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Effect of Xingnaojing Assist Vinpocetine Therapy on Immune Function and Brain Oxygen Metabolism in Elderly Patients with Acute Cerebral Infarction

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Keywords

Xingnaojing injection, Vinpocetine, Acute cerebral infarction, T lymphocyte subset, Brain oxygen metabolism

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Abstract

Objective To explore the effect of Xingnaojing assist vinpocetine therapy on immune function and brain oxygen metabolism in elderly patients with acute cerebral infarction (ACI). **Methods** 124 elderly ACI patients who were treated in our hospital from May 2019 to December 2021 were randomly divided into observation groups and control groups, with 62 cases in each group. Patients in both groups were given conventional treatment, those in the control group were given vinpocetine on this basis, and patients in the observation group were given Xingnaojing injection on the basis of the control group. The national institutes of health stroke scale (NIHSS), activities of daily living (ADL) scores, T lymphocyte subset, vascular endothelial function index, and brain oxygen metabolism index were compared between the two groups. **Results** After treatment, the ADL scores, T lymphocyte CD_3^+, CD_4^+ ratio, serum vascular endothelial growth factor (VEGF) and nitric oxide (NO) in the two groups were significantly higher than those before treatment (P<0.05), and those of the observation group was evidently higher than that in the control group (P<0.05). After treatment, the NIHSS score, T lymphocyte CD_8^+ ratio, endothelin-1 (ET-1), and arterial venous oxygen content difference ($D(a\text{-}jv)O_2$) and cerebral oxygen extraction rate (ERO_2) were obviously lower than those before treatment (P<0.05), and those of the observation group was markedly lower than those of the control group (P<0.05). **Conclusion** Elderly patients with ACI treated with Xingnaojing-assisted vinpocetine can effectively improve nerve function and self-care ability, enhance immunity, promote the recovery of vascular endothelial function and improve blood supply to the brain.

Introduction

Acute cerebral infarction (ACI) is a common clinical neurological disease with high disability rate and mortality rate, which mostly occurs in the elderly and is related to multiple factors such as coronary disease, obesity and diabetes. In recent years, the incidence of ACI has been increasing year by year with the accelerating aging of society and changes in living habits, seriously threatening the life and health of the elderly [1]. Vinpocetine is a cerebral vasodilator, which facilitates vasodilation, increases cranial flow, improves cerebral blood circulation, and plays a neuroprotective role. However, the efficacy of single drug is not ideal. In recent years, with the continuous deepening of the research on traditional Chinese medicine, combined treatment of traditional Chinese medicine and western medicine has become a popular scheme for the treatment of ACI. Xingnaojing is a chinese herbal compound injection, which is derived from Angong Niuhuang pill, a classic first-aid prescription of traditional Chinese medicine, which can dissolve lumps, activate collaterals, clear orifices and restore consciousness. A study suggested that Xingnaojing contains a variety of effective components, which has a definite effect in the treatment of ACI [2]. At present, there are few studies addressing the efficacy of Xingnaojing assisted vinpocetine in the treatment of elderly patients with ACI, let alone the reports highlighting the effect of this treatment on immune function and cerebral oxygen metabolism. The aim of this study is to explore the clinical effect of Xingnaojing in combination with vinpocetine in the treatment of elderly patients with ACI, and its impact on immune function and cerebral oxygen metabolism so as to provide reference for clinical treatment. The results of this research are reported as follows.

Materials and methods

General information

124 elderly ACI patients who were treated in our hospital from May 2019 to December 2021 were selected and randomly divided into an observation group (n=62) and a control group (n=62). Difference in gender, age, onset time, location of infarction and underlying disease between the two groups was not significant (P>0.05), as presented in Table 1. This study was approved by Medical Ethics Committee, and patients were informed and agreed.

Table 1 Comparison of general information between the two groups

Groups		Observation group (n=62)	Control group (n=62)	χ^2/t	P
Gender (cases)	Male	35	33	0.130	0.718
	Female	27	29		
Age (years old)		69.56±5.27	69.69±6.19	-0.126	0.900
Onset time (h)		4.17±1.04	4.50±0.99	-1.810	0.073
Locations of infarction (cases)	Basal ganglia	18	19	0.331	0.988
	Frontal lobe	12	11		
	Parietal lobe	12	14		
	Occipital lobe	11	10		
	Temporal lobe	9	8		
Underlying diseases (cases)	Hypertension	25	26	0.130	0.937
	Diabetes	18	16		
	Hyperlipidemia	21	20		

Inclusion criteria

(1) Patients' symptoms were conformed to the diagnostic criteria of ACI proposed by Chinese Medical Association and confirmed by imaging

examinations such as magnetic resonance imaging (MRI); (2) Patients over 60 years old; (3) Patient was in first-episode ACI and sought medical advice within 12 h after the attack of ACI; (4) Patients with complete clinical data and no history of allergy to related medications.

