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Original Article

Effect and safety of ultrasound-guided continuous stellate ganglion blockade on neurovascular headache

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Abstract: Objective: To analyze the effect and safety of ultrasound-guided continuous stellate ganglion blockade (CSGB) on neurovascular headache. Methods: The clinical data of 137 patients with neurovascular headache treated in the First Affiliated Hospital of Hebei North University from March 2019 to October 2021 were analyzed retrospectively. According to the treatment schemes, the patients were assigned to the control group (69 cases, treated with flunarizine combined with Oryzanol tablets), or the observation group (68 cases, treated with ultrasound-guided CSGB on the basis of the treatment to the control group). The efficacy, headache symptoms, negative emotions, cerebral artery blood flow velocity, vasoactive substance levels and adverse reactions of the two groups were compared. Univariate and logistic multivariate analyses were conducted to explore the risk factors for recurrence of neurovascular headache after treatment. Results: The observation group showed a notably higher total effective rate than the control group (95.59% *vs.* 84.06%, *P*<0.05). In contrast to the control group, the observation group had notably lower self-rating depression scale (SDS) and Self-Rating Anxiety Scale (SAS) scores and showed notably lower posterior cerebral artery (PCA), middle cerebral artery (MCA), basilar artery (BA) and anterior cerebral artery (ACA) levels (P<0.05). After the treatment, the observation group showed higher levels of serum 5-hydroxy tryptamine (5-HT) and Beta-Endorphin (β-EP) than the control group, but a lower serum neurotensin (NT) level than the control group. Moreover, the incidence of adverse reactions in the two groups was not greatly different (10.29% *vs.* 5.80%). The observation group showed a lower recurrence rate within 6 months after treatment than the control group (5.88% *vs.* 18.84%, P<0.05). Univariate and logistic multivariate analyses showed that occupation (physical labor), smoking history and sleep quality (poor) may be the risk factors for recurrence of neurovascular headache after treatment (*OR*>1, *P*<0.05), while CSGB may be the protective factor (OR<1, P<0.05). Conclusion: Ultrasound-guided CSGB has obvious analgesic effect on patients with neurovascular headache, which can shorten the duration of headache, improve the cerebral artery blood flow velocity, regulate the levels of vasoactive substances, relieve negative emotions, and lower the recurrence rate, with a high safety.

Keywords: Neurovascular headache, ultrasound-guided, stellate ganglion catheterization, continuous blockade

Introduction

As a frequently seen disease in clinical scenarios, neurovascular headache refers to the paroxysmal headache caused by abnormal regulation of blood vessels and nerves in the skull [1]. With a long course of disease, it is intractable. Patients are mostly featured with paroxysmal unilateral or bilateral severe head pain, stabbing pain, jumping pain, etc. In severe cases, they even suffer blurred vision, nausea and vomiting, which not only disrupt their normal life and work, but also increase the risk of nervous system diseases and cardiovascular and cerebrovascular diseases [2, 3]. At the current stage, conventional western medicines such as opioid analgesics, non-steroidal anti-inflammatory drugs and ergotamine are often used to treat neurovascular headache [4]. Among them, flunarizine is a kind of selective calcium antagonist, which is a classic and commonly used medicine for treating migraine. It can selectively inhibit the inflow of calcium ions to dilate blood vessels, reduce the spasm of vascular smooth

muscle and protect vascular endothelial cells, thus exerting analgesic and analgesic effects. Oryzanol is a sedative drug, which can act on the central nervous system to activate the hypothalamus and limbic system related to the autonomic nervous system, reduce the endocrine balance disorder, and thus relieve the autonomic nervous dysfunction and pain. However, clinical application has showed that long-term treatment with western medicine is prone to gastrointestinal discomfort, skin itching and other toxic and side effects, and the relapse rate is high after drug withdrawal, which all compromise the long-term curative effect.

Stellate ganglion blockade can maintain normal endocrine function, autonomic nerve function and immune function, regulate hypothalamus to maintain internal environment stability, eliminate excessive tension of sympathetic ganglion and block the vicious circle of pain [5]. Whereas, stellate ganglion blockade can hardly relieve chronic pain at one time, and it usually takes multiple blockades to achieve the goal of complete pain relief [6]. Continuous stellate ganglion blockade (CSGB) can exert a sustained effect on vasodilation in lesion areas, and thus alleviate the vasomotor dysfunction of cerebral vessels [7]. Through consulting relevant references, CSGB has been studied for the treatment of vascular nerve headache for a long time [8]. However, currently, there are few reports about the feasibility and safety of stellate ganglion blockade for neurovascular headache. Accordingly, this study retrospectively analyzed the clinical data of 137 patients with neurovascular headache, explored the influences of ultrasound-guided CSGB on pain, emotion and cerebral artery blood flow velocity of patients, and discussed the related mechanism.

