Therapeutic effect of exercise rehabilitation combined with huatuo reconstructive pills on vascular dementia

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Abstract

Background:Vascular dementia is the second most threatening brain disease, following the Alzeimer's disease, effectuated by the suspension of normal blood flow in the brain as a result of blockage that is caused by cerebrovascular diseases such as stroke.

Objective:Our aim of carrying out this project is to explore the therapeutic effect and significance of exercise rehabilitation combined with huatuo reconstructive pill in the treatment of vascular dementia and to understand the cause of its effect on social determinants health development.

Materials and Methods: 80 patients with vascular dementia were selected for this. Patients were randomly divided into observation group and control group with 40 cases each. The control group was given huatuo reconstructive pill orally on the basis of conventional treatment, and the observation group was given exercise rehabilitation training on the basis of the control group. The two groups were compared before and after treatment with MMSE score, Barthel index (BI) score, blood lipid, vascular function and neurotransmitter related indicators.

Results:After 1 course of treatment, the total effective rate of the observation group was significantly higher than that of the control group ($P < 0.05$). The directivity, language ability and total MMSE scores of patients in the observation group and the control group were significantly higher after treatment than before treatment ($P < 0.05$).

Discussions: After treatment, the directivity, language ability, total MMSE score and BI score of patients in the observation group were significantly higher than those in the control group ($P < 0.05$). Compared with the control group after treatment, the serum levels of homocysteinine (Hcy), thrombin B2 (TXB2), low-density lipoprotein cholesterol (LDL-C) and endothelin (ET) in the observation group after treatment were significantly reduced, while the levels of nitric oxide (NO), norepinephrine (NE) and dopamine (DA) were significantly increased ($P < 0.05$).

Conclusion: The intervention of sports rehabilitation combined with huatuo reconstructive pill can promote the recovery of nerve function, improve vascular endothelial function and cognitive function in patients with vascular dementia, significantly improve the therapeutic effect, and have positive significance for the treatment of vascular dementia.

Key Words: Exercise rehabilitation; huatuo reconstructive pill; vascular dementia; curative effect

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Introduction

Vascular dementia is a severe cognitive dysfunction syndrome caused by cerebrovascular diseases such as stroke. Vascular dementia has a high incidence in middle-aged and elderly people and is on an increasing trend year by year [1-2]. In patients with vascular dementia, memory, spatial and other cognitive functions decline, which may involve the motor and language systems, resulting in the loss of self-care ability and seriously affects the quality of life of patients. Dementia, and its origin resulting from a stroke of high intensity was concluded by a team of investigators under Tomlinson et al but it got its bigger picture when Hachinski et al emphasized on multi-infarct dementia (MID). MID underlines a cumulative result of many strokes, at times asymptomatic as well. Sooner computed tomography (CT) and magnetic resonance imaging (MRI) backed the theory of MID. Non infarct vascular changes were brought to significance which included white matter lesions (WML), small subcortical lacunes and microbleeds. [3-6].Therefore, it is important to explore the effective clinical treatment of vascular dementia.At present, Chinese and western medicine treatment, preventive treatment and rehabilitation treatment are mostly used in clinic, but single therapy can only improve the symptoms of vascular dementia patients within a certain range. Huatuo reconstructive pill comes under the traditional Chinese medicine prescription. It comprises several medicinal herbs, namely Ligusticum wallichii, Angelica sinensis, Borneol, Paeonia albiflora etc. It is essentially used for the treatment of hemiplegia and postoperation of brain stroke. Besides, Huatuo reconstructive pill also shows impressive results in antithrombotic action. It also helps in improving the microcirculation disturbances and protecting cerebral ischemia by modern pharmacology. Studies have also shown that huatuo reconstructive pill has the functions of promoting blood circulation and removing blood stasis, removing phlegm and clearing collateralism. It has a significant effect on the treatment of ischemic stroke [7].Man et al. found in their study that Chinese herbal ingredients such asligusticumwallichii in hutuo reconstructive pills have obvious effects in the treatment of vascular dementia [8].Another study reported that moderate exercise rehabilitation training can significantly improve the cognitive ability of patients with vascular dementia and promote the recovery of neurological function [9].Therefore, in this study, patients with vascular dementia were treated with exercise rehabilitation combined with huatuo reconstructive pill to analyze the efficacy of this regimen and explore its effect on patients' cognitive function, vascular damage and improvement of their condition.

