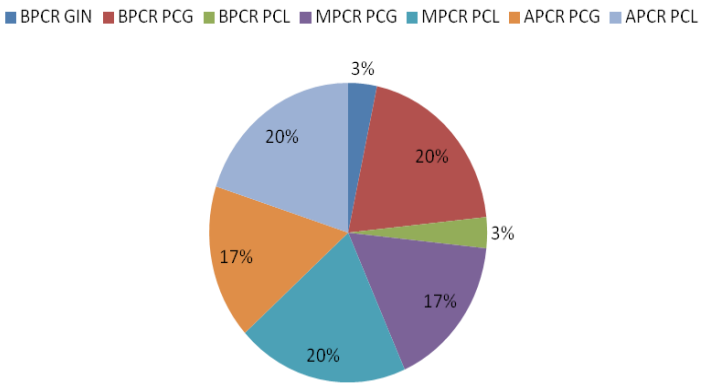

Figure 3. Percentage distribution of patients, according to P-CR content and periodontal diagnosis (UCR, J. Castillo). Note: BPCR GIN=Low P-CR levels (< 1mg/L) and gingivitis; BPCR PCG=Low P-CR levels (< 1mg/L); BPCR PCL=Low P-CR content (< 1mg/L) and localized chronic periodontitis; MPCR PCG=Medium P-CR content (1 to 3mg/L) and chronic generalized periodontitis; MPCR PCL=Medium P-CR content (1 to 3mg/L) and localized chronic periodontitis; APCR PCG=High P-CR content (≥ 3 mg/L) and chronic generalized periodontitis; APCR PCL=High P-CR content (≥ 3 mg/L); and localized chronic periodontitis.

These results are comparable with another published research [16]. The author observed that some individuals with periodontal disease had altered P-CR levels, however, not all individuals with periodontitis has an altered P-CR level. This was similar in this study, where 6 of the 16 subjects diagnosed with chronic generalized periodontitis (37.5%) had values considered to be at low cardiovascular risk, being below 1mg/L of P-CR in blood. The same authors Cite Beck and Offenbacher, who justify this behavior on the basis of genetic evidence, as some people have a hyperinflammatory phenotype, responding in an exaggerated manner to an inflammatory stimulus, such as, periodontal disease.

Periodontitis, like any other disease, is capable of promoting inflammation [17], further lead to increase in the P-CR levels [18]. As a result of the correlation between high P-CR levels and periodontal disease, the study did not show any significant relationship.

5. Conclusion

The results of P-CR levels showed a mean value of 3.72mg/L, equivalent to a high risk of cardiovascular disease. There was no statistically significant relationship between P-CR values and sex, age, metabolic diseases and periodontal condition. The highest PC-R values were found in some patients with no history of metabolic diseases.

Disclosure statement

The authors declare no conflict of interest.

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Mechanisms of Cognitive Improvement After Carotid Endarterectomy: Results of an Autopsy

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Abstract: To develop a clinically meaningful definition of cognitive change before and after carotid endarterectomy (CEA), we categorized patients with "improved postoperative function" and "non-improved postoperative function" based on subjective assessment and neuropsychological tests. The results showed that 11% of the patients showed an improvement in postoperative function. Through single-photon emission computerized tomography (SPECT), positron emission tomography (PET), magnetic resonance imaging (MRI), etc., it was found that improvement of cerebral blood flow by carcinoembryonic antigen (CEA) → improvement of cerebral metabolism → improvement of cerebral cortical neuroreceptor function and cerebral white matter microstructure → improvement of cognitive function. The degree of preoperative cerebral hemispheric white matter lesions was the rate-limiting factor for improvement in cognitive function.

Keywords: Carotid endarterectomy; Cognition; Cerebral blood flow; Cerebral metabolism; Small vessel diseases

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1. Introduction

Carcinoembryonic antigen (CEA) for severe stenosis of the cervical internal carotid artery is a well-established technique for preventing the onset or recurrence of ischemic attacks. Since the 1970s, there have been two schools of thought that cognitive function improves or remains the same after CEA [1-8]. However, no clear conclusion has been reached. Although there are many factors involved, such as differences in the case groups analyzed, the most important reason for this is that the definition of "improvement in cognitive function" for each case is different and has not been clearly defined. In this review, we will describe the concept and definition of improvement in cognitive function after CEA, and then outline the mechanism of improvement based on our own experience [1,9-17]. The study on which the following description is based was approved by the Ethics Committee of the University, including off-label use.

2. Concept of cognitive functional change after CEA

Neuropsychological testing is used to examine changes in cognitive function before and after surgery. Neuropsychological testing is an objective quantitative test of cognitive function, but it has several drawbacks, one of which is the practice effect: It was demonstrated that when the same neuropsychological test was repeated within 3 months, test scores were more likely to improve in patients under 75 years of age due to the practice effect [1,18]. To overcome this drawback, neuropsychological tests with two different test items were created. However, from the standpoint of the examinee, the first neuropsychological test is

often more stressful, while the second time is often less stressful because the examinee has some understanding of the situation. Since neuropsychological tests using two different test items do not solve this problem, the practice effect should always be considered [18]. Moreover, neuropsychological tests include tests with no upper limit to the score, such as the Wechsler Adult Intelligence Scale (WAIS), and tests with an upper limit, such as the Hasegawa Simplified Scale for Dementia (HDS-R) or the mini mental state examination (MMSE). In tests with an upper limit, patients whose cognitive function is higher than the national average by nature cannot be detected before and after surgery. We believe that these tests are not suitable for observing pre- and post-operative changes. Therefore, we examined the changes in cognitive function before and after surgery. First, we performed the WAIS-Revised, WRS, and Rey–Osterrieth Complex Figure (ROCF) test, which are three neuropsychological tests with no upper limit to the scores, twice, in 40 normal subjects with no abnormal findings on MRI over a period of 3 months, and then determined the amount of change (postoperative vs. preoperative). More than 200 CEA cases were subjected to preoperative neuropsychological testing. Next, the surgeon and the patient's family members evaluated whether the patients' cognitive function improved postoperatively in each case. By this subjective definition, 11% of patients showed an improvement in postoperative function. In addition, a postoperative neuropsychological examination was conducted, and the amount of change in the pre- and postoperative neuropsychological scores was calculated. Here, the optimal pre- and postoperative score change for each neuropsychological test to detect postoperative improvement was determined by receiver operating characteristic (ROC) analysis. As a result, postoperative improvement in each case could be detected with a sensitivity and specificity of 80% and above, which means that the pre- and postoperative score change in one of the five items of the WAIS-R (verbal IQ, performance IQ), WRS (MQ), or ROCF test (copy, recall) was the mean change in score of normal subjects + 2 standard deviations or more. It should be noted that these optimal pre- and postoperative score changes are data for patients younger than 76 years of age, and that the practice effect becomes less significant for patients older than 76 years of age, resulting in a smaller difference between pre- and postoperative scores [9].

Subsequent data were based on this definition of neuropsychological testing, and each case was defined as "improved postoperative function" and "non-improved postoperative function".

3. Mechanisms of cognitive improvement after CEA

Theoretically, there is no mechanism for improvement of cognitive function after CEA other than improvement of cerebral blood flow as a result of the release of stenosis, as described at the beginning of this paper. Therefore, to prove this hypothesis, cerebral blood flow SPECT was performed before and after surgery [10]. As a result, the patients who showed postoperative improvement in cognitive function showed an increase in cerebral blood flow at the operated part, and it exceeded a certain threshold (**Figure 1**). However, the increase in cerebral blood flow at the operated part was not necessarily followed by an improvement in cognitive function," with a 50% chance of improvement [10]. This was true even when CEA was limited to asymptomatic lesions [11]. What then is the mechanism of cognitive function improvement when cerebral blood flow in the operated hemisphere increases? In this study, cerebral blood flow in the cerebellar hemisphere was measured in addition to cerebral blood flow in the cerebral hemisphere. In other words, we evaluated the relative postoperative changes in cerebral metabolism in the operated cerebral hemisphere by measuring pre- and postoperative changes in cerebral metabolic status or blood flow, crossed cerebellar diaschisis, or hypoperfusion in the contralateral cerebellar hemisphere, which reflects the cerebral metabolic status of the unilateral cerebral hemisphere. The results showed that in cases of postoperative improvement in cognitive function, in addition to an increase in cerebral blood flow in the operated cerebral hemisphere, there was a significant increase in the contralateral/affected ratio of cerebellar blood flow, that is, the disappearance of crossed cerebellar hypoperfusion (**Figure 1**). This

indicates that in the operated cerebral hemisphere, cognitive function improves only when cerebral blood flow increases → cerebral metabolism improves.

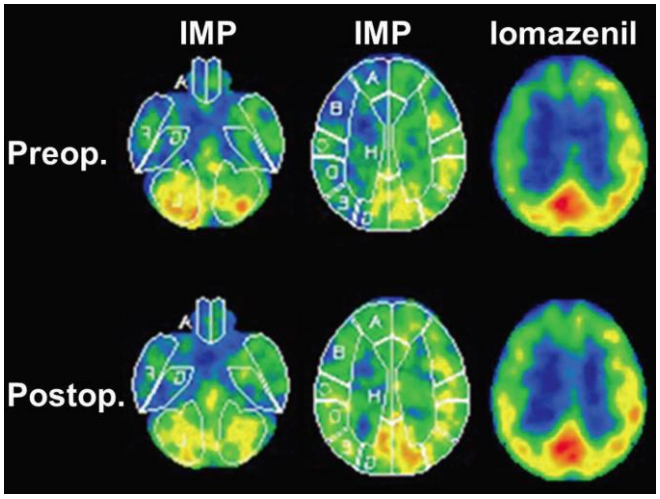

Figure 1 [10]**.** A 70-year-old man with symptomatic right internal carotid artery stenosis (95%) exhibited improvement in cognitive function after CEA. Brain perfusion (IMP) SCET images show postoperative decrease in asymmetry of tracer uptake between bilateral cerebral and cerebellar hemispheres. 123I-iomazenil SCET images showed a postoperative decrease in asymmetry of tracer uptake between bilateral cerebral and cerebellar hemispheres.

Therefore, we investigated three methods to directly measure cerebral hemispheric metabolism. The first method proton MRS, which can determine cerebral metabolism by using the NAA/creatinine ratio or choline/creatinine ratio. The NAA/creatinine ratio or choline/creatinine ratio significantly increased postoperatively in patients whose cognitive function improved after CEA compared to those whose cognitive function did not improve (**Figure 2**) [12]. Another study of glucose metabolism using 18F-FDG PET also demonstrated that patients with improved cognitive function after CEA had a significantly larger area of improved glucose metabolism in the operated cerebral hemisphere postoperatively than those without improvement (**Figure 3**) [13]. The third method was 18F-FRP170PET, which can detect tissues surviving under hypoxic conditions, before and after CEA [14]. The results showed that cognitive function was improved after CEA. As a result, the patients with improved cognitive function after CEA showed increased tracer accumulation in the operative cerebral hemisphere preoperatively, which disappeared postoperatively (**Figure 4**). This finding can be interpreted as the result of a hypoxic environment in which the nervous tissue voluntarily stopped functioning due to hypoperfusion and that oxygen metabolism was reduced as much as possible before surgery. The increased blood supply after CEA then caused the nervous tissue to begin functioning and oxygen metabolism to normalize [14,15].

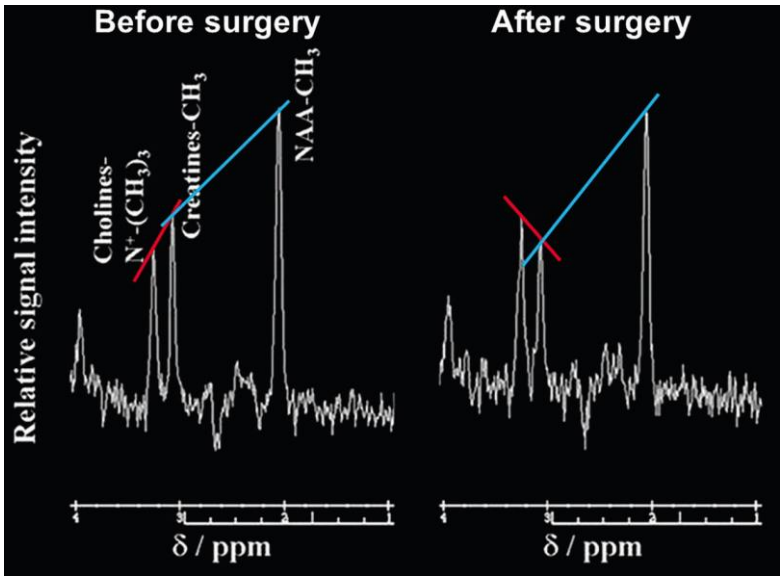

Figure 2 [12]**.** Proton magnetic resonance spectra obtained by using point-resolved spectroscopy in the region of interest in the cerebral hemisphere ipsilateral to the surgical site in a 62-year-old man with improved cognition after endarterectomy for symptomatic right internal carotid artery stenosis. Area for the NAA (cyan lines) or choline peak (red lines) to the area for the creatine peak is relatively increased after surgery (graph on the right) compared to the preoperative spectrum (graph on the left).

