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Original Research

Effects of Floium ginkgo extract and tertram ethypyrazine sodium chloride injection on expression of inflammatory cytokines and cerebral infarction

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Abstract: This experiment was carried out to observe and analyze the effect of floium ginkgo extract and tertram ethypyrazine sodium chloride injection in patients with cerebral infarction. A total of 200 patients diagnosed with cerebral infarction were enrolled in the study. They were randomly divided into a research group and control group, each containing 100 patients. The control group was given routine treatment measures while the research group was given floium ginkgo extract and tertram ethypyrazine sodium chloride injection on the basis of routine treatment. The therapeutic effects of the two groups were observed and compared. After implementing different treatment schemes, the levels of MMP-9, SOD, CBV and CBF in the research group were significantly higher than those in the control group, $p<0.05$. The research group was lower in hs-CRP, MDA, MTT, TTP and TNF-α as compared with the control group, $p<0.05$. In terms of the quality of life of the two groups after six months of treatment, the scores of various indicators in the research group were all significantly superior, $p<0.05$. Conclusion: The treatment of cerebral infarction patients with floium ginkgo extract and tertram ethypyrazine sodium chloride injection can significantly improve the therapeutic effect, which is a relatively ideal treatment.

Key words: Floium ginkgo extract; Tertram ethypyrazine sodium chloride; Injection; Cerebral Infarction; Inflammatory cytokines; Oxidative stress response; Cerebral blood perfusion.

Introduction

Inflammatory cytokines are a group of signaling molecules, called signaling factors, secreted by helper lymphocytes and macrophages and other cells that exacerbate inflammation and increase inflammation. These molecules include interleukin 1, interleukin 12, interleukin 18, alpha tumor necrosis factor, interferon-gamma, Granulocyte-macrophage colony-stimulating factor, all of which play an important role in the function of the innate immune system (1, 2).

The long-term and excessive secretion of inflammatory cytokines can cause inflammation, which is related to the development of certain diseases, such as atherosclerosis and cancer. Abnormal regulation of this system can also cause mood disorders and some neurological diseases. In order to maintain health, it is necessary to strike a balance between inflammatory cytokines and anti-inflammatory cytokines. Aging and exercise also play a role in inflammation caused by inflammatory cytokines (3-5).

Monoclonal antibodies are used to treat inflammatory diseases that can neutralize inflammatory cytokines or inactivate cytokine receptors. Reducing the biological activity of inflammatory cytokines can reduce the damage caused by the disease (6, 7).

Blocking interleukin-1 and alpha tumor necrosis factor has successfully treated patients with rheumatoid arthritis, inflammatory bowel disease and host transplantation (GvHD). But it is not very effective in treating sepsis. Some of these inflammatory cytokines, such as alpha tumor necrosis factor, interleukin 1 beta, interleukin 6 and interleukin 10 (8, 9).

Estrogen has been shown to have curative and therapeutic effects by reducing the production of certain inflammatory cytokines such as alpha tumor necrosis factor, interleukin 6 and "macrophage migration inhibitory factor". Unfortunately, as reported by the American Cancer Society, the use of estrogen has carcinogenic effects, for example, increasing the risk of breast cancer in postmenopausal women receiving replacement hormones (10, 11).

When the various emboli in the blood (such as mural thrombus, inside the heart of atherosclerosis plaques, fat, tumor cells, and fibrous cartilage or air, etc.) flow into the cerebral arteries and blocking blood vessels, and the collateral circulation is not compensated, ischemic necrosis of the brain tissue in the arterial feeding area occurs, resulting in a focal neurological defect, known as cerebral infarction. Cerebral infarction accounts for about 15% ~ 20% of cerebral apoplexy. The mortality rate in the acute phase is 5% ~ 15%, mostly due to encephalopathy, pneumonia and heart failure caused by severe cerebral edema. Cerebral infarction is prone to

relapse, 10% ~ 20% of a cerebral infarction occurs within 10 days of the second embolization, and those who relapsed have a higher mortality rate (12-14).

Cerebral infarction as a sudden neurological disease that can be attributed to focal blood vessels, which interrupts the blood supply to the affected area. According to relevant surveys, the number of people with cerebral infarction is increasing. Drug therapy is an effective treatment model, among which floium ginkgo extract and tertram ethypyrazine sodium chloride injection are often used to treat cerebral infarction. Floium ginkgo extract and tertram ethypyrazine sodium chloride injection contain ginkgo biloba extract and ligustrazine phosphate, which is a compound preparation. This study observed the effect of floium ginkgo extract and tertram ethypyrazine sodium chloride injection in the treatment of cerebral infarction (13-21).

Materials and Methods

General data

In this study, 200 patients who had been treated for cerebral infarction in our hospital from August 2016 to May 2019 were enrolled as research objects. Patients meeting inclusion criteria include those who meet the criteria for the diagnosis of acute cerebral infarction in the diagnosis essentials of various cerebrovascular diseases; those with definite diagnosis after head CT examination; and those with good treatment compliance. Patients and their families had the right to know and signed a formal consent form formulated by our hospital. This study was approved by the hospital ethics association. Patients in the acute stage of a cerebral hemorrhage, patients with serious coagulation diseases, liver and kidney diseases or blood diseases, or patients with mental disorders were excluded.