Materials and Methods

1.1 General information

Since we have limited access and exposure to the hospital data, it is not only more scientific and applicable process but also more agreeable to choose patients randomly. Invariably age, sex, health condition etc are used to determine actual efficacy of the medicine properly. It may also be possible that Alzheimer’s disease is a single mutation gene disorder. This type of mutation is very rare and is usually seen in very rare cases having prior parental history of such disease. Random selection also helped us to study the frequency of this disease occurrence which is highly required for research purpose of this disease. Eighty patients with cerebrovascular dementia admitted to our hospital from June 2015 to June 2019 were selected, and the included patients were randomly divided into observation group and control group with 40 cases each. In the observation group, there were 17 males and 23 females, aged from 52 to 78 years, with an average age of 65.13±12.08 years. In the control

group, there were 19 males and 21 females, aged from 51 to 75 years, with an average age of (64.79±13.17 years).Inclusion criteria: (1) meeting the diagnostic criteria and imaging examination of the 4th edition of the diagnostic and statistical manual of mental disorders [10] of the American psychiatric association, vascular dementia was confirmed. (2) Patients were the first onset, and the course of disease < 4 months. (3) Complete clinical data, informed of the study and signed informed consent.Exclusion criteria: (1) cognitive dysfunction caused by cranial trauma, drug action, etc. (2) Combined with depression, schizophrenia. (3) Combined with tumor disease. (4) serious infection, metabolic and immune system diseases. This study was approved by the ethics committee of our hospital. As shown in table 1, there was no statistically significant difference between the two groups in gender ratio, age, Body mass index (BMI) and educational level (P > 0.05).

Table 1 comparison of general data between the observation group and the control group

Group	Number	Gender(male/female)	Age	BMI （kg/m^2）	course of disease(year)	Education level
Observation	40	17/23	65.13±12.08	22.56±2.53	7.28±2.16	9.27±3.06
Control	40	19/21	64.79±13.17	22.41±2.29	7.47±2.11	9.94±3.15
t/ χ^2	—	0.202	0.120	0.278	0.398	0.965
P	—	0.653	0.905	0.783	0.692	0.338

1.2 Methods

1.2.1 treatment

Patients in both groups received routine treatments such as control of blood pressure, blood sugar, anticoagulation, improvement of cerebral circulation and improvement of brain tissue metabolism. The control group was given huatuo reconstructive pills (Z44020748, made by guangzhoubaiyunshanqixing pharmaceutical co., LTD., 80g) orally on the basis of conventional treatment, 8g each time, 3 times/d, 3 months for a course of treatment. The observation group added exercise rehabilitation training on the basis of the control group, including aerobic exercise training by doing housework, walking, walking in parallel bars, practicing tai chi, and running. Each of the above training exercises should be carried out 40min at a time, morning and evening, 3 months for a course of treatment, patients should exercise rehabilitation training according to their physical conditions to appropriately adjust the training mode and intensity. For the enrolled patients, the administration of huatuo reconstructive pills was supervised by special personnel, and the exercise rehabilitation training was conducted by professional physicians and relevant data was recorded.

1.2.2 evaluation criteria for clinical efficacy

Mini Mental State Examination (MMSE) is a 30-point test or better known as Folstein test. It is widely used in clinical and research arena in order to measure cognitive impairment [34]. According to the scores of the mini-mental State Examination (MMSE) before and after treatment in each group [11], the scoring system was 0 to 30 points, and higher score means the better the cognitive function of the patients. Clinical efficacy was assessed according to the difference of MMSE score before and after treatment: [(post-treatment - pre-treatment)/pre-treatment score] ×100%. If the calculated result is ≥20%, it is effective; if the calculated result is less than 12%, it is effective; if the calculated result is less than 20%, it is invalid [12].

1.2.3 observe indicators

Both groups used Barthel Index (BI) score [13] before and after treatment to assess the Activity of daily living (ADL). The score scale was 0~100. The higher the score means the better the self-care ability of the patients.5mL peripheral venous blood was collected from the both groups before and after treatment, and centrifuged at 4℃ and 3000r for 15min. The supernatant was separated and stored at -80℃ for standby use. Serum Homocycteine (Hcy), High density liptein cholesterol (hdl-c) and Low density liptein cholesterol (ldl-c) were detected by Enzyme linked immune sorbent assay (ELISA). Thromboxane (TXB2), Endothelin (ET), and nitric oxide (NO) correlated with vascular function, Neurotransmitters related to Norepinephrine (NE) and Dopamine (DA) levels were detected by the kit purchased from Taiwan Abnova company and operated in strict accordance.