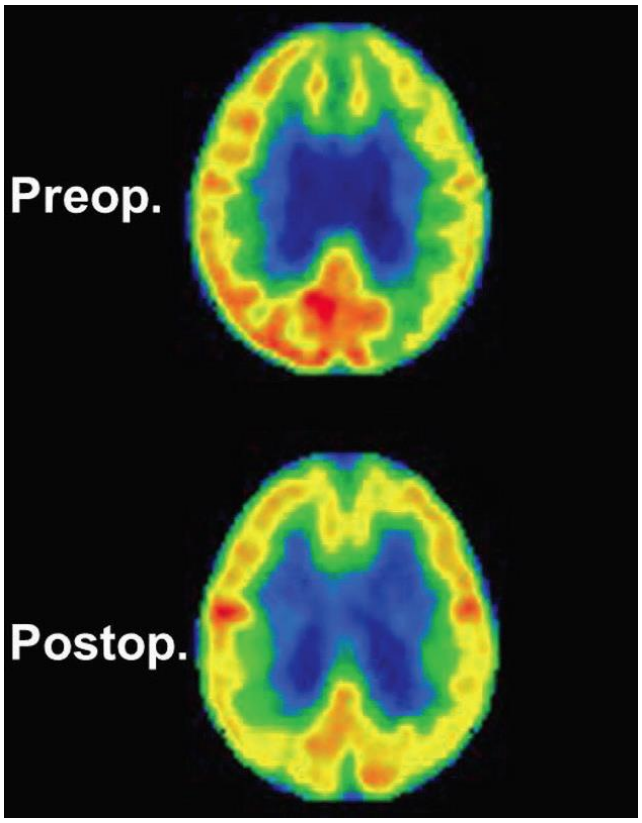

Figure 3 [13]**.** 18F-FDG PET obtained in a 69-year-old male with symptomatic left internal carotid artery stenosis exhibiting cognitive improvement after endarterectomy. Postoperative image reveals increased tracer uptake in the ipsilateral cerebral cortex as compared to preoperative images.

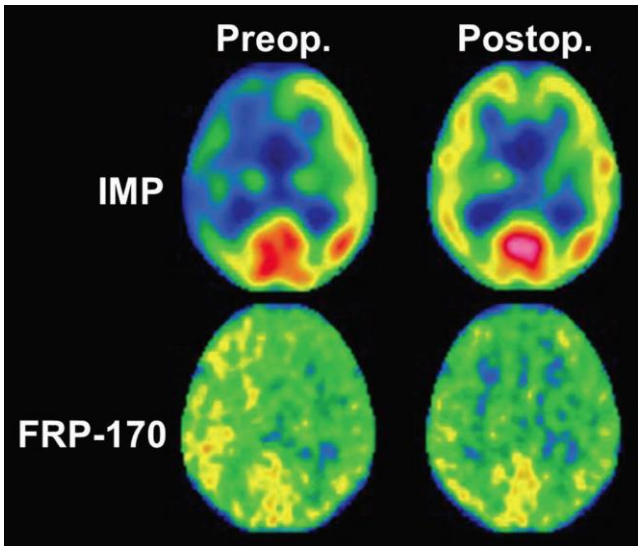

Figure 4 [14]**.** Brain perfusion SPECT (IMP) and FRP170 positron emission tomography images from a 72-year-old man with symptomatic right cervical internal carotid artery stenosis and improved cognition. Cerebral blood flow and FRP170 accumulation were reduced and increased, respectively, in the right cerebral hemisphere compared to the left cerebral hemisphere. These changes resolved after surgery.

We also examined cortical and white matter function in relation to cognitive improvement. We measured cortical neuroreceptor function using 123I-iomazenil, which binds to the abundant central benzodiazepine receptors in the cortex, and SPECT was used to visualize its binding ability [10]. The results showed that the cortical neuroreceptor binding capacity of 123I-iomazenil in the operated cerebral hemisphere increased in patients with improved cognitive function after CEA (**Figure 1**). Moreover, this phenomenon requires increased cerebral blood flow in the operated cerebral hemisphere and is strongly correlated with the disappearance of crossed cerebellar hypoperfusion [10]. For cerebral white matter, the fractional anisotropy (FA) values obtained from diffusion tensor magnetic resonance imaging (DTI) were quantitatively analyzed by tract-based spatial statistics analysis. Patients with improved cognitive function after CEA had a higher FA value than those who showed no improvement in cognitive function (**Figure 5**). Furthermore, this increase was demonstrated to extend to the frontal lobe of the contralateral cerebral hemisphere. The restructuring of cerebral white matter nerve fibers is thought to indicate remyelination of nerve fibers, and the main constituent of myelin is choline. We mentioned above that the choline/creatinine ratio in the operative cerebral hemisphere increased in patients with improved cognitive function after CEA, which is consistent with the increase in FA values using DTI [16].

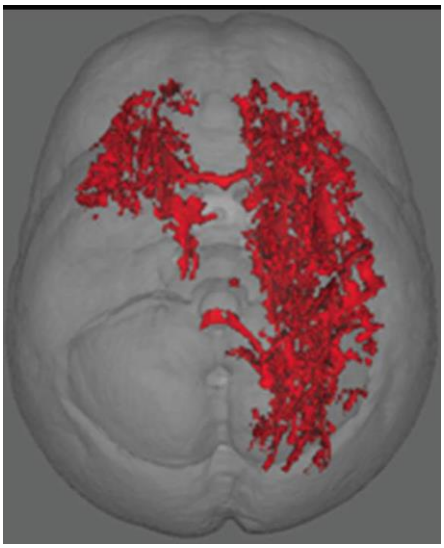

Figure 5 [16]**.** Voxels with significant postoperative increase in cerebral white matter fractional anisotropy in patients with cognitive improvement after carotid endarterectomy are expressed as red-yellow dots on three-dimensional images.

In summary, we can see that there is a flow of improvement of cerebral blood flow by CEA → improvement of cerebral metabolism → improvement of cortical neuroreceptor function and cerebral white matter microstructure → improvement of cognitive function. However, the biggest question here is why the first rate of speed, i.e., the rate at which cerebral blood flow improves with CEA and cognitive function improves thereafter, is so high in half of the cases, while the rate at which cerebral blood flow improves but cognitive function does not improve thereafter is so low in half of the cases? We hypothesized that this rate-limiting factor was irreversible dysfunction of the cerebral hemispheres that already existed prior to CEA. It is well known that small vessel diseases are an independent risk factor for cognitive dysfunction. Therefore, we compared the pre-operative presence of various small vessel diseases, pre- and post-operative changes in cerebral blood flow, and the presence of cognitive improvement, and found that post-operative increased cerebral circulation and pre-operative white matter lesion volume were significantly associated with cognitive improvement [17]. Specifically, if cerebral hemispheric white matter lesions are Fazekas grade 2 or 3, cognitive function does not improve even if there is an increase in cerebral blood flow [17]. Conversely, if cerebral hemispheric white matter lesions are light (Fazekas grade 0 or 1) and cerebral blood flow is increased, cognitive function improves by 89% [17].

4. Conclusion

CEA is a technique that drastically changes cerebral blood flow without touching the brain, and it is a model that allows us to examine changes in cerebral blood flow and brain function in detail. We hope that new discoveries will be made in the future.

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Disclosure statement

The authors have completed a COI self-report to the Japanese Neurosurgical Association.

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Rare Neurodegenerative Disease: Systematization of Nursing Care in Patients Affected by Huntington's Disease

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Abstract: Huntington's disease is a rare neurodegenerative condition of genetic origin, which incapacitates the patient in carrying out daily activities over time and that has no cure. Thus, the monitoring of these individuals through systemized nursing is essential to reduce the impacts of the disease, because it allows a holistic look into the needs of the affected by professionals. This article elaborates on the systematization of nursing care to Huntington's disease patients and their families. 3 clinical cases of the disease were selected, data collection was performed from October 1–November 30, 2018. The study enabled the development of actions based on the real needs of individuals and facilitated the development of nursing care.

Keywords: Rare diseases; Huntington's disease; Nursing care; Genetics; Nursing diagnoses

Online publication: May 24, 2023

1. Introduction

According to the Ministry of Health, rare diseases affect 65 people per 100 thousand individuals. Most of these diseases are chronic, degenerative conditions that have no cure or specific treatment, with high morbidity and mortality rates. It is estimated that there are 6000-8000 types of rare diseases (RDs), and 80% of them are of genetic origin. Approximately 8% of the world population is affected by one of these diseases; in Brazil, it is estimated that there are between 13 and 15 million people affected by rare diseases [1].

Huntington's disease (HD) stands out as a rare neurodegenerative condition of autosomal dominant character and genetic origin. The condition is caused by the expansion of the cytosine-adenine-guanine (CAG) trinucleotide contained in the DNA. The normal amount of CAG triplet varies from 10 to 35 repeats, while patients with HD has 36 or more repeats. This disease appears between 30 and 60 years of age, regardless of gender. However, it can be detected earlier in the clinical picture; in this case, with the denomination of juvenile HD, in which greater impacts and anticipation of signs and symptoms are observed [2-3].

Clinically, there are three stages of HD. In the first stage, the affected individual has subtle changes in coordination, like chorea and bradylalia, such as involuntary movements, as well as mild cognitive decline, irritability, and depression. In the second stage, speech and swallowing are also affected, which results in

dysphagia, aphasia, muscle atony, and decline in logical thinking abilities. In the third and last stage, bradykinesia, joint stiffness, and severe cognitive decline are manifested, even reaching a vegetative state, which eventually leads to death [4].

With the progression of symptoms, the patient gradually loses his/her ability to perform daily activities, the loss of autonomy will become the main challenge faced by both the affected person and the family, because as the disease progresses, more care will be needed. In addition, these people usually lack knowledge and information about the disease and end up having difficulties in access to diagnosis and treatment, and the situation is aggravated by the lack of qualified health teams and professionals [5].

Professional nurses will be the most important discipline for this disease, because professional nurses are the ones who will be in constant contact with patients and their families, and provide care according to the relevant guidelines, such as the Systematization of Nursing Care-SAE [2].

For patients with neurodegenerative diseases, specifically HD, the SAE becomes even more necessary due to the symptoms that the affected individuals present. The neural deterioration caused by these diseases results in the inability of the individual to perform activities of daily living, requiring individual and comprehensive care, as recommended by the SAE. Thus, the role of the nursing team will be based on the early identification of the symptoms that will result from the disease. In addition, they will monitor and improve the condition of the individual as much as possible, in order to promote a better quality of life [2].

This study aimed to develop and apply the SAE to three people with HD to improve the monitoring of affected patients and reduce the impacts of the disease. Thus, given the above and the ideas developed so far, the following guiding question of this study was presented: what are the main highlights of the SAE in the care of patients with HD for a continuous care and higher quality?

2. Methods

A descriptive study of clinical cases was carried out through the elaboration of the SAE, based on the Theory of Basic Human Needs (NHB), by Wanda Aguiar Horta, which is based on the psychobiological, psychosocial and psychospiritual needs of individuals and that can influence human behavior. Based on this, the nurse can evaluate and prioritize the patient's main concerns, provide necessary care and promote the recovery and rehabilitation of the patient [6].

According to the Horta model, the nurse takes the nursing history, highlights the identified problems and then prepares the care prescription, which will be implemented by the nursing team. Later, the nurse evaluates the resoluteness of the care provided and modifies the plan if necessary [6].

The following steps were considered for the study: nursing history, identification of the main problems found in the affected individuals, and elaboration of problems, diagnoses, and nursing interventions according to the diagnostic classification of NANDA-I (2015-2017). The subjects of this study were three individuals from the same family with a confirmed molecular diagnosis of HD, residing who were residing in a rural area in the municipality of Porto Velho, Rondônia.

Data collection was performed from 10/01 to 11/30/2018 through periodic home visits. The information was obtained through a form previously structured and tested for this purpose and the Katz Scale (KSS).

The selection of the participants was made through the scores obtained from the Katz Scale of Activities of Daily Living (ADL), which the individuals are scored based on the activities they can perform independently: A – completely independent; B – independent for all activities but one; C – independent for all activities but bathing and another activity; D – independent for all activities but bathing, dressing and one more activity; E - independent for all activities except bathing, dressing, toileting, and one more activity; F – independent for all activities except bathing, dressing, toileting, transferring, and one more activity; G – dependent for all activities or at least two functions, but does not qualify for C, D, E, or F [7].

By obtaining the degree of independence in ADLs through the Katz Scale (KS), it was possible to determine the relationship between the stage of HD and dependence on others [7]. Thus, the scores A, B, and C were associated with the initial stage; D and E with the intermediate stage, and F and G with the final stage.

This study is part of a matrix project, coordinated by researchers from Human Genetics Laboratory of the Federal University of Rondônia, submitted and approved by the Ethics Committee on Research with Humans (CEP) under opinion 1.849.777 and CAEE59260516.0.0000.5300, and met the ethical principles required by Resolution 466/12 of the National Health Council.

3. Results

3.1. Clinical case reports

The three cases discussed in this study belong to a family with several HD-affected members. The cases are described in the table below.

Table 1. Clinical case reports

Case 1
(i) Female, 38 years old, HD carrier with diagnosed in 2015 through molecular analysis with 44 CAG repeats. Her symptoms began seven years ago, and she had severe neuropsychomotor impairment. (ii) Symptoms: dyslalia, dysarthria, spasticity, dystonia, bradykinesia, irritability, aggressiveness, chorea, and dementia. It is also noteworthy that she was bedridden for most of the day due to severe motor impairment. She could not walk properly and needed integral care, such as skin care, and needed help with bathing, eating, and constant dressing change due to decubitus in bed. (iii) During the application of the AVD scale it was identified that the patient is totally dependent on others, in this case, the person who does most of the care is her father. She is divorced and the mother of three children. (iv) She got a score of G on the EK, which meant that she was at the final stage of HD.
Case 2
(i) Male, 33 years old, also a carrier of HD and with molecular diagnosis confirmed also in 2015, showing 43 CAG repeats. He was separated from his family and had two daughters who lived with their mother. (ii) Symptoms: he presented the same symptoms as case 1 but less severe. During the home visits, it was identified that the patient, despite presenting motor and cognitive impairment and needing help from others, he could still perform some daily activities with great difficulty, which in most cases represents a risk factor, since he is exposed to vulnerable situations, such as riding motorcycles. (iii) He scored a B on the EK, which classifies him as early-stage HD.
Case 3
(i) Male, 26 years old, carrier of HD with 46 CAG repeats, diagnosed in 2016. (ii) His symptoms manifested before the age of 20, which made him a juvenile HD. (iii) He manifested severe psychological and cognitive impairment, especially irritability, aggressiveness, hallucinations, delusions, and sometimes psychotic outbreaks, requiring special care. It is worth mentioning that he did not present severe motor impairment. However, due to cognitive and psychological alterations, he could not perform the ADLs and also depended on the caregiver to perform daily activities. (iv) He obtained score G in the EK and presented intermediate stage of HD.

