

CLINICAL RESEAPCH

Effect of Yangxue Qingnao Pills Combined with Plavix on Blood Coagulation Function and Barther Index in Patients with TIA

Yu Lin

Department of Pharmacy, Putuo Hospital, Zhoushan City, Zhejiang Province

Keywords

Yangxue Qingnao pills, Plavix, Transient ischemic attack, Blood coagulation function, Barther index

Correspondence

Yu Lin, Department of Pharmacy, Putuo Hospital, Zhoushan City, Zhejiang Province, No. 19 Wenkang Street, Donggang Street, Putuo District, Zhoushan City, Zhejiang Province. Tel: 18058028767; E-mail: linyu604@163.com

Received: 8 December 2020; Accepted: 7

January 2021; Published online: 8

February 2021

Diagnostic Brain Medicine 2021; 2(1):

144–149

Abstract

Objective To explore the clinical efficacy of treatment of Yangxue Qingnao pills combined with Plavix in patients with transient ischemic attack (TIA), and the effect on blood coagulation function of patients and Barther index. **Methods** A total of 116 cases of TIA patients in our hospital from Jan. 2018 to Aug. 2020 were randomly divided into the control group (n=58) and the observation group (n=58). With the basic regular treatment of the both groups, the control group was treated with Plavix, the observation group was treated with Yangxue Qingnao pills combined with Plavix. The clinical efficacy, blood coagulation function, Barther index and incidence of adverse reactions of the both groups were compared before and after treatment. **Results** The total effective rate was obviously higher in the observation group than that in the control group ($P<0.05$); The prothrombin time (PT), activated partial thromboplastin time (APTT) and Barther index score of both groups after treatment were obviously increased in comparison with those before treatment ($P<0.05$), and the observation group was obviously increased in comparison with those in the control group ($P<0.05$); The level of fibrinogen (FIB) of both groups after treatment was obviously decreased in comparison with that before treatment ($P<0.05$), and the observation group was obviously decreased in comparison with that in the control group ($P<0.05$); The incidence rate of adverse reactions of the observation group and the control group were 8.62% and 12.07% respectively, no significant difference was observed in the incidence rate of adverse reactions between both groups ($\chi^2=0.372$, $P=0.542$). **Conclusion** The combination of Yangxue Qingnao pills and Plavix has shown significant efficacy in treating patients with TIA, improving their blood coagulation function and neurological function.

Introduction

Transient ischemic attack (TIA) is a common cerebrovascular disease in which patients suffer from clinical symptoms such as dizziness, unilateral sensory disturbance, motor dysfunction, aphasia and monocular vision disorder [1]. Clinically, patients with TIA are usually treated with drugs such as Tirofiban, Clopidogrel, Aspirin, Argatroban anhydrous, Rivaroxaban and Warfarin which mainly focus on antiplatelet aggregation, antithrombotic formation and anticoagulation [2]. Plavix is a thienopyridine compound that has shown significant efficacy in the clinical treatment of TIA by effectively inhibiting platelet aggregation and reducing thrombosis, however its single application is limited, detrimental to the prognosis of TIA and may increase the risk of cerebral infarction [3]. In recent years, integrated traditional Chinese and Western medicine therapy has been gradually applied to the clinical treatment of patients with TIA. Juanqiang Shi applied Yiqi Huoxue Jiangzhu decoction combined with western drug to treat patients with TIA and found that the combination was effectively in reducing clinical symptoms and improving cerebral artery hemodynamics [4]. Yangxue Qingnao pill is made from a variety of Chinese herbs and has significant efficacy in the clinical treatment of acute cerebral infarction by improving neurological function and reducing inflammatory response of the body [5]. This study was expected to use the combined treatment of Yangxue Qingnao pills and Plavix for patients with TIA, and explore its clinical efficacy as well as the effects on the coagulation function and neurological function, hoping to be used for reference in the clinical treatment of TIA, and the results of the study are reported below.

Information and methods

Clinical information

Basic information

A total of 116 cases of patients with TIA diagnosed in our hospital from January 2018 to August 2020 were randomly divided into the control group (n=58) and the observation group (n=58). The control group: 35

males and 23 females, aged 38-72 years, mean age (49.52±7.26) years. The observation group: 37 males and 21 females, aged 35-70 years, mean age (48.34±8.40) years. There was no statistically significant difference between the two groups in terms of basic information ($P>0.05$), and the data were clinically comparable. The study was approved by the Ethics Committee of the hospital, with informed consent form all patients.

Inclusion and exclusion criteria

Inclusion criteria

Patients who were diagnosed with TIA met the diagnostic criteria in the *Chinese Guidelines for the Prevention and Treatment of Cerebrovascular Diseases* [6]; patients were not recently treated with either antithrombotic or antiplatelet medication.

