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ORIGINAL RESEARCH

Effects of Hyperbaric Oxygen-Assisted Naoxintong Capsule Therapy on Hemodynamics and Hemorheology in Patients with Hypertensive Cerebral Hemorrhage

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Keywords

Hyperbaric oxygen, Naoxintong capsule, Hypertensive cerebral hemorrhage, Hemodynamics, Hemorheology

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Abstract

Objective To investigate the effect of hyperbaric oxygen-assisted Naoxintong capsule therapy on hemodynamics and hemorheology in patients with hypertensive intracerebral hemorrhage (HICH). **Methods** A total of 110 patients with HICH who were treated in our hospital from March 2019 to December 2021 were selected and divided into control group and observation group by random number table method, with 55 cases in each group. The control group was given routine treatment combined with Naoxintong capsule, and the observation group was given hyperbaric oxygen therapy on the basis of the control group. The clinical efficacy, neurological function, hemodynamics and hemorheology of the two groups were compared. **Results** The total effective rate in the observation group was apparently higher than that in the control group (P<0.05). After treatment, brain-derived neurotrophic factor (BDNF) level , the mean cerebral vascular velocity (Vmean) and cerebral vascular mean flow (Qmean) of the patients in the two groups were significantly higher, while the levels of dynamic resistance (DR) , peripheral blood flow resistance (R),myelin basic protein (MBP) and neuron-specific enolase (NSE) in the two groups were apparently lower as compared with those before treatment (P<0.05), and the change trend of each index in the observation group was more obvious than that in the control group (P<0.05). After treatment, viscosity high shear, whole blood viscosity low shear, and plasma viscosity were apparently lower than those before treatment (P<0.05), and those indicators in the observation group were apparently lower than those in the control group (P<0.05). **Conclusion** Hyperbaric oxygen-assisted Naoxintong capsule has a significant effect on HICH patients, which can effectively reduce the degree of neurological impairment, and improve the hemodynamics and hemorheology in the body.

Introduction

Hypertensive intracerebral hemorrhage (HICH) is a common disease in clinical neurosurgery, which refers to the rupture of small arteries after a sudden increase of the blood pressure, resulting in the intracranial hematoma, abnormal changes in cerebral blood flow, neurological impairment, and increased intracranial pressure. The disability rate and mortality rate of this disease are high, which seriously threatens people's health and quality of life [1-2]. Previous clinical treatment of HICH was based on the basic measures, including lowering intracranial pressure and controlling blood pressure. Although it has certain curative effects, most patients will suffer from following sequelae: neurological impairment and decreased ability of daily living, which affect the quality of patients' life. Therefore, it is necessary to explore a more effective treatment to improve the prognosis of HICH patients. Chinese medicine believes that HICH belongs to the category of "stroke", and its lesions are in the brain. Thus, the treatment of HICH should be mainly focused on promoting blood circulation and removing blood stasis. Naoxintong is a Chinese patent medicine capsule preparation composed of *astragali radix*, *salvia miltiorrhiza bunge*, *angelicae sinensis radix*, etc. It has the effects of promoting blood circulation for removing blood-stasis, alleviating Qi-deficiency and relaxing collaterals, which is mainly used for the treatment of cerebral infarction, coronary disease, angina pectoris, etc [3]. In addition, hyperbaric oxygen therapy is the one which provides high concentration oxygen under atmospheric pressure. It can increase the oxygen concentration in brain tissues to relieve the hypoxia of the brain tissues, which is widely used in clinical treatment of cerebrovascular diseases [4]. In recent years, many studies have found that clinical effects of integrated traditional Chinese and Western medicine has been confirmed in various diseases [5,6]. At present, there are few studies on hyperbaric oxygen combined with naoxintong capsule in treating patients with HICH. Based on this, this study explored the effect of hyperbaric oxygen-assisted naoxintong capsule therapy on hemodynamics and hemorheology in patients with HICH, providing an insight for the clinical treatment of patients with HICH. The study was shown as follows.

Materialsand methods

General data

A total of 110 patients with HICH who were treated in our hospital from March 2019 to December 2021 were selected and divided into control group and observation group by random number table method, with 55 cases in each group. The general data between the two groups were not significantly different and were comparable (P>0.05), which was seen in Table 1. This study was approved by the ethics committee of our hospital, and all patients signed the written informed consent. Inclusion criteria: the patient with hypertension, or cerebral hemorrhage diagnosed by head CT or MRI; patients with stable vital signs and complete clinical data. Exclusion criteria: patients with heart, liver, kidney and other functional insufficiency; patients with traumatic brain injury or other cerebrovascular diseases; patients with coagulation disorders; patients with contraindications to the treatment in this study, such as pneumothorax; patients with poor treatment compliance who interrupted the study during the way.