Source: Prepared by the authors in 2019

3.2. Systematization of nursing care

In view of the cases described, the main problems identified symptoms presented by each patient, as well as the diagnoses and diagnoses and nursing interventions.

Table 2. Main nursing diagnoses and interventions for the cases

Case 1	
Problems identified: frequent choking (dysphagia), spatial and temporal disorientation, communication difficulty (dyslalia and dysarthria), difficulty ambulation (chorea, spasticity), bed ridden.	
Nursing diagnoses	**Interventions**
Impaired swallowing related to neurological problems, characterized by choking before swallowing.	(i) Evaluation by speech therapy and nutrition. (ii) Swallowing and emptying of the mouth was observed during meals. (iii) Cough reflex was monitored during the visits. (iv) Mushy foods were prepared, and the food was ingested fractionally. (v) Appropriate utensils were used for the ingestion of liquids.
Decreased personal hygiene related to altered cognitive function and musculoskeletal impairment, evidenced by impaired ability to perform body hygiene.	(i) Evaluation by occupational therapy. (ii) Assistance in bathing to avoid imbalances and falls. (iii) Assistance in cleaning genital areas and maintaining oral hygiene. (iv) Special care for nails, perineum, eyes and prioritize wearing comfortable clothes. (v) Ensuring that patient has personal hygiene material.
Impaired physical mobility related to muscle stiffness and neuromuscular impairment as evidenced by altered gait, difficulty in turning around and uncoordinated movements.	(i) The caregiver was guided on the use of ambulation aids. (ii) The patient's ability to transfer was determined. (iii) The patient was assessed at the end of the transfer for correct body alignment and comfort. (iv) Anti-impact protectors were placed around the bed. (v) Referral to multidisciplinary care: psychology, speech therapy, physical therapy, and occupational therapy. (vi) Ergonomic evaluation of the environment to avoid accidents and traumas.
Risk of impaired skin integrity related to immobility, pressure on bony protrusion, and inadequate nutrition.	(i) The caregiver was guided on the use of moisturizing oils on the skin after bathing. (ii) Gelatinous coverings were used to protect the bony extremities and prevent pressure lesion (LP). (iii) Guidance was given on bed rest and ambulation. (v) Guidance was given regarding massages and the use of improvised cushions.

Case 2	
Problems identified: mood swings and difficulty walking.	
Nursing diagnoses	**Interventions**
Impaired physical mobility related to impaired muscle control, characterized by uncoordinated movements and movement-induced tremor.	(i) Referral to physical therapy was provided for evaluation of passive and active exercises. (ii) Caregivers were required to assist the patient in walking around the home for at least 30 minutes a day. (iii) Support was built on walls of the home and/or canes were used in the ambulation.
Impaired mood regulation related to chronic illness characterized by aggressiveness, anxiety, and agitation.	(i) Stressful factors such as noise were reduced. (ii) The patient was referred to a psychiatrist. (iii) Guidance was provided on the importance of correct and continuous use of prescribed medications.
Case 3	
Problems identified: insomnia, poor hygiene, low weight, and pain in the lower limbs.	
Nursing diagnoses	**Interventions**
Inadequate self-care due to neuromuscular impairment, characterized by fetid odor and dirty scalp.	(i) The importance of performing body hygiene was explained. (ii) The caregiver was guided on the supervision of the patient's use of hygiene products such as shampoo, conditioner, and soap.
Anxiety-related insomnia characterized by repetitive movements, wandering, and reports of insomnia.	(i) Guidance was given on the importance of sleep regulation, avoiding naps in the morning or afternoon, and prioritizing sleeping at night. (ii) Guidance was given on the importance of supervising strenuous activities such as walking. (iii) Guidance was provided on the correct use of the prescribed medications. (iv) The patient underwent evaluations from a psychiatrist, a psychologist, and an occupational therapist.
Unbalanced diet: malnutrition characterized by excessive weight loss.	(i) The patient's food preferences should be understood during visits (ii) The acceptance/refusal of the diet and the reason should be noted. (iii) Guidance should be provided on the importance of a healthy diet, considering the availability of food and the financial situation of the family (v) The patient should be encouraged to drink more water and the caregiver should be aware of its importance; the patient should be referred to a nutritionist.

Source: Prepared by the authors in 2019

4. Discussion

The identification of the onset of the first symptoms allowed us to identify the early involvement in one of the three cases studied. HD usually appears between 35 and 44 years of age, with a life expectancy of 15 to 18 years after diagnosis [8]. However, there is a relationship between the number of CAG trinucleotide repeats and the decrease in survival after the onset of symptoms and the speed of progression, i.e., the higher the number of CAG repeats, the earlier the symptoms will manifest in the affected individual, which is the case of juvenile HD identified in the study (Case 3) [5]. The age groups of the patients in the study and the number of CAG repeats presented in each one of them are noteworthy.

Because it is an autosomal dominant disease, that is, it manifests itself in all generations, at least one person in each generation of the family studied inherited a normal copy of the gene and an affected copy. Therefore, knowledge not only of the symptomatology of the disease, but also regarding the management of genetic conditions allows professionals to use tools such as reproductive planning in the identification of risk and referral and/or correct monitoring of affected patients and their families [2].

Currently, HD has become a major challenge for health professionals, because in addition to requiring care and specific knowledge about the pathology, it is also necessary to provide total assistance to patients and families. In this case, the caregiver was overworked (the father), since the patient needs integral care along the progression of the disease [9].

Therefore, literature also points out that the caregiver's follow-up by health professionals is also essential to maintain the physical and emotional integrity of the whole family for a better quality of life [10].

This highlights the importance of a multidisciplinary approach in the three cases discussed here, to meet the different needs presented as the disease progresses, from symptomatic therapy, psychological support for patients and caregivers, and genetic counseling for family members, to palliative care [11].

In this context, the elaboration of the SAE enabled the development of actions based on the real needs presented by each individual, according to the stage of the disease. It can be observed that the individual in Case 1 is in the final stage of the disease and requires comprehensive care. On the other hand, the Case 3 is in the intermediate stage and is dependent for some activities. Case 2 is in the initial stage, but already with manifest difficulties in performing ADLs.

Regarding the diagnoses listed as priorities at the time of the development of this work, we observed the need to implement interventions according to the clinical evolution of HD and its peculiarities, namely the presence of different manifestations of neurological involvement, thus requiring a multifocal and specific approach [12].

For the elaboration of the SAE, it is necessary to know these specificities in order to reach the expected goals, i.e., based on standardized diagnoses, it is necessary to elaborate intervention strategies considering the complexity of HD and the need to involve not only the affected individuals, but also the caregiver and the whole family in the care plan, since the patients will become increasingly dependent on them [2,13].

Among the symptoms manifested in the final stage of HD are difficulty swallowing and the inability to eat due to joint stiffness and chorea, as presented by the individual in Case 1. Dysphagia is one of the most serious symptoms of HD, since it can lead to bronchoaspiration, which could potentially trigger pneumonia, and even cause death. Thus, in addition to a paste-like diet, it is necessary to guide the caregiver and the family on feeding the patient, and train them to perform first aid [14-15].

Nurses must educate the caregiver, such as identifying the signs and performing the Heimlich maneuver, a technique used while somebody is choking to expel the object from the victim's trachea. Thus, it is essential to provide health education to family members and caregivers [16].

In the intermediate stage of HD, the nurse should provide guidance on minimizing the risks arising from difficulty in walking due to motor impairment, chorea, and muscle spasms. Aspects related to safety at home must also be addressed, aiming at preventing the risk of falls. Using a walker, removing physical

barriers, padding the walls near the bed, wearing appropriate shoes, and active and passive exercises are examples of strategies to slow the progression of motor symptoms are [17].

In the early stages, as observed in Case 2, the motor symptoms may be subtle with predominance of the psychiatric and cognitive symptoms. Thus, psychological follow-up was emphasized in addition to clear and objective explanation for the individual and his family about the initial symptoms, including the possibility of psychotic episodes and mental confusion [3].

Although studies showed that the signs and symptoms of HD can be predetermined [4], in this study, the stages and manifestations of the disease occurred differently in each individual. Furthermore, it is necessary to characterize the socioeconomic and cultural characteristics of these people, so that it is possible to understand the real needs of the patients, and care can be provided according to their social reality [14].

According to research, the functional capacity of these individuals may be impaired by several socio-demographic aspects, including gender, age, income, and education. Low level of educational and poor economic conditions may also contribute to a higher risk of dependence, thus influencing the daily lives of this population. Therefore, it is crucial to create programs and public policies that are in line with the maintenance and recovery of functionality of such individuals, along with a multidisciplinary approach [18].

In this context, the SAE stands out as one of the original and autonomous methodological tools for nursing practice it is ideal for the organization of critical-reflexive thinking through the steps adopted in this work, because there is a need for technical-scientific knowledge by health professionals, since those affected by this disease require differentiated care compared to DRs [19].

5. Conclusion

It can be concluded that nursing care associated with multidisciplinary care to the individual affected by HD is one of the main care strategies. Thus, the use of the SAE makes this care particularized, allowing interventions to be made according to the stage of the disease and the needs of the moment.

Although there are similarities between the nursing diagnoses, the care strategies and interventions were completely different. Thus, it is believed that this study can also promote reflections about the need for productions based on scientific evidence and thus arouse the interest of public health agencies for this problem that has its magnitude not yet measured.

Therefore, it is important to emphasize the relevance of the scientific deepening on the health care provided to HD patients in Brazil, because although there is no official data, there is a significant number of families affected by this pathology. In this context, it should also be considered that, since it is a hereditary pathology, several generations of the same family will be affected, which generates an even greater impact on society, especially within the Unified Health System (SUS).

Disclosure statement

The authors declare no conflict of interest.

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Evaluation of Optic Nerve Sheath Diameter Measurement in the Management of Patients Admitted to the Emergency Department with Head Trauma

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Abstract: *Objective:* Ultrasonographic measurements of optic nerve sheath diameter is associated with increased intracranial pressure. Intracranial pressure measurements are usually performed on critical areas or intensive care unit patients. The effect of ultrasonographic measurement of optic nerve sheath diameter in predicting pathology or the need for surgery in mild or moderate head trauma has not been evaluated. In our study, we compared ultrasonographic optic nerve sheath diameter measurements with cranial computed tomography (CT) findings and clinical outcomes of patients with head trauma. *Materials and methods:* Patients with head trauma admitted to the emergency department who were diagnosed with mild, moderate, and severe brain injury were selected for this retrospective study. The optic nerve sheath diameters were measured by ultrasonography. The findings were compared with the outcome and cranial tomography characteristics of the patients. *Results:* Of the 58 patients admitted to the emergency department with head trauma, mild traumatic brain injury was most common. Hospitalization or operation was required in 51.7% of the patients (30 patients). The mean optic nerve sheath diameter was 4.96 ± 1.02 mm (3.1–7.3 mm) on the right and 4.92 ± 1.02 mm (3.3–7.8) on the left. Optic nerve sheath diameter of 5 mm or more were statistically significant in predicting hospitalization, the presence of pathology, and increased intracranial pressure on cranial CT ($P < 0.05$). *Conclusion:* Optic nerve sheath diameters of patients with moderate and mild head trauma may provide information about the need for hospitalization or surgery and can be used as a triage criterion in determining the need for monitoring and follow-up and imaging priorities.

Keywords: Head trauma; Optic nerve sheath diameter measurement; Ultrasonography; Emergency department

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1. Introduction

Traumatic brain injury is a common cause of early death [1,2]. Patients usually have time to reach the hospital. Although altered consciousness is one of the most common findings, the Glasgow Coma Score (GCS) cannot be a direct indicator of traumatic brain injury because it may also occur due to metabolic reasons [3,4]. In patients with suspected traumatic brain injury, cranial computed tomography (CT) is used to form a diagnosis and to detect increased intracranial pressure (ICP) with a mortal course [2,4,5]. Since intracerebral hemorrhage (ICH) is a major cause of mortality, many diagnostic studies have been done [5]. Measurements can be performed with ventriculostomy or intraparenchymal transducer in patients with GCS ≤ 8 [2,6]. However, the fact that invasive interventions cannot be performed in the emergency department, not all

patients have GCS ≤ 8 and cranial CT shows indirect findings, and this has led to the search for a new diagnostic method. Accordingly, diagnostic classifications in cranial CT have been developed and associated with mortality [1,2]. Optic nerve sheath diameter (ONSD) measurement has been evaluated as one of these methods [3]. Especially in intensive care unit patients, ONSD was found to be effective in diagnosing increased intracranial pressure non-invasively compared to intracranial pressure measurement [6-8].

Most cases of traumatic brain injury presenting to the emergency department are mild or moderate [9]. In the literature, no study was found in which ONSD measurements were compared with cranial CT results or that ONSD was used as an outcome indicator in patients with mild head trauma.

In our study, we compared the ONSD measurements of patients with traumatic brain injury with their cranial CT results.

2. Materials and methods

The prospective cross-sectional study was conducted in the emergency department of a university hospital with a level 3 trauma center. During a nine-month period, 58 patients who met the inclusion criteria were recruited from patients admitted with trauma. After obtaining the approval of the local ethics committee (Decision number: 12-10.1/41), the study was conducted in accordance with the 1975 Declaration of Helsinki.

