Effect of clopidogrel combined with atorvastatin on NIHSS and Barthel score in patients with progressive cerebral infarction

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Objective: Study the clinical effect of atorvastatin combined with clopidogrel on patients with progressive cerebral infarction of intracranial aortic stenosis.

Methods: Chose eighty-eight patients with progressive cerebral infarction in our hospital from June 2014 to October 2015. They were randomly divided into study group and study group, 44 cases in each group. The patients in the control group were treated with oral clopidogrel. On the basis of this, the patients in the study group were treated with atorvastatin; all patients were treated for 4 weeks. Compared the total effective rate, adverse reaction rate, coagulation function index and blood lipid level between the two groups, and compared the NIHSS score and daily life ability (ADL) score between the two groups before and after treatment.

Results: The total effective rate (90.90%) was significantly higher in the study group than in the control group (72.73%). After treatment, the NIHSS score of the study group was significantly lower than that of the control group. The levels of LDL-C, TG and TC in the study group were significantly lower than those in the control group, and HDL-C was significantly higher than that in the control group. There was no significant difference between the two groups.

Conclusion: Clopidogrel combined with atorvastatin has a significant effect on the patients with intracranial large artery stenosis and improve the neurological function and quality of life. It is safe and reliable. It is worthy to be popularized.

1. Introduction

Progressive Cerebral Infarction (SIP) is a disease with a higher incidence in the elderly patients, which is a more severe clinical subtype in acute cerebral infarction. Progressive or progressive increase in neurological deficits of patients[1], which can lead to severe neurological deficits, and with the difficulty of treatment and poor prognosis. Related statistics show[2], intracranial aortic stenosis is an independent risk factor for progressive cerebral infarction, combined with intracranial artery stenosis of the SIP has a high disability rate, more complications, high mortality. It is a serious threat to the lives and health of patients. At present, intracranial arterial stenosis SIP is mainly used anti-platelet aggregation drug combined with stent intervention for treatment. Clopidogrel is the most commonly used effective anti-platelet aggregation drug in clinic, the main pharmacological mechanism was inhibition of adenosine diphosphate (ADP) agonist effect, blocking its mediated glycoprotein and GPIIb / IIIa complex activation[3], to achieve inhibition of platelet aggregation, usually used to treat ischemic stroke. However, for those who could not use interventional therapy, a single use of anti-platelet aggregation drugs are often with poor efficacy. The studies have found that intracranial arterial stenosis is usually caused by atherosclerosis, statins is currently the prevention and treatment of cardiovascular and cerebrovascular disease line and second line of drugs, a number of studies show that[4,5], Statins are the first-line and second-line drugs for the prevention and treatment of cardiovascular and cerebrovascular diseases, which has a good effect on coronary atherosclerotic heart disease. However, there is currently less coverage of clopidogrel combined with atorvastatin in the treatment of intracranial arterial stenosis. In this study, we report the efficacy of combination of two drugs for the treatment of SIP, to provide guidance for the clinical.
2. Materials and methods

2.1 General Information

88 intracranial artery stenosis progressive cerebral infarction cases were selected as subjects from our hospital from October 2015 to December 2016, included in the standard[6]: (1) All accord with the 2005 edition of ‘Guidelines for the prevention and treatment of cerebral blood diseases in China’ about the SIP diagnostic criteria for intracranial arterial stenosis, and confirm the stenosis of intracranial artery by CT/MRI and other imaging examinations; (2) No bleeding occurred after infarction; (3) No serious complication of heart, kidney, lung and other organ diseases; (4) Both the family members and the patients volunteered to sign the informed consent. Exclusion criteria: (1) Previous severe cerebrovascular events or brain organic disease leading to neurological deficits; (2) Recently received anticoagulation or thrombolytic therapy or larger surgery within 1 month; (3) With severe infectious diseases, immune function, hematologic diseases or malignant tumors; (4) With hemorrhagic cerebrovascular diseases; (5) Water-Electrolyte disorders, hypotension and other factors led to the progress of the disease; (6) Allergic to the study drug or accompanied the disease affected drug absorption. The subjects were randomly divided into control group and treatment group, each group of 44 cases, there were 26 males and 18 females in the control group, ages among 42-80 years old. The average age was (55.71 ± 6.82), the average course of disease was (35.76 ± 3.95) h, of which 6 cases were parietal lobe infarction, 19 cases of basal ganglia infarction , 5 cases of temporal lobe infarction,11 cases of lacunar infarction and 3 cases of multiple infarcts; There were 23 males and 21 females in the treatment group , aged 44-71 years, the mean age was (56±7) years, the course of disease is 11-46 h, the average course of disease was (34.67±5.09) h, including 6 cases of temporal lobe infarction, 11 cases of lacunar infarction, 9 cases of lacunar infarction, 4 cases of multiple infarction. There was no significant difference between the two groups in general data such as sex, age, course of disease and type of infarction. The results showed no significant difference (P>0.05).