Exclusion criteria

Patients who were allergic to Plavix and Yangxue Qingnao pills; patients with coagulation disorders; patients with server anemia; patients with a previous history of cerebral infarction or cerebral hemorrhage; patients accompanied with central system infections and craniocerebral injury; patients with hematological disorders; patients with brain hemorrhage caused by brain tumors such as cerebral aneurysms and brain tumors.

Treatment methods

Both groups were given regular treatment, including blood circulation activation, blood stasis dissipation and cerebrovascular protection. At the same time, all vital indicators of patients were required to monitor.

Control group

Patients were given Plavix (Clopidogrel Bisulfate Tablets, Sanofi (Hangzhou) Pharmaceutical Co., Ltd, national drug approval number: H20056410, specification: 75 mg × 7 tablets) by oral administration (75 mg/time, 1 time/day) for total 2 weeks.

Observation group

On the basis of the control group, patients in the observation group were given Yangxue Qingnao pills (Tasly Pharmaceutical Group Co., Ltd, national drug approval number: Z20063808, specification: 2.5 g × 15 bags) by oral administration (5 g/time, 1 time/day) for total 2 weeks.

Observation and indication

(i) Clinical efficacy: The clinical efficacy of patients in the two groups was evaluated with reference to the efficacy criteria in the *Guiding principles for Clinical Research of New Chinese Medicines* [7]. Significant effectiveness: patients showed significant improvement in clinical symptoms, and TIA was well controlled, with no recurrence at follow-up. Effectiveness: patients showed improvement in clinical symptoms with < 2 recurrences of follow-up. Ineffectiveness: no improvement was observed in clinical symptoms, TIA control and number of attacks from patients. Total effective rate of treatment = (significant effectiveness + effectiveness) number of cases/total number of cases × 100%.

(ii) Coagulation function: Before and after treatment, 5 ml of elbow venous blood was taken from each fasting patient in the two groups, and then was performed centrifugation (2500 r/minute, 15 minutes) for obtaining serum which was used to detect prothrombin time (PT), activated partial

thromboplastin time (APTT) and fibrinogen (FIB) level by an automatic biochemistry analyzer (BS-280, Shenzhen Mindray Biomedical Electronics Co., Ltd).

(iii) Neurological function: The Barther index scale was applied to assess the neurological function of patients in the two groups. The total score of the scale was 100 with 10 items, the higher the total score the better the neurological function of the patients.

(iv) Adverse reactions: We monitored the adverse reactions such as nausea and vomiting, dizziness, gingival bleeding and gastrointestinal hemorrhage in both groups.

Statistically analysis

SPSS software (version 22.0) was used for statistical analysis. Count data were compared using χ^2 test. Quantitative data was demonstrated as the mean ± standard, with comparison using the *t*-test. There was statistical significance if $P < 0.05$.

Results

Comparison of clinical efficacy between the two groups

There was a significant difference between the two groups in term of total treatment effectiveness, and the observation group showed a significantly higher effective rate than the control group ($P < 0.05$), as shown in table 1.

Table 1. Comparison of clinical efficacy between the two groups [case (%)]

groups	cases	significant effectiveness	effectiveness	ineffectiveness	total effective rate
observation group	58	37 (63.79)	16 (27.59)	5 (8.62)	53 (91.38)
control group	58	25 (43.10)	17 (29.31)	16 (27.59)	42 (72.41)
χ^2					7.036
<i>P</i>					0.008

Comparison of coagulation function between the two groups

Before treatment, there was no significant difference in PT, APTT and FIB level between the two groups ($P > 0.05$). Compared with the pre-treatment, PT and

APTT were significantly higher ($P < 0.05$) and FIB level were significantly lower ($P < 0.05$) in both groups after treatment. Besides, PT and APTT were significantly higher ($P < 0.05$) and FIB level were significantly lower ($P < 0.05$) in the observation group

compared with the control group, as shown in Table 2.

Table 2. Comparison of coagulation function between the two groups

groups	cases	PT (s)		FIB (g/L)		APTT (s)	
		pre-treatment	post-treatment	pre-treatment	post-treatment	pre-treatment	post-treatment
		nt	nt	nt	nt	nt	nt
observation group	58	9.85±1.84	13.24±1.56*	3.56±1.15	2.34±0.54*	25.74±4.85	34.74±4.22*
control group	58	10.03±1.92	11.85±2.04*	3.74±1.24	2.93±0.85*	26.13±5.26	30.86±6.23*
<i>t</i>		-0.515	4.122	-0.811	-4.462	-0.415	3.927
<i>P</i>		0.607	0.000	0.419	0.000	0.679	0.000

Note: compared to pre-intervention, * $P < 0.05$

Comparison of Barther index between the two groups

Before treatment, no significant difference in Barther index score was observed between the two groups ($P > 0.05$). Compared with the pre-treatment, the

Barther index score was significantly higher in both groups after treatment ($P < 0.05$), and significantly higher in the observation group compared to the control group ($P < 0.05$), as shown in Table 3.