2.1. Selection of patients

Patients over 18 years of age who presented to the emergency department with head trauma were included in the study. Patients under 18 years of age and patients with head trauma but no symptoms of intracranial pathology were excluded. Headache, nausea, vomiting, and anisocoria, motor deficits, altered consciousness, and loss of light reflexes were considered as indicators of intracranial pathology. Therefore, head trauma patients with these symptoms were included in the study. Hemodynamically unstable patients, patients requiring emergency operation, and patients with eye trauma that would interfere with the measurements were excluded.

2.2. Study method

Bedside measurement of ONSD was performed by an emergency physician with basic ultrasonography training and two or more years of experience in the emergency department. The presence of pathology or indirect signs of increased intracranial pressure in cranial CT taken after ONSD measurement was evaluated. The predictive effect on the need of hospitalization and surgery was investigated. If the patients met the inclusion criteria after presentation to the emergency department, the patient was asked to undergo an ultrasound examination without knowledge of tomography or additional injuries. The decision for hospitalization or operation was made by the neurosurgeon.

2.3. Evaluation of pathologic findings in cranial CT

Cranial CT images were evaluated by a radiologist and concluded according to the presence of increased intracranial pressure and intracranial lesions. Tomography results were obtained from official reports. Midline shifting, fading of sulcus and cisternae, ventricular compression and diffuse edema were interpreted in favor of increased intracranial pressure. Intracranial pathologies (subdural, epidural, subarachnoid hemorrhage, contusion, etc.) were evaluated separately.

2.4. Optic nerve sheath diameter (ONSD)

ONSD were performed by emergency medicine residents who had received basic and advanced ultrasound

training, had performed at least 25 ONSD measurements under the supervision of an expert, and had more than two years of experience working in the emergency department. The eyes of the patient lying in supine position were protected with transparent gloves and transverse measurement was made from the upper eyelid with a linear probe, and the measurements were taken 3 mm posterior to the junction of the optic nerve with the eyeball (**Figure 1**). Both eyes were measured with a Sonosite Micromaxx ultrasound machine and a 7.5 Mhz linear probe, and values of 5 mm and above were considered pathologic [6-8].

2.5. Statistical method

Patients were divided into three groups according to traumatic brain injury classification: severe (< 9), moderate (9–13), and mild (14–15). Their age, gender, presence of increased ICP, presence of pathology findings on tomography, mean OSND, and clinical outcome were evaluated. The demographic of the patients with one of the primary outcome measures were analyzed according to the need for operation and hospitalization. Numerical data were given as mean and standard deviation. Chi-square test was used in the presence of independent variables that fit the normal distribution. Continuous and normally distributed independent variables were tested with *t*-test. ROC analysis was performed to evaluate the effect of OSND measurement in determining the need for hospitalization for more than 24 hours for follow-up and surgery.

2.6. Findings

Among the head trauma patients admitted to the emergency department, 16 (27.6%) were female and 42 (72.4%) were male. The mean age was 45.10 ± 17.93 (18–80) years. The causes of head trauma were falls (*n* = 28 48.5%), traffic accidents (*n* = 21 36.2%), and direct blows to the head (*n* = 9 15.5%). When classified according to GCS, there were 42 patients with severe (72.4%), moderate (13.8%), and mild (13.8%) traumatic brain injury. The mean OSND was 4.96 ± 1.02 mm (3.1–7.3 mm) for the right eye and 4.92 ± 1.02 mm (3.3–7.8 mm) for the left eye. The OSND of 31 (53.4%) patients were < 5mm, whereas 27 patients (46.6%) had an OSND > 5 mm. Among these patients, 7 (13.8%) underwent surgery and 23 (37.9%) patients were hospitalized for more than 24 hours. The characteristics of the patients according to their outcomes are shown in **Tables 1 and 2**.

Table 1. Characteristics of head trauma patients admitted to the emergency department according to their clinical outcome

	Patients who underwent surgery (*n* = 7)	**Inpatients (*n* = 23)**	**Patients who were discharged (*n* = 28)**	***P***
Gender				0.113
Female	2 (28.6)	3 (13.1)	11 (39.3)	
Male	5 (71.4)	20 (86.9)	17 (60.7)	
Average age	38.42 ± 17.39	50.04 ± 18.13	42.71 ± 17.46	0.203
(Min.–Max.)	(21.00–63.00)	(18.00–80.00)	(21.00–73.00)	
Traffic accident	3 (42.9)	11 (47.8)	7 (25)	
Blow to the head	-	4 (17.4)	5 (17.9)	
Falling	4 (57.1)	8 (34.8)	16 (57.1)	
GCS				N/A
< 9	4 (57.1)	4 (17.4)	–	
9–13	1 (14.3)	7 (30.4)	–	
14–15	2 (37.5)	12 (52.2)	28 (100.0)	

Table 2. Distribution of head trauma patients admitted to the emergency department according to diagnostic test findings and outcomes

Diagnostic tests	Patients who underwent surgery (*n* = 7)	Inpatients (*n* = 23)	Patients who were discharged (*n* = 28)	*P*
OSND (mm)				< 0.05
< 5	1 (14.3)	4 (17.4)	26 (92.9)	
> 5	6 (85.7)	19 (82.6)	2 (7.1)	
Right OSND	5.50 ± 0.92 (3.60–6.90)	5.47 ± 0.97 (3.70–6.80)	4.39 ± 0.79 (3.10–5.70)	< 0.05
Left OSND	5.62 ± 1.16 (3.60–7.00)	5.38 ± 1.05 (3.50–7.80)	4.36± 0.59 (3.30–5.70)	< 0.05
Cranial CT				
Pathology				N/A
Yes	7 (100.0)	23 (100.0)	–	
No	–	–	28 (100.0)	
ICP				N/A
Positive	3 (42.9)	6 (26.1)	–	
Negative	4 (57.1)	17 (73.9)	28 (100.0)	

Table 3. OSND measurements of patients according to hospitalization-discharge decision

Outcome	OSND > 5 mm *n* (%)	OSND < 5 mm *n* (%)	*P*
Hospitalized/underwent surgery	25 (83.3)	5 (16.7)	**< 0.05**
Discharged	2 (7.1)	26 (92.9)	

Table 4. Evaluation of OSND on tomography finding and positive ICP

OSND		> 5 mm	< 5 mm	*P*
Presence of pathology on CT scan	Yes	25	5	**< 0.05**
	No	2	26	
ICP	Positive	9	0	< 0.05
	Negative	18	31	

At the time of presentation to the emergency department, 50 (86.2%) patients had moderate to mild head trauma. Hospitalization or operation was required in 51.7% (30) of the patients.

In 9 patients with positive ICP elevation, the mean OSND was 5.74 ± 0.51 mm on the right and 5.75 ± 0 .95 mm on the left. When the OSND cut-off value above 5 mm was considered significant, the sensitivity of OSND measurement in predicting the need for hospitalization and operation was 83.33% (65.28–95.36%), with a specificity of 92.86% (76.51–99.12%), positive predictive value of 92.59% (76.51–97.96%), and negative predictive value of 83.87% (69.89-92.1). The positive likelihood ratio was 11.67 (3.04–44.79%), while the negative likelihood ratio was 0.18 (0.08–0.4), with an accuracy of 87.93% (76.7–95.01%), as shown in **Table 3**.

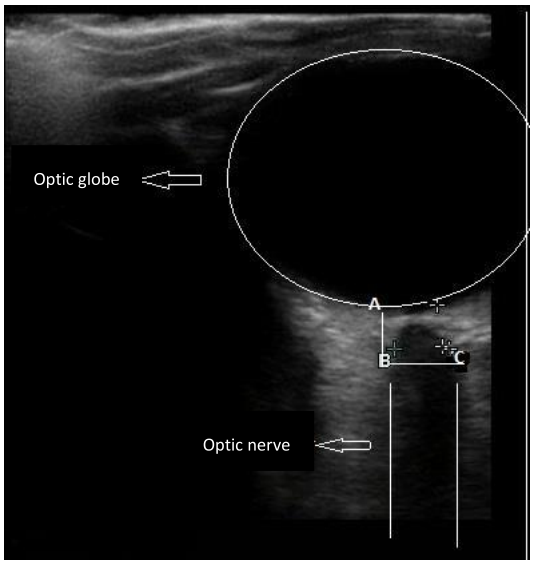

Figure 1. Ultrasonographic image of optic nerve sheath diameter measurement. (A) Optic nerve exit from the eyeball. (B) 3 mm posterior to the exit from the eyeball for OSND measurement. (C) Transverse measurement of OSND.

The area under the curve (AUC) was 0.805 for the right side and 0.802 for the left side as a result of the evaluation of the OSND measurement with ROC analysis in determining the need for hospitalization and operation (**Figure 2**).

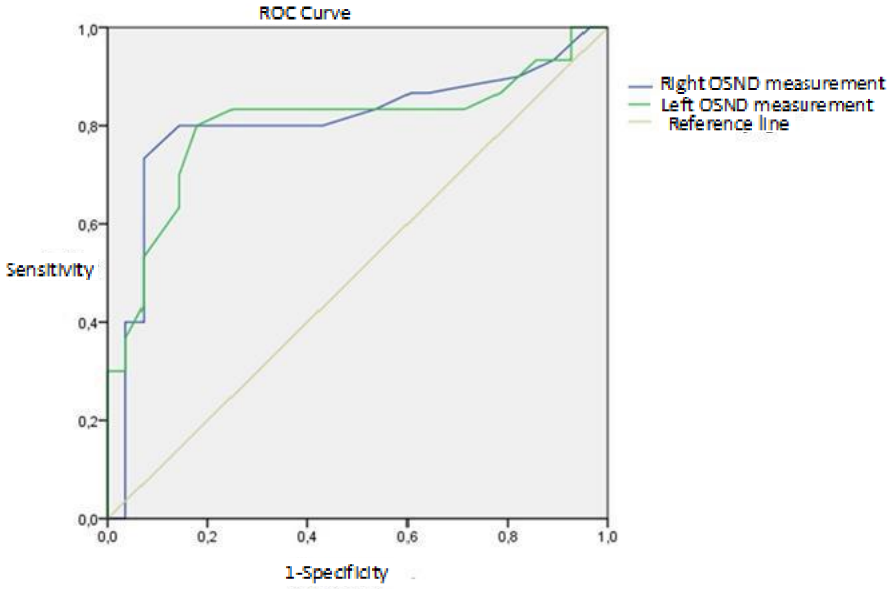

Figure 2. OSND measurement evaluation of patients in need of hospitalization and operation.

OSND over 5 mm was found to be statistically significant with the presence of pathologic findings and increased ICP on tomography ($P < 0.05$). The sensitivity, specificity, PPD, and NPD of OSCT measurement over 5 mm in predicting the presence of ICP on tomography were 33.33% (16.52–53.96%), 100%, 100%, and 63.27% (56.88–69.22%), respectively. The negative likelihood ratio was 0.67 (0.51–0.87), and the accuracy was 68.97% (55.46–80.46%), as shown in **Table 4**.

3. Discussion

In our study in which patients with head trauma admitted to the emergency department were examined,

most patients suffered mild to moderate head trauma according to the GCS score at the time of admission. However, half of these patients required hospitalization or surgery. Among the hospitalized and operated patients, OSND values above 5 mm were found to be statistically significant for pathology. An OSND measurement of 5 mm or more was also found to be statistically significant In the detection of increased intracranial pressure or cranial pathology. We found that OSND measurement is a good test to indicate the need for hospitalization or operation in patients with head trauma.

OSND measurement is considered as a noninvasive measurement method of increased intracranial pressure [7,8,10–12], and most of the studies involve intensive care unit patients [6,11]. Studies on patients with head trauma in emergency department usually involve severe head trauma [5,7]. The most important difference of our study was that OSND was measured in patients with moderate and mild head trauma. Most patients presenting to the emergency department with head trauma suffer from mild head trauma [9]. Half of the patients with moderate and mild head trauma in our study required operation and hospitalization. The diagnosis of these patients is made by cranial CT [13,14]. Considering the density of the emergency department, it is important for emergency physicians to be able to use a bedside imaging method in addition to the examination in the critical area follow-up of patients with mild or moderate head trauma or in determining imaging priority. Our study suggests that OSND measurement is a useful test for predicting hospitalization or operation of patients with mild or moderate head trauma, which makes a unique contribution to medical literature since no such comparison has been made before.

We found that OSND more than 5 mm was statistically significant in predicting the pathology through cranial CT. There were also patients with OSND above 5 mm who did not have signs of increased ICP when evaluated with tomography. In a study, the sensitivity for increased ICP was 86% and specificity was 100%, while the sensitivity for detecting intracranial pathology was 60% and specificity was 100% [14]. In our study, although OSND measurement was statistically significant in detecting intracranial pathology, sensitivity, and specificity were low. In our study, no pathology was detected through cranial CT in two patients with OSND of more than 5 mm. One of these patients had hypertension and this supports the increase in OSND in hypertensive patients reported in literature [15]. Although the sensitivity of OSND in predicting ICP was low, its specificity was 100%, supporting its use as a triage test in critical patient follow-up. The fact that the accuracy of OSND in predicting ICP was found to be 68.97% may be associated with the low number of patients with ICP.

In a review by Restrepro et al., it was emphasized that the determination of ICP increase is useful for emergency services and intensive care units, but more studies are needed for daily use [3]. The data obtained in our study suggest that OSND measurement can be used in addition to the clinical findings of the patient without ICP. In the study by Das et al. evaluating OSND measurements from cranial tomography sections, it was stated that it could be used as a triage tool in determining the decision or time of tomography in patients with mild head trauma [16], which is also consistent with our study.

When we evaluated the measurement of ICP and OSND and the relationship of OSND of more than 5 mm with increased ICP. Raffız et al. found head trauma patients of OSND 5.22 mm and Jean et al. 5.6 mm experienced increased ICP [17,18]. In our study, the mean OSND was found to be 5.7 mm in patients with ICP.

4. Limitations

Due to the limited sample size of our study, stronger evidence cannot be obtained from our results alone, and the inability to perform invasive measurement of ICP in the emergency department and the use of CT may have led to limitations in the definitive diagnosis of ICP. One of the important limitations of the study is that there was no agreement obtained between ultrasound practitioners.