Table 1 Comparison of general data in two groups

Project	Control group （55 cases）	Observation group （55 cases）	$t/\chi^2/Z$	P value
Sex（case）			0.146	0.702
Male	30	28		
Female	25	27		
Age	65.23±2.36	64.15±2.69	1.549	0.124

Course of hypertension（year）	8.65±1.55	8.69±1.46	0.139	0.890
Amount of cerebral hemorrhage（mL）	22.13±2.68	22.56±2.71	0.837	0.404
Bleeding part（case）			0.577	0.564
Basal ganglia	26	28		
Encephalocoele	13	14		
Cerebral ganglia	10	9		
brainstem	6	4		
Time of disease onset to hospital admission（d）	34.42±4.93	35.16±4.69	0.807	0.421

Methods

Both groups were given routine treatment, including lowering intracranial pressure, controlling blood pressure, and preventing infection with antibiotics. On the basis of routine treatment, the control group was additionally orally treated with Naoxintong capsule for one month, 3 capsules/time and 3 times/d. The observation group was given hyperbaric oxygen therapy on the basis of the control group. Hyperbaric oxygen therapy was performed when the patient's vital signs were stable. The pressure was set to 0.2 MPa with 20-minute compression, 80-minute stable oxygen inhalation by air pressure mask, 10-minute rest in between, and 20-minute decompression, once a day, for 1 month.

Observational indicators

Clinical efficacy

Clinical Neurological Impairment Degree Scoring Standard for Stroke Patients [7] was used to evaluate the clinical efficacy of the patients in both groups. Recovery: neurological impairment score is decreased by more than 90%; significant improvement: neurological impairment score is decreased by 46%-90%; improvement: neurological impairment score is decreased by 18%-45%; invalid: neurological impairment score is decreased less than 17%. The total effective rate = (the number of recovery cases + the number of significantly improved cases + the number of improved cases)/the total number of cases × 100%.

Neurological function

Before treatment and one month after treatment, 5 ml of fasting vein blood was collected from the two groups of patients on morning, and the serum was collected after centrifugation. Brain-derived neurotrophic factor (BDNF) myelin basic protein (MBP) and neuron-specific enolase (NSE) levels were detected by enzyme-linked immunosorbent assay. The kits were purchased from EK-Bioscience, and all operations were performed strictly following instructions in the kits.

Hemodynamics

Before treatment and one month after treatment, Shanghai Shenzhou GT-3000 automatic cerebrovascular function detector was used to detect the mean cerebral vascular velocity (Vmean), cerebral vascular mean flow (Qmean), and dynamic resistance (DR), and peripheral blood flow resistance (R) levels in the two groups.

Hemorheology

Before treatment and one month after treatment, Hailifu HF5000 automatic blood rheology analyzer was used to detect viscosity high shear, whole blood viscosity low shear, and plasma viscosity in both groups.

Statistical methods

The data are described as mean ± standard deviation and the clinical efficacy of the two groups is compared by rank sum test. The comparison between before and after treatment in the same group is carried out by paired-sample *t*-test. The comparison of the observation group before and after treatment is achieved via Independent-sample *t*-test. All data were processed using SPSS 20.0 software, and $P<0.05$ was

considered statistically significant.

Results

Comparison of clinical efficacy between the two groups

The total effective rate in the observation group was significantly higher than that in the control group (P<0.05), as shown in Table 2.

Table 2 Comparison of clinical efficacy between the two groups

Group	Case	Recovery	Significant improvement	Improvement	Invalid	Total effective rate [case (%)]
Observation group	55	13	13	14	15	40（72.7）
Control group	55	28	17	5	5	50（90.9）
Z						3.724
P value						0.001

Comparison of neurological function between the two groups

Before treatment, there was no significant difference in the levels of BDNF, MBP and NSE between the two groups (*P*>0.05). After treatment, the level of BDNF in the two groups was significantly higher than that before treatment (*P*<0.05) while the levels of MBP and NSE in the two groups were apparently lower than those before treatment (*P*<0.05). The variation tendency of each indicator in the observation group was more obvious than that in the control group (*P*<0.05), as displayed in Table 3.