Exclusion criteria

(1) Patients with contraindication of vinpocetine, such as those with uncontrolled intracranial hemorrhage, ischemic heart disease or arrhythmia; (2) Patients with dysfunction of important organs such as heart, lung, liver and kidney; (3) Patients with mental disorders, cognitive dysfunction, blood system and immune system disorders; (4) Pregnant women.

Treatment methods

Patients in both groups were given routine treatment such as respiratory support, anticoagulation, intracranial pressure reduction and neuroprotection. In the control group, 30 mg vinpocetine injection (Hunan Wuzhoutong Pharmaceutical Co., Ltd., SFDA Approval No.: H20143089, specification: 2 mL:10 mg) was diluted into 500 ml normal saline, and used for intravenous drip once a day. The observation group was given Xingnaojing injection (Henan Tiandi Pharmaceutical Co., Ltd., SFDA Approval No.: Z41020665, specification: 2 mL) on the basis of the control group. 10 ml Xingnaojing injection was diluted with 250 mL normal saline and then used for intravenous drip. Both groups were treated for 14 days.

Observation indexes

(1) National institutes of health stroke scale (NIHSS) [4], activities of daily living (ADL) [5] scores: Before and 14 days after treatment, NIHSS was used to evaluate the neurological function of the two groups. The lower the NIHSS score, the stronger the neurological function. At the same time, ADL was used to evaluate the quality of life of the two groups. The higher the ADL score, the higher the quality of life. (2) Immune function: Before and 14 days after treatment, the levels of CD_3^+, CD_4^+ and CD_8^+ in the two groups were detected by a flow cytometer (Brand: BD, model: FACSVia). (3) Vascular endothelial function and brain oxygen metabolism indexes: Before and 14 days after treatment, 5 mL of fasting venous blood of the two groups were taken for examination. Vascular endothelial growth factor (VEGF), nitric oxide (NO) and endothelin-1 (ET-1) were detected by enzyme-linked immunosorbent assay (ELISA, EK-Bioscience). At the same time, the blood gas analyzer (Brand: Radiometer, model: ABL80 FLEX) was used to detect arterial venous oxygen content difference ($D(a\text{-}jv)O_2$) and cerebral oxygen extraction rate (ERO_2) levels.

Statistical methods

SPSS 20.0 was used to perform statistical analysis, and the enumeration data were compared using χ^2 test. The measurement data were expressed as mean ± standard deviation ($\bar{x}\pm s$). Comparison between two groups was performed using the independent sample *t*-test. Comparison between different time points in the same group was analyzed using the paired sample *t*-test. The data with $P<0.05$ were considered to be statistically significant.

Results

Comparison of NIHSS and ADL scores between the two groups

Before treatment, there was no significant difference in NIHSS and ADL scores between the two groups ($P>0.05$). After treatment, the ADL score of the two groups was evidently higher than that before treatment ($P<0.05$), and the score of the observation group was markedly higher than that of the control group ($P<0.05$). After treatment, the NIHSS score of the two groups was significantly lower than that before treatment ($P<0.05$), and the score of the observation group was distinctly lower than that of the control group ($P<0.05$), as shown in Table 2.

Table 2 Comparison of NIHSS and ADL scores between the two groups ($\bar{x}\pm s$, points)

Groups	Number of cases	ADL score		NIHSS score	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	62	28.53±9.39	46.52±10.39*	23.79±3.36	11.45±2.07*
Control group	62	28.78±8.87	37.10±10.72*	24.16±3.04	15.58±2.66*
t		-0.152	4.968	-0.643	-9.648
P		0.879	0.000	0.521	0.000

Note: compared with before treatment: *P<0.05

Comparison of immune function between the two groups

Prior to the treatment, difference in the levels of CD_3^+, CD_4^+ and CD_8^+ between the two groups was not significant (P>0.05); however, after treatment, the levels of CD_3^+ and CD_4^+ in the two groups were obviously higher than those before treatment (P<0.05), and the levels in the observation group were significantly higher than those in the control group (P<0.05). After treatment, the level of CD_8^+ in the two groups was evidently lower than that before treatment (P<0.05), and CD_8^+ level in the observation group was markedly lower than that in the control group (P<0.05), as presented in Table 3.

