76131_Auto_Edited.docx

Retrospective Study

Qixue Shuangbu decoction and acupuncture combined with Western medicine in acute severe stroke patients

Abstract

BACKGROUND

Stroke is a common and frequently occurring disease of the nervous system and one of the three major diseases leading to human death. The incidence and mortality of stroke in China increase with age. Overall, 70 % of patients with stroke have serious disability, which results in heavy burden to their families and the society.

AIM

To analyze the effects of Qixue Shuangbu decoction and acupuncture combined with Western medicine on immune indexes and digestive tract function in patients with acute severe stroke.

METHODS

A total of 68 patients with acute severe stroke admitted to Lanzhou Second People's Hospital between March 2018 and September 2021 were selected and divided into the control and observation groups according to a random number table method. The control group was administered routine Western medicine treatment, such as dehydration, lowering intracranial pressure, anticoagulation, improving cerebral blood circulation and cerebral nerve protection according to the "Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke in China." The observation group was administered Qixue Shuangbu decoction *via* nasal feeding tube on the basis of the

routine Western medicine treatment with simultaneous acupuncture. The two groups were compared.

RESULTS

The acute physiology and chronic health evaluation II, organ dysfunction syndrome score, National Institutes of Health Stroke Scale, and traditional Chinese medicine syndrome scores of the two groups were significantly decreased compared with those measured before treatment, and the complements C3 and C4, and immunoglobulins (Ig) M and G were significantly increased compared with those observed before treatment ($P < 0.05$). After treatment, the scores of the observation group were lower than those of the control group, and the complement and Ig levels were higher than those of the control group ($P < 0.05$). The levels of diamine oxidase (DAO), D-lactic acid (D-LA), and calcitonin gene-related peptide (CGRP) in the two groups were significantly higher than those before treatment, while the levels of lipopolysaccharide, ubiquitin carboxyl-terminal hydrolase 1 (UCH-L1), tumor necrosis factor-α (TNF-α), interleukin (IL) -2, and IL-8 were significantly lower than those before treatment ($P < 0.05$). After treatment, DAO, D-LA, and CGRP were higher in the observation group than in the control group, while lipopolysaccharide, UCH-L1, TNF-α, IL-2, and IL-8 were lower than in the control group ($P < 0.05$). The hospitalization time of individuals in the observation group was shorter than that of the control group ($P < 0.05$).

CONCLUSION

Qixue Shuangbu decoction and acupuncture combined with Western medicine for the treatment of acute severe stroke can regulate intestinal flora, reduce inflammation, improve intestinal mucosal barrier function and immune function related indicators, and promote recovery.

INTRODUCTION

Severe stroke is a common disease of the nervous system with high mortality. Due to the most common sensory and motor dysfunction caused by neurological impairment, patients cannot eat independently; therefore, they require nutritional support treatment. However, long-term nutritional support treatment leads to abnormal intestinal flora, imbalance of gastrointestinal hormone secretion, and eventually systemic inflammatory response and even flora disorder[1]. The disease belongs to "apoplexy" category of traditional Chinese medicine. Because the brain is the capital of the gods, the disorder of qi and blood leads to the occurrence of apoplexy and the imbalance of qi movement in spleen and stomach. Additionally, the stagnation of intestinal dross leads to the accumulation of blood stasis and heat, which disturbs the gods. Both form a vicious circle. Therefore, traditional Chinese medicine (TCM) advocates the principle of promoting qi and activating blood, dredging the fu organs and reducing turbidity. Qi and blood Shuangbu decoction is mainly used to supplement qi and blood deficiency in patients with stroke, and acupuncture treatment focuses on regulating gastrointestinal function[2]. In this study, the effects of Qixue Shuangbu decoction and acupuncture combined with Western medicine on patients with acute severe stroke were assessed. The immune function and digestive tract function indexes were selected as the observation objects to analyze the therapeutic effect of integrated traditional Chinese and Western medicine to provide the corresponding basis for clinical practice.

MATERIALS AND METHODS

General information

A total of 68 patients with acute severe stroke admitted to Lanzhou Second People's Hospital between March 2018 and September 2021 were selected and divided into two groups according to the random number table method. A total of 34 cases were included in the control group, of whom 19 and 15 were men and women, respectively, and were aged 42–75 years (average, 60.84 ± 5.32 years). The time from onset to treatment was 0.5–6 h, with an average of 2.74 ± 0.46 h. The locations of lesions were the basal ganglia, lobe, and brainstem in 19, 10, and 5 cases, respectively. The Glasgow

coma scale (GCS) was 6.25 ± 1.04. A total of 34 cases were included in the observation group, of whom 17 were men and 17 were women, aged 41–75 years (average, 61.01 ± 5.05 years). The time from onset to treatment was 0.5–6 h, with an average of 2.69 ± 0.47 h, and the locations of lesions were the basal ganglia, brain lobe, and brain stem for 17, 12, 5 cases, respectively. The gCS score was 6.22 ± 1.01 points. General data were balanced between the two groups, with no statistical significance being observed ($P > 0.05$).