Table 3. Comparison of Barther index between the two groups (point)

groups	cases	pre-treatment	post-treatment
observation group	58	68.74±9.56	86.33±7.50*
control group	58	67.12±8.57	80.62±10.34*
<i>t</i>		0.961	3.404
<i>P</i>		0.339	0.001

Note: compared to pre-intervention, * $P < 0.05$

Comparison of adverse reactions between the two groups

The incidence rate of adverse reactions in the observation group was 8.62% (5/58), including 2 cases of nausea and vomiting, 2 cases of dizziness and 1 case of gingival bleeding. The incidence rate of adverse reactions in the control group was 12.07% (7/58), including 3 cases of nausea and vomiting, 2 cases of dizziness, 1 case of gingival bleeding and 1 case of gastrointestinal hemorrhage. There was no significant difference in the incidence rate of adverse reactions between the two groups ($\chi^2 = 0.372$, $P = 0.542$).

Discussion

TIA is a transient neurological deficits caused by cerebral ischemia and hypoxia, and is an ischemic cerebrovascular disease that mostly affects middle-aged and elderly people. The pathogenesis of TIA remains unknown yet, but some studies suggest that its onset is related to atherosclerosis, cerebral vasospasm, cardiac disease, altered blood composition and hemodynamics [9]. If left untreated, TIA can deteriorate further into cerebral infarction. In traditional Chinese medicine, TIA is regarded as a kind of stroke portent which mainly caused by the triggered disorder of qi and blood circulation in the zang-fu viscera, blockage and malnutrition of the brain induced by wind-phlegm and blood stasis. Therefore, the treatment of patients with TIA should be based on strengthening vital qi to eliminate

pathogenic factor, dissipating stasis to activate qi flow and expelling phlegm for removing obstruction in collaterals [10]. In this study, patients in both groups were given basic treatment, based on which the control group was given Plavix and the observation group was given Yangxue Qingnao pills combined with Plavix. As a result, the total effective rate of treatment in the observation group was significantly higher than that in the control group, indicating that Yangxue Qingnao pills combined with Plavix has a better effect on treating patients with TIA.

patients with TIA are accompanied with inflammatory injury to nerve cells, and the inflammatory response can trigger damage to the vessel wall, prompting platelet activation and aggregation, leading to abnormal coagulation [11]. Simultaneously, patients with TIA have inadequate blood supply to the carotid or basilar arteries, causing ischemia and hypoxia in brain tissue, leading to nerve damage and triggering neurological dysfunction. PT refers to the time required for the conversion of prothrombin to thrombin, resulting in the coagulation of plasma, and can be used as an indicator to determine whether the exogenous coagulation of the body is normal. APTT refers to the time required for the plasma to clot when special substances are added to the plasma during the test, and can be used to determine the state of the endogenous coagulation system. FIB is the precursor protein of fibrin and has the effect of coagulation, and its level can be used to determine the state of coagulation. Our study found that PT, APTT and Barther index score were significantly elevated and FIB level were significantly decreased in both groups after treatment. Besides, PT, APTT and Barther index score were significantly higher and FIB level were significantly lower in the observation group compared with the control group, indicating that Yangxue Qingnao pills combined with Plavix for the treatment of TIA could improve patients' coagulation and neurological functions. Plavix is an adenosine diphosphate (ADP) receptor inhibitor that blocks the binding of ADP to platelet receptors and inhibits the activation of the glycoprotein IIb/IIIa complex, further inhibiting platelet aggregation and preventing

