

CLINICAL RESEARCH

Analysis on the Application Value of Tongqiao Huoxue Decoction Combined with Cognitive Rehabilitation Training in the Treatment of Cognitive Impairment in Stroke

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Key words

Tongqiao Huoxue Decoction, Rehabilitation training, Stroke, Cognitive function, Blood coagulation function

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Abstract

Objective To analyze the application value of Tongqiaoxuoxue Decoction combined with cognitive rehabilitation training in the treatment of cerebral apoplexy cognitive impairment. **Methods:** A total of 96 stroke patients with cognitive impairment admitted to our hospital from January 2019 to January 2022 were selected and divided into control group and observation group by random number table method, with 48 cases in each group. Patients in the control group received conventional treatment combined with cognitive rehabilitation training, and those in the observation group were additionally given Tongqiao Huoxue Decoction on the basis of the control group. Clinical efficacy, cognitive function and hemorheology were compared between the two groups. **Results:** The clinical efficacy in observation group was significantly higher than that in control group ($P<0.05$). The scores of Summary Mental State Scale (MMSE), Montreal Cognitive Assessment Scale (MoCA) and Neurobehavioral Cognitive State Test (NCSE) in two groups after treatment were significantly increased ($P<0.05$), and the scores in the observation group were higher than those in the control group ($P<0.05$). Compared with before treatment, the levels of high whole blood viscosity, low whole blood viscosity, plasma viscosity and fibrinogen in two groups after treatment were significantly decreased ($P<0.05$), and the levels in the observation group were significantly lower than those in the control group ($P<0.05$). **Conclusion:** Tongqiao Huoxue Decoction combined with cognitive rehabilitation training has good clinical efficacy in the treatment of stroke patients with cognitive impairment, which can effectively improve the patients' cognitive function and hemorheology.

Introduction

Stroke is an acute cerebrovascular disease, which is a group of diseases that cause brain tissue damage due to the severe shortage of blood supply to the brain caused by the sudden rupture or blockage of cerebral blood vessels. Due to the large damage to the cerebral blood vessels of stroke patients, the neurons in the brain cannot normally transmit nerve signals, and the patients may have cognitive impairment^[1-2]. A study has shown that cognitive rehabilitation training has a certain effect on improving the cognitive impairment of stroke patients, but it is time-consuming and laborious with poor effect^[3]. In order to make up for the shortcomings of cognitive rehabilitation training, traditional Chinese medicine therapy can be used to further improve the cognitive impairment of stroke patients in clinic. The main components of Tongqiao Huoxue Decoction are jujuba, fresh ginger, peach kernel, etc., and its main effects are promoting blood circulation and arousing consciousness, eliminating blood stasis and dredging collaterals, etc. Clinically, it is commonly used to treat the symptoms caused by blood stasis, such as transient blindness, headache and

dizziness^[4]. At present, there are relatively few clinical studies on the use of Tongqiao Huoxue Decoction to assist in the treatment of stroke patients with cognitive impairment. Therefore, this study explored the clinical effect of Tongqiao Huoxue Decoction on stroke patients with cognitive impairment, and explored a reliable method to treat stroke patients with cognitive impairment. The research results are reported as follows.

Materials and methods

General information

A total of 96 stroke patients with cognitive impairment admitted to our hospital from January 2019 to January 2022 were selected and divided into control group and observation group by random number table method, with 48 cases in each group. This study was approved by the Ethics Committee of the hospital, and all patients signed the informed consent. Difference in the general information between the two groups was not significant ($P>0.05$), which was comparable, as presented in Table 1.

Table 1 Comparison of general information between two groups

Groups	Number of cases	Gender		Age (years old)	Average course of disease (months)	Body weight (kg)
		Male	Female			
Observation group	48	25	23	66.93±5.87	2.42±0.97	52.52±4.61
Control group	48	26	22	67.01±7.27	2.54±1.04	51.03±4.50
t/χ^2			0.838	-0.059	-0.585	1.602
P			1.000	0.953	0.560	0.112

Diagnostic criteria

Western medicine diagnostic criteria: ①refer to the diagnostic criteria of stroke from *Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke 2014*^[5]; ②refer to the diagnostic criteria of cognitive impairment from *Expert Consensus on Management of Post-stroke Cognitive Impairment*^[6].

