

The Effect of Tongqiao Huoxue Tang on Cognitive Function and Serum Inflammatory Factor Levels in Patients with Vascular Dementia of Phlegm Stasis Obstruction Type

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Abstract: *Objective:* To observe the improvement effect of Tongqiao Huoxue Tang on cognitive function in patients with vascular dementia (VaD) of phlegm stasis obstruction type, and to explore its possible mechanism of action from the changes in serum inflammatory factor levels. *Method:* A randomized controlled trial was conducted to divide 90 patients with phlegm stasis obstruction type VaD into a control group and an observation group. The control group received routine Western medicine treatment, while the observation group received oral administration of Tongqiao Huoxue Tang in addition to the control group, for a continuous treatment period of 8 weeks. This study compared MoCA, MMSE, TCM-DSS, mRS, and BI scores before and after treatment, measured serum IL-6 and CRP levels, and recorded the occurrence of adverse reactions. *Results:* The cognitive function scores (MMSE, MoCA) and Barthel Index (BI) of the observation group increased after treatment compared to before treatment, and the scores of the Traditional Chinese Medicine Syndrome Differentiation Scale (TCM-DSS), Modified Rankin Scale (mRS), and blood IL-6 and CRP were all lower than before treatment, with statistical significance ($p < 0.05$) compared to the control group. *Conclusion:* Based on conventional Western medicine treatment, the combination therapy of Tongqiao Huoxue Tang for patients with phlegm stasis obstruction type VaD can assist in improving patients' postoperative cognition and independent living ability through targeted treatment of traditional Chinese medicine pathogenesis and syndrome, or be related to the regulation and inhibition of central inflammatory response by the combination of prescription and bioactive ingredients contained in decoction pieces.

Keywords: Vascular dementia; Tongqiao Huoxue Tang; Phlegm stasis obstructing collaterals syndrome; Cognitive function; Inflammatory factors; Clinical research

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1. Introduction

Vascular dementia is an acquired cognitive dysfunction syndrome caused by cerebrovascular disease and its risk factors. Pathological damage to the patient's brain tissue and central nervous system can lead to progressive degenerative changes in memory and executive function, as well as language disorders and personality changes, which can seriously affect the patient's daily living abilities ^[1]. The incidence rate of VaD is increasing year by year in China and has become the second largest type of dementia after Alzheimer's disease. At present, the overall efficacy of Western medicine in treating VaD is not satisfactory, while the advantages of traditional Chinese medicine treatment are prominent. The formula of Tongqiao Huoxue Tang originated from "Yi Lin Gai Cuo" and is a classic formula for the treatment of head and face blood stasis syndrome. It can be combined with the formula to exert the effects of promoting blood circulation, unblocking orifices, and removing blood stasis, in order to regulate the pathogenesis and improve the symptoms of patients ^[2]. In recent years, this formula has been widely used in the treatment of neurological diseases such as ischemic stroke and vascular dementia. Clinical studies have shown that it can improve brain microcirculation and alleviate neurological deficits.

2. Data and methods

2.1. Research object

Select 90 patients with phlegm stasis obstruction type VaD admitted to the Brain Disease Department of Shangqiu Traditional Chinese Medicine Hospital, Zhecheng Traditional Chinese Medicine Hospital, and Minquan County Traditional Chinese Medicine Hospital from May 2025 to May 2026, and conduct treatment research.

2.2. Diagnostic criteria

The diagnostic criteria for Western medicine: The clinical diagnosis of Western medicine conforms to the diagnostic criteria of VaD ^[3].

The diagnostic criteria of traditional Chinese medicine: The diagnosis based on TCM syndrome differentiation meets the diagnostic criteria for VaD in the syndrome of phlegm and blood stasis blocking the meridians ^[4].

2.3. Inclusion criteria

- (1) Age 50–80 years old, gender not limited;
- (2) Meets the diagnostic criteria of Western and Traditional Chinese Medicine mentioned above;
- (3) The disease course is ≥ 3 months, and the condition is stable;
- (4) MoCA score ranges from 10 to 26 points;
- (5) Failure of vital organs such as the heart, liver, and kidneys;
- (6) Patients and their families are informed, confirm treatment, and sign the 'Consent Form'.