Data and methods

Research objects

The clinical data of 137 patients with neurovascular headache treated in the First Affiliated Hospital of Hebei North University from March 2019 to October 2021 were analyzed retrospectively, including 56 males and 81 females with age ranged from 33 to 70 years and an average of 40.43±4.42 years. The course of disease ranged from 5 months to 7 years, with an average of 4.67±1.41 years. The years of education ranged from 5 to 16 years, with an average of 9.91±2.42 years. The patients were divided into groups according to different treatment schemes. This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Hebei North University (No. 201844687).

Inclusion and exclusion criteria

(1) Inclusion criteria: Patients who met the diagnostic criteria of neurovascular headache according to the International Classification of Headache Disorders (ICHD) [9]; patient without abnormality in head CT/MRI, transcranial Doppler and electroencephalogram; patients with bilateral or lateral pulsating headache; patients who usually suffered nausea, vomiting and photophobia in the onset of the disease; patients with disease frequency ≥5 times/month; patients whose symptoms seriously hindered daily activities, or halted daily activities in severe cases; patients who had not taken any drugs that impacted vascular tension within 1 month before admission; and those with detailed clinical data. (2) Exclusion criteria: Patients with headache triggered by other reasons, such as epilepsy, stroke, severe hypertension and brain organic diseases; patients with contraindications of stellate ganglion blockade; patients with coagulation dysfunction or bleeding tendency; patients with comorbid diseases or uncontrollable diseases; patients comorbid with malignant tumor, liver dysfunction, kidney dysfunction or systemic failure; patients with mild headache; patients without requirement for medication; or patients unable to tolerate the treatment.

Methods

Control group: Each patient was orally administrated with oryzanol tablets (Henan Guangkang Pharmaceutical Co., Ltd./Henan Runhong Pharmaceutical Co., Ltd., specification: 10 mg; State Food and Drug Administration (SFDA) approval number: H41023241) 3 times/d, 10 mg/time, and also orally administrated with Flunarizine Hydrochloride Capsules (Shanxi Zhendong Anxin Biological Pharmaceutical Co., Ltd., specification: 5 mg; SFDA approval number: H14020844) 1 time/d, 5 mg/time, for four consecutive weeks. On the basis of the control group, the observation group was treated with ultrasound-guided CSGB. Specifically, the pa-

tient was required to take a supine position, with a thin pillow below, and then the color Doppler diagnostic ultrasound (model: HI VISION-preirus, Hitachi) was used to display transverse process of the sixth cervical vertebra (C6) and the common carotid artery. The medial edge of sternocleidomastoid muscle was used to extrapolate the mastoid muscle and carotid sheath to separate the trachea and carotid artery and expose the puncture point. After successful puncture, the catheter in the conduit was placed and immobilized, and one end was connected to the 9300 portable patient-controlled analgesia pump with 100 ml 0.8% lidocaine (Guilin Pharmaceutical Co., Ltd., specification: 20 ml:0.4 g; SFDA approval number: H45020823). The single self-controlled analgesic dose was 1.5 ml and the blockade time was 20 min. The continuous injection speed was 1 ml/h and the catheter was placed continuously for 2 weeks.