Traditional Chinese medicine diagnostic criteria: refer to the diagnostic criteria of “dementia” from *Guidelines for Diagnosis and Treatment of Internal*

Diseases in Traditional Chinese Medicine: Traditional Chinese Medicine Diseases and Syndromes^[7].

Inclusion criteria

①Those who met the diagnostic criteria of traditional Chinese medicine and Western medicine; ②Conscious people; ③Patients first caught by stroke.

Exclusion criteria

①Patients with severe primary diseases of brain, liver

and kidney; ②Those who are allergic to the ingredients of Tongqiao Huoxue Decoction; ③Patients with malignant tumor; ④Patients with cognitive impairment caused by other factors; ⑤Patients with history of craniocerebral trauma, encephalitis and other intracranial diseases.

Treatment methods

The patients in both groups were given conventional treatment for post-stroke cognitive impairment: a. Anti-platelet agents (aspirin). b. Nerve protection (edaravone or vitamin). c. Hyperbaric oxygen therapy. Cognitive rehabilitation training was carried out based on it: Patients were assisted to complete tasks according to different instructions, which is used to improve patients' executive ability, mainly including: (1) Orientation training including specific training such as time, person and place. (2) Attention training: Patients were trained through games, movies, etc. (3) Computing power training: Patients were trained through arithmetic and logical operations. (4) Memory ability training: Patients were trained by memorizing pictures, characters, story lines, etc. On the basis of the control group, patients in the observation group were treated with Tongqiao Huoxue Decoction, which was decocted to 150 ml and boiled. The residue was removed. The potion was added with musk, followed by boiling again. It was taken once a day at bedtime. The ingredients include 10 g jujuba (cores removed), 9 g fresh ginger (chopped), 9 g peach kernel (ground), 9 g crocus sativus, 5 g thick green onion (chopped), 3 g Ligusticum wallichii, 3 g red peony roots and 250 ml yellow wine. The treatment course of both groups was 4 weeks.

Observational indexes

①Clinical efficacy: after treatment, the criteria of therapeutic effects were drawn up according to the *Chinese Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke*^[5], and the clinical effects between the two groups were compared.
②Cognitive function: before and after treatment, the cognitive functions in the two groups were evaluated with the Mini-Mental State Examination (MMSE)^[8],

Montreal Cognitive Assessment Scale (MoCA)^[8] and Neurobehavioral Cognitive Status Examination (NCSE)^[9]. The main test contents of MMSE scale include time orientation, place orientation, attention and calculation, short-term memory, naming, repetition, execution, etc. MoCA scale mainly includes time orientation, place orientation, attention and calculation, short-term memory, naming, repetition, execution, etc. NCSE scale mainly evaluates some aspects, such as memory, attention and executive ability. The higher the total score, the better the cognitive function of patients.

③Hemorheology: before and after treatment, 5 ml of venous blood was taken from patients in the two groups, and the whole blood viscosity (high and low), plasma viscosity and fibrinogen level of patients were measured by GD3LBY-N6 automatic blood rheometer.

Statistical methods

The statistical analysis was conducted using SPSS 20.0, and the enumeration data were compared using χ^2 test. The ranked data were compared by rank sum test. The measurement data were presented as mean \pm standard deviation ($\bar{x} \pm s$). Additionally, *t*-test was used for comparison. $P < 0.05$ was considered to be statistically significant.

Results

Comparison of clinical efficacy between the two groups

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

Comparison of cognitive function between the two groups before and after treatment

Before treatment, there was no significant difference in MMSE, MoCA and NCSE scores between the two groups ($P > 0.05$). Compared with those before the treatment, the MMSE, MoCA and NCSE scores of the two groups were significantly increased after treatment ($P < 0.05$), and the scores in the observation group were higher than those in the control group

($P<0.05$), as shown in Table 3.