Selected patients were randomly divided into a research group and control group, each containing 100 cases. There were 52 male patients and 48 female patients in the research group, with an average age of (66.7±2.1) years old. There were 49 male patients and 51 female patients in the control group, respectively, with an average age of (67.3±2.8) years old. There were no significant differences in general data between the two groups before treatment, $p>0.05$.

Methods

Patients in both the research group and the control group were given routine comprehensive treatment, including administration of aspirin (Guangdong Jiuming Pharmaceutical Co., Ltd., SFDA approval number H44021139), at a dose of 25 mg per each time, once a day; Intravenous infusion of compound Danshen injection (Sichuan Shenghe Pharmaceutical Co., Ltd., SFDA approval number H20162583), once a day; routine neuro-nutrition, oxygen absorption, dehydration and blood pressure reduction; symptomatic treatment for patients with diabetes, hyperlipidemia or hypertension, blood sugar control, lipid regulation and blood pressure reduction. On this basis, patients in the research group were also treated with an intravenous drip of floium ginkgo extract and tertram ethypyrazine sodium chloride injection (Honghe Pharmaceutical Co., Ltd., SFDA approval number H22026583), at a dose of 250mL per each time, once a day. The patients were treated for a complete course of two weeks.

Floium ginkgo extract and tertram ethypyrazine sodium chloride injection is a compound preparation, which mainly contains ginkgo biloba extract and ligustrazine phosphate (C 8H 12N 2•H 3PO 4•H 2O). It is mainly used to treat ischemic cardiovascular and cerebrovascular diseases such as cerebral insufficiency, cerebral thrombosis, cerebral embolism, angina pectoris, myocardial infarction; peripheral circulation disorders such as arterial obliterans, vasculitis, diabetes caused by microcirculation disorders, hearing loss, chronic glaucoma; cerebral insufficiency, senile dementia, hypertension, hyperlipidemia and other diseases. Compound salvia miltiorrhiza injection is suitable for angina pectoris and acute myocardial infarction, treating cerebrovascular accident, chronic hepatitis, epidemic hemorrhagic fever and renal failure and other diseases. Its main effects include the protection of myocardial ischemia and hypoxia, scavenging of free radicals, protection of liver damage, sedation and improvement of hemorheology. The molecular chemical formula of aspirin is C9H8O4, the molecular structure formula is CH3COOC6H4COOH, and the molecular relative mass is 180.16. Aspirin is a derivative of salicylic acid, which can inhibit platelet aggregation and prevent thrombosis, and is used to prevent transient ischemic attacks and myocardial infarction.

Observational indicators

The levels of inflammatory factors, oxidative stress response and cerebral blood perfusion related indexes in the two groups were analyzed and compared. Inflammatory cytokines involve hypersensitive c-reactive protein (hs-CRP) and tumor necrosis factor-alpha (TNF-α), where were measured by immune rate nephelometry and radioimmunoassay, respectively. The oxidative stress indicators include peroxide dismutase (SOD) and malondialdehyde (MDA), which were measured by the enzymatic method and chemical method using the kit purchased from Bode Company, Wuhan. Cerebral blood perfusion indicators include mean transit time, peak time, cerebral blood flow, cerebral blood volume (MTT, TTP, CBF, CBV). The SF-36 scale was used to objectively evaluate the quality of life of the two groups.

Statistical method

Statistical analysis software SPSS21.0 was used to process data. The measurement data were expressed by mean ± average ($\bar{x} \pm s$), with a t-test conducted for intergroup comparison. Enumeration data were expressed by natural (n) and percentage (%), with X2 used for intergroup comparison. The intergroup difference is of statistical value when $P < 0.05$.

Results

Comparison of levels of inflammatory cytokines and oxidative stress response indicators between the two groups

As shown in Table 1, the reduction of hs-CRP and TNR-α of the two groups was significantly lower in the research group than in the control group, $p<0.05$. Compared with the control group, the research group had a

Table 1. Comparison of levels of inflammatory cytokines and oxidative stress response indicators between the two groups ($\bar{x}$ ±s)

Group	Time	MMP-9 (μg/L)	hs-CRP (mg/L)	SOD (nU/mL)	MDA (nmol/mL)
Research group	Before treatment	436.50±30.69	6.24±3.10	276.88±32.18	4.87±0.19
	After treatment	254.30±28.70	2.82±1.20	275,33±30.82	2.23±0.31
Control group	Before treatment	428.05±36.59	6.40±3.21	277.50±20.36	4.85±0.39
	After treatment	140.28±30.83	4.05±1.79	375.40±19.05	3.94±0.22

Table 2. Comparison of cerebral blood perfusion indexes of the two groups ($\bar{x}$ ±s)