Outcome measures

(1) Efficacy: Based on the diagnostic criteria in the ICHD, the efficacy was evaluated as follows: Cured: The score of Visual Analogue Scale (VAS) decreased by >80%, and the headache and accompanying symptoms disappeared completely; Markedly effective: The VAS score decreased by 50-80%, and the duration of each attack and the number of attacks decreased notably within 4 weeks of treatment, with most of the headaches and concomitant symptoms alleviated; Effective: The VAS score decreased by 30-49%, and the duration of each attack and the number of attacks decreased notably within 4 weeks of treatment, with most of the headaches and concomitant symptoms alleviated to a certain extent; Ineffective: Within 4 weeks of treatment, the VAS score, duration of each attack, number of attacks, headache and concomitant symptoms were not relieved, or even aggravated. Total effective rate = cure rate + markedly effective rate + effective rate. (2) The duration, frequency and degree of headache attack. The VAS scale was used to evaluate the degree of headache. It covers a range of 0-10 points, and a higher score indicates more severe headache. (3) Negative emotions. The self-rating depression scale (SDS) and self-rating anxiety scale (SAS) covered 20 items, separately, and each item was scored by 4 grades. The critical values of SDS and SAS were 53 and 50 respectively. The two scales were used for evaluation before therapy and 4 weeks after therapy. (4) Cerebral arterial blood flow velocity. The cerebral arterial blood flow velocity, including posterior cerebral artery (PCA), middle cerebral artery (MCA), basilar artery (BA) and anterior cerebral artery (ACA), was measured by a transcranial Doppler blood flow analyzer (EMS-9A, Delikai) before treatment and after 4 weeks of treatment. (5) The levels of vasoactive substances. Fasting peripheral venous blood (4 ml) was sampled, followed by 30-min still standing and 10-min centrifugation (rotational speed: 2500 r/min, radius: 6 cm) to separate the serum. The supernatant was acquired, and the serum 5-hydroxytryptamine (5-HT) was determined by enzyme-linked immunosorbent assay (ELISA) with kit provided by Shenzhen Kerunda Bioengineering Co., Ltd. (Lot number: 20180505), and neurotensin (NT) and β-endorphin (β-EP) were measured by radioimmunoassay with kits from Shanghai Kemin Biotechnology Co., Ltd. (Lot number: 20180321). All operations were carried out under strict instructions. (5) Adverse reactions. Adverse reactions included gastrointestinal reaction, transient upper limb numbness, rash, hoarseness, pain at puncture site, etc. (6) Recurrence: After treatment, the patients were followed up for 6 months, and the recurrence rate was counted.

Statistical analyses

This study adopted SPSS25.0 software package for data analysis. The measurement data were described by mean ± SD, and analyzed via the independent-samples t test. Counting data were descried by cases (%), and analyzed via the χ^2 test. Logistic regression analysis was performed to analyze the risk factors for the recurrence of neurovascular headache. $P<0.05$ indicated a significant difference.

Results

General data

No significant difference was found in gender, age, course of disease and years of education between the observation group and the control group (all P>0.05, **Table 1**).

Efficacy

The observation group showed a notably higher total effective rate than the control group (95.59% vs. 84.06%, $P<0.05$, **Table 2**).

Table 1. Comparison of general data between the two groups (n, $\bar{x} \pm$ Sd)

Group	Cases	Male/female	Age (year)	Course of disease (Year)	Years of education (Year)
Control group	69	29/40	40.09±4.91	4.72±1.43	9.86±2.24
Observation group	68	27/41	40.74±4.18	4.62±1.37	9.99±2.73
χ^2/t		0.076	0.834	0.418	0.305
P		0.782	0.406	0.677	0.761

Table 2. Comparison of efficacy between the two groups n (%)

Group	Case	Cured	Markedly effective	Effective	Ineffective	Total effective
The control group	69	3 (4.35)	23 (33.33)	32 (46.38)	11 (15.94)	58 (84.06)
Observation group	68	8 (11.76)	26 (38.24)	31 (45.59)	3 (4.41)	65 (95.59)
χ^2						4.963
P						0.026