1.3 statistical treatment

Traditional medicines are generally safe. The contraindication and drug interaction or side effects are even lesser. Though a very conclusive and detailed studies are not yet available. Statistical software SPSS 22.0 was used for analysis. Measurement data conforming to normal distribution were expressed as mean ± standard deviation（$\bar{X} \pm s$）. Independent sample t test was used for comparison between two groups, and one-way analysis of variance was used for comparison between multiple groups. Enumeration data were represented by (%). $P < 0.05$ was considered statistically significant.

Results

2.1 comparison of clinical efficacy between the two groups

As shown in table 2, after one course of treatment, the total effective rate of the observation group was 92.50%, significantly higher than that of the control group (75.00%, $P < 0.05$).As shown in figure 1, the apparent efficiency of the observation group reached 67.50%, significantly higher than that of the control group (40.00%).The inefficiency of the observation group was 7.50%, significantly lower than that of the control group at 25.00% ($P < 0.05$).The results showed that exercise rehabilitation combined with huatuo reconstructive pill intervention can significantly improve the curative effect of vascular dementia.

Table 2 Comparison of clinical efficacy between the two groups

Group	Number	Excellent	Effective	Invalid	Total effective rate
Observation	40	27（67.50）	10（30.00）	3（7.50）	37（92.50）
Control	40	16（40.00）	11（27.50）	13（25.00）	27（75.00）

χ^2	6.084	0.065	7.813	7.813
p	0.014	0.799	0.005	0.005

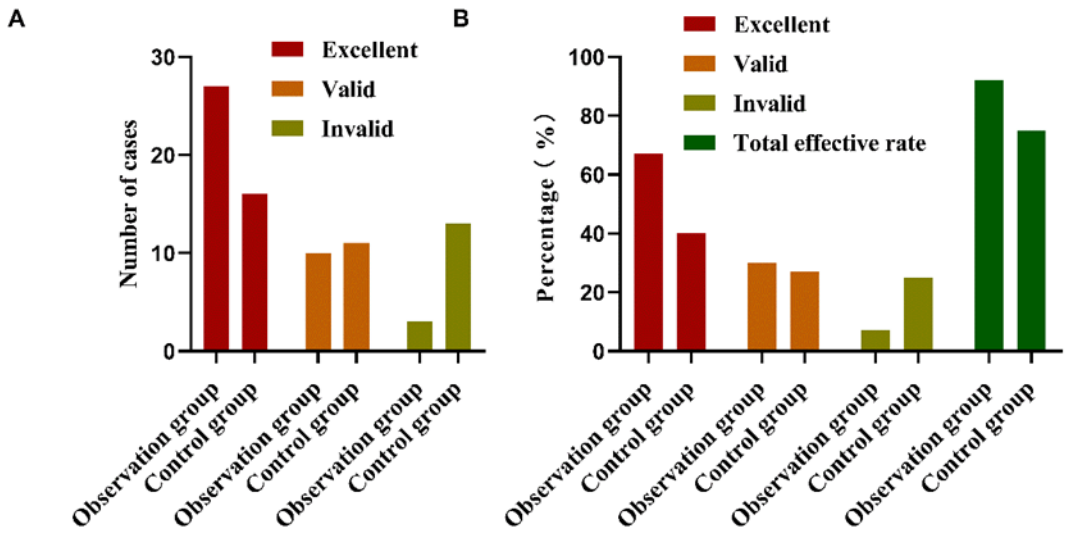

Figure 1. Comparison of clinical efficacy between the two groups

A: number of patients with different curative effects in the two groups; B: the percentage of patients with different curative effects in the two groups

Note: observation group: sports rehabilitation combined with huatuo reconstituted pills; Control group: huatuo reconstructive pills.

2.2 comparison of MMSE scores between the two groups before and after treatment

Before treatment, there was no significant difference in the orientation, memory, recall ability, attention, calculation power, language ability and MMSE scores between the two groups (P > 0.05).The orientation, language ability and total MMSE scores of patients in the observation group and the control group were significantly higher after treatment than before treatment (P < 0.05).After treatment, the orientation, language ability and total MMSE scores of patients in the observation group were significantly higher than those in the control group (P < 0.05), as shown in table 3. The results showed that the exercise rehabilitation combined with huatuo reconstructive pill intervention could significantly improve the orientation, language ability and overall cognitive function of patients with vascular dementia.

Table 3 comparison of MMSE scores between the two groups before and after treatment (±s, n=40)

Group	Number	Orientation	Memory	Recall	Attention and calculation	Language	Total score
Observatio							

n							
Before	40	5.78±0.43	4.14±0.32	0.97±0.24	1.93±0.59	5.94±0.32	15.38±1.17
After	40	#*6.91±0.37	4.39±0.25	1.06±0.26	1.95±0.58	#*6.46±0.27	#*18.95±1.43
Control							
Before	40	5.83±0.46	4.08±0.35	0.92±0.25	1.92±0.61	6.05±0.26	15.62±1.49
After	40	*6.55±0.41	4.16±0.38	0.94±0.23	1.93±0.56	*6.22±0.31	*16.86±1.31

Note: *P < 0.05 compared with that before treatment in the same group; #P < 0.05compared with the control group.