The inclusion criteria were as follows: (1) stroke defined in line with the "Chinese guidelines for the diagnosis and treatment of acute ischemic stroke 2014" criteria for ischemic stroke[3]: (a) acute onset; (b) focal neurological deficit; (c) unlimited duration of symptoms or signs; (d) excluding non-vascular causes; and (e) excluding cerebral hemorrhage; (2) stroke defined in line with the "common diagnostic criteria of traditional Chinese medicine" in the Qixue deficiency syndrome standard[4], including dizziness, fatigue, insomnia, amnesia, shortness of breath, pale lips, pale tongue, weak pulse, and other syndromes; (3) ≥ 40 years of age, ≤ 75 years of age; (4) GCS score of ≤ 8 and National Institutes of Health Stroke Scale (NIHSS) score of ≥ 17; and (5) family members sign informed consent.

The exclusion criteria were as follows: (1) a history of mental illness; (2) a history of serious underlying digestive diseases or abdominal surgery; (3) complicated with severe visceral lesions; and (4) thyroid dysfunction, coagulation dysfunction, malignant tumors, or severe malnutrition.

Methods

In the control group, routine Western medicine treatment, including dehydration and intracranial pressure reduction, anticoagulation, improvement of cerebral blood circulation, and cerebral nerve protection, was adopted. Patients were administered enteral nutrition support treatment. Enteral nutrition suspension (commodity name: Nengquanli, Newdihiya Pharmaceutical Co., Ltd., Batch No. 20180318) was

administered 1500–2500 mL/day with 50–100 mL/h dripping speed using a gastric tube.

In the observation group, the patients were administered with Qixue Shuangbu decoction using a nasal feeding tube and simultaneous acupuncture treatment was performed. Prescriptions of Qixue Shuangbu decoction included *Codonopsis* (15 g), *Atractylodes* (15 g), *Poria* (12 g), *Angelica* (12 g), *Paeoniae Alba* (12 g), *Rehmannia glutinosa* (15 g), *Chuanxiong* (9 g), and *Radix Glycyrrhizae* (6 g). The above drugs were decocted for 150 mL and administered using a nasal feeding tube daily for 14 d. The acupuncture points were Neiguan, Zusanli, Guanyuan, Qihai, Shangjuxu, Zhongwan, and Xiawan. One-time acupuncture was performed using the twirling small lifting insertion technique, following the use of a gas needle for 20 min. Acupuncture was performed twice a day as a continuous treatment of 14 d.

Observation indicators

Acute physiology and chronic health evaluation II (APACHE II)[5] and organ dysfunction syndrome (MODS)[6] scores were used to evaluate the overall severity of the disease and severity of organ failure. The two scores were proportional to the overall severity of the disease and severity of organ failure, respectively. NIHSS[7] was used to evaluate the degree of neurological deficit, and it was proportional to the degree of neurological deficit. TCM syndrome score was estimated based on symptoms, including dizziness, laziness, amnesia, fatigue, insomnia, dreaminess, blurred vision, palpitations, shortness of breath, loss of appetite, slim body, and luxuriant face. The above symptoms were categorized from light to heavy using the Likert 4 grade scoring method, ranging from 0–3 points.

The incidence of gastrointestinal complications (diarrhea, constipation, gastrointestinal bleeding, vomiting), pressure sores, ventilator-associated pneumonia (VAP), offline success rate, hospitalization time, and 28-d mortality in the two groups were recorded[8].

Detection method

Fasting venous blood (3 mL) was extracted from patients and centrifuged at 2000 r/min for 30 min. Hitachi 7600i automatic biochemical analyzer was used for determination of biochemical parameters. The kit was provided by Nanjing Jiancheng Biological Products Co., Ltd. The calcitonin gene-related peptide (CGRP), ubiquitin carboxyl-terminal hydrolase 1 (UCH-L1), tumor necrosis factor-α (TNF-α), interleukin (IL)-2, IL-8, diamine oxidase (DAO), and D-lactic acid (D-LA) were estimated using enzyme-linked immunosorbent assay. The changes of the lipopolysaccharide concentration were determined using a radioimmunoassay. The changes of complement C3, complement C4, immunoglobulin (Ig) M, and IgG were detected by flow cytometry.

The patient's feces weighing 1 g were diluted with 5 mL of distilled water and inoculated in appropriate culture medium to determine the number of *Bifidobacterium*, *Lactobacillus*, *Enterococcus*, and *Enterobacter*.