2.4. Exclusion criteria

- (1) The clinical diagnosis suggests that they meet the diagnostic criteria for Alzheimer's disease, Lewy body dementia, or other primary or pathological dementia;
- (2) Individuals who are allergic or intolerant to the drugs used in this study;

- (3) Patients with other cognitive health-influencing diseases;
- (4) Individuals who have received other treatment plans within the past 3 months prior to enrollment;
- (5) Patients with poor treatment cooperation or inability to complete follow-up.

2.5. Treatment methods

2.5.1. Control group

The control group was given conventional Western medicine treatment:

- (1) Cholinesterase inhibitor

Donepezil hydrochloride tablets 5mg/time, taken orally once a night;

- (2) Control vascular risk factors

Based on the patient's underlying disease, symptomatic treatment should be combined with glucose and lipid metabolism, blood pressure regulation, antiplatelet aggregation, and other standardized treatments.

2.5.2. Observation group

- (1) Received Western medicine treatment similar to the control group.

- (2) Treatment with Tongqiao Huoxue Tang

The formula contains peach kernels, safflower, and wolfberry; 6 g of red peony, Chuanxiong, and scallion; 10 g of Acorus calamus and Yujin; 9 g of ginger; 5 jujubes; and 0.2g of artificial musk. Except for artificial musk, the rest of the medicinal herbs are soaked in water for 30 minutes, added to 250 mL of yellow wine, boiled over high heat and then turned to low heat for 40 minutes, concentrated to about 150mL, filtered to remove residue, and added with artificial musk (wrapped in fine cloth) for 5 minutes. Take one dose daily, warm twice in the morning and evening, and take it half an hour after meals. Continuous treatment for 8 weeks. All traditional Chinese medicine decoction pieces are provided by the Chinese Medicine Pharmacy of Shangqiu Traditional Chinese Medicine Hospital, and artificial musk is purchased from Beijing Tongrentang Co., Ltd. The quality meets the standards of the Pharmacopeia of the People's Republic of China.

2.6. Efficacy evaluation criteria

According to the "Guidelines for Clinical Research of Traditional Chinese Medicine New Drugs" and relevant literature, the following are formulated:

- (1) Significant effect

MoCA score increased by ≥ 5 points, MMSE score increased by ≥ 4 points, TCM-DSS score decreased by $\geq 70\%$;

- (2) Effective

MoCA score increased by 2–4 points, MMSE score increased by 1–3 points, TCM-DSS score decreased by 30–69%;

- (3) Invalid

MoCA score increased by < 2 points or decreased, MMSE score increased by < 1 point or decreased, TCM-DSS score decreased by $< 30\%$. Total effective rate = (significant effect + effective) cases/total cases $\times 100\%$.

2.7. Statistical methods

SPSS 26.0 software was used to complete data statistics; Normal distribution metric data,

represented by ($\bar{x} \pm s$), uses paired *t*-test for intra-group comparisons and independent-samples *t*-test for inter-group comparisons; Count data, represented by [n (%)], chi-square test; composition ratio data, chi-square test; rank data, rank-sum test. The difference is statistically significant with $p < 0.05$.

3. Results

3.1. Baseline data

The baseline data comparison showed no statistically significant difference between the groups ($p > 0.05$), as shown in **Table 1**.

Table 1. Comparison of baseline data between two groups ($\bar{x} \pm s/\text{case}$)

Item	Observation group (n = 45)	Control group (n = 45)	<i>t</i> / χ^2 value	<i>p</i> value
Gender (male/female)	27/18	25/20	0.180	0.671
Age (years)	68.5 $\pm$ 7.3	67.8 $\pm$ 7.6	0.446	0.657
Disease duration (years)	2.5 $\pm$ 1.2	2.6 $\pm$ 1.3	0.376	0.708
Educational level	—	—	0.528	0.768
Primary school or below	15	17	—	—
Secondary school	22	20	—	—
Junior college or above	8	8	—	—
Hypertension	32	30	0.202	0.653
Diabetes mellitus	18	16	0.184	0.668
Hyperlipidemia	25	23	0.180	0.671
History of stroke	38	36	0.346	0.556
MoCA score (points)	18.5 $\pm$ 3.4	18.2 $\pm$ 3.5	0.414	0.680
MMSE score (points)	20.8 $\pm$ 3.6	20.5 $\pm$ 3.8	0.385	0.701

3.2. Clinical efficacy

The total clinical effective rate of the observation group was 86.67%, which was higher than that of the control group ($Z = 2.518$, $p = 0.012$), as shown in **Table 2**.