2.3 comparison of BI scores between the two groups before and after treatment

As shown in table 4 and figure 2, there was no statistically significant difference in BI score between the two groups before treatment (P > 0.05).After treatment, both the observation group and the control group had significantly higher BI scores (P < 0.05).After treatment, the BI score of the observation group was significantly higher than that of the control group (P < 0.05).The results showed that the exercise rehabilitation combined with huatuo reconstructive pill intervention could significantly improve the daily living ability of patients with vascular dementia.

Table4 comparison of BI score before and after treatment between the two groups ($\bar{x}$ ±*s*, n=40)

Group	Number	Before	After
Observation	40	49.24±16.35	#*68.39±18.09
Control	40	49.73±17.46	*59.28±18.41

Note: *P < 0.05 compared with that before treatment in the same group; #P < 0.05 compared with the control group.

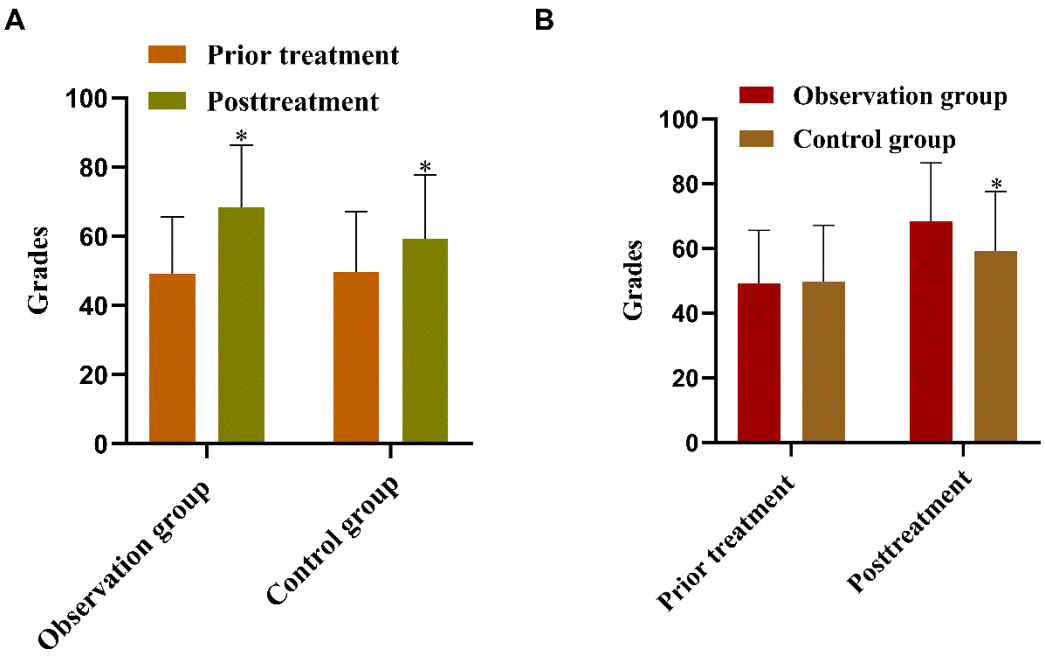

Figure 2. Comparison of BI scores between the two groups before and after treatment

A: comparison of BI scores before and after treatment between the observation group and the treatment group; B: comparison of BI scores between the two groups before and after treatment

Note: observation group: sports rehabilitation combined with huatuo reconstructive pills; Control group: huatuo reconstructive pills.

2.4 comparison of serum routine indexes, vascular function related indexes and neurotransmitter related indexes between the two groups before and after treatment

After treatment, the levels of Hcy, TBX2, ldl-c and ET were significantly decreased in the observation group and the control group, while hdl-c, NO, NE and DA were significantly increased ($P < 0.05$). Compared with the control group after treatment, the levels of Hcy, TBX2, ldl-c and ET in the observation group after treatment were significantly reduced, and the levels of NO, NE and DA were significantly increased ($P < 0.05$), as shown in table 5. The results showed that the intervention of exercise rehabilitation combined with huatuo reconstructive pills could significantly improve blood lipid level, vascular function and neurotransmitter delivery level in patients with vascular dementia.