5. Conclusion

ONSD is not only useful for patients with severe head trauma but also for patients with mild and moderate head trauma. In addition to clinical findings, its measurement can be used as a predictor in determining the need for operation or hospitalization by determining the need for tomography and its duration. It can be used as a useful diagnostic tool other than ICP, especially in critically ill patients.

Disclosure statement

The authors declare no conflict of interest.

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Does Sinapic Acid Provide Neuroprotection Against Cisplatin-Induced Toxicity in HT-22 Cells?

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Abstract: *Objective:* The aim of this study was to explain the benefits and possible protective mechanisms of sinapic acid (SA) against cisplatin-induced oxido-inflammatory damage in HT-22 rat hippocampal cells by biochemical and molecular methods. *Materials and methods:* Sinapic acid (SA) was applied at different concentrations (100, 400, and 800 μM) before cisplatin treatment on HT-22 cells under *in vitro* conditions to elicit neuroprotective activity. Half an hour after SA treatment, 5.5 μM cisplatin was added to all wells except the control group and incubated for 24 hours. Cell viability was determined by 3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and cytotoxicity was determined by lactate dehydrogenase (LDH) assays. Oxidative stress was evaluated by total antioxidant capacity (TAC), catalase (CAT), glutathione reductase (GSH), malondialdehyde (MDA), and superoxide dismutase (SOD) assays. In addition, the effect of SA on Caspase-3 gene regulation in HT-22 cells was investigated by real-time PCR. *Results:* Cisplatin decreased cell viability by approximately 40% and increased LDH level in HT-22 cells. In SA-treated groups, cell viability increased and LDH level decreased dose-independently. SA showed neuroprotective activity by inhibiting the cytotoxic activity of cisplatin and increasing the antioxidant activity in cells. Similarly, Caspase-3, which was up-regulated by cisplatin, approached the control value upon SA administration. SA eliminated the neurotoxicity of cisplatin and significantly reduced cell death and oxidative stress. *Conclusion:* The results of this study indicate that SA protects HT-22 cells against cisplatin by inhibiting both the formation of oxidative stress and induction of cell apoptosis.

Keywords: Catalase; Caspase-3; Oxidative stress

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1. Introduction

Cisplatin (CP) is a platinum-based chemotherapeutic agent. It is widely used in the treatment of many solid tumors such as lung, stomach, ovarian, testicular, colorectal, and bladder cancers [1]. Despite its widespread use, CP does not act in a targeted manner in the body. Instead, it acts on healthy cells as well as cancerous cells and causes significant neurotoxic side effects such as peripheral neuropathy, impaired recognition, tremor, and ataxia, which limit its clinical use [2]. Oxidative stress, DNA damage, mitochondrial dysfunction, and increased production of proinflammatory cytokines play an important role in the neurotoxicity caused by CP [3]. Although some clinical and preclinical studies have reported that CP causes cognitive dysfunction, learning difficulties, and memory loss [2,4], information on the effects of CP on the hippocampal structure, biochemical changes, and cognitive behaviors is still limited. Therefore, in this study, we investigated the effects of CP on proinflammatory cytokines and oxidative stress markers in hippocampal cells and rats.

Minimizing the neurotoxic damage caused by frequent use of CP has recently become an important research topic [5]. Due to their antioxidant properties, polyphenolic compounds have recently been suggested to be useful in reducing the toxic effect of CP on brain tissue [6]. Sinapic acid (SA) is a polyphenol derived from hydroxycinnamic acid, which is cinnamic acid with 3,5-dimethoxyl and 4-hydroxyl structures in the phenyl group. It has been reported that SA has pharmacological activities such as anti-inflammatory, antioxidant, antibacterial, and antitumor [7]. At the same time, it has been reported to stabilize the increase in lipid peroxidation in neurodegenerative diseases such as Alzheimer's and Parkinson, suppress oxidative stress, and show neuroprotective effect by preventing cell apoptosis [7,8]. However, there has been no study on the effect of SA on CP-induced hippocampal neurotoxicity.

CP-induced neurotoxicity is mediated by various mechanisms. In this study, the benefits and possible protective mechanisms of SSA against oxido-inflammatory damage induced by cisplatin in HT-22 rat hippocampal cells by biochemical and molecular methods are discussed.

2. Materials and methods

2.1. Chemicals and reagents

CP (CAS 15663-27-1), Phosphate buffer solution (PBS), Dulbecco's Modified Eagles Medium F12 (DMEM-F12), Fetal Bovine Serum (FBS), dimethylsulfoxide (DMSO), 3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), Trypsin (with EDTA) and antibiotics were obtained from Sigma-Aldrich (St. Louis, MO, USA), and Elisa kits were obtained from Elabscience (Houston, USA). Primers and reagents required for gene expression by real time-PCR were obtained from Roche (Darmstadt, Germany).

2.2. Cell culture experiments

2.2.1. HT-22 cell culture

HT-22 (CVCL_0321) was purchased from ATCC for our study and stored at -196℃ until use. For the experiment, the thawed cells were first centrifuged for 5 min. Cells were suspended in fresh medium, 10% fetal bovine serum (FBS) and 1% antibiotic (penicillin, amphotericin B and vestreptomycin) and seeded in different well plates for each assay. Cells seeded in 96-well plates (Corning, USA) for MTT and LDH activity assays and 6-well plates (Corning, USA) for PCR assays were stored in an incubator (5% CO_2; 37 °C) under appropriate ambient conditions (9).

2.2.2. *In vitro* drug administration

Firstly, different concentrations of SA (100, 400 and 800 μM) were administered to ensure neuroprotective activity (10). Half an hour later, 5.5 μM CP was applied to all groups except the control group (11). 24 hours were incubated under optimum conditions. After 24 hours of incubation, the study was terminated for analyses (12).

2.2.3. MTT assay

After 24 h of treatment, MTT (10 μL) was added to each well of a 96-well plate and the plate was incubated in a CO_2 incubator for 4 h. After 4 h, DMSO (100 μL) solution was added (to liquefy formazan crystals). The optical density was read at 570 nm by a spectrophotometer.

2.2.4. Lactate dehydrogenase (LDH)

LDH level was examined in the LDH detection kit. HT-22 cells at a density of 103-106 cells/well were seeded in 200 μL medium in a 96-well plate and and incubated for 24 h. The cells were then removed from the incubator to measure the LDH level. 6 wells were prepared for each concentration. TritonX-100 (10%)

and assay buffer were added, and the wells were incubated at room temperature for one hour. After centrifugation, the cell supernatant was transferred to a new 96-well assay plate. LLDH reaction solution was added to each well and the plate was incubated at 37 °C for 30 min with gentle shaking on an orbital shaker. A microplate reader was used to measure the absorbance optical density (OD) at 490 nm [13].

Table 1. Gene sequences of specific primers

Gene	Forward	Reverse
β-actin	5'-CCAACCGCGAGAAGATGA-3'	5'-CCAGAGGCGTACAGGGATAG-3'
Caspase-3	5'-CAGTGGAGGCCGACTTCTTG-3'	5'-ATCCAGTCGCTTTGTGCCA-3'

2.3. Biochemical analyses

2.3.1. Total antioxidant capacity (TAC)

TAC levels were measured spectrophotometrically (Multiskan™ GO Microplate Spectrophotometer). The number of oxidants and antioxidants in the sample was determined based on the intensity of the color.

2.3.2. Analysis of catalase (CAT), glutathione (GSH), malondialdehyde (MDA), superoxide dismutase (SOD), TNF-α, and IL-1β assay

CAT, GSH, MDA and SOD, TNF-α, and IL-1β were determined by ELISA kits (Elabscience, USA). ELISA analyses were performed according to the manufacturer's instructions. Absorbance was measured with a spectrophotometer at 450 nm.

2.3.3. Real-time PCR

Total RNA was extracted with the High Pure RNA Isolation Kit (Roche Mannheim Germany). Cells were extracted with absolute methanol. We performed a real-time Polymerase Chain Reaction (PCR) using a High Capacity Single-strand cDNA Synthesis Kit and specific primers for RT-PCR (AMW) from Roche (Darmstadt, Germany). The sequences of the genes used are listed in **Table 1**. Results were expressed as fold changes in relative expression changes between SA (100, 400 and 800 μg/mL), CP (positive control), and control group (healthy cells). We normalized the expression of target genes to beta-actin (reference control gene) using the ΔΔCt method [14].

2.4. Statistical analysis: Data obtained from experiments were analyzed with SPSS 26.0. All data are expressed as mean ± SD. Differences between experimental groups were compared by One-Way ANOVA. $P < 0.05$ were considered significant.

3. Results

3.1. MTT test results

After 24 hours of application, the cytotoxicity results of all groups were determined by MTT assay and the cell viability graph is shown in **Figure 1**. Cell viability in the control group (negative control) was considered as 100%. In 5.5 μM CP, the cell viabilty was 62.47% after 24 hours, which meant that the cell viability was significantly decreased in 5.5 μM CP ($P < 0.001$). This approximately 40% decrease in viability proves the cytotoxic effect of CP. In 100 μM SA, the cell viability was 85.31% ($P < 0.05$). After 24 hours, the highest cell viability was found to be 97.01% in 400 μM SA ($P < 0.001$). In our study, SA offered an effective treatment option at all doses. However, the most prominent neuroprotective activity was detected at a concentration of 400 μM. 400 μM SA eliminated the cytotoxic effect of CP and had a near 100% cell viability.

3.2. LDH results

Since LDH is released by necrotic cells, it is an excellent metabolic marker of cell viability. The effect of SA treatment on the LDH activity of HT-22 cells was determined using an LDH kit (**Figure 1**). The LDH activity of treated cells were expressed as % of the standard (shown as 100%). The LDH level in 5.5 µM CP was 26.96%, which was significant compared to the control group ($P < 0.01$). For neuroprotective activity, the LDH level decreased gradually in a dose-dependent manner in the SA-treated groups before 5.5 µM CP administration. The best result was found in the concentration of of 400 µM SA. In this group, LDH level was found to be 10.29, which was close to the control (8.73), and protected the cells against CP cytotoxic effect. However, LDH level also decreased significantly in the other two concentrations ($P < 0.05$ and $P < 0.01$). These data show that SA significantly decreases the cytotoxic effect of cisplatin.

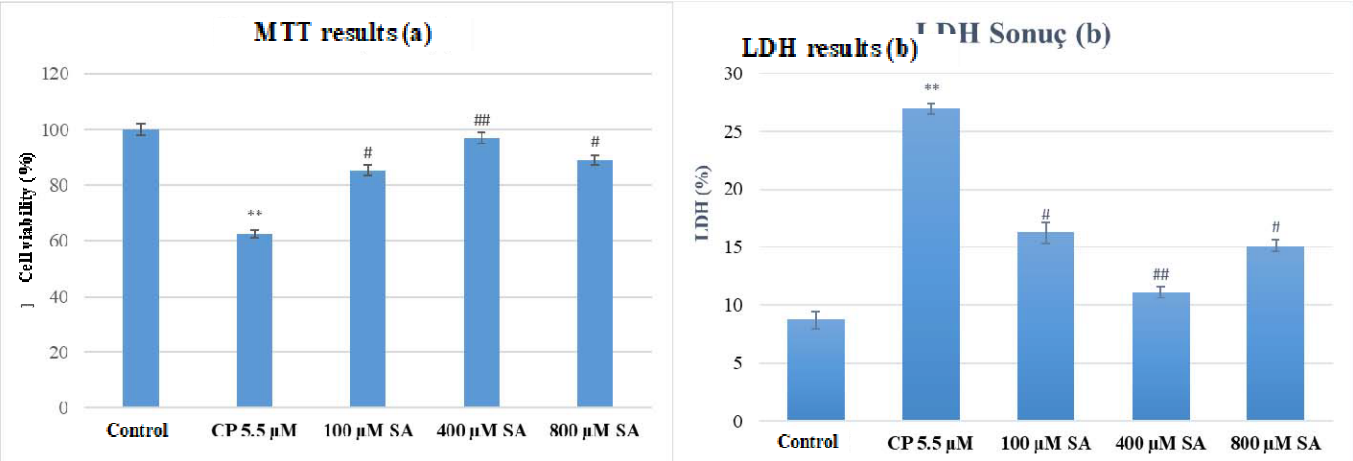

Figure 1. MTT results (left) and LDH activity results (right). Data are expressed as mean ± SD. $^{**}P < 0.01$ indicates significant differences compared to the control; $^{\#}P < 0.05$, $^{\#\#}P < 0.001$ indicate significant differences compared to CP.

3.3. Redox status in HT-22 cells treated with SA

3.3.1. TAC results

The spectrophotometrically determined TAC value of HT-22 cells in the control group was 12.66 mmol Trolox/L, while the TAC value in 5.5 µM CP was 2.99 mmol Trolox equivalent/L (**Figure 2**). Compared to the control group, cisplatin decreased cellular antioxidant activity and induced cytotoxicity ($P < 0.01$). The antioxidant activity of cells was significantly increased by SA. The TAC value was 8.99 mmol Trolox/L in 100 µM SA, 11.815 in 400 µM SA and 10.97 mmol Trolox/L in 800 µM SA (**Figure 2**). TAC value in 400 µM group approached the control group at the highest level.