Table 2. Comparison of clinical efficacy between two groups [Example (%)]

Group	Markedly effective	Effective	Ineffective	Total effective rate
Observation group (n = 45)	16 (35.56)	23 (51.11)	6 (13.33)	39 (86.67)
Control group (n = 45)	9 (20.00)	22 (48.89)	14 (31.11)	31 (68.89)

3.3. Cognitive function

After treatment, the MoCA and MMSE scores of the patients increased compared to the treatment group, and the observation group was higher than the control group ($p < 0.05$), as shown in **Table 3**.

Table 3. Comparison of cognitive function scores between two groups ($\bar{x} \pm s$, points)

Group	Time	MoCA	MMSE
Observation group (n = 45)	Before treatment	18.5 $\pm$ 3.4	20.8 $\pm$ 3.6
	After treatment	24.2 $\pm$ 2.7 ^{ab}	26.0 $\pm$ 2.6 ^{ab}

Control group (n = 45)	Before treatment	18.2 ± 3.5	20.5 ± 3.8
	After treatment	21.4 ± 3.0 ^a	23.0 ± 3.1 ^a

Note: Compared with before treatment in the same group, ^a $p < 0.05$; Compared with the control group after treatment, ^b $p < 0.05$

3.4. Traditional Chinese Medicine (TCM) syndrome score

After treatment, the TCM-DSS scores of patients decreased compared to before treatment, and the observation group was lower than the control group ($p < 0.05$), as shown in **Table 4**.

Table 4. Comparison of Traditional Chinese Medicine syndrome score between two groups ($\bar{x} \pm s$, points)

Group	Number of cases	Before treatment	After treatment
Observation group	45	18.7 ± 4.2	8.8 ± 3.0 ^{ab}
Control group	45	18.4 ± 4.5	13.0 ± 3.7 ^a

Note: Compared with before treatment in the same group, ^a $P < 0.05$; Compared with the control group after treatment, ^b $p < 0.05$

3.5. Neurological function, daily living ability

After treatment, the mRS score of the observation group decreased compared to before treatment and the control group, and the BI score increased compared to before treatment and the control group ($p < 0.05$), as shown in **Table 5**.

Table 5. Comparison of neurological function and daily living ability between two groups ($\bar{x} \pm s$, points)

Group	Time	mRS	BI
Observation group (n = 45)	Before treatment	3.5 ± 0.8	52.2 ± 12.6
	After treatment	2.2 ± 0.7 ^{ab}	74.5 ± 10.8 ^{ab}
Control group (n = 45)	Before treatment	3.4 ± 0.9	51.8 ± 13.0
	After treatment	2.8 ± 0.8 ^a	63.2 ± 11.5 ^a

Note: Compared with before treatment in the same group, ^a $p < 0.05$; Compared with the control group after treatment, ^b $p < 0.05$

3.6. Inflammatory factors

After treatment, the levels of IL-6 and CRP in the patients' blood decreased compared to before treatment, and the observation group was lower than the control group ($p < 0.05$), as shown in **Table 6**.

Table 6. Comparison of inflammatory cytokine levels between two groups ($\bar{x} \pm s$)

Indicator	Group	Before treatment	After treatment
IL-6 (pg/mL)	Observation group	35.8 ± 8.3	18.2 ± 5.2 ^{ab}
	Control group	35.2 ± 8.6	25.8 ± 6.2 ^a
CRP (mg/L)	Observation group	12.6 ± 3.7	6.0 ± 2.1 ^{ab}
	Control group	12.3 ± 3.9	8.8 ± 2.5 ^a

Note: Compared with before treatment in the same group, ^a $p < 0.05$; Compared with the control group after treatment, ^b $p < 0.05$

3.7. Comparison of safety between two groups

During the treatment period, there were 2 cases of mild gastrointestinal discomfort (nausea, bloating) in the observation group, with an incidence rate of 4.44%. After adjusting the medication time, the symptoms improved, and continued treatment was not affected. In the control group, there were 2 cases of dizziness and 1 case of mild liver dysfunction, with an incidence rate of 6.67%. After symptomatic treatment, the condition improved. There was no statistically significant difference in the incidence of treatment-related adverse reactions between the groups ($\chi^2 = 0.212$, $p = 0.645$). During both treatment periods, no abnormalities were observed in blood routine, renal function, or electrocardiogram indicators.

