Effect of Salvia Miltiorrhiza Polyphenolic Acid Combined with Salvia Miltiorrhiza Ligustrazine Injection on Cognitive Function in Patients with Cerebral Infarction

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Objective: To investigate the effect of salvia miltiorrhiza polyphenolic acid combined with salvia miltiorrhiza ligustrazine injection on cognitive function in patients with cerebral infarction. Methods: 60 patients with cerebral infarction from December 2017 to December 2019 were randomly divided into control group (n = 30) and observation group (n = 30) by random number table method. The control group was treated with salvia miltiorrhiza ligustrazine injection, and the observation group was treated with salvia miltiorrhiza polyphenolic acid on the basis of the control group. After 4-week treatment, the effect of the patients was evaluated, and the hemorheological level, cognitive function and drug safety of the two groups were compared. Results: The levels of high blood and low shear viscosity, high whole blood and plasma viscosity in the observation group were lower than those in the control group 4 weeks after treatment (P<0.05); the cognitive function scores in the observation group were higher than those in the control group 2 and 4 weeks after treatment (P<0.05); the incidence rates of liver and kidney function damage, mild diarrhea, dizziness and somnolence, nausea and vomiting, and blood pressure fluctuation in the treatment of the two groups had no statistical significance (P>0.05). Conclusion: The combination of salvia miltiorrhiza polyphenolic acid and salvia miltiorrhiza ligustrazine injection can improve the hemorheology of patients with cerebral infarction. It is helpful to improve the cognitive function of patients. The drug is safe and worthy of being popularized.

Keywords : Salvia miltiorrhiza polyphenolic acid; Salvia miltiorrhiza ligustrazine injection; Cerebral infarction; Application effect; Cognitive function; Hemorheology
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Cerebral infarction is a cardiovascular disease with a clinical incidence due to necrosis or softening of brain tissue with various causes [1]. In clinical practice, cerebral infarction was divided into three types: cerebral thrombosis, lacunar infarction and cerebral embolism, while cerebral infarction accounted for 80.0% of all strokes [2]. The etiology of cerebral infarction is complicated, which is generally related to diabetes, arrhythmia, hypertension and all kinds of arterial pressure. The clinical manifestations include sudden collapse, speech disorder and mental retardation, which affect the patients' health and life.

According to the study of domestic scholars [3]: If the patients with cerebral infarction fail to receive effective treatment, they will cause visual disturbance, increase paralysis and mortality. Salvia miltiorrhiza ligustrazine injection is a commonly used injection of traditional Chinese medicine, which can improve local microcirculation, anti-platelet and other functions, and can also improve the patient's neurological function and obtain good prognosis [4]. In contrast, salvianolate can maintain the function of antioxidant enzyme and inhibit lipid peroxidation [5]. At present, salvia miltiorrhiza polyphenolic acid and salvia miltiorrhiza ligustrazine injection have a lot of clinical application, but their combined use has less effect on cognitive function of patients with cerebral infarction. Therefore, the aim of this study was to investigate the effect of salvia miltiorrhiza polyphenolic acid injection combined with salvia miltiorrhiza ligustrazine injection on cognitive function in patients with cerebral infarction.

DATA AND METHODS

Clinical data

60 patients with cerebral infarction from December 2017 to December 2019 were randomly divided into two groups by random number table method. In the control group, there were 30 patients, 16 males and 14 females, aged (41-82) years, mean (59.48 ± 6.71) years; mean (1-4) days, mean (2.16 ± 0.61) days; body mass index (21-25 kg/m^2, average (23.15 ± 1.73) kg/m^2; among them, there were 15 patients with hypertension,10 patients with hyperlipidemia and 8 patients with diabetes mellitus. There were 30 cases in the observation group, 17 males and 13 females, aged (41-82) years, mean (59.53 ± 6.75) years; mean (1-5) days, mean (2.21 ± 0.66) days; body mass index (20-26) kg/m^2, mean (23.22 ± 1.76) kg/m^2; among them, there were 13 patients with hypertension, 11 patients with hyperlipidemia and 9 patients with diabetes mellitus.

Inclusion and exclusion criteria

Inclusion criteria: (1) Enrolled patients met the diagnosis criteria of cerebral infarction [6]; (2) All patients were finally diagnosed by CT/MRI, with stable disease condition and clear ideology; (3) Met the indications of salvia miltiorrhiza polyphenolic acid combined with salvia miltiorrhiza ligustrazine injection, and the patients were tolerable.