thrombus formation [12]. Meanwhile, Plavix can also dilate blood vessels to improve microcirculation, and increase blood and oxygen supply to the brain for promoting nerve cell recovery and improving neurological function. The main ingredients of Yangxue Qingnao pills are Chinese angelica, Sichuan lovage rhizome, debark peony root, prepared rehmannia root, gambir plant nod, suberect spatholobus stem, common selfheal fruit-spike and cassia seed. In terms of medicinal value, Chinese angelica has the effect of activating blood circulation and relieving pain as well as clearing intestine and facilitating feces excretion; Sichuan lovage rhizome has the effect of activating blood circulation and qi flow as well as dispelling pathogenic wind to relieve pain; debark peony root has the effect of nourishing blood and relieving pain as well as inhibiting liver yang; prepared rehmannia root has the effect of nourishing yin and tonifying blood as well as strengthening and nourishing marrow and essence; gambir plant nod has the effect of clearing heat and suppressing hyperactive liver as well as relieving spasm by calming endogenous wind; suberect spatholobus stem has the effect of regulating blood circulation and replenishing blood as well as relieving rigidity of muscles and activating collaterals; common selfheal fruit-spike has the effect of clearing heat-fire and resolving static blood and removing edema; cassia seed has the effect of removing liver-fire for improving eyesight and relaxing bowels. The combined effect of these herbs is to invigorate blood circulation to activate collaterals, remove blood stasis to subdue swelling and relieve paralysis and pain. Furthermore, the component of Sichuan lovage rhizome is found to reduce thrombin and prothrombin activity, inhibit platelet aggregation, reduce thrombosis and mitigate vascular endothelial damage, while improving microcirculation, increasing cerebral cortical blood flow and promoting recovery of neurological function. The component of Chinese angelica is found to increase coronary flow, inhibit platelet aggregation, improve ischemia and hypoxia in peripheral nerve endings, promoting repair of damaged nerves. The volatile oil components in

debarb peony root are found to improve cell membrane permeability, enhance the body's ability to resist hypoxia, reduce cellular lipid peroxidation, and reduce ischemia-reperfusion damage to nerve cells, while improving blood circulation, promoting hematoma absorption, reducing neural tissue edema, improving neural ischemia and hypoxia, and accelerating neurological function recovery. What's more, no significant difference in the incidence rate of adverse reactions between the two groups was observed during the study, suggesting that Yangxue Qingnao pills combined with Plavix has a certain safety profile in the treatment of patients with TIA.

In conclusion, the combination of Yangxue Qingnao pills and Plavix has shown significant efficacy in treating patients with TIA, improving their blood coagulation function and neurological function.

Declaration of conflict-of-interest

The authors declare no conflict-of-interest.

References

- [1] Wenwu Ding Xiaoliang Xu. Clinical efficacy of naoxintong combined with rosuvastatin in the treatment of patients with transient cerebral ischemia[J]. *Medical & Pharmaceutical Journal of Chinese People's Liberation Army*,2020,32(10):84-87.
- [2] Hou X, Chen H. Proposed antithrombotic strategy for acute ischemic stroke with large-artery atherosclerosis: focus on patients with high-risk transient ischemic attack and mild-to-moderate stroke[J]. *Ann Transl Med*. 2020, 8(1):16.
- [3] Guangyu Xiang. Effect of clopidogrel combined with atorvastatin calcium in the treatment of transient ischemic attack[J]. *Journal of Xinxiang Medical College*,2019,36(01):81-84.
- [4] Junqiang Shi. Effect of Yiqi Huoxue Jiangzhuo Decoction on on secondary prevention of transient ischemic attack[J]. *World Journal of Integrated Traditional and Western Medicine*,2020,15(02):296-300.
- [5] Linjun Li, Yanan Wang, Ping Xiao, et al. Clinical study on Yangxue Qingnao Granules combined with clopidogrel in treatment of acute cerebral infarction[J]. *Drugs & Clinic*,2019,34(12):3563-3567.
- [6] Dandan Chen. Clinical study on argatroban combined with clopidogrel in treatment of transient ischemic attack[J]. *Drugs & Clinic*,2019,34(12):3573-3576.
- [7] Lichao Yang, Yinping Li, Rong Yang. Clinical study on niergoline combined with defibrase in treatment of transient ischemic attack[J]. *Drugs & Clinic*,2020,35(01):65-69.
- [8] Shu Wang. Effect of cerebrotein hydrolysate combined with urinary kallidinogenase in the treatment of transient ischemic attack and its influence on neurological function and cerebral hemodynamics[J]. *Chinese Remedies & Clinics*,2020,20(17):2835-2837.
- [9] Chun Li, Bo Huang, Chaoyang Wei. Research Advances in Etiology of Transient Ischemic Attack[J]. *Journal of Preventive Medicine of Chinese People's Liberation Army*,2018,36(02):279-282.
- [10] Meilin Zheng, Yue Cai. Clinical study of compound Danshen dropping pills combined with aspirin in the treatment of transient ischemic attack[J]. *Hainan Medical Journal*,2020,31(06):696-698.
- [11] Mingming Zhang, Wenming Ban, Weiwei Tong. Effects and Mechanism of Buqi Tongzhi Decoction Combined with Butylphthalide on Transient Ischemic Attack with Qi Deficiency and Blood Stasis Syndrome[J]. *World Chinese Medicine*,2019,14(11):3020-3023.
- [12] Chengxia Lin. Clinical Observation on the Combination of Clopidogrel and Nimodipine in the Treatment of Transient Ischemic Attack[J]. *Sichuan Medical Journal*,2019,40(06):588-592.