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Comparison of Clinical Effects of Ginkgolide and Ginkgo Biloba Extract on Acute Cerebral Infarction

Guozhen Lu[1, #], Liming Jiao[1, #], Na Shi[1], Na Guo[1], Liang An[1], Lingyun Zhang[1] and Junfeng Kang[2, *]

[1]Shanxi Provincial Hospital of Traditional Chinese Medicine, 030000 Taiyuan, Shanxi, China

[2]Affiliated Hospital of Shanxi University of Chinese Medicine, 030000 Taiyuan, Shanxi, China

Keywords

Ginkgo biloba extract, Ginkgolide, Acute cerebral infarction

***Correspondence**

Junfeng Kang, Affiliated Hospital of Shanxi University of Traditional Chinese Medicine, No. 75 Jinci Road, 030000 Taiyuan, Shanxi, China. E-mail: 36171696@qq.com

[#]These authors contributed equally.

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Abstract

Objective To compare the clinical effects of ginkgolide and ginkgo biloba extract on acute cerebral infarction. **Methods** 120 patients with acute cerebral infarction admitted to our hospital from February 2019 to February 2022 were selected and divided into group A and group B by random number table method, with 60 cases in each group. Patients in group A was given ginkgo biloba extract on the basis of routine treatment, while patients in group B was given ginkgolide on the basis of routine treatment. The clinical efficacy, inflammatory factors, coagulation function and hemorheology of the two groups were compared. **Results** After treatment, the total effective rate of clinical efficacy in group B was higher than that in group A (P<0.05). Compared with before treatment, the levels of monocyte chemoattractant protein-1 (MCP-1) , Matrix metalloproteinase-9 (MMP-9), plasma fibrinogen (FIB), erythrocyte aggregation index, plasma viscosity (PSV), hematocrit (HCT) in the two groups after treatment were significantly declined (P<0.05), and those data mentioned above in observation group were significantly lower than those in control group (P<0.05). Compared with pre-treatment data, the levels of activated partial thromboplastin time (APTT) and prothrombin time (PT) in the two groups after treatment was significantly increased (P<0.05), and the levels of APTT and PT in observation group were obviously higher than those in control group (P<0.05). **Conclusion** Ginkgolide is effective in treating acute cerebral infarction, effectively improving the level of inflammatory factors and coagulation function, and promoting the recovery of hemorheology.

Introduction

Acute cerebral infarction refers to cerebral ischemia and necrosis caused by sudden occlusion of cerebral vessels due to various reasons, and patients often have symptoms such as hemiplegia, sensory disturbance, aphasia, ataxia, etc [1]. Tian-tian Meng et al. suggested [2] that ginkgo leaf tablets can improve the elasticity and permeability of blood vessels in patients with acute cerebral infarction so as to promote the recovery of patients as soon as possible. In addition, ginkgolide and ginkgo biloba extract are common clinical ginkgo-processed products. Ginkgo biloba extract can not only resist oxidation, but also increase the cerebral blood flow of patients, so it is often used to treat coronary heart disease [3]. Ginkgolide exerts the effects of promoting blood circulation, removing blood stasis, dredging channels and collaterals, making it often used to improve symptoms such as dizziness, facial distortion and numbness of limbs [4]. Therefore, in this study, ginkgolide and ginkgo biloba extract were applied to the treatment of acute cerebral infarction, and the curative effects of these two treatment methods were compared, with the hope to provide some reference for the clinical treatment for this kind of diseases. The results were reported as follows.

Data and methods

General information

120 patients with acute cerebral infarction treated in our hospital from February 2019 to February 2022 were selected and randomly divided into group A (n=60) and group B (n=60). This study was approved by the ethics committee of our hospital, and all patients signed the informed consent in the written form. There was no significant difference in general data between the two groups (P>0.05), which was comparable, as shown in Table 1.