Exclusion criteria: (1) Patients with organic disease, cognitive function abnormality and quadriplegia; (2) Patients with progressive hypertension, cerebral infarction or complicated infection; (3) Patients with blood system disease, organic disease or disease of self-immune system.

Methods

Both groups were given conventional treatment after admission, such as medical treatment including group B vitamin and energy mixture, thrombolysis, thrombectomy, anticoagulation and antiplatelet therapy, and mannitol therapy for patients with cerebral edema [7]. Control group: treated with salvia miltiorrhiza ligustrazine injection. For each time,10 mL of salvia miltiorrhiza ligustrazine injection (Guizhou Baite Pharmacy Co., Ltd., SFDA Approval No. H52020959, specification: 5 mL) mixed with normal saline (250 mL) was given via intravenous drip, once a day, for 4 consecutive weeks (1 treatment course). Observation group: treated by combining with salvia miltiorrhiza polyphenolic acid on the basis of control group. For each time, take salvia miltiorrhiza polyphenolic acid injection (Tianjin Tasly Pride Pharmaceutical Co., Ltd., SFDA Approval No. Z20110011, specification: 0.13 g/vial (containing 100 mg salvia miltiorrhiza polyphenolic acid)) 200mg, mix with 250 mL of 0.9% sodium chloride injection, intravenous drip, once daily, for consecutive 4 weeks (1 treatment course).

Observational indexes

(1) The level of hemorheology. Before and 4 weeks after treatment, SH210B automatic blood flow detector was used to measure high blood and low shear viscosity, high whole blood shear viscosity and plasma viscosity of patients [8]; (2) Cognitive function. Cognitive function was assessed by Montreal Cognitive Assessment (MOCA) and Mini-Mental State Examination before and 2 and 4 weeks after treatment, and the higher the score, the better the cognitive function [9,10]; (3) Drug safety. The incidence of hepatic and renal function impairment, mild diarrhea, dizziness and somnolence, nausea and

vomiting, and blood pressure fluctuation during treatment were recorded in both groups.

Statistical analysis

SPSS18.0 software was used for processing, χ^2 test was performed for counting data, expressed by n (%), t test was performed for measuring data, expressed by ($\bar{x} \pm s$), ANOVA was used for repeated data measurement, and the difference was statistically significant (P<0.05).

RESULTS

Hemorheology comparison between the two groups

There was no statistical significance in hemorheology before drug use in the two groups (P>0.05); the hemorheology level in both groups was lower than that before treatment at 4 weeks after treatment (P<0.05); the high blood and low shear viscosity, high whole blood shear viscosity and plasma viscosity in the observation group were lower than that in the control group at 4 weeks after treatment (P<0.05). See Table 1.

Table 1
Comparison of hemorheology levels in the two groups ($\bar{x} \pm s$)

Group		High blood low shear viscosity (mPa · s)	High whole blood shear viscosity (mPa · s)	Plasma viscosity (mPa · s)
Observation group (n = 30 cases)	Before treatment	11.68±2.15	7.28±0.64	1.92±0.41
	4 weeks after treatment	9.57±0.71[ab]	5.11±0.41[ab]	1.42±0.36[ab]
Control group (n = 30)	Before treatment	11.69±2.16	7.31±0.66	1.93±0.42
	4 weeks after treatment	10.73±1.32[b]	6.24±0.49[b]	1.57±0.39[b]

Compared with the control group, [a]P<0.05; compared with that before treatment, [b]P<0.05

Cognitive function comparison between the two groups

There was no statistical significance in cognitive function scores before treatment in the two groups (P>0.05); MMSE and MOCA scores in the observation group were higher than that in the control group 2 and 4 weeks after drug combination (P<0.05), see Table 2.

Table 2.
Cognitive function comparison between the two groups (scores, $\bar{x} \pm s$)

Group	Number of cases	MOCA score			MMSE score		
		Before treatment	2 weeks after treatment	4 weeks	Before treatment	2 weeks after treatment	4 weeks
Observation group	30	15.34±1.24	17.53±1.31	19.48±1.46	22.11±2.69	24.87±3.21	27.43±3.42
Control group	30	15.36±1.25	15.81±1.27	17.51±1.33	22.10±2.63	23.41±3.05	25.69±3.21
Inter-group		F=6.195	P=0.027		F=5.758	P=0.033	
Inter-time point		F=4.589	P=0.028		F=6.332	P=0.018	
Inter-group · inter-time point		F=9.184	P=0.019		F=5.093	P=0.032	

Comparison of drug safety between the two groups

The incidence rates of liver and kidney function damage, mild diarrhea, dizziness and somnolence, nausea and vomiting, and blood pressure fluctuation during the treatment in the two groups had no statistical significance (P>0.05). See Table 3.