Table 3 Comparison of neurological function between the two groups

Group	BDNF（μmol/L）		MBP（mg/mL）		NSE（mg/mL）	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	1.65±0.16	2.48±0.21	20.38±3.21	15.75±2.51	32.46±4.58	20.34±2.28
Observation group	1.63±0.15	3.32±0.23*	21.08±3.95	7.52±1.27*	31.85±3.32	15.09±2.24*
t	0.676	20	1.02	21.7	0.799	12.18
p	0.5	<0.001	0.31	<0.001	0.425	<0.001

Note: Compared with before treatment: **P*<0.05

Comparison of hemodynamics between the two groups

Before treatment, there was no significant difference in the levels of Vmean, Qmean, DR and R between the two groups (*P*>0.05). After treatment, the Vmean and Qmean in the two groups were apparently higher than those before treatment (*P*<0.05). The levels of DR and R were apparently lower than those before treatment (*P*<0.05), and the variation tendency of each indicator in the observation group was more obvious than that in the control group (*P*<0.05), as displayed in Table 4.

Table 4 Comparison of hemodynamics between the two groups

Group	Vmean（cm/s）		Qmean（mL/s）		DR[（kPa·s）/m]		R[（kPa·s）/m]	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment

Control group	12.06±1.95	18.16±2.31*	8.37±1.16	11.59±1.51*	491.26±20.18	311.24±22.31*	2102.38±55.36	1759.34±45.51*
Observation group	12.65±1.69	22.29±2.32*	8.26±1.11	13.83±1.39*	489.58±22.35	246.11±19.88*	2117.64±48.85	1304.33±39.14*
t	1.696	9.355	0.508	8.094	0.414	16.16	1.533	56.22
P	0.092	<0.001	0.612	<0.001	0.680	<0.001	0.128	<0.001

Note: Compared with before treatment: *P<0.05

Comparison of hemorheology between the two groups

Before treatment, there was no significant difference in viscosity high shear, whole blood viscosity low shear, and plasma viscosity between the two groups (P>0.05). After treatment, the viscosity high shear, whole blood viscosity low shear, and plasma viscosity were apparently lower than those before treatment (P<0.05), and the observation group were apparently lower than those in the control group (P<0.05), as shown in Table 5.

Table 5 Comparison of Hemorheology between the two groups

Group	Viscosity high shear（kPa·s）		Whole blood viscosity low shear（kPa·s）		Plasma viscosity（kPa·s）	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	7.21±0.51	5.68±0.45*	15.03±1.11	11.32±1.03*	1.96±0.21	1.35±0.15*
Observation group	7.18±0.54	4.54±0.28*	14.98±1.32	8.65±0.58*	1.89±0.16	1.12±0.12*
t	0.299	15.95	0.215	16.75	1.966	8.88
p	0.765	<0.001	0.830	<0.001	0.051	<0.001

Note: Compared with before treatment: *P<0.05

Discussion

In recent years, with the change of people's diet and lifestyle, the incidence of hypertension has continued to rise, along with the increased incidence of HICH, which seriously affects the quality of patients' life [8]. Western medicine believes that the pathological mechanism of HICH is mainly related to cleavage products of hematoncus, hematoma mass effect, and brain tissue damage, which stimulates the body to release certain active substances, resulting in intracranial hypertension, cerebral edema, etc. [9]. In traditional Chinese medicine, cerebral hemorrhage belongs to blood disease and stroke. As shown in *Su Wen·Tiaojing Theory*: Blood and qi go up along the meridians together, and a coma will occur, causing people to faint suddenly like sudden death. It shows that the inversion of qi and blood is the main reason for the occurrence of HICH, indicating that the disorder of qi and blood causes blood not flow through the meridians, and extravasates blood out of the veins, causing the upper orifices to be blocked, and poor mental condition [10]. Clinical treatment should focus on promoting blood circulation and nourishing qi, and dispersing blood stasis and dredging collateral.