Table 3 Comparison of immune function between the two groups ($\bar{x}\pm s$, %)

Groups	Number of cases	CD_3^+		CD_4^+		CD_8^+	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	62	50.23±8.25	60.27±5.19*	29.12±3.66	35.39±4.10*	37.60±4.08	31.60±2.33*
Control group	62	50.18±7.00	56.21±5.14*	29.05±3.87	33.16±4.21*	37.98±4.14	34.41±2.86*
t		0.036	4.377	0.103	2.988	-0.515	-5.998
P		0.971	0.000	0.918	0.003	0.608	0.000

Note: compared with before treatment: *P<0.05

Comparison of vascular endothelial function between the two groups

Before treatment, there was no significant difference in the levels of VEGF, NO and ET-1 between the two groups (P>0.05). After treatment, the levels of VEGF and NO in the two groups were distinctly higher than those before treatment (P<0.05), and the levels in the observation group were significantly higher than those in the control group (P<0.05). After treatment, the level of ET-1 in the two groups was obviously lower than that before treatment (P<0.05), and ET-1 level in the observation group was markedly lower than that in the control group (P<0.05), as exhibited in Table 4.

Table 4 Comparison of vascular endothelial function between the two groups ($\bar{x}\pm s$)

Groups	Number of cases	VEGF (ng/L)		NO (μmol/L)		ET-1 (pg/mL)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observatio	62	163.39±32.2	235.77±33.45	50.81±5.2	65.83±6.48	83.73±12.0	61.31±11.73

n group		4	*	2	*	3	*
Control group	62	163.52±34.03	191.08±28.91*	51.02±4.91	55.72±5.94*	83.02±14.68	75.89±11.85*
t		-0.022	7.959	-0.231	9.056	0.295	-6.885
P		0.983	0.000	0.818	0.000	0.769	0.000

Note: compared with before treatment: *P<0.05

Comparison of brain oxygen metabolism index between the two groups

The difference in the levels of D(a-jv)O_2 and ERO_2 between the two groups was not significant before treatment (P>0.05). After treatment, the levels of D(a-jv)O_2 and ERO_2 in the two groups were obviously lower than those before treatment (P<0.05), and the levels in the observation group were markedly lower than those in the control group (P<0.05), as shown in Table 5.

Table 5 Comparison of brain oxygen metabolism index between the two groups ($\bar{x}\pm s$)

Groups	Number of cases	D(a-jv)O_2		ERO_2 (%)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	62	7.23±1.70	3.14±0.96*	37.01±8.48	15.57±5.03*
Control group	62	7.17±1.37	4.98±1.09*	36.65±8.54	26.89±4.44*
t		0.216	-9.975	0.236	-13.285
P		0.829	0.000	0.814	0.000

Note: compared with before treatment: *P<0.05

Discussion

ACI refers to the stenosis or occlusion of cerebral supplying artery lumen, resulting in insufficient cerebral blood flow and ischemic necrosis of local brain tissue, which causes damage to relevant physical functions in this area. The patients' clinical manifestations include hemiplegia, language disorder, coma, and even death in a short time. Brain cells cannot be repaired after death, but studies have shown that there is an "ischemic penumbra" between necrotic brain tissue and healthy brain tissue when ACI occurs, in which there are a large number of dormant brain cells with complete morphology. Timely restoration of cerebral blood perfusion and promotion of the transformation of "ischemic penumbra" into healthy brain tissue are the key to improve the clinical treatment effect of ACI [6]. At present, the main clinical therapeutic methods for ACI include thrombolysis, anticoagulation and neuroprotection. Vinpocetine is an indole alkaloid extracted from Vinca minor, which can improve cerebral blood flow and protect nerves. Traditional Chinese medicine believes that ACI belongs to "stroke", and its pathogenesis is deficiency of inborn vitality and poor blood circulation, resulting in blood stasis and phlegm turbidity and blocking of clear orifices, which leads to stroke. Xingnaojing is an intravenous drug modified from Angong Niuhuang Pill. It excludes dangerous medicinal materials, such as *cinnabar* and *realgar*, and is made of artificial *musk*, *tulip*, *borneol* and *gardenia*, which can activate blood circulation, remove blood stasis, induce resuscitation and restore consciousness. This paper explored the clinical effect of Xingnaojing assisted vinpocetine in the treatment of ACI patients. The results showed that Xingnaojing assisted vinpocetine has better clinical effect than vinpocetine alone.