Table 1. Comparison of general data between the two groups

Group		Group A（n=60）	Group B（n=60）	χ^2/t	P
Gender (case)	male	33	35	0.136	0.713
	female	27	25		
Age (year)		67.37±10.81	66.68±10.68	0.352	0.726
Body mass（kg）		63.42±10.21	63.57±10.80	-0.078	0.938
The time of diagnosis（h）		7.02±1.03	6.97±0.84	0.291	0.771
Complication (case)	Hypertension	44	42	0.404	0.939
	Coronary heart disease	15	13		
	Hyperlipoidemia	28	31		
	Diabetes	29	31		
Lesion site (case)	Brain lobe	17	16	0.556	0.906
	Cerebellum	8	9		
	Basal ganglia	29	31		
	Multi-site	6	4		

Diagnostic criteria

Diagnostic criteria of Western medicine referred to the diagnostic criteria of acute cerebral infarction recovery period in *Chinese guideline for diagnosis and treatment of acute ischemic stroke 2018* [5]. Diagnostic criteria of traditional Chinese medicine referred to the diagnostic criteria of "apoplexy" and "thoracic obstruction" in *Effect of TCM comprehensive management on 172 patients with convalescent cerebral infarction* [6].

Inclusion criteria

① Patients' symptoms met the diagnostic criteria of Chinese and Western medicine; ② All patients were

diagnosed for the first time; ③ Patients with stable vital signs.

Exclusion criteria

① Patients with severe primary diseases of brain, liver and kidney; ② Patients were allergic to ginkgo biloba; ③ Patients with malignant tumors; ④ Patients who had undergone early intravenous thrombolysis and interventional therapy; ⑤ Patients with coagulation dysfunction.

Treatment methods

Patients in both groups were given routine treatment for acute cerebral infarction: a. antiplatelet aggregation therapy (aspirin combined with clopidogrel); b. defibration therapy; c. oxygen therapy; d. hypotensive therapy (nifedipine); e. lipid-lowering therapy (fenofibrate). On the basis of routine treatment, 25 ml ginkgo biloba extract injection (package specification: 5 ml: 17.5 mg*10 pieces; approval number of National Medical Products Administration: H20070226; manufacturer: Youcare Pharmaceutical Group Co., Ltd.) was added into 250 ml 0.9% sodium chloride injection that was administered intravenously to patients in A Group, once a day. B group was treated with 10 ml ginkgolide injection (package specification: 2ml; approval number of National Medical Products Administration: Z20110035; manufacturer: Chengdu Baiyu Technology Pharmaceutical Co., Ltd.) was added into 250ml of 0.9% sodium chloride injection that was administered intravenously to the patients in B Group, once a day. Both groups were treated for 10 days.

Observation indicators

① Clinical curative effect [7]: after treatment, the clinical curative effect of the two groups of patients was evaluated according to the changes of NIHSS score. Recovery: NIHSS score decreased by > 90% compared with that before treatment; obvious effect: reduction ≤90%, > 45%; effective: reduction ≤45%, > 18%; ineffective: reduction ≤18% or increase. Total clinical effective rate=(recovery+ obvious effect +effective) cases/total cases ×100%.

② Levels of inflammatory factors, coagulation function and hemorheology: before and after treatment, fasting elbow venous blood of patients in the two groups was collected, and then centrifuged at room temperature for 5 minutes (min) at 3000r/min. The upper serum samples were taken, and monocyte chemoattractant protein-1 (MCP-1) and matrix metalloproteinase-9 (MMP-9) were detected by enzyme-linked immunosorbent assay. The levels of activated partial thromboplastin time (APTT) and prothrombin time (PT) and plasma fibrinogen (FIB) were detected by ACL9000 automatic blood coagulation analyzer. The levels of plasma viscosity (PSV) and hematocrit (HCT) were measured by hemorheology tester. 5ml fasting venous blood of patients in two group was drawn that was added into 100IU heparin for testing, and the erythrocyte aggregation index was measured with a usage of an erythrocyte aggregation tester (model: LG-B-190).

Statistical methods

SPSS 20.0 was used for statistical analysis. The counting data were compared by χ^2 test, and the measurement data were expressed by mean ± standard deviation ($\bar{x}\pm s$). The comparison between the two groups was made by independent sample *t* test, and the comparison between different time points in the same group was made by paired sample *t* test. Besides, the data with $P<0.05$ were considered as statistically significant.

Results

Comparison of clinical efficacy of patients between the two groups

After treatment, the total effective rate of clinical efficacy in B group was significantly higher than that in A group ($P<0.05$), as described in Table 2.