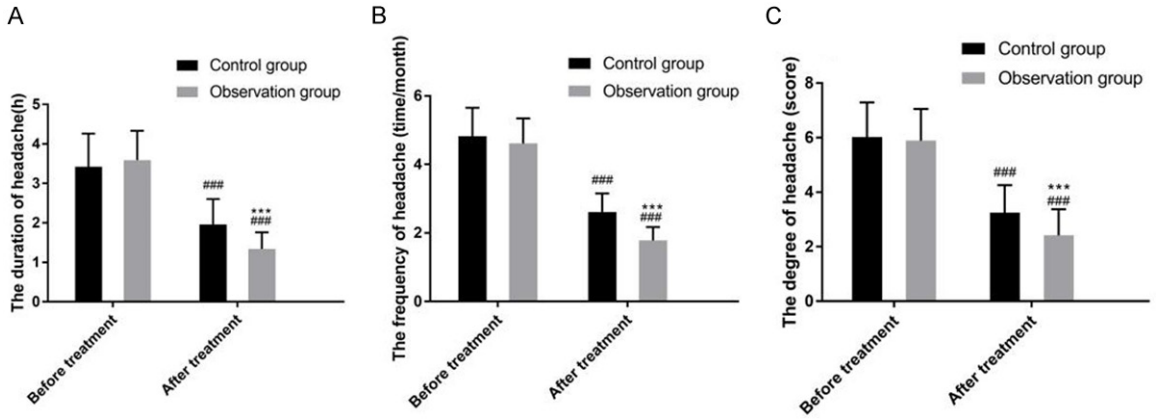

Figure 1. Comparison of the duration, frequency and degree of headache attack between the two groups before and after treatment. Note: A: The duration of headache; B: The frequency of headache; C: The degree of headache. ###*P*<0.001 *vs.* the same group before treatment; ***P*<0.001 *vs.* the control group.

Duration, frequency and degree of headache

Before the treatments, the two groups were similar in the duration, frequency and degree of headache (all *P*>0.05), while after the treatments, the duration, frequency and degree of headache in the observation group were all lower than those in the control group (all P<0.05, **Figure 1**).

Negative emotions

Before the therapy, the SDS and SAS scores of the two groups were not notably different (both *P*>0.05), while after the treatments, the observation group got notably lower SDS and SAS scores than the control group (both *P*<0.05, **Figure 2**).

Cerebral artery blood flow velocity

Before the treatment, the two groups were similar in the blood flow velocity of PCA, BA, MCA and ACA (P>0.05), while after the treatment, the blood flow velocities of PCA, BA, MCA and ACA in the observation group were lower than those in the control group (all P<0.05, **Figure 3**).

Vasoactive substance levels

Before the treatment, the two groups were similar in serum NT, 5-HT, and β-EP levels (all *P*>0.05), while after it, the observation group showed higher levels of serum 5-HT and β-EP but a lower serum NT level than the control group (all *P*<0.05, **Figure 4**).

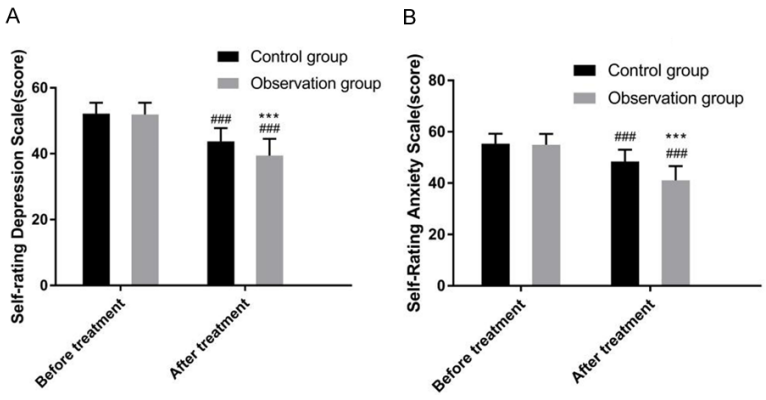

Figure 2. Comparison of SDS and SAS scores between the two groups before and after treatment. Note: A: Self-rating Depression Scale score; B: Self-Rating Anxiety Scale score. ###*P*<0.001 *vs.* the same group before treatment; ***P*<0.001 *vs.* the control group.