Table 5 comparison of serum routine indexes, vascular function related indexes and neurotransmitter related indexes between the two groups before and after treatment （$\bar{x} \pm s$，n=40）

Group	Number	Hcy (μmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	TBX2 (ng/L)	ET (ng/L)	NO (ng/L)	NE (nmol/mL)	DA (nmol/mL)
Observation									
Before	40	24.19±7.25	1.16±0.25	3.89±1.24	402.03±127.15	78.74±19.36	37.03±8.95	8.13±2.43	8.27±1.98

After	40	#*14.73±4.97	*1.39±0.31	#*2.45±0.93	#*257.96±71.85	#*46.32±14.29	#*65.02±13.35	#*13.74±3.86	#*11.51±2.62
Control									
Before	40	24.72±7.38	1.13±0.23	3.82±1.21	398.52±121.48	76.51±18.62	37.08±9.16	8.25±2.48	8.43±2.13
After	40	*19.63±5.82	*1.29±0.27	*3.06±1.02	*339.18±96.73	*57.35±15.72	*49.44±11.23	*10.16±3.19	*9.89±2.65

Note: *P < 0.05 compared with that before treatment in the same group; #P < 0.05 Compared with the control group.

Discussion

Vascular dementia is mainly manifested as mood is difficult to control emotion, memory decline, concentration, thinking, dizziness, thought retardation, headache and other symptoms. Serious people can develop depression, aphasia, unable to live independently.Atherosclerosis leads to cerebral artery stenosis, reduced brain volume, or ischemic hypoperfusion caused by ischemia in important parts of cerebral cortex, furthermore, neuronal injury and cognitive dysfunction induced are important pathogenesis of vascular dementia [14-16].

According to the theory of traditional Chinese medicine, deficiency of kidney essence, stagnation of qi and phlegm, and blood stasis of collateral-vein are the basis of vascular dementia after stroke. After cerebral apoplexy, the liver wind impairs the phlegm and causes the cerebral pulse to be blocked and the essence of blood cannot be filled in the brain,and the essence of time withersbecome dementia [17]. Huatuo reconstructive pill is derived from the secret recipe of Mr. Ran xuefeng, a famous doctor. The main ingredients are Ligusticumwallichii, angelica sinensis, safflower carthamus, white peony root, red ginseng, strychniastrychnii,Schisandrachinensis, borneol and nanxing, which have the functions of promoting blood circulation and removing blood stasis, removing phlegm and clearing collateralism.it can relieve pain and nourish kidney and fill essence. Among them, angelica sinensis and ligusticumwallichii have the effect of inhibiting thrombosis, Radix paeoniae alba and nanxing have the effects of lowering blood lipid and blood pressure, strychniastrychnii has the effect of improving atherosclerosis,Schisandrachinensis has the effect of improving nerve center function, and borneol has the effect of refreshing the mind and awakening the brain [18].The results of this study showed that the total effective rate of huatuo reconstructive pills was 75.00%, indicating that huatuo reconstructive pills had a certain effect on vascular dementia.Zhang et al. [19] reported that huatuo reconstructive pills could improve hippocampal dependent memory defects and improve synaptic dysfunction by reversing long-term enhancement (LTP) injury. Duan et al. [4] found that huatuo reconstructive pills treatment can promote the recovery of nerve function after stroke by inducing an increase in the number of neurons. It is suggested that huatuo reconstructive pill in this study may reduce the neuron damage and increase the number of neurons in patients with vascular dementia, promote the recovery of nerve function, and achieve the therapeutic effect [20-27]. Further study found that, after treatment, language ability, MMSE score, BI directional force ratings, HDL -

C, NO, NE, DA were significantly higher than that of before treatment, after treatment of Hcy, TBX2, LDL - C, ET level is decreased obviously. It is suggested that huatuo constructive pill may have effects on regulating blood lipid, improving vascular endothelial function, increasing neurotransmitter secretion and promoting recovery of brain injury [28-33].

Conclusion

The limited research shows that it is generally safer. It can be applied for patients with diabetic conditions or patients under invasive care or patients with co-morbidities; moreover, there is generally no contraindication of drug interaction with any kind of allopathic medicine. But under supervision of medical practitioners or clinical supervisor it yields the best result.

In summary, the intervention of sports rehabilitation combined with huatuo reconstructive pill can promote the recovery of nerve function, improve vascular endothelial function and cognitive function in patients with vascular dementia, significantly improve the therapeutic effect, and have positive significance for the treatment of vascular dementia. However, due to the small sample size and short time of exercise rehabilitation training in this study, the long-term efficacy of the combination of the two still needs to be further verified by accumulating samples.

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