According to reports [11], the cerebral arterial wall becomes thinned or hardened and its elasticity decreases in the long-term hypertensive state of the human body. During this time, a sharp increase in blood pressure can easily lead to brain rupture and

cerebral hemorrhage, resulting in secondary cranial nerve damage. BDNF is a protective neural factor, which has the functions of maintaining neuron survival, promoting nerve cell regeneration and repair, etc. The neurological function of patients with HICH is damaged, and the level of BDNF is significantly decreased. After cranial nerve damage, MBP, as an important component protein of myelin sheath, can quickly enter the cerebrospinal fluid and involve in the blood circulation through the blood-brain barrier. As an acid protease, the higher the level of NSE is, the more severe the nerve damage is [12-14]. In this study, the total effective rate in the observation group was apparently higher than that in the control group. After treatment, the level of BDNF in the two groups was significantly higher than that before treatment while the levels of MBP and NSE in the two groups were apparently lower than those before treatment, and the change trend of each index in the observation group was more obvious than that in the control group. The results showed that hyperbaric oxygen-assisted Naoxintong capsule has a significant effect on HICH patients, which can effectively improve the neurological function of patients. Naoxintong capsule is made from 16 kinds of traditional Chinese medicines, including *astragali radix, paeoniae radix rubra, salviae miltiorrhizae radix et rhizoma, angelica sinensis, carthami flos, persicae semen, chuanxiong rhizoma, scorpion, whitmania pigra whitman, achyranthes*, etc. Among them, *astragali radix* has the functions of tonifying middle-jiao and qi, and elevating yang; *paeoniae radix rubra* has the effects of promoting blood circulation for removing blood stasis, and removing pathogenic heat from blood; *salviae miltiorrhizae radix et rhizoma*, *angelica sinensis*, *carthami flos*, and *persicae semen* have the functions of nourishing blood, promoting blood circulation, regulating menstruation and relieving pain; *chuanxiong rhizome* has the effects of dispelling rheumatism, relieving pain, promoting blood circulation and promoting qi. *Scorpion* has the effects of relieving endogenous liver wind and activating meridians to stop pain. The combination of above medicine can reach the effects of promoting blood circulation and benefiting qi, and removing blood stasis and dredging collaterals. At the same time, hyperbaric oxygen increases the physically dissolved oxygen in the blood, the partial pressure of blood oxygen, and the oxygen content in the brain tissues, improves the ischemia and hypoxia state of the brain tissues, and promotes the mitochondrial metabolism of neuron cells and the recovery of nerve function. Besides, hyperbaric oxygen can inhibit the effect of harmful factors caused by brain tissue ischemia and hypoxia and relieve the degree of brain tissue damage, thereby effectively improving neurological function and regulating the levels of neurological function indicators BDNF, MBP, and NSE in the body [15]. It can be seen that the hyperbaric oxygen-assisted Naoxintong capsule has a significant effect on HICH patients, which can effectively reduce the degree of neurological impairment and effectively improve neurological function of patients

Study has found that a lot of toxic substances will be released after the occurrence of HICH, causing abnormal changes in the body's hemorheology and microcirculation [16]. Vmean, Qmean, DR and R are clinically important markers to reflect the cerebral vascular function and the patency of cerebral vascular microcirculation. When the cerebral blood supply is insufficient, the levels of Vmean and Qmean are decreased significantly, while the levels of DR and R are increased significantly. In this study, after treatment, the Vmean and Qmean in the two groups were apparently higher than those before treatment, and the levels of DR and R were apparently lower than those before treatment. The change trend of each index in the observation group was more obvious than that in the control group. After treatment, viscosity high shear, whole blood viscosity low shear, and plasma viscosity were apparently lower than those before treatment, and those indicators in the observation group were apparently lower than those in the control group. The results showed that hyperbaric oxygen-assisted naoxintong capsule has a significant effect on HICH patients, which can effectively improve the body hemodynamics and hemorheology. Hui Wang et al. showed that the important

components of naoxintong capsule, such as carthami flos and paeoniae radix rubra, can inhibit platelet aggregation, reduce blood viscosity, and improve hemorheology; and scorpions and leeches can dissolve thrombus and improve the body's coagulation function [17]. In addition, hyperbaric oxygen can expand the blood vessels of ischemic tissues, increase the diffusion distance of blood oxygen and the reserve state of tissue oxygen, improve the microcirculation of the body and hemorheology, and reduce the proportion of hematocytes and blood viscosity [18].

In conclusion, hyperbaric oxygen-assisted Naoxintong capsule has a significant effect on HICH patients, which can effectively reduce the degree of neurological impairment, and improve the hemodynamics and hemorheology in the body.

Acknowledgement

Not applicable.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization, Data curation and Writing-Original draft, Y.D and S.C.W; Writing-review and editing, Q.L; All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee, and the patients were informed and consented.

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Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Material

Not applicable.

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