2.2 Method

Two groups of patients received reduction of intracranial pressure, antibiotics, brain cell protection, regulation of blood glucose and lipid and other conventional treatment intervention after admitted to hospital, all patients were treated with oral Clopidogrel Bisulfate Tablets (Shenzhen XinliTai Pharmaceutical Co., Ltd., H20000542, 75 mg), the initial treatment dose was 300 mg, additional dose of 75 mg/d, 1 times/d. On the basis of drug use in the control group, the treatment group were treated with Atorvastatin Calcium Tablets (Beijing Jialin Pharmaceutical Co., Ltd., H19990258, 10 mg), the dose of 20 mg/d, with warm water delivery in the daily before bedtime. All patients were treated continuously for 4 weeks.

2.3 Observe indicators

(1) The clinical cure rate, the obvious effective rate, the effective rate and the total effective rate of the two groups were compared.
(2) The NIHSS score and the ADL score were evaluated before and after treatment, and the differences between the two groups were compared. (3) The adverse reaction rate of gastrointestinal bleeding, gross hematuria, black stool, liver and kidney dysfunction, coagulation dysfunction, blood routine and urine routine abnormality were compared between the two groups; (4) Comparison of two groups of the indexes of blood coagulation function and blood lipid level.

2.4 Efficacy criteria and detection methods

The neurological function was evaluated by NIHSS score. Total score is, the higher the score, the worse the neurological deficit. The quality of life was evaluated by the ADL score, The score is among 0-100, the higher the score, the higher the quality of life. Referring to related literatures, the improvement degree of NIHSS score was used as the criterion of efficacy evaluation[7], divided into (1) cure: NIHSS score decreased> 90.0% after treatment, clinical symptoms, signs and daily living ability returned to normal; (2) the obvious effective: NIHSS score decreased by 46.0%-90.0% after treatment, while all the symptoms and signs improved significantly, basically realize self-care; (3) effective: NIHSS score decreased in 18.0% to 45.0%, symptoms and signs improved, be able to complete a simple daily life behavior; (4) invalid: NIHSS score decreased <18.0% or aggravated after treatment, symptoms, signs and daily living ability no significant improvement or aggravated. The total effective rate of treatment = (cure rate + obvious effective rate+ effective rate) ×100.0%. Two groups of patients extracted 5ml of the peripheral venous blood of the morning fasting for detecting the blood coagulation function and blood lipid indexes before medication and after treatment for 7 d.

2.5 Statistical method

The statistical data involved in this study were analyzed by SPSS 21.0. NIHSS score and ADL score were expressed as mean ± standard deviation form, and performed t test (P<0.05). And the treatment grade, the incidence of adverse reactions and other count data is expressed by used (%) form, and performed χ² test There was a significant difference between the each groups or comparison before and after treatment (P<0.05).
3. Result

3.1 The total effective rate of treatment in both groups was compared

The cure rate and the total effective rate of the treatment group were 27.27% and 90.90% respectively. The cure rate and the total effective rate of the control group were 9.10% and 72.73% respectively. The cure rate and the total effective rate in the treatment group were significantly higher than the control group ($\chi^2 = 4.88, P = 0.02$), See Table 1 for details.

3.2 Comparison of NIHSS scores and ADL scores of two groups before and after treatment

There was no significant difference of the NIHSS score and ADL score between the two groups before treatment ($P>0.05$). After treatment, NIHSS scores of both groups were significantly lower than those before treatment ($P<0.01$), while ADL scores was significantly higher than before treatment ($P<0.01$), at the same time, The NIHSS score of patients in the treatment group was $(8.21 \pm 1.93)$ points, which was significantly lower than that in the control group $(10.23 \pm 2.19)$ (4.69, $P = 0.00$). The ADL score of patients in the treatment group was (67.32 ± 7.21) points, which was significantly higher than those of the control group $(59.34 \pm 6.39)$ ($t = 5.62, P = 0.00$), See Table 2 for details.

3.3 Comparison of two groups of blood lipid index

Before treatment, there was no significant difference in serum lipids between the two groups ($P>0.05$). After treatment, the LDL-C, TG and TC in the treatment group were significantly lower than those in the control group, and the HDL-C was significantly higher than that of the control group, the difference between the two groups was obvious ($P<0.05$). The details are shown in Table 3

3.4 The incidence of adverse reactions was compared between the two groups

Two groups of patients during treatment were not serious liver and kidney dysfunction, coagulation dysfunction, blood routine and urine routine examination results abnormal. Among the patients in the control group, there were 2 cases of stools, 2 cases of gastrointestinal bleeding, 1 cases of gross hematuria, and the total incidence of adverse reactions was 11.36%. There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$), and all adverse reactions were improved after targeted treatment.