Statistical analysis

The data were processed using the SPSS19.0 software. The data were assessed for normal distribution and uniform variance was described using mean ± SD. The *t* test was used for comparison, and the number of cases (%) for enumeration data were used for description. The χ^2 test was used for comparison, and statistical significance was set at $P < 0.05$.

RESULTS

Comparison of scores between and within groups

Before treatment, APACHE II, MODS, NIHSS, and TCM syndrome scores were not significantly different between the groups ($P > 0.05$). Table 1 shows that APACHE II, MODS, NIHSS, and TCM syndrome scores were significantly lower than those before treatment for both groups ($P < 0.05$). After treatment, the scores of the observation group were lower than those of the control group ($P < 0.05$).

Comparison of complement and Ig system indexes between and within groups

Complement (complement C3, complement C4) and Ig system (IgM, IgG) indexes were not significantly different before treatment ($P > 0.05$). Table 2 shows that the complement and Ig system indexes were significantly higher than those before treatment in both groups ($P < 0.05$). After treatment, complement C3, complement C4, IgM, and IgG were higher in the observation group than in the control group ($P < 0.05$).

Comparison of intestinal mucosal barrier function indexes between groups and within groups

Before treatment, the intestinal mucosal barrier function indexes were not significantly different between the groups ($P > 0.05$). Table 3 shows that DAO and D-LA were significantly increased ($P < 0.05$), while lipopolysaccharide was significantly decreased ($P < 0.05$) in the two groups. After treatment, DAO and D-LA were higher in the observation group than in the control group, while lipopolysaccharide was lower than that in the control group ($P < 0.05$).

Comparison of CGRP, UCH-L1, TNF-α, IL-2, IL-8 between and within groups

Before treatment, CGRP, UCH-L1, TNF-α, IL-2 and IL-8 were not significantly different ($P > 0.05$). Table 4 shows that CGRP was significantly increased ($P < 0.05$), and UCH-L1, TNF-α, IL-2 and IL-8 were significantly decreased ($P < 0.05$) in the two groups. After treatment, CGRP was higher, while UCH-L1, TNF-α, IL-2 and IL-8 were lower in the observation group than in the control group ($P < 0.05$).

Comparison of intestinal flora between groups and within groups

The number of intestinal flora before treatment were not significantly different between the groups ($P > 0.05$). As shown in Table 5, *Bifidobacterium*, *Lactobacillus*, and *Enterococcus* numbers were significantly higher in the two groups than those before treatment ($P < 0.05$), while the number of *Bacteroides* was significantly lower than that before treatment ($P < 0.05$). After treatment, *Bifidobacterium*, *Lactobacillus*, and

Enterococcus numbers were higher in the observation group than in the control group, while the number of *Bacteroides* was lower than in the control group ($P < 0.05$).

Comparison of the incidence of gastrointestinal complications and pressure ulcers between groups

There were seven cases of gastrointestinal complications and one case of pressure sore in the control group. The overall complication rate was 23.53%, which was higher than that of the observation group (8.82%); however, no statistical significance was reached ($P > 0.05$) (Table 6).

Comparison of VAP incidence, weaning success rate, hospital stay, and 28-d mortality between groups

The incidence of VAP and the success rate of weaning were higher in the observation group than those in the control group, while the 28-d mortality rate was lower than that in the control group; however, no statistical significance was reached ($P > 0.05$). The hospitalization time of the observation group was significantly shorter than that of the control group ($P < 0.05$) (Table 7).

DISCUSSION

Severe stroke refers to the brain tissue necrosis or softening caused by hypoxia and ischemia due to cerebral blood circulation disorder, which is a common cerebrovascular disease in clinic. The occurrence of patients with stroke is generally developed on the basis of atherosclerosis changes. Inflammatory reaction is one of the reasons for cell loss, which has a serious impact on life safety and physical and mental health of patients[9]. Most critically ill patients experience disturbance of consciousness, swallowing dysfunction, and metabolic exuberance; therefore, they have higher nutritional needs. However, limited intake leads to high stress response, resulting in malnutrition and reduced immune function[10]. Western medicine mainly relies on intestinal nutrition support in the aspect of supplemental nutrition; however, it can

cause reproduction of pathogenic bacteria and formation of flora disorder, which would eventually lead to excessive activation of systemic inflammatory response. At the same time, the loss of neurological function in patients with stroke would lead to the inactivation of gastrointestinal hormones and change in neurotransmitter secretion, affecting the function of human intestinal mucosa and causing intestinal flora disorder.