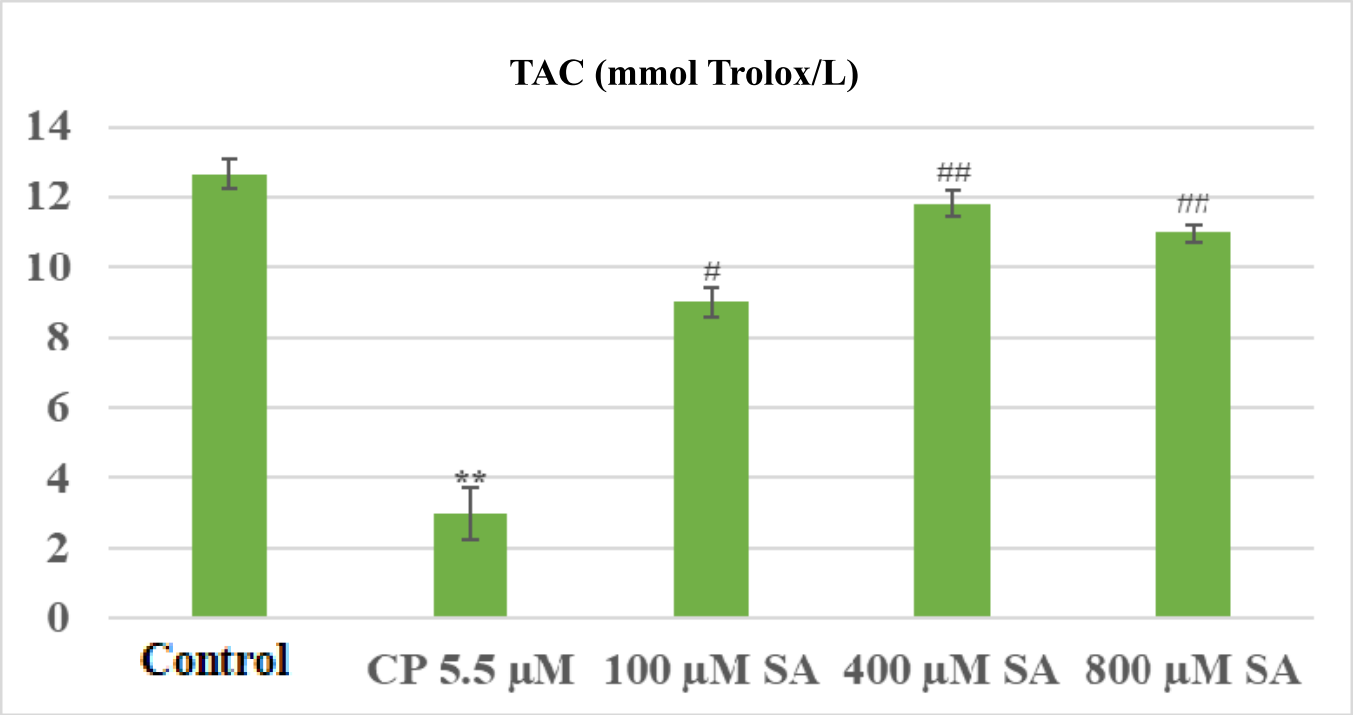

Figure 2. TAC results. Data are expressed as mean ± SD. $^{**}P < 0.01$ indicates significant differences compared to the control; $^{\#}P < 0.05$, $^{\#\#}P < 0.001$ indicate significant differences compared to CP.

3.3.2. CAT, GSH, MDA, and SOD levels

As shown in **Figure 3**, the CAT, GSH and SOD levels decreased significantly in 5.5 µM CP compared to the control, while MDA levels increased significantly ($P < 0.001$). The cells treated with showed a significant increase in SA, CAT, GSH, and SOD activities, and decrease in MDA levels compared to the 5.5 µM CP ($P < 0.001$). Antioxidant activity, which decreased with cisplatin administration, reached normal levels in SA groups. These findings were consistent with TAC, MTT, and LDH results (**Figure 3**).

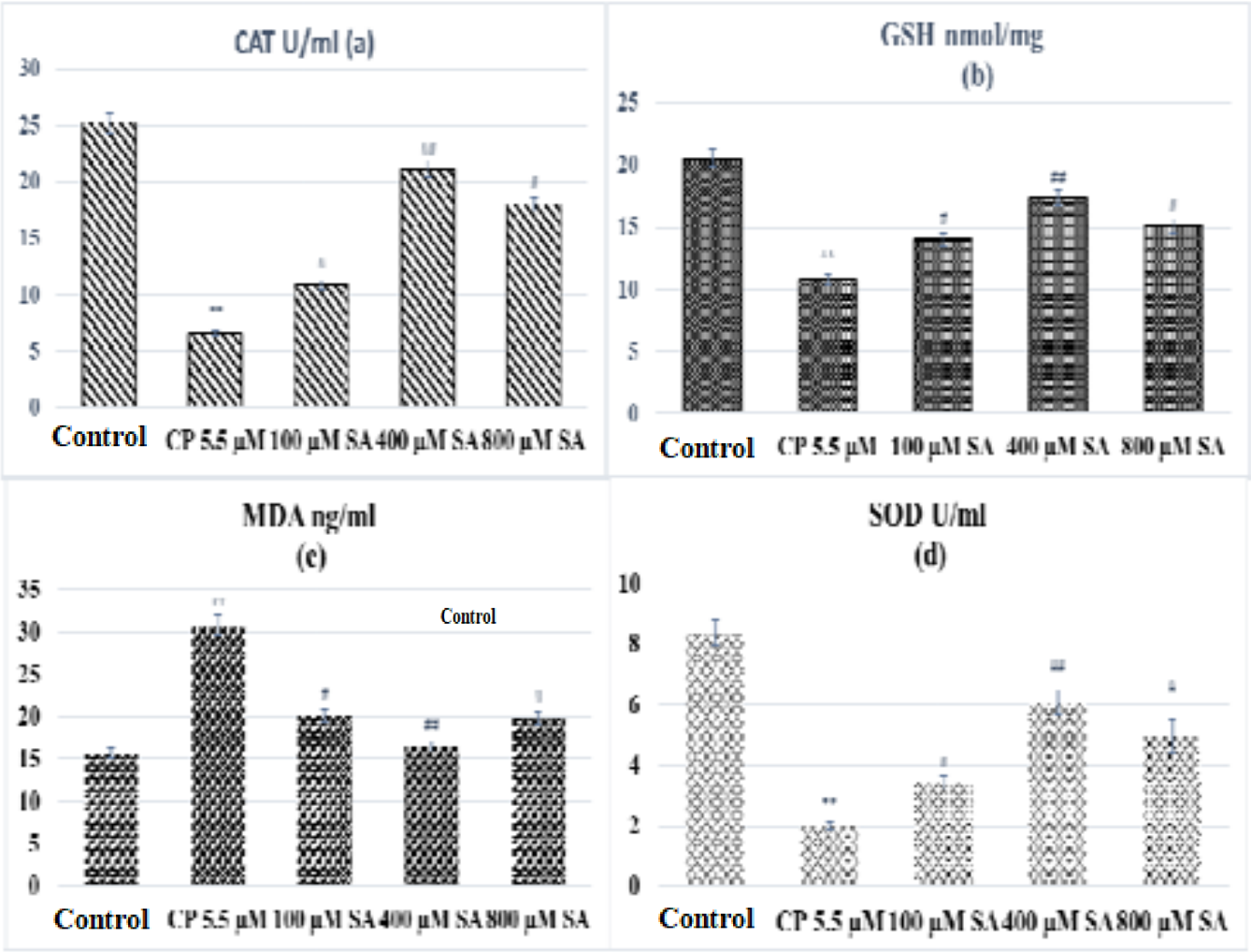

Figure 3. CAT, GSH, MDA and SOD results. Data are expressed as mean ± SD. $^{**}P < 0.01$ indicates significant differences compared to the control; $^{\#}P < 0.05$, $^{\#\#}P < 0.001$ indicate significant differences compared to CP.

3.4. Inflammation status in HT-22 cells treated with SA

IL-1β and TNF-α mediate the development of numerous inflammatory diseases and IL-1β is typically activated when TNF-α is produced. According to our results, CP treatment significantly increased IL-1β and TNF-α levels in cells (24.49 pg/ml) ($P < 0.01$). SA treatment decreased cellular inflation. This decrease was dose-independent, and the most significant result was obtained in 400 µM SA. These findings were consistent with the results other tests in this study (**Figure 4**).

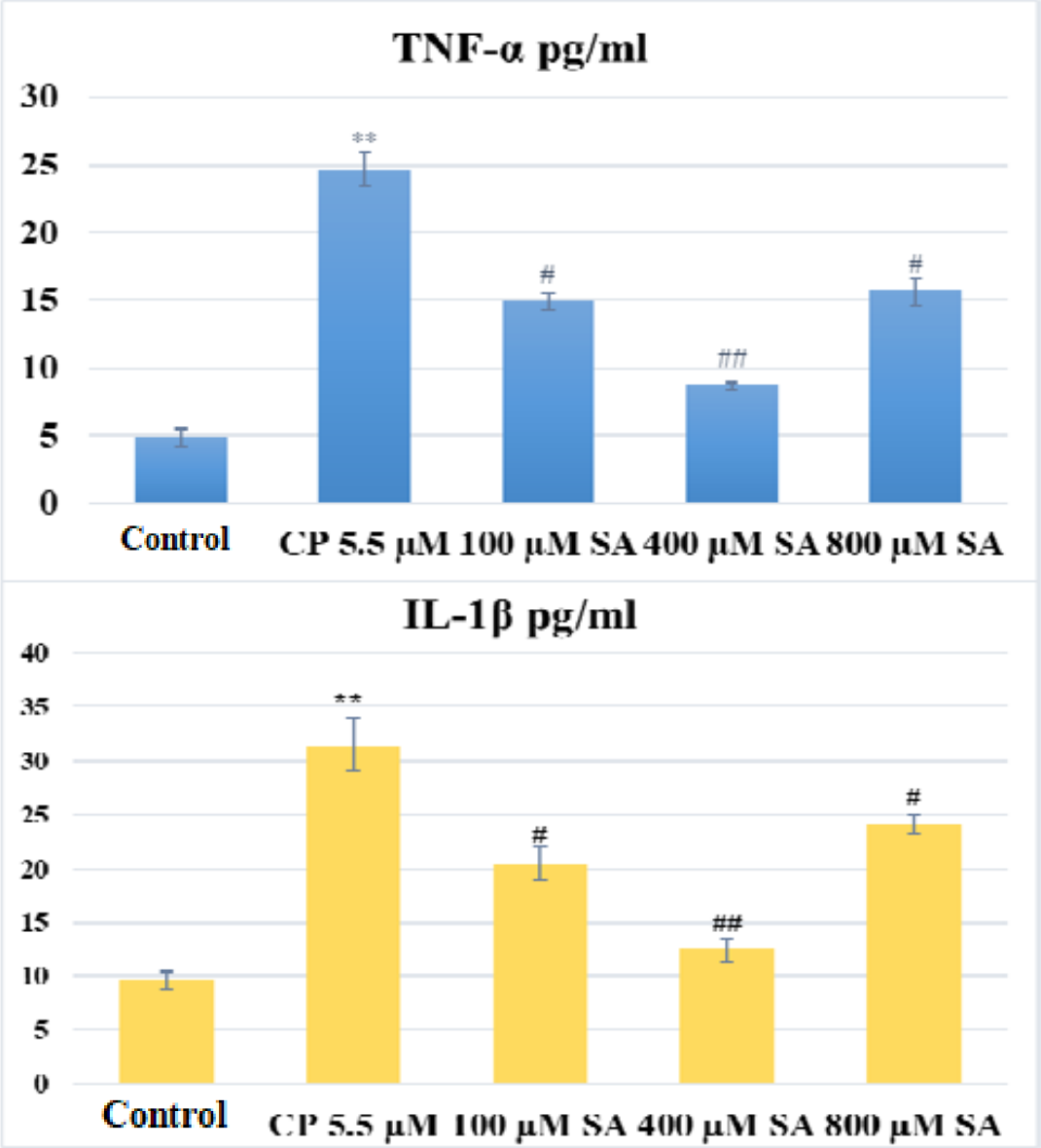

Figure 4. TNF-α and IL-1β results. Data are expressed as mean ± SD. Data are expressed as mean ± SD. $^{**}P < 0.01$ indicates significant differences compared to the control; $^{\#}P < 0.05$, $^{\#\#}P < 0.001$ indicate significant differences compared to CP.

3.5. Real-time PCR results

Caspase-3 gene expression was measured by real-time PCR analysis after 24 h of treatment. The results of this study showed that CP 5.5 μM significantly up-regulated Caspase-3 expression ($P < 0.01$). Specifically, a 1.69-fold increase is one of the most important indicators of cisplatin-induced apoptotic factors in HT-22 cells. SA reversed the apoptotic stimulus occurring in the cells regardless of the dose change and down-regulated Caspase-3 activity, thus protecting the cells from the apoptotic effect of cisplatin (**Figure 5**).

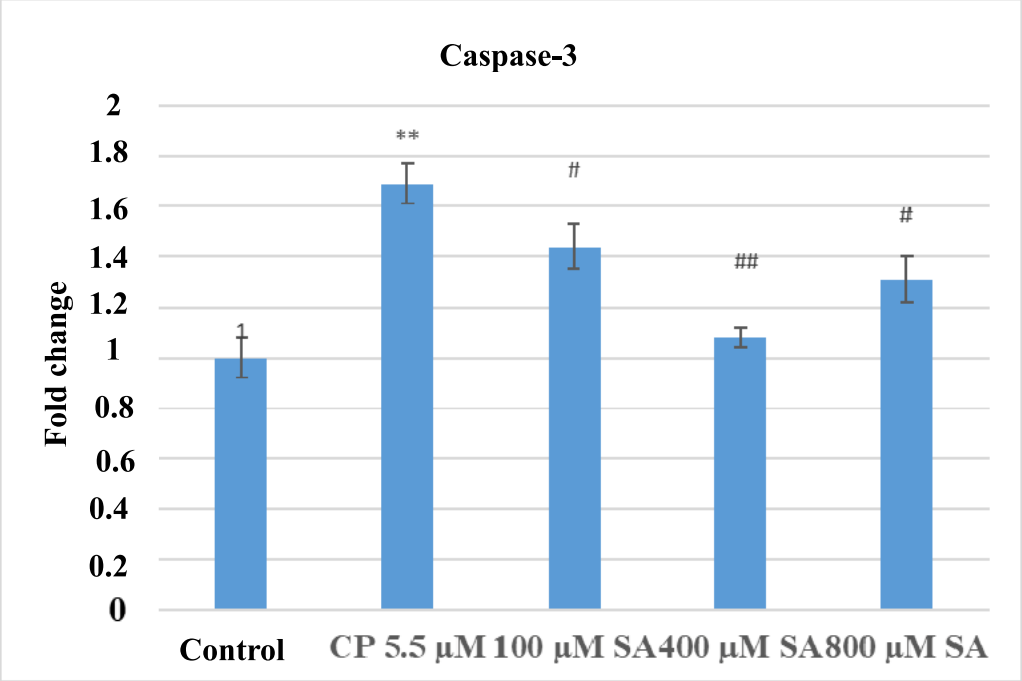

Figure 5. Caspase-3 gene regulation results, expressed as mean ± SD. $^{**}P < 0.01$ indicates significant differences compared to the control; $^{\#}P < 0.05$, $^{\#\#}P < 0.001$ indicate significant differences compared to CP.