4. Discussion

Vascular dementia is an acquired cognitive impairment caused by cerebrovascular disease, and its pathogenesis is complex. Among them, chronic inflammatory response plays an important role in the occurrence and development of VaD. Therefore, inhibiting the central inflammatory response and reducing neuroinflammatory damage have become important targets for current VaD treatment^[5].

Traditional Chinese Medicine believes that VaD is located in the brain and is closely related to the heart, liver, spleen, and kidneys. The overall pathogenesis is based on deficiency of the essence and excess of blood. Deficiency of the essence is caused by deficiency of Qi and blood, and deficiency of kidney essence. The excess is caused by phlegm turbidity and blood stasis blocking the brain meridians. Clinical observations have found that phlegm stasis and obstruction of the brain are extremely common syndromes in the course of VaD, especially in post-stroke dementia patients. Therefore, promoting blood circulation and removing blood stasis, resolving phlegm and unblocking collaterals, and awakening the mind and opening the orifices are the basic treatment methods for treating phlegm stasis obstructing collaterals type VaD^[6].

The formula of Tongqiao Huoxue Tang contains peach kernels and red flowers, which promote blood circulation, remove blood stasis, unblock meridians, and relieve pain, and are considered royal medicines; *Paeonia lactiflora* and *Ligusticum chuanxiong* promote blood circulation and Qi circulation, dispel wind and relieve pain, and enhance the power of promoting blood circulation and removing blood stasis. They are medicinal herbs of the emperor; *Acorus tatarinowii* and *Polygonum multiflorum* are used to clear phlegm and open up the body, awaken the mind and enhance intelligence, and eliminate phlegm and turbidity to clear the body; Artificial musk fragrance travels and awakens the mind, leading various medicines to ascend directly to the disease site; Scallion and ginger warm and promote Yang Qi, promote blood circulation, and help spread medicinal power; Jujube can nourish Qi and spleen, and harmonize various medicines. The key pathogenesis of VaD is to use a combination of full formula, promoting blood circulation and resolving phlegm, balancing the circulation of orifices and supporting the body, and cutting through the phlegm and stasis obstructing collaterals^[7,8].

The results of this study showed that after treatment, when observing cognitive function (MMSE, MoCA), the BI score increased compared to the control group, and the mRS score and TCM-DSS score were lower than those of the control group. The total clinical effective rate was better than that of the control group. Analysis suggests that the clinical application of Tongqiao Huoxue Tang can assist Western medicine treatment in promoting cognitive function and daily living ability improvement in patients with phlegm stasis obstruction type VaD, delaying the pathological progression of neurological deficits, and alleviating clinical

manifestations of traditional Chinese medicine.

Inflammatory response is a core link in the pathological process of VaD. IL-6 is an important pro-inflammatory cytokine that can be secreted by activated microglia and astrocytes. It exacerbates brain injury by inducing neuronal apoptosis, promoting amyloid deposition, and disrupting the integrity of the blood-brain barrier^[9]. In recent years, a large number of studies have confirmed that the levels of serum IL-6 and CRP in VaD patients are significantly elevated and positively correlated with the degree of cognitive impairment. In modern pharmacological research, active ingredients such as amygdalin in peach kernels, safflower yellow pigment in safflower, and ligustrazine in *Ligusticum chuanxiong* can all inhibit the activation of the nuclear factor kappa B (NF - κ B) signaling pathway, reducing the transcription and release of pro-inflammatory factors. In addition, muscone can pass through the blood-brain barrier, alleviate brain tissue inflammation, and protect neurons. The β - asarone in the volatile oil of *Acorus tatarinowii* has dual anti-inflammatory and antioxidant effects and can improve cerebral ischemia-reperfusion injury^[10].

5. Conclusion

In summary, Tongqiao Huoxue Tang can regulate the TCM pathogenesis and syndrome manifestations of patients with phlegm stasis obstruction type VaD, assist Western medicine treatment to optimize the improvement of cognitive and neurological deficits after treatment, and assist in maintaining healthy daily living abilities. Its mechanism of action may be related to reducing serum IL-6 and CRP levels and inhibiting inflammatory reactions. This method has good safety and is worthy of clinical promotion and application. In the future, large-scale, multicenter, long-term follow-up clinical studies can be conducted, and combined with network pharmacology, molecular biology, and other technical means, the targets and signaling pathways of Tongqiao Huoxue Tang in the treatment of VaD can be explored in depth, providing a more comprehensive scientific basis for its clinical application.

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Disclosure statement

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