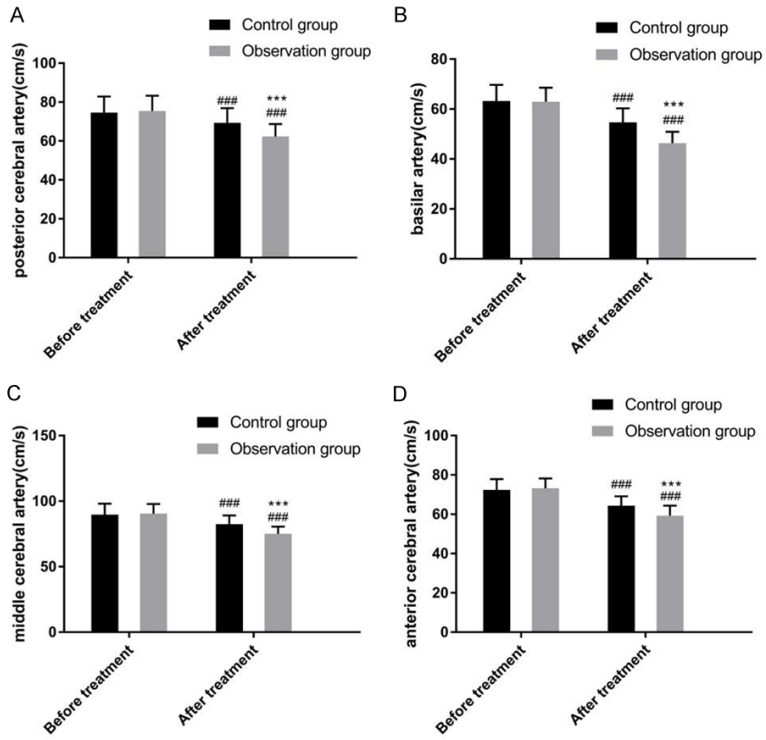

Figure 3. Comparison of cerebral artery blood flow velocity between the two groups before and after treatment. Note: A: Posterior cerebral artery; B: Basilar artery; C: Middle cerebral artery; D: Anterior cerebral artery. ###*P*<0.001 *vs.* the same group before treatment; ***P*<0.001 *vs.* the control group.

Adverse reactions

In the control group, there were 2 cases of gastrointestinal reaction, 1 case of somnolence and 1 case of skin rash, showing a total incidence of 5.80% (4/69). In the observation group, there was 1 case of gastrointestinal reaction, 1 case of rash, 2 cases of hoarseness (disappeared within 1 hour of rest), 1 case of puncture site pain and 2 cases of transient upper limb numbness, showing a total incidence of 10.29% (7/68). The two groups were not notably different in the incidence of adverse reactions (χ^2=0.938, *P*=0.333).

Prognosis

In the control group, 13 cases recurred within 6 months after treatment, showing a recurrence rate of 18.84% (13/69). In the observation group, 4 cases recurred within 6 months after treatment, showing a recurrence rate of 5.88% (4/68). The observation group showed a lower recurrence rate within 6 months after treatment than the control group (χ^2=5.291, *P*=0.021).

Univariate analysis on influencing factors for recurrence of neurovascular headache

The recurrence and non-recurrence groups were not greatly different in sex, age, course of disease, years of education and drinking history (all *P*>0.05), but the two groups were greatly different in occupation (physical labor), smoking history, sleep quality (poor) and therapeutic regimen (**Table 3**).

Multivariate analysis on influencing factors for recurrence of neurovascular headache

Multivariate logistic analysis showed that occupation (physical labor), smoking history and sleep quality (poor) may be the risk factors for recurrence of neurovascular headache after treatment (all *OR*>1, P<0.05), while CSGB may be the protective factor (OR<1, P<0.05, **Table 4**).

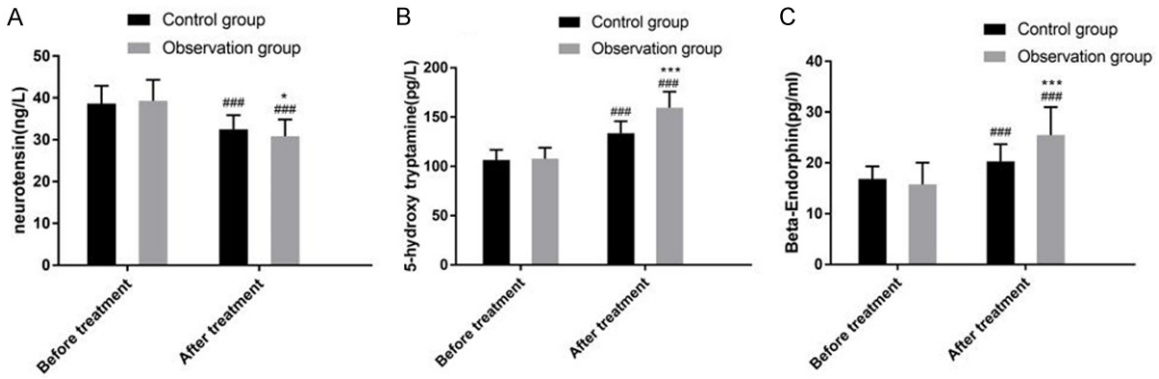

Figure 4. Comparison of vasoactive substance levels between the two groups before and after treatment. Note: A: Neurotensin; B: 5-hydroxy tryptamine; C: Beta-Endorphin. $^{###}P<0.001$ *vs.* the same group before treatment; $^{*}P<0.05$, $^{***}P<0.001$ *vs.* the control group.