Table 2. Comparison of clinical efficacy between the two groups of patients [cases (%)]

Group	Case	Recovery	The effect appeared	Effective	Ineffective	Total clinical effective rate

A group	60	9（15.00）	19（31.67）	18（30.00）	14（23.33）	46（76.67）
B group	60	15（25.00）	29（48.33）	12（20.00）	4（6.67）	56（93.33）
χ^2						0.536
P						0.011

Comparison of inflammatory factors of patients between the two groups

There was no significant difference in MCP-1 and MMP-9 levels between the two groups before treatment (P>0.05). After treatment, the levels of MCP-1 and MMP-9 in the two groups were decreased significantly (P<0.05), and the levels of MCP-1 and MMP-9 in B group were significantly lower than those in A group (P<0.05), as listed in Table 3.

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

Group	Case	MCP-1（μg/L）		MMP-9（mg/L）	
		Before treatment	After treatment	Before treatment	After treatment
A group	60	138.17±49.31	118.27±39.06*	320.78±45.34	230.60±44.10*
B group	60	137.31±40.95	101.21±33.84*	326.60±44.10	169.00±43.81*
t		0.104	2.572	-0.713	7.676
P		0.917	0.011	0.477	0.000

Note: Compared with the data before treatment: *P<0.05

Comparison of coagulation function between the two groups

Before treatment, there was no significant difference in the levels of FIB, PT and APTT between the two groups (P>0.05). After treatment, the level of FIB in the two groups was significantly decreased and the level of PT and APTT in the two groups were enhanced (P<0.05). Besides, the level of FIB in B group were significantly lower than that in A group (P<0.05) and the levels of PT and APTT were higher than those in A group (P<0.05), as described in Table 4.

Table 4. Comparison of coagulation function between the two groups of patients ($\bar{x}$±s)

Group	Case	FIB (g/L)		PT (s)		APTT (s)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
A group	60	5.65±0.44	5.06±0.50*	8.76±1.17	10.83±2.23*	23.47±3.13	30.17±3.78*
B group	60	5.66±0.43	3.37±0.39*	8.80±1.06	12.44±1.77*	24.00±3.32	37.59±2.06*
t		-0.126	20.644	-0.196	-4.380	-0.900	-13.351
P		0.900	0.000	0.845	0.000	0.370	0.000

Note: Compared with the data before treatment: *P<0.05

Comparison of hemorheology between the two groups

Before treatment, there was no significant difference in erythrocyte aggregation index, PSV and HCT levels between the two groups (P>0.05). After treatment, the levels of erythrocyte aggregation index, PSV and

HCT in the two groups were decreased obviously (P<0.05), and the levels of erythrocyte aggregation index, PSV and HCT in B group were significantly lower than those in A group (P<0.05), as shown in Table 5.

Table 5. Comparison of hemorheology between the two groups of patients ($\bar{x}\pm s$)

Group	Case	erythrocyte aggregation index		PSV（mPa·s）		HCT（%）	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
A group	60	2.53±0.38	2.03±0.45*	3.82±0.80	2.38±0.81*	47.40±5.28	44.15±4.49*
B group	60	2.58±0.38	1.64±0.26*	3.74±0.78	1.24±0.44*	47.56±5.12	39.42±4.63*
t		-0.721	5.813	0.555	9.580	-0.169	5.681
P		0.473	0.000	0.580	0.000	0.866	0.000

Note: Compared with the data before treatment: *P<0.05

Discussion

Acute cerebral infarction is usually caused by atherosclerosis in the arteries that supply blood to the brain. In addition, hypertension, coronary heart disease, diabetes, hyperlipidemia, etc. are risk factors that induce acute cerebral infarction [8]. Acute cerebral infarction is characterized by high morbidity and mortality, which will not only increase the burden on families, but also affect the quality of life of patients. A previous study has shown that Chinese medicine has a good curative effect on acute cerebral infarction, and can effectively improve the neurological function of patients [9]. According to the syndrome characteristics, this disease belongs to the category of "apoplexy" in traditional Chinese medicine. Although the occurrence and pathogenesis of apoplexy are complicated, it is mostly caused by the obstruction of meridians due to the failure of water to nourish wood, the incompetency of yin to control yang, hyperactivity of liver yang, hyperactivity of yang transforming wind and disturbance of wind yang to clear orifices. Treatment should be based on the basic principles of eliminating phlegm, smoothing liver Yang and wind, promoting blood circulation, dredging collaterals, restoring consciousness and inducing resuscitation [10].