Table 3
Comparison of safety between the two groups [n (%)]

Group	Number of cases	Liver and kidney function damage	Mild diarrhea	Dizziness and somnolence	Nausea and vomiting	Blood pressure fluctuation	Incidence rate
Observation group	30	0（0.00）	1（3.33）	0（0.00）	1（3.33）	1（3.33）	3（10.00）
Control group	30	1（3.33）	2（6.67）	1（3.33）	1（3.33）	0（0.00）	5（16.67）
χ^2	/						1.215

P	/	0.749

DISCUSSION

Cerebral infarction occurs in the middle-aged and elderly population, which refers to ischemia and hypoxic necrosis of local brain tissue caused by blood circulation disorder, etc., resulting in corresponding neurological deficit, leading to abnormal limb and speech function, affecting the cognitive function and quality of life of the patient [11]. Traditional Chinese medicine thinks that [12], cerebral infarction belongs to the stroke category, and it is mainly because the patient's physique is weak, the vital qi is insufficient, causes the qi-blood reflux, thus causing the body yin-yang imbalance. Therefore, the treatment of cerebral infarction by traditional Chinese medicine is mainly based on the treatment of activating blood circulation and removing blood stasis and dredging collaterals [16].

In recent years, salvia miltiorrhiza polyphenolic acid combined with salvia miltiorrhiza ligustrazine injection has been used in patients with cerebral infarction with satisfactory results. In this study, the high blood and low shear viscosity, high whole blood shear viscosity and plasma viscosity in the observation group were lower than those in the control group 4 weeks after treatment ($P<0.05$), indicating that salvia miltiorrhiza polyphenolic acid combined with salvia miltiorrhiza ligustrazine injection could improve the local blood flow level of patients with cerebral infarction, which was beneficial to the recovery of patients. Salvia miltiorrhiza ligustrazine injection is a commonly used drug in clinical practice, which can reduce blood viscosity and accelerate red blood cell flow rate, thereby improving the local cerebral microcirculation [13]. At the same time, the drug has anti-myocardial ischemia and myocardial infarction effect, and is widely used in occlusive cerebrovascular disease, thromboangiitis obliterans, myocardial infarction and other cardiovascular diseases. The modern pharmacological results show that the clinical application of salvia miltiorrhiza ligustrazine injection can accelerate the flow rate of red blood cells, exert the effect of anti-platelet aggregation, dilate coronary artery, improve microcirculation, play the role of anti-myocardial ischemia and myocardial infarction, and obtain a good therapeutic prognosis. Salvia miltiorrhiza polyphenolic acid is mainly composed of salvia miltiorrhiza polyphenols, which has the function of promoting blood circulation and dredging collaterals. It is widely used in patients with mild and moderate cerebral infarction in recovery period, and can also be used in patients with symptoms such as hemiplegia, skew of mouth and tongue and hemianesthesia. Modern pharmacological results show that [14]: Salvia miltiorrhiza polyphenolic acid can inhibit the production of intracellular reactive oxygen species (ROS), eliminate superoxide anion and free radicals, reduce the apoptosis of brain cells, protect half dark zone of ischemia to the maximum extent, and protect ischemic brain tissues. Clinically, the combination of salvia miltiorrhiza polyphenolic acid and salvia miltiorrhiza ligustrazine injection in the treatment of patients with cerebral infarction can play different therapeutic advantages, help to improve the cognitive function of patients, and the combination of the two drugs is safe and can improve the treatment tolerance and compliance of patients [15]. In this study, the cognitive function scores of the observation group were higher than that of the control group at 2 and 4 weeks after the combined treatment ($P<0.05$); the incidence rates of liver and kidney damage, mild diarrhea, dizziness and drowsiness, nausea and vomiting, and blood pressure fluctuation during the treatment of the two groups had no statistical significance ($P>0.05$), indicating that salvia miltiorrhiza polyphenolic acid combined with salvia miltiorrhiza ligustrazine injection could improve the cognitive function of the patients with cerebral infarction, without increasing the incidence rate of adverse reactions, and had a good prognosis.

In conclusion, the combination of salvia miltiorrhiza polyphenolic acid and salvia miltiorrhiza ligustrazine injection can improve the hemorheology of patients with cerebral infarction. It is helpful to improve the cognitive function of patients. The drug is safe and worthy of being

popularized.

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