Table 3. Univariate analysis on influencing factors for recurrence of neurovascular headache

Group	Number of cases	Male/ female	Age (years)	Course of disease (years)	Years of education (years)	Occupation (physical labor)	Smoking history	Drinking history	Sleep quality (poor)	Therapeutic regimen A/B
Non-recurrence group	120	50/70	39.65±4.51	4.58±1.36	9.63±2.02	25	13	44	30	56/64
Recurrence group	17	6/11	41.03±5.02	5.02±1.48	10.09±2.34	8	6	5	12	13/4
χ^2/t		0.250	1.164	1.235	0.861	5.601	7.459	0.341	14.557	5.543
P		0.617	0.246	0.219	0.391	0.018	0.006	0.559	0.000	0.019

Note: A: Flunarizine combined with oryzanol tablets; B: Ultrasound-guided continuous stellate ganglion blockade.

Table 4. Multivariate analysis on influencing factors for recurrence of neurovascular headache

Correlative factor	*B*	Standard error	*Wald*	*P*	*OR*	95% CI
Occupation (physical labor)	1.217	0.535	5.169	0.023	3.378	1.183-9.646
Smoking history	1.502	0.586	6.559	0.010	1.423	1.423-14.169
Sleep quality (poor)	1.974	0.573	11.889	0.001	7.200	2.344-22.114
Ultrasound-guided continuous stellate ganglion blockade	-1.312	0.600	4.777	0.029	0.269	0.083-0.873

Discussion

At present, the clinical pathogenesis of neurovascular headache remains unclear. It is mostly considered to be bound up with trigeminal neurovascular theory, neurovascular theory, vascular theory, cortical diffusion inhibition theory, etc., among which vasomotor dysfunction is the primary cause [10, 11]. Cerebrovascular system is primarily under the regulation of sympathetic nerves and parasympathetic nerves. Inhibition and excitement of sympathetic nerves can induce cerebral vasodilation and contraction, resulting in persistent chronic pain [12]. Therefore, inhibiting the corresponding neurotransmitter levels in sympathetic nerves and blocking signal transmission are particularly critical in relieving neuropathic pain and improving the function of pain regulation.

Stellate ganglion is a sympathetic nerve formed by the fusion of C6-7 and T1 ganglia, which takes an essential part in regulating immune response and autonomic nerve function of neck, head and shoulder [13, 14]. Therefore, injecting blockade into the stellate ganglion contributes to improving the regulation function of central and peripheral nerve and bi-directional regulation of vasoconstriction, and maintaining the stability of the internal environment, which can be used to treat neurovascular headache from the etiology. Wen et al. [15] have reported that stellate ganglion blockade can relieve upper limb pain-related syndrome and

reduce intraoperative complications such as cerebral blood flow insufficiency and reentrant tachycardia. Moon et al. [16] have revealed that stellate ganglion blockade can alleviate the degree of neurovascular headache and improve the quality of life. However, according to recent studies, the influence of single daily stellate ganglion blockade is limited, and repeated puncture will reduce the comfort and satisfaction of patients [17]. In CSGB, after the first successful puncture, the stellate nerve ganglion catheter can be retained for 1-2 weeks. Long-term sympathetic ganglion blockade can relieve the puncture pain and reduce the side effects caused by nerve damage. In this study, compared with the control group, the observation group showed a notably higher total effective rate, experienced a lower duration of headache attack, attack frequency, and headache degree, had lower SDS and SAS scores and showed a lower recurrence rate within 6 months after treatment, but no notable difference was found in adverse reactions between the two groups. The results indicate that ultrasound-guided CSGB could alleviate the pain degree, shorten the duration of headache attack and relieve negative emotion, and lower the recurrence risk in patients with neurovascular headache, without greatly increasing adverse reactions. Yu et al. [18] found that stellate ganglion blockade via lateral cervical approach under real-time guidance of high-frequency ultrasound has a high success rate, with few adverse reactions and obvious analgesic effect, and the frequency and duration of headache are greatly relieved after treatment with it, which finding is similar to the result of this study. According to analysis, its analgesic mechanism is linked to the following two points: (1) Central function. CSGB can regulate hypothalamic function and autonomic nerve, maintain the stability of internal environment, keep endocrine function and immune function normal, inhibit bradykinin free, and thus relieve pain. (2) Peripheral action. It can suppress the function of sympathetic preganglionic and postganglionic fibers, dilate blood vessels, block vascular dyskinesia, inhibit pain conduction, relieve vasospasm and head blood supply, and then achieve the purpose of relieving pain. Additionally, the puncture position guided by ultrasound is accurate, which can avoid adverse reactions such as pain at the puncture site caused by improper operation. Moreover, in this study, 0.8% lidocaine was adopted as a therapeutic drug. Lidocaine has a high affinity with nerve tissue, which can help block the conduction function, thus regulating autonomic nerve function, nerve block and reducing the release of pain-causing substances. Anxiety or depression is the direct consequence or inherent part of pain experience, while pain is the physical symptom of anxiety or depression, which may have the same pathological basis or pathogenic factors. After the treatment, the pain degree of the patients with vascular headache was obviously relieved, so the degree of anxiety or depression was reduced accordingly.