Comparison on the level of each hemorheology index between two groups before and after treatment

Before treatment, there was no significant difference in high whole blood viscosity, low whole blood viscosity, plasma viscosity and fibrinogen level

between the two groups ($P>0.05$). Compared with those before the treatment, the high whole blood viscosity, low whole blood viscosity, plasma viscosity and fibrinogen level in the two groups were decreased evidently after treatment ($P<0.05$), and those in the observation group were distinctly lower than those in the control group ($P<0.05$), as presented in Table 4.

Table 2 Comparison of clinical efficacy between the two groups [%]

Groups	Number of cases	Basically controlled	Markedly improved	Improved	Unchanged	Deteriorating	Effective rate/%
Observation group	48	15	15	15	3	0	62.5
Control group	48	17	20	10	1	0	77.08
χ^2							5.084
P							0.018

Table 3 Comparison of cognitive function between the two groups before and after treatment ($\bar{x}\pm s$, points)

Groups	Number of cases	MMSE		MoCA		NCSE	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	48	16.55±2.23	20.24±2.76 ^a	22.03±1.76	25.01±1.71 ^a	53.11±7.56	65.88±7.14 ^a
Observation group	48	16.99±2.45	24.33±1.37 ^a	21.61±2.33	27.56±2.31 ^a	52.77±8.06	70.00±7.49 ^a
t value		-0.920	-9.196	0.997	-6.147	0.213	-2.758
P value		0.360	0.000	0.322	0.000	0.832	0.007

Note: compared with before treatment: ^a $P<0.05$

Table 4 Comparison on the level of each hemorheology index between two groups before and after treatment (n=48)

Groups	Time	Whole blood viscosity/mPa·s		Plasma viscosity/mPa·s	Fibrinogen/g·L ⁻¹
		High 200 s ⁻¹	Low 30 s ⁻¹		
Control group	Before treatment	6.74±1.43	10.34±2.56	2.74±0.98	6.32±1.45
	After treatment	5.01±0.88 ^a	7.33±2.70 ^a	1.93±0.57 ^a	4.75±0.97 ^a
Observation group	Before treatment	6.55±1.36	10.11±3.01	2.69±1.02	6.82±1.55
	After treatment	4.09±2.45 ^{ab}	6.38±1.42 ^{ab}	1.56±0.44 ^{ab}	4.01±0.76 ^{ab}

Note: compared with before treatment: ^a $P<0.05$; Compared with the control group: ^b $P<0.05$

Discussion

Cognitive impairment in stroke is characterized by high incidence, mortality and disability rates. Some data show that the prevalence of cognitive impairment among ten-year stroke survivors is 61%. With the progression of the disease, patients' cognitive function continues to decline, their functional independence is weakening, and their social participation ability significantly deteriorates. In addition, post-stroke cognitive dysfunction will aggravate the disability of patients and reduce their life satisfaction. However, there is no clear method to prevent or treat cognitive impairment except for the enhanced secondary prevention of stroke. Therefore, the main purpose of this study is to explore whether traditional Chinese medicine combined with cognitive rehabilitation training can improve the cognitive function of stroke patients with cognitive impairment^[10-11]. Traditional Chinese medicine believes that the cognitive impairment in stroke belongs to "dementia", which is a syndrome of deficiency in origin and excess in superficiality. Although the disease is primarily located in the brain, its incidence is closely related to the heart, liver, spleen and kidney. The main pathogenesis is that long illness is accompanied by stasis, blood stasis damages the collaterals, and that internal static blood obstruction causes brain collaterals to be affected by pathogenic factors. Therefore, the treatment of this disease should focus on activating blood circulation and dredging collaterals^[4].