TCM believes that stroke belongs to the category of stroke. In early stages of the disease, wind, fire, phlegm, and silt are the main factors, while in late stages, deficiency and silt are the main factors. TCM theory believes that qi is the handsome of blood, blood is the mother of qi, qi is the blood, qi is the vitality and movement, and qi deficiency is unable to promote the operation of blood, which will lead to blood stasis. This study adopts the TCM treatment method of Qixue Shuangbu decoction combined with acupuncture treatment. Qixue Shuangbu decoction consists of Sijunzi decoction and Siwu decoction. Reinforcing qi by *Dangshen*, strengthening healthy qi and expelling pathogenic factors, reinforcing qi by *Shaoyao Ganhuayin*, replenishing blood by *Danggui Shudihuang* and activating blood by *Chuanxiong*. *Rhizoma Atractylodis Macrocephalae* and *Poria* can nourish qi and blood by invigorating spleen, while stir-fried licorice can reconcile various drugs. Ginger and jujube can support spleen and stomach, give consideration to tonifying qi and blood, play the role of nourishing blood, invigorating spleen and kidney, tonifying qi and blood, and harmonizing qi and blood[11-14].

Acupuncture treatment is the external treatment of TCM. This study selected acupoints that are commonly used in the treatment of gastrointestinal diseases. Zusanli is a strong point, can strengthen the body, spleen and stomach, while Shangjuxushichangchangchangxiahe point can reconcile gastrointestinal function. Guanyuan and Qihai can strengthen the spleen and kidney, while Buyuanqi and Zhongwan can reduce adverse stomach. Xiawan is Tongzhi and Neiguan and can open the orifices to wake up the min. Therefore, the acupuncture treatment of the above acupoints helps regulate the intestinal function of patients and improve the imbalance of flora. This study found that DAO and D-LA were higher, while lipopolysaccharide was lower in the observation group than in the control group after treatment, indicating

that the regulation of TCM combined therapy on intestinal flora was significant. The above indicators are commonly used for the observation of intestinal mucosal loss. There is a bidirectional regulation between the human intestinal tract and the brain. Reducing intestinal loss through combined treatment can be administered back to the brain, thereby reducing the neurological deficit symptoms of patients[15,16].

In this study, the APACHE II, MODS, NIHSS and TCM syndrome scores were significantly decreased in the two groups compared with those before treatment, and the scores in the observation group were lower than those in the control group after treatment, indicating that the combined treatment of TCM had good effects on improving the symptoms of neurological deficit and reducing the severity of patients. Chinese medicine prescriptions can improve blood flow, improve vascular reserve capacity of patients, and alleviate the corresponding clinical signs caused by stroke. In this study, the complement and Ig system indexes of the two groups were significantly improved compared with those before treatment. The complement C3, complement C4, IgM and IgG were higher in the observation group than those in the control group after treatment, indicating that the immune function of the patients was significantly improved after TCM combined treatment. TCM and acupuncture treatment can promote the secretion of IL-2, thereby promoting lymphocyte proliferation and differentiation, as well as antibody formation, and playing an important role in human immune response. In this study, the changes of inflammatory factors in patients were also analyzed. TNF-α, IL-2, and IL-8 are the commonly used cellular inflammatory factors in clinic. The increase in their concentration suggested that the inflammatory response in patients was aggravated, and it could mediate the cascade activation process of inflammatory response. UCH-L1 was mainly expressed in the brain, testis, or ovary tissue, belonging to neuron-specific protein, which was of great significance to maintain the normal function of the nervous system. CGRP was a vasodilator polypeptide substance in the peripheral and central nervous system, which could form a strong antagonistic effect on cardiovascular and cerebrovascular contraction. Therefore, the severe response of patients in this study was reduced. The decrease of

vasoconstrictive substance concentration suggests the possible mechanism of TCM combined therapy[17,18].

This study also analyzed the complications. The two main complications were gastrointestinal complications and pressure sores, which could be alleviated through active treatment. In contrast, the observation group showed significantly shortened hospitalization time, indicating that the combined treatment of TCM used multiple ways to regulate the clinical signs and symptoms of patients helping reduce the hospitalization time of patients. In terms of the changes of bacterial flora in patients after treatment, *Bifidobacterium*, *Lactobacillus*, and *Enterococcus* numbers were higher in the observation group than in the control group, and the number of *Bacteroides* was lower than in the control group. Under normal conditions, beneficial and harmful bacteria in the human body were inhibited and reached a balance. The balance of bacterial flora is helpful for the digestion and absorption in the human body. Through the combined treatment of TCM, the beneficial bacteria in patients with severe stroke were increased, and the reproduction of harmful bacteria was inhibited, so as to protect the gastrointestinal function and promote the absorption of nutrients, which played an important role in maintaining the balance of bacterial flora in the human body[19,20].

In this study, patients with severe stroke were selected as the research objects, and the improvement effect of the combined treatment of TCM on patients was emphatically analyzed. At the same time, a variety of observation indexes were selected, including inflammatory factors, immune factors, intestinal flora, and other factors, which further confirmed the effect of the combined treatment of TCM and Western medicine, and could provide certain basis for the clinical comprehensive treatment of severe stroke. However, the number of cases included in this study is limited, and the cases derived from the same hospital, which may introduce a bias in case selection, and the follow-up time was relatively short. Follow-up studies should have been further confirmed by increasing the quality of life and living ability of patients outside the hospital.