Modern studies have shown that when the body has stress response or sympathetic nerve excitation, vasoactive substances such as substance P, NT, 5-HT and catecholamine will be released, aggravating the disturbance of regulation of intracranial vasomotor function, thus inducing a series of vascular and neurological headache symptoms [19, 20]. 5-HT is a kind of auto-active substance. During the onset of neurovascular headache, 5-HT is released from platelets, resulting in a transient increase in plasma 5-HT content, which leads to an increase in norepinephrine secretion. These neurotransmitters act on meningeal blood vessels, which can lead to severe contraction of blood vessels and induce visual precursors of neurovascular headache. Subsequently, 5-HT attaches to the blood vessel wall, and results in the rapid decrease of plasma 5-HT content, causing vasodilative headache in the attack period and rebound dilatation of scalp blood vessels, and then inducing headache. β-EP is an endogenous morphine-like substance in human body, which can achieve analgesic effect by inhibiting pain from being transmitted to thalamus, and can reflect the changes of neurotransmitters in central pain regulation pathway.

Wu et al. [21] established a migraine rat model induced by nitroglycerin, and found decreased contents of plasma 5-HT and β-EP in the rats. In this study, after treatment, the serum NT level and the blood flow velocity of PCA, BA, MCA and ACA in the observation group were all lower than those in the control group, while the serum 5-HT and β-EP levels in the observation group were higher than those in the control group. NT can excite many neurons, and the

increase of its level can lead to the decrease of pain threshold.

The results indicate that ultrasound-guided CSGB can regulate the vasoactive substance levels, improve the cerebral artery blood flow velocity, alleviate autonomic nerve dysfunction, relax the nervous sympathetic nerve, and promote the gradual restore of the relaxation balance in the autonomic nervous system to eliminate the burning sensation produced by the autonomic nerve, so as to achieve the purpose of treating headache.

To sum up, ultrasound-guided CSGB has obvious analgesic effect for patients with neurovascular headache, which can shorten the duration of headache, improve the cerebral artery blood flow velocity, regulate the vasoactive substance levels, and relieve negative emotions, with high safety. However, this study still has some limitations. For example, the study is a retrospective cohort study, so there may be some deviation in data collection. The limitations also include small sample size and single sample source. Moreover, the follow-up time is short, so the long-term prognosis of patients and the related factors influencing that have not been analyzed. Therefore, in future studies, we can focus on the analysis on factors influencing the long-term prognosis of patients given CSGB, with a larger sample size and more sources, through a longer follow-up time, and make further analysis.

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Disclosure of conflict of interest

None.

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References

[1] Zhang T, Xiao Y and Li S. Safety and efficacy of nimodipine combined with flunarizine in patients with angioneurotic headache. Am J Transl Res 2022; 14: 511-517.

[2] Jeong SH and Kim H. Acute intractable headache and oculomotor nerve palsy associated with nicorandil: a case report. Am J Emerg Med 2017; 35: 1988.e3-1988.e5.

[3] Liu LL, Li X, Chang G, Zhang SJ and Ju XN. Sibelium in combination with dibazole in the treatment of angioneurotic headache. J Biol Regul Homeost Agents 2017; 31: 653-657.

[4] Xie X, Shang K and Li X. Tuling Wendan Decoction combined with flunarizine in the treatment of migraine patients and the effect of intervention on serum cyclooxygenase-2, endothelin-1 and nitric oxide. Cell Mol Biol (Noisy-le-grand) 2020; 66: 34-40.