The results of this study showed that the clinical efficacy in the observation group was significantly higher than that in the control group. Compared with before treatment, MMSE, MoCA and NCSE scores in the two groups were obviously increased after treatment, and the scores in the observation group were higher than those in the control group. It indicates that Tongqiao Huoxue Decoction combined with cognitive rehabilitation training has a good clinical effect on stroke patients with cognitive impairment, and can effectively improve their cognitive function. Cognitive rehabilitation training can improve the cognitive dysfunction of stroke

patients by inducing the formation of new information in their brains^[12]. Tongqiao Huoxue Decoction consists of jujuba, fresh ginger, peach kernel, crocus sativus, thick green onion, *Ligusticum wallichii*, red peony roots, musk and yellow wine. Of them, Jujuba can strengthen spleen and stomach, and supplement blood and Qi. Fresh ginger has the effects of perspiration, cooling and removing wind chill. Peach kernel can remove blood stasis, moisturize dryness and smooth intestines. Crocus sativus can activate blood circulation, cool blood, relax tendons and dredge collaterals. The thick green onion can tonify the kidney and Yang, expel toxin and strengthen the body. *Ligusticum wallichii* can promote Qi, relieve depression, expel wind and relieve pain. Red peony roots can clear away heat and cool blood, disperse blood stasis and relieve pain. Musk can induce resuscitation, invigorate blood circulation and dredge menstruation. Yellow wine has the effect of activating blood circulation, dispelling cold, dredging meridians and activating collaterals. Modern pharmacological studies have shown that the aqueous extract of peach kernel in Tongqiao Huoxue Decoction can increase the concentration of extracellular acetylcholine in patients' hippocampus to promote the activation of brain nerve conduction function, improve the speed of information transmission and enhance brain memory ability, which comprehensively improves patients' cognitive function. Its ethanol extract can improve the activity of glutathione peroxidase (GSH-Px) in brain tissue. Selenium is a component of GSH-Px enzymes, which reduces toxic peroxides to non-toxic hydroxyl compounds by catalyzing glutathione to glutathione disulfide, so as to protect the structure of nerve cell membrane from peroxide interference and damage, which further improves the cognitive function of patients^[13]. Total paeony glycoside can inhibit the accumulation of advanced glycation end products (AGEs) in the body, slow down protein modification by AGEs, protect the physiological function of protein, inhibit glycosylation-oxidative stress reaction, and maintain the normal genotype and phenotype of nerve cells, so as to protect the nerve cells of patients and further improve the cognitive function of patients^[14].

The factors such as whole blood viscosity, plasma viscosity and fibrinogen increase will cause a large amount of "atherosclerotic substances" to deposit in the blood vessel wall of patients, making the blood vessel wall of the brain thicker and harder, and further aggravating the condition of stroke patients with cognitive impairment. This study showed that after the treatment, high whole blood viscosity, low whole blood viscosity, plasma viscosity and fibrinogen level in the two groups were decreased significantly compared with those before treatment, and those in the observation group were obviously lower than those in the control group. It suggests that Tongqiao Huoxue Decoction combined with cognitive rehabilitation training can improve the hemorheology of stroke patients with cognitive impairment. Cognitive rehabilitation training is conducive to promoting functional reorganization around cerebral ischemia, stimulating the thinking vitality of stroke patients with cognitive impairment by increasing their memory ability, so as to ameliorate their brain microcirculation and further improve their hemorheology^[12]. Modern pharmacology reports that sodium ferulate in *Ligusticum wallichii* in Tongqiao Huoxue Decoction can inhibit tryptophan hydroxylase from being catalyzed to 5-hydroxytryptamine, interrupt the vicious cycle of abnormal vasodilatation in patients' brain, and thus improve patients' hemorheology. It can also reduce blood viscosity and further improve cerebral microcirculation^[15]. Jujuba itself is rich in vitamins, trace elements and bioactive substances. Vitamin P₄ can effectively adjust the caliber of blood vessels, which is conducive to maintaining smooth microcirculation blood flow, so as to effectively improve patients' hemorheology. In addition, vitamin E can improve the blood viscosity of patients by regulating the level of fibrin^[4].

In conclusion, Tongqiao Huoxue Decoction combined with cognitive rehabilitation training has a good clinical effect on the treatment of stroke patients with cognitive impairment, and can effectively improve the cognitive function and hemorheology of patients.

Declaration of conflict-of-interest

The authors declare no conflict-of-interest.

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