Group	Time	MTT (s)	TTP (s)	CBF (ml/100mg)	CBV (ml/100mg)
Research group	Before treatment	241.56±90.73	125.05±20.16	30.89±12.46	70.89±24.16
	After treatment	128.33±98.22	96.55±18.22	78.33±10.27	97.68±26.13
Control group	Before treatment	243.08±95.72	125.48±16.58	30.42±11.80	70.52±23.12
	After treatment	180.31±92.84	106.46±16.59	55.43±12.06	80.47±20.45

Table 3. Comparison of quality of life between the two groups ($\bar{x}$ ±s)

Group	Number of cases	Physiological function	Emotional function	Social function	General health state	Mental function	Energy
Research group	100	79.80±3.25	78.96±3.20	82.35±2.18	60.78±3.22	75.63±4.02	65.79±2.04
Control group	100	72.20±2.46	66.88±2.58	73.20±2.59	49.06±3.01	65.80±2.06	55.49±3.28
t		6.70	20.19	6.79	8.53	11.22	13.27
p		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

significantly higher SOD level while lower MDA level, $p<0.05$.

Comparison of cerebral blood perfusion indexes of the two groups

As shown in Table 2, there was no significant difference in MTT, TTP, CBV and CBF between the two groups before treatment, $p>0.05$. After treatment, the MTT and TTP of the study group were significantly lower than those of the control group, $p<0.05$. Meanwhile, CBF and CBV in the research group were significantly higher than those in the control group, $p<0.05$.

Comparison of quality of life between the two groups

As shown in table 3, after the implementation of different treatments for patients in the research group and the control group, the quality of life of patients in the research group was better than that in the control group, $p<0.05$.

Discussion

Studies have shown that free radical injury plays a key role in cerebral ischemia-reperfusion injury, and both oxidative stress response and inflammatory response play an important role in the degeneration and apoptosis of ischemic nerve cells in patients with cerebral infarction. Serum hs-CRP can promote vascular or endothelial cells in an inflammatory state, which is an important marker of non-specific inflammatory response. TNF- alpha plays a positive role in the accumulation of a large number of neutrophils in the focus area, promoting white blood cells and damaged tissue cells to secrete cytokines, and making the inflammatory reaction worse (22).

Currently, the oxidation level indexes determined in the laboratory mainly include MDA and SOD, etc. SOD is a common enzyme in organisms to eliminate free radicals, of which the activity can directly affect the scavenging of oxygen free radicals. MDA is a metabolite in lipid peroxidation reaction, which can indirectly react to the effects of free radicals on tissue cells. For cerebral blood perfusion, MTT, TTP, CBV, CBF and other parameters were analyzed in CT perfusion imaging, which clearly showed the changes of blood flow at the early stage of cerebral infarction and after treatment (23, 24).

Floium ginkgo extract and tertram ethypyrazine sodium chloride injection contain ginkgo biloba extract, ligustrazine phosphate and other components, which is a compound preparation. Ginkgo biloba extract can reduce the content of MDA in brain tissue and effectively improve the activity of SOD in brain tissue. The action mechanism of Floium ginkgo extract and tertram ethypyrazine sodium chloride is to remove free radicals from the blood, dilate the blood vessels and improve the symptoms of cerebral ischemia or hypoxia. At the same time, it can relieve brain edema, form certain antagonistic effects on platelet activation factor, and significantly enhance the learning and memory ability of patients. Ligustrazine plays a role in dilating blood vessels, blocking platelet aggregation, reducing platelet activity, reducing the levels of inflammatory factors such as hs-CRP and TNF-α, and achieving the effect of microcirculation optimization (25-28).

It has been pointed out that ligustrazine inhibits platelet function and prevents the utilization and release of calcium in patients. After the occurrence of cerebral infarction, the amount of local blood perfusion in the infarction area will be correspondingly reduced, affecting the function of brain cells. After reperfusion, oxygen-free radicals can cause damage to the cell membrane, mediate Ca2+ intracellular flow in the infarct area, af-

fect morphine A2 or endogenous opioid, induce cerebral ischemia or hypoxia and necrosis symptoms, and cause problems such as disturbance of consciousness or movement. However, the treatment with floium ginkgo extract and tertram ethypyrazine sodium chloride injection can eliminate free radicals while avoiding lipid peroxidation, and actively improve the injury caused by cerebral ischemia-reperfusion (29-34).

The results of this study showed that after implementing different treatment regiments, the levels of MMP-9, SOD, CBV and CBF were significantly higher in the research group than those in the control group, $p<0.05$. In terms of levels of hs-CRP, MDA, MTT, TTP and TNF-α, the research group was lower than the control group, $p<0.05$. The study group was significantly superior in quality of life and scores of various indicators after six months of treatment, $p<0.05$, which is consistent with the relevant research results.

In conclusion, the conventional treatment combined with Floium ginkgo extract and tertram ethypyrazine sodium chloride injection can achieve good results for patients with cerebral infarction. On the one hand, it can reduce the level of inflammatory cytokines in patients, on the other hand, it can weaken the oxidative stress response. The application of floium ginkgo extract and tertram ethypyrazine sodium chloride injection can improve the indexes of cerebral blood perfusion in patients with cerebral infarction, and can help to improve the quality of life of patients. However, due to the limited sample size of this study, larger sample data studies are needed to fully demonstrate in the future.

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