CONCLUSION

In summary, Qixue Shuangbu decoction and acupuncture combined with Western medicine in the treatment of acute severe stroke can regulate intestinal flora, reduce inflammation, improve intestinal mucosal barrier function and immune function related indicators, and promote recovery.

REFERENCES

1 **Khandelwal P**, Martínez-Pías E, Bach I, Prakash T, Hillen ME, Martínez-Galdámez M, Arenillas JF. Severe Epistaxis after Tissue Plasminogen Activator administration for Acute Ischemic Stroke in SARS-COV-2 Infection. *Brain Circ* 2021; 7: 135-138 [PMID: 34189359 DOI: 10.4103/bc.bc_17_21]

2 **Elsaid N**, Mustafa W, Saied A. Radiological predictors of hemorrhagic transformation after acute ischemic stroke: An evidence-based analysis. *Neuroradiol J* 2020; 33: 118-133 [PMID: 31971093 DOI: 10.1177/1971400919900275]

3 **Riou-Comte N**, Zhu F, Cherifi A, Richard S, Nace L, Audibert G, Achit H, Costalat V, Arquizan C, Beaufils O, Consoli A, Lapergue B, Loeb T, Rouchaud A, Macian F, Cailloce D, Biondi A, Moulin T, Desmettre T, Marnat G, Sibon I, Combes X, Lebedinsky AP, Vuillemet F, Kempf N, Pierot L, Moulin S, Lemmel P, Mazighi M, Blanc R, Sabben C, Schluck E, Bracard S, Anxionnat R, Guillemin F, Hossu G, Gory B; DIRECT ANGIO Investigators. Direct transfer to angiosuite for patients with severe acute stroke treated with thrombectomy: the multicentre randomised controlled DIRECT ANGIO trial protocol. *BMJ Open* 2021; 11: e040522 [PMID: 33722864 DOI: 10.1136/bmjopen-2020-040522]

4 **Obayashi S**, Takahashi R, Onuki M. Upper limb recovery in early acute phase stroke survivors by coupled EMG-triggered and cyclic neuromuscular electrical stimulation. *NeuroRehabilitation* 2020; 46: 417-422 [PMID: 32310196 DOI: 10.3233/NRE-203024]

5 **Forti P**, Maioli F, Nativio V, Maestri L, Coveri M, Zoli M. Association of prestroke glycemic status with stroke mortality. *BMJ Open Diabetes Res Care* 2020; 8 [PMID: 32079614 DOI: 10.1136/bmjdrc-2019-000957]

6 **Naito Y**, Kamiya M, Morishima N, Ishikawa T. Association between out-of-bed mobilization and complications of immobility in acute phase of severe stroke: A retrospective observational study. *J Stroke Cerebrovasc Dis* 2020; **29**: 105112 [PMID: 32912565 DOI: 10.1016/j.jstrokecerebrovasdis.2020.105112]

7 **Amarenco P**, Denison H, Evans SR, Himmelmann A, James S, Knutsson M, Ladenvall P, Molina CA, Wang Y, Johnston SC; THALES Steering Committee and Investigators[a]. Ticagrelor Added to Aspirin in Acute Nonsevere Ischemic Stroke or Transient Ischemic Attack of Atherosclerotic Origin. *Stroke* 2020; **51**: 3504-3513 [PMID: 33198608 DOI: 10.1161/STROKEAHA.120.032239]

8 **Shen S**, Hou N. Adverse Drug Reactions Caused by Antimicrobials Treatment for Ventilator-Associated Pneumonia. Front Pharmacol 2022; 13: 921307 [PMID: 35712710 DOI: 10.3389/fphar.2022.921307]

9 **Ansari S**, McConnell DJ, Velat GJ, Waters MF, Levy EI, Hoh BL, Mocco J. Intracranial stents for treatment of acute ischemic stroke: evolution and current status. *World Neurosurg* 2011; 76: S24-S34 [PMID: 22182268 DOI: 10.1016/j.wneu.2011.02.031]

10 **Moshayedi P**, Liebeskind DS, Jadhav A, Jahan R, Lansberg M, Sharma L, Nogueira RG, Saver JL. Decision-Making Visual Aids for Late, Imaging-Guided Endovascular Thrombectomy for Acute Ischemic Stroke. *J Stroke* 2020; **22**: 377-386 [PMID: 33053953 DOI: 10.5853/jos.2019.03503]

11 **Warach SJ**, Dula AN, Milling TJ Jr. Tenecteplase Thrombolysis for Acute Ischemic Stroke. *Stroke* 2020; **51**: 3440-3451 [PMID: 33045929 DOI: 10.1161/STROKEAHA.120.029749]