4. Discussion

In this study, the effect of SA against CP-induced hippocampal neuronal damage in HT-22 cells was investigated by biochemical and molecular methods. When we evaluated the neurotoxicity induced by CP using MTT and LDH assays, we found that 5.5 µM CP caused significant toxicity compared to control cells at the end of 24 h. Our results were consistent with other studies on the toxic effects of cisplatin on neuronal cell viability [2]. We found that SA significantly reduced CP-induced hippocampal toxicity. So far, there has been no information on the protective effect of SA against CP-induced neurotoxic damage in hippocampal cells was found. *In vitro* and *in vivo* studies have reported that CP causes oxidative damage and lipid peroxidation by increasing free radical in brain tissue [3,15]. MDA is the end product of lipid peroxidation. MDA exacerbates the damage caused by lipid peroxidation by causing cross-linking and polymerization of membrane components [16,17]. The fact that high MDA levels were found in cisplatin-treated cells in our study shows that our findings are compatible with other studies. It is also known that impaired redox balance is closely related with CP-related neuronal toxicity [18,19]. Therefore, the effect of cisplatin on SOD, GSH, CAT, and TAC levels, which are important indicators of antioxidant capacity, was investigated in our study. As seen from our findings, a significant decrease in SOD, GSH, CAT, and TAC levels was detected in parallel with the increase in MDA in hippocampal cells as a result of cisplatin administration. In *in vivo* and *in vitro* studies, it was reported that cisplatin significantly decreased antioxidant enzyme levels and total antioxidant capacity in hippocampus tissue [2,20]. SA significantly suppressed CP-induced increase in MDA and decrease in SOD, GSH, CAT and TAC levels in HT-22 cells. Verma et al. showed that SA protected hippocampus tissue from oxidative stress by increasing antioxidant enzyme levels and preventing MDA increase in Alzheimer's disease rat models [7]. The results of this study support the previous studies and suggest that SA protects the hippocampus tissue against oxidative damage thanks to its antioxidant properties. It has been reported that the increase in free radical production in hippocampus damage accelerates neuroinflammation by triggering excessive production of proinflammatory cytokines such as TNF-α and IL-1β in neuronal cells [2,3]. In our study, TNF-α and IL-1β levels in hippocampal cells were found to increase with CP. In the study conducted by Cankara *et al.* [2], it

was reported that there was a significant increase in TNF-α and IL-6 proinflammatory levels following oxidative stress as a result of CP application in HT-22 cells. SA treatment significantly decreased TNF-α and IL-6 levels compared to the cisplatin group, indicating that it antagonized CP-induced hippocampal inflammation. In the literature, it has been reported that SA reduces neurodegeneration by suppressing proinflammatory cytokine release [21]. Shahmohamady *et al.* (22) showed that SA improves inflammation in hippocampal tissue by inhibiting the increase of TNF-α inflammatory cytokines. It has been shown that oxidative stress induces apoptosis in cisplatin-induced hippocampal toxicity [14]. At the same time, it is known that high TNF-α and IL-1β levels caused by cisplatin in the hippocampus are related to apoptosis [23]. In our study, cisplatin caused a significant increase in the expression level of Caspase-3, an important component of the mitochondrial apoptotic pathway, in hippocampal cells. In *in vivo* studies, it was reported that Caspase-3 mRNA level increased significantly in hippocampus tissue [2]. In addition, Binnetoglu *et al.* [24] found an increase in Caspase-3, 9, and TNF alpha expression levels due to cisplatin toxicity in primary neuron culture. However, in our study, SA administration significantly suppressed the increase in caspase-3 caused by cisplatin. Our findings support the findings of other studies by showing that increased Caspase-3 level in neurodegenerative diseases is decreased by SA [25].

5. Conclusion

In conclusion, the results of this study suggest that SA is an effective molecule in the prevention of CP-induced neurotoxicity in HT-22 hippocampal cells. SA preserves the viability of HT-22 cells against cisplatin toxicity and reduces apoptosis through the mitochondrial intrinsic pathway by reducing oxido-inflammatory damage. However, further *in vivo* and clinical studies are needed in addition to *in vitro* studies to clarify the molecular basis of the neuroprotective properties of SA.

Disclosure statement

The authors declare no conflict of interest.

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Effect of Antipsychotic Drugs on the Cardiac Function of Patients with Schizophrenia and Analysis of Echocardiogram Results

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Abstract: *Objective:* To explore and analyze the effect of antipsychotic drug treatment on the cardiac function of patients with schizophrenia. *Methods:* From January 2021 to December 2022, 30 patients with schizophrenia were divided into three groups, group A (n = 10), group B (n = 10), and group C (n = 10), by random number table. Patients in group A were treated with risperidone, patients in group B were treated with quetiapine, and patients in group C were treated with aripiprazole. The Positive and Negative Syndrome Scale (PANSS) and Lowenstein Occupational Therapy Cognitive Assessment (LOTCA) scores, electrocardiogram results, and echocardiogram results were compared among the three groups. *Results:* There were no significant differences in PANSS and LOTCA scores among the three groups after treatment ($P > 0.05$). Electrocardiogram showed that the incidence of prolonged QT interval in group C was higher than that in groups A and B ($P < 0.05$); echocardiogram showed that the left ventricular ejection fraction (LVEF) and left ventricular end-diastolic volume (LVEDV) in group C were lower than those in group A and group B ($P < 0.05$). *Conclusion:* Risperidone, quetiapine, and aripiprazole can improve the symptoms and cognitive function in patients with schizophrenia. Aripiprazole has a greater impact on cardiac function, as evidenced on electrocardiogram and echocardiogram. Therefore, close monitoring must be done to ensure drug safety.

Keywords: Antipsychotic drugs; Schizophrenia; Cardiac function; Echocardiography

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1. Introduction

Schizophrenia is a chronic mental disorder. Its etiology is related to genetics, environment, and abnormal neuronal function. Patients with schizophrenia are unable to distinguish reality from imagination. They tend to behave abnormally and react slowly, and normal communication is an issue for them. Typical symptoms include hallucinations, delusions, abnormal thinking and behavior, depression, and anxiety; some patients may even display violent behaviors or have suicidal tendencies [1,2]. Clinically, antipsychotic drugs are often used to treat schizophrenia. The commonly used drugs include risperidone, quetiapine, and aripiprazole. These drugs can effectively relieve positive and negative symptoms as well as control the progression of the disease [3]. Several studies have pointed out that antipsychotic drugs can affect the cardiac function of patients, as evidenced by abnormal electrocardiogram results. Hence, they should be used with caution [4]. In this study, 30 schizophrenia patients were selected to explore the effects of different antipsychotic drugs on the patients' cardiac function, as observed on electrocardiogram and echocardiogram.

2. Materials and methods

2.1. General information

The research process and patient selection plan were approved by the medical ethics committee of Zhangjiagang Fourth People's Hospital. From January 2021 to December 2022, 30 patients with schizophrenia divided into three groups by random number table: group A (n = 10), group B (n = 10), and group C (n = 10). Group A consisted of 7 males and 3 females, age ranging from 13 to 70, with a mean of 41.48 ± 2.66 years. Group B consisted of 6 males and 4 females, age ranging from 15 to 68, with a mean of 41.52 ± 2.62 years. Group C consisted of 8 males and 2 females, age ranging from 15 to 69, with a mean of 41.51 ± 2.74 years. The baseline data of the three groups of patients were comparable ($P > 0.05$).

Inclusion criteria: (i) patients who met the diagnostic criteria for schizophrenia based on the Chinese Mental Disorders Classification and Diagnostic Criteria after comprehensive examination; (ii) patients with no contraindications to medication; and (iii) patients who understood the research content and provided informed consent.

Exclusion criteria: (i) patients with hypersensitivity to the drugs used in the study; (ii) patients with heart disease; (iii) patients with organ dysfunction; or (iv) patients who were uncooperative.

2.2. Methods

Patients in group A were treated with risperidone, orally, once a day: 1 mg on the first day of treatment, 2 mg on the second day of treatment, and 3 mg on the third day of treatment, followed by a maintenance dose of 3 mg for 8 weeks.

Patients in group B were treated with quetiapine, orally, 150 mg after breakfast and dinner. Upon improvement in symptoms, the dosage was gradually increased to 300 mg/time, and the duration of treatment was 8 weeks.

Patients in group C were treated with aripiprazole, orally, 10–15 mg once a day after dinner. The dosage was gradually increased to 30 mg with improvement in symptoms, and the duration of treatment was 8 weeks.

2.3. Evaluation indicators

(i) Positive and Negative Syndrome Scale (PANSS) and Lowenstein Occupational Therapy Cognitive Assessment (LOTCA) scores before treatment and after 8 weeks of treatment (PANSS score ranges from 30 to 210 points; the higher the score, the more severe the symptoms; LOTCA score ranges from 0 to 30 points; higher scores indicate better cognitive function).

(ii) Electrocardiogram after 8 weeks of treatment: incidence of prolonged QT interval, abnormal T wave, sinus tachycardia, and ST depression.

(iii) Echocardiography before treatment and after 8 weeks of treatment using an ultrasonic diagnostic instrument in our hospital: patients were kept in a supine position, the ultrasonic parameters were set, and their left ventricular ejection fraction (LVEF) and left ventricular end-diastolic volume (LVEDV) were determined.

2.4. Statistical analysis

SPSS 23.0 was used to calculate various data; measurement data were expressed as mean ± standard deviation, and *t*-test was used; count data were expressed as percentage (%), and χ^2 test was performed. $P < 0.05$ indicated a significant difference between groups.

3. Results

3.1. PANSS and LOTCA scores before treatment and after 8 weeks of treatment

As shown in **Table 1**, there were no significant differences in PANSS and LOTCA scores among the three groups before and after treatment ($P > 0.05$).

Table 1. Comparison of PANSS and LOTCA scores between the three groups before treatment and after 8 weeks of treatment

Group	PANSS score		LOTCA score	
	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 10)	69.75 ± 4.83	36.25 ± 2.71	14.26 ± 2.75	23.77 ± 2.08
Group B (n = 10)	69.88 ± 4.79	36.33 ± 2.68	14.29 ± 2.81	23.82 ± 1.98
Group C (n = 10)	69.64 ± 4.82	36.38 ± 2.66	14.21 ± 2.69	23.71 ± 2.04

Note: Data are shown as mean ± standard deviation.

3.2. Electrocardiogram results

As shown in **Table 2**, the incidence of prolonged QT interval in group C was higher than that in groups A and B ($P < 0.05$).

Table 2. Comparison of electrocardiogram results among the three groups

Group	Prolonged QT interval	Abnormal T wave	Sinus tachycardia	ST depression
Group A (n = 10)	1 (10.0)	0 (0.0)	1 (10.0)	0 (0.0)
Group B (n = 10)	6 (60.0)*	2 (20.0)	1 (10.0)	1 (10.0)
Group C (n = 10)	1 (10.0)	1 (10.0)	2 (20.0)	1 (10.0)

Note: Data are shown as n (%). *$P < 0.05$, comparing group A with group B.

3.3. Echocardiogram results

As shown in **Table 3**, the LVEF and LVEDV in group C were significantly lower than those in group A and group B ($P < 0.05$).

Table 3. Comparison of echocardiogram results among the three groups

Group	LVEF (%)		LVEDV (ml)	
	Before treatment	After treatment	Before treatment	After treatment
Group A (n = 10)	30.68 ± 3.75	40.59 ± 3.77	108.44 ± 12.79	141.75 ± 16.29
Group B (n = 10)	30.75 ± 3.69	34.68 ± 2.96*	108.49 ± 12.83	122.47 ± 10.87*
Group C (n = 10)	30.81 ± 3.64	40.62 ± 3.84	108.52 ± 12.74	141.69 ± 16.33

Note: Data are shown as mean ± standard deviation. *$P < 0.05$, comparing group A with group B.

4. Discussion

According to statistics from the World Health Organization, the total number of schizophrenic patients worldwide has exceeded 23 million, and the lifetime prevalence is about 5% [5]. The age distribution of schizophrenia is wide, and its causes include abnormal brain neurotransmitters, genetics, environment, *etc*. The main symptoms are delusion, hallucination, confusion, abnormal behavior, and inability to distinguish reality from imagination [6]. Drug therapy is the most fundamental intervention for patients with

schizophrenia. Physicians must choose antipsychotic drugs that have significant efficacy and safety based on the patient's condition.