4. Discussion

Progressive cerebral infarction is a cerebral infarction subtypes which neurological deficit showed progressive development from 6
have confirmed that reperfusion injury and the edema of brain tissue obstruction, the decrease of cerebral blood perfusion, the ischemia that the main pathogenesis of SIP is local cerebral blood supply insufficiency. It is closely related with the expansion of thrombus, the instability of cerebral fat plaques, the collateral circulation obstruction, the decrease of cerebral blood perfusion, the ischemia reperfusion injury and the edema of brain tissue[8,9]. The intracranial atherosclerotic stenosis is an independent risk factor for progressive cerebral infarction; studies have shown that patients with progressive cerebral infarction in the detection rate of intracranial artery stenosis up to 40%, approximately 50% of transient ischemic attacks are associated with intracranial arterial stenosis. In addition, platelet aggregation is one of the major factors leading to brain tissue blood supply disorder[10,11]. Domestic studies have also confirmed that platelet-leukocyte polymer is closely related to the progression of SIP, its level increases can aggravate SIP illness, and meanwhile, inhibiting the formation of the polymer can improve the SIP and reduce the neurological deficit.

The study found that the nerve defect in the early stage of cerebral infarction is mostly caused by the disease itself, the formation of cerebral ischemic penumbra is the main mechanism, in the late stage, the patient was mainly caused by secondary factors, such as infection, deep vein thrombosis and fever[12]. A number of studies have confirmed that[13,14], antiplatelet aggregation is currently the main method of clinical treatment of SIP, which can inhibit platelet aggregation in the cerebrovascular, thereby improving blood supply to the brain tissue and repair the ischemic penumbra, to save the brain cells which be close to necrosis. Clopidogrel is a powerful anti-platelet aggregation drug commonly used in clinic, the pharmacological mechanism is through the inhibition of ADP[15], blocking its surface receptor and platelet binding, inhibition of its mediated glycoprotein and GPIIb / IIa complex activation process, in order to inhibit platelet aggregation. Studies have shown that clopidogrel is more pronounced in the inhibition of platelet aggregation than the commonly used antiplatelet agents aspirin, often replacing it for the treatment of ischemic cerebrovascular disease[16]. But for intracranial artery stenosis SIP, a single use of anti-platelet aggregation drug effect is often poor, need to use arterial stent implantation for treatment. The clinical experience shows that some patients cannot afford the high cost of medical care or no stent implantation indications, so often need to use drugs to intervene. Studies have confirmed that abnormal lipid metabolism plays an important role in the pathogenesis of intracranial arterial stenosis SIP, all patients with intracranial arterial stenosis and SIP are accompanied with various degrees of hyperlipidemia, while lowering serum lipids can significantly promote the prognosis of patients[17].

Atorvastatin is a commonly used statin, modern pharmacological studies found that it not only has a strong lipid-lowering effect, but also has improved vascular endothelial cell function, anti-platelet aggregation, promote endothelial cell regeneration, inhibition of inflammation, which can block the process of thrombosis and stabilization of atherosclerotic plaques and other effects, long-term use of atorvastatin can significantly inhibit the development of atherosclerosis, scavenging free radicals, delay the progression of the disease, and even repair damaged nerve cells, so as to promote the recovery of nerve function[18]. The data show that LDL-C, TG and TC in the treatment group were significantly lower than those in the control group; HDL-C was significantly higher than the control group, consistent with the current report. In clinical practice, atorvastatin is often adjuvant to treat various types of ischemic cerebrovascular disease, but there is still insufficient literature support about the efficacy and safety of clopidogrel combined with atorvastatin in the treatment of SIP. The results of this study show that the total effective rate of treatment and the ADL scores after treatment of the treatment group were significantly higher than the control group, while the NIHSS score was significantly lower than the control group, confirmed that the two drugs combined therapy can achieve synergistic effect, promoted together the recovery of neurological function and quality of life in SIP patients. At the same time, there was not found significant adverse reactions in the two groups of patients in the study, confirmed the safety and reliable of the two drugs, consistent with the current report[9,20].

In conclusion, this study used clopidogrel combined with atorvastatin in the treatment of intracranial arterial stenosis SIP, which confirmed that the combination of drugs can improve the efficacy, and promote the recovery of neurological function, improve quality of life, and with higher safety. However, this study only for the drug intervention in atherosclerotic stenosis and platelet aggregation and other aspects, and the selected subjects are less, therefore, further intervention in the disease relies on a large sample study which currently conducted.

Reference


[3] Zang RS, Zhang H, Xu Y. Serum C-reactive protein, fibrinogen and