12 **Liao Z**, Bu Y, Li M, Han R, Zhang N, Hao J, Jiang W. Remote ischemic conditioning improves cognition in patients with subcortical ischemic vascular dementia. *BMC Neurol* 2019; **19**: 206 [PMID: 31443692 DOI: 10.1186/s12883-019-1435-y]

13 **Saver JL**, Adeoye O. Intravenous Thrombolysis Before Endovascular Thrombectomy for Acute Ischemic Stroke. *JAMA* 2021; **325**: 229-231 [PMID: 33464293 DOI: 10.1001/jama.2020.22388]

14 **Rioux B**, Keezer MR, Gioia LC. Occult cancer diagnosed following acute ischemic stroke. *CMAJ* 2020; **192**: E1037-E1039 [PMID: 32900764 DOI: 10.1503/cmaj.200725]

15 **Salwi S**, Cutting S, Salgado AD, Espaillat K, Fusco MR, Froehler MT, Chitale RV, Kirshner H, Schrag M, Jasne A, Burton T, Grory BM, Saad A, Jayaraman MV, Madsen TE, Dakay K, McTaggart R, Yaghi S, Khatri P, Mistry AM, Mistry EA. Mechanical Thrombectomy in Ischemic Stroke Patients with Severe Pre-Stroke Disability. *J Stroke Cerebrovasc Dis* 2020; **29**: 104952 [PMID: 32689611 DOI: 10.1016/j.jstrokecerebrovasdis.2020.104952]

16 **Yamagami H**, Sakaguchi M, Furukado S, Hoshi T, Abe Y, Hougaku H, Hori M, Kitagawa K. Statin therapy increases carotid plaque echogenicity in hypercholesterolemic patients. *Ultrasound Med Biol* 2008; **34**: 1353-1359 [PMID: 18378381 DOI: 10.1016/j.ultrasmedbio.2008.01.019]

17 **Scaravilli V**, Guzzardella A, Madotto F, Beltrama V, Muscatello A, Bellani G, Monti G, Greco M, Pesenti A, Bandera A, Grasselli G. Impact of dexamethasone on the incidence of ventilator-associated pneumonia in mechanically ventilated COVID-19 patients: a propensity-matched cohort study. *Crit Care* 2022; **26**: 176 [PMID: 35698155 DOI: 10.1186/s13054-022-04049-2]

18 **Ahmed Y**, Bardia N, Judge C, Ahmad S, Malozzi C, Calderon E. *Aerococcus urinae*: A Rare Cause of Endocarditis Presenting With Acute Stroke. *J Med Cases* 2021; **12**: 65-70 [PMID: 34434432 DOI: 10.14740/jmc3612]

19 **Ebinger M**, Siegerink B, Kunz A, Wendt M, Weber JE, Schwabauer E, Geisler F, Freitag E, Lange J, Behrens J, Erdur H, Ganeshan R, Liman T, Scheitz JF, Schlemm L, Harmel P, Zieschang K, Lorenz-Meyer I, Napierkowski I, Waldschmidt C, Nolte CH, Grittner U, Wiener E, Bohner G, Nabavi DG, Schmehl I, Ekkernkamp A, Jungehulsing GJ, Mackert BM, Hartmann A, Rohmann JL, Endres M, Audebert HJ; Berlin_PRehospital Or Usual Delivery in stroke care (B_PROUD) study group. Association Between Dispatch of Mobile Stroke Units and Functional Outcomes Among Patients With Acute Ischemic Stroke in Berlin. *JAMA* 2021; **325**: 454-466 [PMID: 33528537 DOI: 10.1001/jama.2020.26345]

20 **Ehtesham M**, Mohmand M, Raj K, Hussain T, Kavita F, Kumar B. Clinical Spectrum of Hyponatremia in Patients with Stroke. *Cureus* 2019; **11**: e5310 [PMID: 31592365 DOI: 10.7759/cureus.5310]

Table 1 Comparison of scores between and within groups (mean ± SD)

Indicators	Time	Control group (*n* = 34)	Observation group (*n* = 34)	*t* value	*P* value
APACHE II score (points)	Before treatment	17.58 ± 3.21	17.62 ± 3.08	0.052	0.958
	After treatment	13.25 ± 2.14[a]	10.11 ± 1.83[a]	6.502	0.000
MODS score (points)	Before treatment	14.55 ± 2.53	14.48 ± 2.61	0.112	0.911
	After treatment	9.89 ± 1.67[a]	8.21 ± 1.43[a]	4.456	0.000
NIHSS score (points)	Before treatment	19.97 ± 2.07	20.01 ± 2.13	0.079	0.938
	After treatment	10.74 ± 1.74[a]	8.56 ± 1.55[a]	5.455	0.000
TCM syndrome points (points)	Before treatment	24.12 ± 2.58	23.97 ± 2.61	0.238	0.812
	After treatment	11.41 ± 1.25[a]	7.85 ± 1.06[a]	12.666	0.000

[a]$P < 0.05$ *vs* before treatment.