The present study showed that there were no significant differences in PANSS and LOTCA scores among the three groups of patients after treatment, suggesting that all three drugs (risperidone, quetiapine, and aripiprazole) can improve the positive and negative symptoms of schizophrenia as well as the cognitive function of patients with schizophrenia. Analyzing the reasons, risperidone can bind to 5-hydroxytryptamine (5-HT) and α2-adrenergic receptors, reduce central nervous system activity, inhibit dopamine receptor activity, and relieve schizophrenia-related symptoms [7]. Quetiapine, an antipsychotic drug that is widely used clinically, can specifically bind to dopamine D2 and 5-HT receptors and inhibit histamine, thereby reducing the severity of mental disorders and improving various symptoms and cognitive function. Aripiprazole can bidirectionally regulate the dopaminergic nervous system and has high affinity to 5-HT1A, 5-HT2A, D2, and D3 receptors, antagonizing 5-HT2A receptors and partially exciting 5-HT1A receptors, thereby alleviating schizophrenia-related symptoms [8]. Risperidone, quetiapine, and aripiprazole have similar binding receptors, mechanisms of action, and therapeutic effects on schizophrenia. Therefore, no significant differences in PANSS and LOTCA scores were observed among the three groups of patients after treatment.

The present study also showed that the incidence of prolonged QT interval after treatment in group C was higher than that in groups A and B, suggesting that aripiprazole may have adverse effects on the electrical activity of the heart. Analyzing the reasons, aripiprazole has anticholinergic effects and can block dopamine receptors. Long-term medication can weaken the negative feedback effect of dopamine receptors on the presynaptic membrane of cardiovascular nerve endings and induce the release of norepinephrine, causing abnormal coronary contraction and resulting in abnormal myocardial electrical activity. As a result, hypoxic-ischemic necrosis of myocardial tissue may occur, and prolonged QT interval can be observed on electrocardiogram [9,10]. Risperidone and quetiapine have weak anticholinergic effects and minimal effects on the function of the cardiovascular system through coronary artery contraction. Therefore, the incidence of prolonged QT interval was significantly lower in group C, as compared with group A and group B.

In the present study, the three groups of patients were examined by echocardiography. The results showed that the LVEF and LVEDV after treatment were lower in group C, as compared with groups A and B, suggesting that aripiprazole may have adverse effects on the cardiac function of patients with schizophrenia. The advantage of echocardiography is its simple operation and non-invasiveness. High-frequency ultrasonic probes are used by doctors to scan the patient's heart, allowing the arterial wall structure and blood flow to be observed and LVEF, LVEDV, and other indicators to be measured. Through these processes, the patient's cardiac function can be determined [11,12]. The anticholinergic effect of aripiprazole is stronger than that of risperidone and quetiapine. With long-term medication, the myocardial tissue may be partially necrotic, and the diastolic and systolic function may be abnormal, thus resulting in abnormal echocardiogram results [13]. This study postulates that risperidone, quetiapine, and aripiprazole have good therapeutic effects on schizophrenia, but aripiprazole may affect the patient's cardiac function. Hence, it is necessary to strengthen monitoring and evaluation during treatment, especially if the patient experiences chest discomfort; in such a case, the treatment plan needs to be adjusted immediately [14,15].

In conclusion, the use of risperidone, quetiapine, and aripiprazole in patients with schizophrenia can improve their symptoms and cognitive function, although aripiprazole has a greater impact on cardiac function, as evidenced by echocardiography. The sample size of this study is relatively small, improvement and adjustments need to be made to the analysis, and further research on the mechanism is required.

Disclosure statement

The author declares no conflict of interest.

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Analysis of Factors of Complications in Patients with Moyamoya Disease After Revascularization

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Abstract: *Objective:* In this study, the driving factors of complications in patients with moyamoya disease after revascularization are analyzed and discussed. *Methods:* A total of 1500 cases with moyamoya disease after revascularization in Yunan Shuifu People's Hosptial and Beijing University of Chinese Medicine Third Affiliated Hospital from November 2017 to November 2022 were selected retrospectively, and they were divided into an observation group (with postoperative complications) and a control group (with no complications), resulting in 313 cases and 1187 cases in each group, respectively. Univariate and multivariate analysis were performed to screen out independent risk factors for complications in patients with moyamoya disease after revascularization. *Results:* Univariate analysis showed that the proportion of patients with cerebral ischemia, history of hypertension, and modified Rankin scale (mRs) score of 3-5 in the observation group were significantly higher than those in the control group. Complications were used as the dependent variable, and the indicators with statistically significant differences based on the univariate analysis were included as independent variables in the logistic regression analysis. The results showed that the first symptoms before operation were cerebral ischemia, history of hypertension, and mRs score of 3 to 5 were risk factors for complications in patients with moyamoya disease after revascularization, and there were significant differences in the data (OR = 1.781, 1.811, 1.859, all $P < 0.05$). *Conclusion:* Cerebral ischemia is the first symptom before operation, and history of hypertension and mRs score of 3 to 5 are all risk factors for complications in patients with moyamoya disease after revascularization. Therefore, clinical prevention should be strengthened, and corresponding treatment measures should be given in time to reduce the risk of postoperative complications in patients with moyamoya disease.

Keywords: Moyamoya disease; Revascularization; Complications; Driving factors

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1. Introduction

Moyamoya disease is a type of progressive cerebrovascular disease caused by occlusion of the skull base arteries. The main feature of the disease is progressive stenosis or occlusion of the end of the internal carotid artery and its branches, combined with an abnormal vascular network of the skull base. The etiology is yet to be determined, and the course of the disease is complex, which can pose varying degrees of threats to the lives and health of patients [1-2]. Nowadays, revascularization has become the main treatment method for patients with moyamoya disease. This surgical method can repair the broken blood vessels in the body, and then restore the patency of blood flow in the blood vessels [3-4]. The application of revascularization in the treatment of moyamoya disease can significantly reduce the risk of bleeding and improve the blood

circulation of their distal extremities, which has a good therapeutic effect. However, due to the differences in the patients' conditions and symptoms, there is still a risk of postoperative complications [5-6]. Determining the influencing factors of complications in patients with moyamoya disease after revascularization can aid subsequent prevention and treatment measures [7-8]. Therefore, in this study, the driving factors of complications in patients with moyamoya disease after revascularization are analyzed and discussed, and the research content and results are summarized in the following sections.

2. Materials and methods

2.1. General information

1,500 patients with moyamoya disease after revascularization in Yunan Shuifu People's Hosptial and Beijing University of Chinese Medicine Third Affiliated Hospital from November 2017 to November 2022 were selected retrospectively, and they were divided into observation group (with postoperative complications) and control group (with no postoperative complications), resulting in 313 cases and 1187 cases in each group, respectively. This study was approved by the Medical Ethics Committee of our hospital. The diagnostic criteria were based on the Diagnostic Criteria for Moyamoya Disease [9]. Inclusion criteria: those who were highly in line with the above diagnostic criteria, with complete clinical data and normal blood vessels after postoperative reexamination. Exclusion criteria: those with mental disorders and unable to cooperate and those with carotid atherosclerosis or abnormal heart and kidney function.

2.2. Assessment method

The age, gender, first preoperative symptom, history of hypertension, history of diabetes, preoperative modified Rankin scale (mRs) score [10], Suzuki staging [11], etc. were investigated and recorded through the self-made questionnaire of the hospital.

2.3. Observation indicators

(i) The clinical baseline data of all subjects were collected, and univariate analysis was carried out. (ii) Multivariate logistic regression analysis was performed with the occurrence of complications in patients with moyamoya disease after revascularization as the dependent variable, and the indicators with statistically significant differences from the univariate analysis as independent variables.

2.4. Statistical methods

SPSS 20.0 statistical software was used to analyze the data, the count data was represented by [case (%)], and the χ^2 test was used; the measurement data was represented by (mean ± SD), and t test was performed; multivariate logistic regression analysis was performed to screen relevant risk factors, where $P < 0.05$ was considered statistically significant.

3. Results

3.1. Univariate analysis

The results of univariate analysis showed that the proportion of patients with cerebral ischemia, history of hypertension, and mRs score of 3-5 in the observation group were significantly higher than those in the control group (mean $P < 0.05$), see **Table 1**.

Table 1. Univariate analysis affecting the occurrence of complications in patients with moyamoya disease after revascularization

Factor	Observation group (n = 313)	Control group (n = 1187)	χ^2/t	P
Gender [example (%)]			0.034	> 0.05
Male	159 (50.80)	596 (50.21)		
Female	154 (49.20)	591 (49.79)		
Age (mean ± SD)	46.59 ± 4.22	46.62 ± 4.24	0.111	> 0.05
Preoperative symptoms [cases (%)]			147.075	< 0.05
Cerebral ischemia	134 (42.81)	150 (12.64)		
Cerebral infarction	62 (19.81)	343 (28.90)		
Epilepsy	59 (18.85)	345 (29.06)		
Asymptomatic	58 (18.53)	349 (29.40)		
History of hypertension			90.887	< 0.05
Yes	192 (61.34)	379 (31.93)		
No	121 (38.66)	808 (68.07)		
History of diabetes			0.003	> 0.05
Yes	155 (49.52)	590 (49.71)		
No	158 (50.48)	597 (50.29)		
mRs score			123.641	< 0.05
0–2	103 (32.91)	801 (67.48)		
3–5	210 (67.09)	386 (32.52)		
Suzuki staging			0.210	> 0.05
I–II	104 (33.23)	398 (33.53)		
III–IV	101 (32.27)	395 (33.28)		
V–VI	108 (34.50)	394 (33.19)		

3.2. Multivariate analysis

Multivariate logistic regression analysis was carried out with the complication of patients with moyamoya disease after revascularization as the dependent variable and included the indicators with statistically significant differences in the univariate analysis results as independent variables. The results showed that the cerebral ischemia being the first preoperative symptom, history of hypertension, and mRs score of 3 to 5 were all risk factors for complications in patients with moyamoya disease after revascularization, and there were significant differences in the data (OR = 1.781, 1.811, 1.859, all $P < 0.05$), see **Table 2** .

Table 2. Logistic regression analysis of factors of the complications of patients with moyamoya disease after revascularization

Variable	*β*	*SE*	*Wald* χ^2	*P*	*OR* (95% *CI*)
Cerebral ischemia being the first preoperative symptom	0. 577	0. 149	14.966	< 0.05	1.781 (1. 330–2.385)
History of hypertension	0.594	0. 155	14.686	< 0.05	1.811 (1. 337–2.454)
mRs score 3~5 points	0.620	0.132	22.062	<0.05	1.859 (1.435–2.408)

4. Discussion

Moyamoya disease is a cerebrovascular disease caused by occlusion or stenosis of the terminal branches of the internal carotid artery, and its incidence has been increasing year by year [12-13]. Revascularization can effectively control the progression of the patient's condition, prevent the development of stroke, and improve the prognosis, but postoperative complications are still relatively common. Common postoperative complications include cerebral infarction and secondary cerebral hemorrhage, which can seriously threaten the lives of patients [14-16]. Therefore, clinical factors that affect the occurrence of complications of moyamoya disease patients after revascularization should be identified.

The results of this study showed that cerebral ischemia as the first preoperative symptom, history of hypertension, and mRs score of 3–5 were all risk factors for complications in patients with moyamoya disease after revascularization. It is mainly caused by blood circulation disorder caused by intracranial vascular disease in patients, and the body's blood supply reduces as the disease progresses [17-18]. In patients with a history of hypertension, blood vessels are often blocked to varying degrees, which can reduce the regulatory function of cerebral blood vessels [19-20]. Patients with mRs scores of 3 to 5 points have decreased internal regulatory function, are prone to abnormal perfusion, and have an increased risk of complications [21-22]. Besides, patients with cerebral ischemia as the first symptom before operation should be closely observed, and the compensatory contraction and expansion of small arteries and capillary smooth muscle should be adjusted in time to ensure the dynamic stability of cerebral blood flow in patients and avoid postoperative complications [23]. As for patients with hypertension, their blood pressure should be strictly monitored, relevant drug treatment should be given, and patients should be instructed to quit smoking and drinking. Besides, the patients should also exercise regularly to improve blood pressure and reduce the probability of complications. Patients with an mRs score of 3 to 5 should be evaluated for brain function, undergo revascularization as soon as possible. In addition, the patients' condition changes were closely observed during the whole treatment process to reduce the incidence of postoperative complications.

5. Conclusion

In conclusion, cerebral ischemia as the first symptom before operation, history of hypertension, and mRs score of 3 to 5 are all risk factors for complications in patients with moyamoya disease after revascularization, and clinical prevention should be strengthened, and corresponding treatment measures should be given in time, so as reduce the risk of postoperative complications. However, since the research subjects in this study were all from our hospital and the sample size is relatively small, there may be some limitations in the data and results. Therefore, multicenter studies should be done with a bigger sample size to further demonstrate the risk factors affecting complications in patients with moyamoya disease after revascularization.

Disclosure statement

The author declares no conflict of interest.

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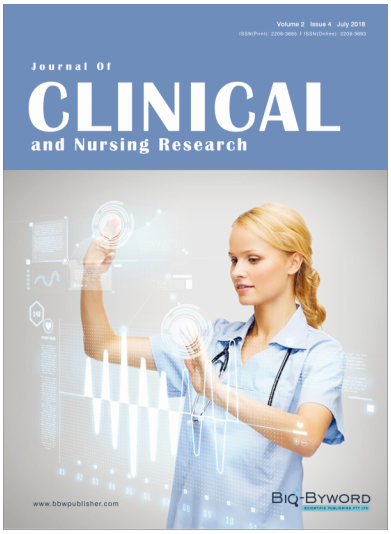

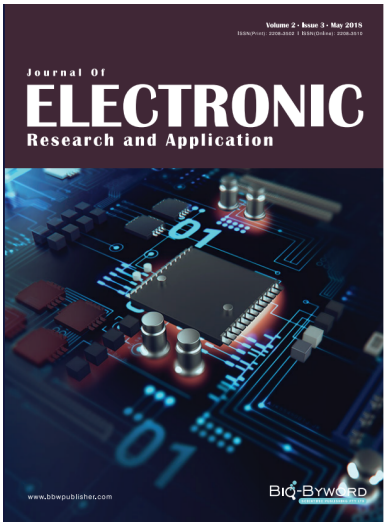

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