Brain tissue mainly relies on aerobic metabolic supply of glucose, and local hypoxia in the brain will lead to irreversible necrosis of brain cells, resulting in limb or consciousness dysfunctions in patients with ACI. Brain oxygen metabolism index D(a-jv)O_2 and ERO_2

levels can intuitively reflect the oxygen uptake of brain tissue and are important indexes for evaluating central nervous function. The results of this study showed that after treatment, ADL scores of the two groups were significantly higher compared with before treatment, and the score of the observation group was obviously higher than that of the control group. After treatment, the NIHSS scores, ET-1, $D(a\text{-}jv)O_2$ and ERO_2 levels of the two groups were distinctly lower than those before treatment, and those of the observation group were obviously lower than those of the control group. It is suggested that Xingnaojing assisted by vinpocetine can relieve the clinical symptoms of ACI patients and improve the body's brain oxygen metabolism. Vinpocetine acts on calcium ion phosphodiesterase, which can promote cyclic adenosine monophosphate (cAMP) expression, thereby relaxing vascular smooth muscle, inducing vasorelaxation, and increasing cerebral blood flow. Second, vinpocetine has an anti-platelet agglutinating effect, which may reduce blood viscosity and improve blood microcirculation in the brain. In addition, vinpocetine can promote the uptake of glucose by brain tissue, enlarge the oxygen dissociation degree of hemoglobin, relieve cerebral hypoxia, improve the metabolism of brain tissue, and play a role in protecting nerve [7-8]. In Xingnaojing, *musk* is used as the principal drug to invigorate blood, unblock circulation tracts and induce resuscitation, *gardenia* is used as the ministerial drug to purge intense heat and detonicate, clear away heat and dissipate stasis, *tulip* is used as an adjuvant to promote Qi flow and remove blood-stasis, clear away the heart-fire and remove depression, and *borneol* was used as a conductant drug to assist *musk* to arouse consciousness [9]. Modern pharmacological research shows [10] that *musk* and *borneol* in Xingnaojing can repair blood-brain barrier (BBB) damage, regulate BBB permeability, and play a role in reducing brain edema; Secondly, Xingnaojing can promote the secretion and release of vascular growth factors such as VEGF, which can promote angiogenesis and endogenous neurovascular remodeling, with the effect of improving microcirculation.

Immune disorders are closely related to vascular endothelial dysfunction and the occurrence and development of ACI [11-12]. T lymphocytes are an important part of the immune system. CD_3^+ refers to all mature T lymphocytes. CD_4^+ interacts with CD_8^+ to maintain the stability of cellular immune function. Brain tissue injury in patients with ACI will activate the immune system, cause abnormal expression of T lymphocyte subsets, lead to high levels of CD_8^+ and low levels of CD_3^+ and CD_4^+, and reduce the immune capacity of the body, which is not conducive to ACI treatment [13]. In addition, NO and ET-1 are endogenous vascular regulators, which jointly regulate vasomotor. VEGF is a highly specific vascular endothelial growth factor, which can participate in the regulation of endothelial cell migration and proliferation. When ACI occurs, the levels of NO and VEGF decrease significantly, while the level of ET-1 increases obviously, resulting in vasoconstriction, spasm and increase of blood viscosity, which aggravates cerebral hypoxia [14]. The results showed that after treatment, the levels of CD_3^+, CD_4^+, VEGF and NO in the two groups were significantly higher than those before treatment, and the levels in the observation group were distinctly higher than those in the control group. After treatment, the levels of CD_8^+ and ET-1 in the two groups were obviously lower than those before treatment, and those in the observation group were significantly lower than those in the control group. It is suggested that Xingnaojing combined with vinpocetine can enhance the immune function and reduce the injury of vascular endothelial function in elderly patients with ACI. Vinpocetine can improve cerebral oxygen metabolism to promote neovascularization, improve vascular endothelial function, establish collateral circulation and improve cerebral blood circulation. In addition, vinpocetine has anti-inflammatory and antioxidant effects, which can reduce the damage of vascular endothelium caused by inflammation and oxidative stress, and regulate the immune function of the body [15]. Modern pharmacological research suggests that [9-10], Xingnaojing can reduce blood viscosity and vascular resistance, eliminate oxygen free radicals, inhibit

inflammatory reaction, and reduce vascular endothelial function damage; In addition, Xingnaojing can reduce the content of adhesion factors, thus inhibiting the expression of inflammatory factors and playing an immunomodulatory role.

In conclusion, Xingnaojing combined with vinpocetine can effectively alleviate the clinical symptoms of elderly patients with ACI, help to improve their neurological function and ability in daily life, enhance immunity, promote the recovery of vascular endothelial function and improve the blood supply to the brain.

Acknowledgement

Not applicable.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization, Data curation, Writing-Original draft,Writing-review and editing, H.L.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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