APACHE II: Acute physiology and chronic health evaluation II; MODS: Organ dysfunction syndrome; NIHSS: National Institutes of Health Stroke Scale; TCM: Traditional Chinese medicine.

Table 2 Comparison of complement and immunoglobulins system indexes between and within groups (mean ± SD)

Indicators	Time	Control group (n = 34)	Observation group (n = 34)	t value	P value
Complement C3 (g/L)	Before treatment	1.04 ± 0.12	1.02 ± 0.13	0.659	0.512
	After treatment	1.28 ± 0.17[a]	1.43 ± 0.21[a]	3.237	0.002
Complement C4 (g/L)	Before treatment	0.22 ± 0.05	0.23 ± 0.04	0.911	0.366
	After treatment	0.31 ± 0.07[a]	0.37 ± 0.09[a]	3.068	0.003
IgM (g/L)	Before treatment	0.74 ± 0.11	0.73 ± 0.14	0.327	0.744
	After treatment	1.11 ± 0.15[a]	1.36 ± 0.18[a]	6.221	0.000
IgG (g/L)	Before treatment	9.74 ± 0.41	9.68 ± 0.38	0.626	0.534
	After treatment	10.64 ± 0.52[a]	11.47 ± 0.61[a]	6.038	0.000

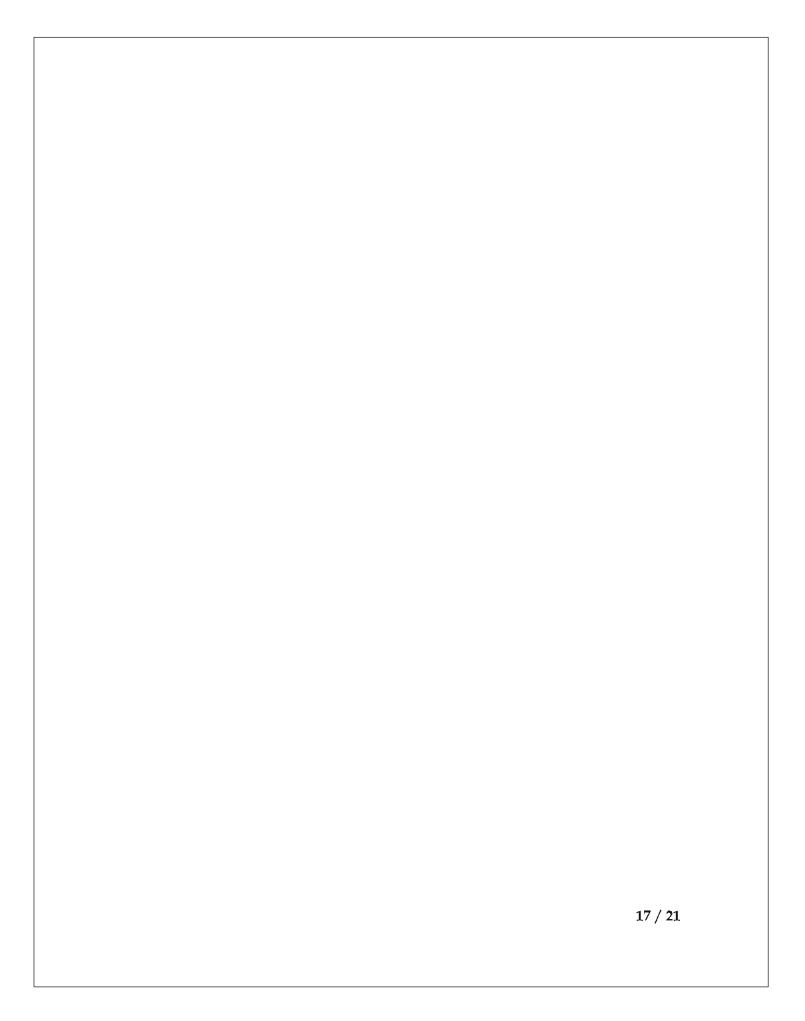[a]$P < 0.05$ vs before treatment.

Ig: Immunoglobulins.

Table 3 Comparison of intestinal mucosal barrier function indexes between groups and within groups (mean ± SD)

Indicators	Time	Control group (n = 34)	Observation group (n = 34)	t value	P value
DAO (U/mL)	Before treatment	3.28 ± 0.34	3.31 ± 0.30	0.386	0.701
	After treatment	4.15 ± 0.38[a]	4.63 ± 0.45[a]	4.752	0.000
D-LA (mmol/L)	Before treatment	0.18 ± 0.07	0.19 ± 0.06	0.632	0.529
	After treatment	0.27 ± 0.08[a]	0.36 ± 0.10[a]	4.098	0.000
Lipopolysaccharide (ng/L)	Before treatment	17.41 ± 4.52	17.35 ± 4.67	0.054	0.957
	After treatment	11.14 ± 2.05[a]	8.21 ± 1.61[a]	6.554	0.000

[a]$P < 0.05$ vs before treatment.