Some cytokines released by neurons and axons of patients with cerebral ischemia have chemotaxis, which can promote the migration of white blood cells from blood vessels to ischemic brain tissues and stimulate the inflammatory response of the body. At the same time, inflammatory reaction will also damage the blood vessel wall and cause platelet aggregation, which will make the blood vessel wall form unstable plaque. The common inflammatory indexes are MCP-1 and MMP-9. As for MCP-1, it can induce and activate monocytes/macrophages, which is closely related to inflammatory reaction. Besides, MMP-9 can help neutrophils pass through basement membrane and induce inflammatory reaction [11]. Clinically, the coagulation function of the body is often judged by evaluating the levels of FIB, PT and APTT. The results of this study showed that the levels of MCP-1 and MMP-9 in the two groups were markedly decreased after treatment, and the levels of MCP-1 and MMP-9 in B group were obviously lower than those in A group. It showed that ginkgolide is usefully in treating acute cerebral infarction and can effectively improve the level of inflammatory factors in patients. Moreover, flavonoids in ginkgo biloba extract can not only reduce the concentration of malondialdehyde (MDA) in neurons, but also alleviate the lipid peroxidation between oxygen free radicals and unsaturated fatty acids in biofilm. It can also significantly increase the activity of superoxide dismutase (SOD), increase the speed of scavenging

oxygen free radicals, relieve the inflammatory reaction of the body, and improve the coagulation function of patients [12]; Ginkgolide B can inhibit the nuclear translocation of nuclear factor κB, prevent the activation of inflammatory bodies of natural immune factor NLRP3, reduce the level of inflammatory factors in cerebral ischemia area, and alleviate brain tissue injury induced by ischemia. It can also obviously promote the production of anti-platelet activating factor (PAF), inhibit platelet aggregation and improve the coagulation function of the body [13].

In view of the fact that the increase of PSV in ACI patients is not conducive to the smooth circulation of microcirculation and the establishment of collateral circulation, it may enlarge the scope of local infarction and further aggravate the patient's condition. Common hemorheological indexes include some related to erythrocyte aggregation, namely, PSV and HCT. Among them, the aggregation index of red blood cells usually indicates the aggregation degree of red blood cells, thus reflecting the viscosity of blood, and the higher the aggregation index is calculated, the thicker the blood is formed. HCT refers to the percentage of red blood cells in plasma volume, and the larger the value is calculated, the more viscous the blood is formed. The results of this study showed that the levels of erythrocyte aggregation index (PSV and HCT) in patients of the two groups were clearly reduced after treatment, with those in B group were distinctly lower as compared with A group. It thus manifested that ginkgolide can effectively regulate the level of hemorheology in patients with acute cerebral infarction. Besides, ginkgo biloba extract can obviously prolong the recalcification time of the body, slow down the increase rate of blood viscoelasticity, reduce the maximum viscoelasticity of blood, and effectively improve the hemorheology of patients. Likewise, ginkgolide can not only improve the deformability of red blood cells, dilute the blood viscosity of patients, but also maintain the sufficient blood supply in infarcted areas. It can also stimulate the production of vascular endothelial relaxing factor, dilate cerebral vessels, reduce vascular resistance, increase cerebral blood flow, and effectively improve the cerebral hemorheology level of patients [14].

To sum up, ginkgolide has a good therapeutic effect on acute cerebral infarction, which can improve the level of inflammatory factors and coagulation function, and promote the recovery of hemorheology.

Acknowledgement

Not applicable.

Conflict of Interest

The authors declare no conflicts of interest.

Author Contributions

Conceptualization, Data curation, L.G.Z and N.S; Formal analysis, N.A; Methodology, L.A and L.Y.Z; Writing-Original draft, L.G.Z and J.L.M; Writing-review and editing, J.F.K; All authors have read and agreed to the published version of the manuscript.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee, and the patients were informed and consented.

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Availability of Data and Materials

The data presented in this study are available on request from the corresponding author.

Supplementary Material

Not applicable.

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