[5] Rae Olmsted KL, Bartoszek M, Mulvaney S, McLean B, Turabi A, Young R, Kim E, Vandermaas-Peeler R, Morgan JK, Constantinescu O, Kane S, Nguyen C, Hirsch S, Munoz B, Wallace D, Croxford J, Lynch JH, White R and Walters BB. Effect of stellate ganglion block treatment on posttraumatic stress disorder symptoms: a randomized clinical trial. JAMA Psychiatry 2020; 77: 130-138.

[6] Liu LD and Duricka DL. Stellate ganglion block reduces symptoms of long COVID: a case series. J Neuroimmunol 2022; 362: 577784.

[7] Davis J, Ozcan MS, Kamdar JK and Shoaib M. Stellate ganglion block used to treat reversible cerebral vasoconstriction syndrome. Reg Anesth Pain Med 2021; 46: 732-734.

[8] Makharita MY, Amr YM and El-Bayoumy Y. Effect of early stellate ganglion blockade for facial pain from acute herpes zoster and incidence of postherpetic neuralgia. Pain Physician 2012; 15: 467-474.

[9] Headache Clawificatim Gommittee of Inkernational Healathe Socidy. Classification and diagmstie criveria for healache disorders, cranial mauralgia, and farial pain. Cephalalgia 2004; 24 Suppl: 1.

[10] Ailani J, Burch RC and Robbins MS; Board of Directors of the American Headache Society. The American Headache Society consensus statement: update on integrating new migraine treatments into clinical practice. Headache 2021; 61: 1021-1039.

[11] Khan J, Asoom LIA, Sunni AA, Rafique N, Latif R, Saif SA, Almandil NB, Almohazey D, AbdulAzeez S and Borgio JF. Genetics, pathophysiology, diagnosis, treatment, management, and prevention of migraine. Biomed Pharmacother 2021; 139: 111557.

[12] Feigin G, Wang NN and Flamer D. Stellate ganglion block as a diagnostic and therapeutic option in chronic pericardial pain: a case report. A A Pract 2021; 15: e01375.

[13] Hou J, Pu S, Xu X, Lu Z and Wu J. Real-time ultrasound-guided stellate ganglion block for migraine: an observational study. BMC Anesthesiol 2022; 22: 78.

[14] Lu F, Tian J, Dong J and Zhang K. Tonic-clonic seizure during the ultrasound-guided stellate ganglion block because of an injection into an unrecognized variant vertebral artery: a case report. Medicine (Baltimore) 2019; 98: e18168.
[15] Wen S, Chen L, Wang TH, Dong L, Zhu ZQ and Xiong LL. The efficacy of ultrasound-guided stellate ganglion block in alleviating postoperative pain and ventricular arrhythmias and its application prospects. Neurol Sci 2021; 42: 3121-3133.
[16] Moon S, Lee J and Jeon Y. Bilateral stellate ganglion block for migraine: a case report. Medicine (Baltimore) 2020; 99: e20023.
[17] Li J, Yin Y, Ye L and Zuo Y. Pulsed radiofrequency of C2 dorsal root ganglion under ultrasound guidance for chronic migraine: a case report. J Pain Res 2018; 11: 1915-1919.
[18] Yu Q, Zheng E, Li X and Ding X. Ultrasound image guided lateral cervical approach to stellate ganglion block for cervical headache. Neurosci Lett 2020; 735: 135139.
[19] Giniatullin R. 5-hydroxytryptamine in migraine: the puzzling role of ionotropic 5-HT3 receptor in the context of established therapeutic effect of metabotropic 5-HT1 subtypes. Br J Pharmacol 2022; 179: 400-415.
[20] Vila-Pueyo M, Page K, Murdock PR, Loraine HJ, Woodrooffe AJ, Johnson KW, Goadsby PJ and Holland PR. The selective 5-HT1F receptor agonist lasmiditan inhibits trigeminal nociceptive processing: implications for migraine and cluster headache. Br J Pharmacol 2022; 179: 358-370.
[21] Wu X, Zhang M and Huang H. Effect of qilongtoutong granule on calcitonin gene-related peptide, beta-endorphin, serotonin, dopamine, and noradrenalin in migraine model rats and mice. J Tradit Chin Med 2014; 34: 188-193.