DAO: Diamine oxidase; D-LA: D-lactic acid.

Table 4 Comparison of calcitonin gene-related peptide, ubiquitin carboxyl-terminal hydrolase 1, tumor necrosis factor-α, interleukin-2, interleukin-8 between and within groups (mean ± SD)

Indicators	Time	Control group (n = 34)	Observation group (n = 34)	t value	P value
CGRP	Before	21.52 ± 5.36	20.97 ± 5.71	0.409	0.683

Indicators	Time	Control group	Observation group	t value	P value
(pg/mL)	treatment				
	After treatment	28.26 ± 6.17ᵃ	36.58 ± 6.78ᵃ	5.292	0.000
UCH-L1 (µg/L)	Before treatment	0.40 ± 0.18	0.41 ± 0.13	0.263	0.794
	After treatment	0.25 ± 0.11ᵃ	0.17 ± 0.10ᵃ	3.138	0.003
TNF-α (pg/mL)	Before treatment	44.52 ± 5.89	42.97 ± 6.01	1.074	0.287
	After treatment	21.02 ± 4.15ᵃ	14.63 ± 3.85ᵃ	6.582	0.000
IL-2 (pg/mL)	Before treatment	15.89 ± 2.16	15.81 ± 2.24	0.150	0.881
	After treatment	10.13 ± 1.92ᵃ	6.78 ± 1.52ᵃ	7.977	0.000
IL-8 (pg/mL)	Before treatment	5.23 ± 0.82	5.18 ± 0.91	0.238	0.813
	After treatment	4.64 ± 0.53ᵃ	3.47 ± 0.42ᵃ	10.088	0.000

[a]$P < 0.05$ *vs* before treatment.

CGRP: Calcitonin gene-related peptide; UCH-L1: Ubiquitin carboxyl-terminal hydrolase 1; TNF-α: Tumor necrosis factor-α; IL: Interleukin.

Table 5 Comparison of intestinal flora between groups and within groups (mean ± SD)

Indicators	Time	Control group (n = 34)	Observation group (n = 34)	t value	P value

Bifidobacterium (× 10⁷ CFU)	Before treatment	9.74 ± 1.14	9.67 ± 1.21	0.246	0.807
	After treatment	11.11 ± 1.25ᵃ	12.78 ± 1.34ᵃ	5.314	0.000
Lactobacillus (× 10⁷ CFU)	Before treatment	9.42 ± 1.14	9.36 ± 1.08	0.223	0.824
	After treatment	10.78 ± 1.27ᵃ	12.63 ± 1.41ᵃ	5.685	0.000
Enterococcus (× 10⁷ CFU)	Before treatment	8.85 ± 1.14	8.79 ± 1.21	0.210	0.834
	After treatment	9.75 ± 1.21ᵃ	11.41 ± 1.37ᵃ	5.296	0.000
Bacteroides (× 10⁷ CFU)	Before treatment	7.96 ± 0.21	8.02 ± 0.26	1.047	0.299
	After treatment	6.41 ± 0.17ᵃ	6.02 ± 0.14ᵃ	10.326	0.000

$^aP < 0.05$ *vs* before treatment.

Table 6 Comparison of the incidence of gastrointestinal complications and pressure ulcers between groups, n (%)

Group	Gastrointestinal complications			Vomit	Pressure ulcer	Total complications
	Diarrhea	Constipate	Gastrointestinal bleeding			
Control group (n = 34)	2 (5.88)	1 (2.94)	1 (2.94)	3 (8.82)	1 (2.94)	8 (23.53)
Observation	1 (2.94)	0 (0.00)	0 (0.00)	2	0 (0.00)	3 (8.82)

group (n = 34)		(5.88)	
χ^2 value		2.711	
P value		0.100	

Table 7 Comparison of ventilator-associated pneumonia incidence, weaning success rate, hospital stay, and 28-d mortality between groups, n (%)

Group	Incidence of VAP	Offline success rate	Hospital stay (d)	28 d case fatality rate (%)
Control group (n = 34)	11 (32.35)	18 (52.94)	20.56 ± 5.82	7 (20.59)
Observation group (n = 34)	5 (14.71)	23 (67.65)	16.78 ± 4.53	2 (5.88)
χ^2/t value	2.942	1.536	2.989	3.202
P value	0.086	0.215	0.004	0.074

VAP: Ventilator-associated pneumonia.

76131_Auto_Edited.docx