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Original Research Article

Efficacy of diterpene ginkgolide meglumine injection in convalescent cerebral infarction and hemorheology

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Abstract

Purpose: *To investigate the effect of diterpene ginkgolide meglumine injection (DGMI) compared to betahistine in convalescent cerebral infarction (CI).*

Methods: *80 convalescent patients with CI from March 2021 and March 2022 were randomly grouped into control and study groups comprising 40 participants each. Control and study groups received 20 mg betahistine and 25 mg DGMI respectively in 250 mL normal saline for 1 week. The efficacy, National Institute of Health Stroke Scale (NIHSS) score, hemorheology, and adverse effects were investigated in control and study groups*

Results: *Total effective rate was significantly higher in study group compared to control group ($p < 0.05$). Also, the National Institute of Health Stroke Scale (NIHSS) score, plasma viscosity (PV), whole blood reduced viscosity, fibrinogen (FIB), erythrocyte aggregation index (EAI), and incidence of adverse effect were significantly lower in study group compared to control group ($p < 0.05$).*

Conclusion: *Administration of DGMI to patients in the recovery period of CI improves neurological deficit, and average blood flow velocity in the brain, and reduces the incidence of adverse effects. Further studies with larger sample sizes and multi-center approaches will be required to validate these findings.*

Keywords: *Diterpene ginkgolide meglumine injection, Cerebral infarction recovery period, Clinical efficacy, Hemorheology*

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INTRODUCTION

Cerebral infarction (CI) is mainly caused by the interruption of blood supply to the brain due to a variety of factors, thus inducing cerebral ischemia [1-3]. According to incomplete epidemiological statistics, the incidence of CI in China exceeds 1.2 / 100,000, and approximately 2 million new patients are added every year [4]. Compared with developed countries, morbidity and mortality of CI in China ranked among the highest in the world, and it has become a serious medical challenge. The recovery period of CI ranged from two weeks to six months after onset. Because the disease is usually acute, patients experience sudden fainting, loss of consciousness, speech impairment, and intellectual disability. Most patients face clinical manifestations such as slurred speech, hemiplegia, numbness of limbs, and even cognitive dysfunction after acute treatment. Therefore, treatment in the recovery period is extremely important. Clinical trials have reported that the active ingredients of *Ginkgo biloba*, such

as flavonoids and salmon, exert unique pharmacological effects and have a significant effect on improving cerebral circulation. In recent years, preparations of *Ginkgo biloba* extract have been widely used in clinical settings, such as Ginkgo Damo injection, Shuxuening injection, and Ginkgo biloba extract injection (Ginaton), all with varying pharmacological effects [5,6]. Diterpene ginkgolides meglumine injection (DGMI), which belongs to the 4th generation of Ginkgo preparations, has been proven to be safe and effective in treating CI. It mainly contains ginkgolide A, B, and K, which activate blood circulation and remove blood stasis [7,8]. Since 2012, it has been used in clinical treatment of CI. At present, some clinical studies have reviewed its efficacy and safety, but no consistent conclusion has yet been reached. This study aimed to investigate the effectiveness of DGMI in treating CI convalescence and its effect on the hemorheology of patients.

METHODS

Participants

A total of 80 convalescent patients with CI from March 2021 and March 2022 were randomly assigned to control and study groups comprising 40 participants each. Participants and their families voluntarily signed the informed consent form. This study was carried out after approval from the ethics committee of Anhui Second People's Hospital, China (approval no. R-2024-032) and conducted in accordance with the guidelines of the Declaration of Helsinki [9].

Inclusion criteria

Adult patients whose symptoms were all consistent and had been clinically diagnosed as CI, in the recovery period of CI, complied with the relevant diagnostic criteria in traditional Chinese medicine, having the syndrome of phlegm and blood stasis obstruction, and complete clinical data.

Exclusion criteria

The presence of abnormal liver and kidney function or autoimmune system disease, presence of bleeding or bleeding tendency, presence of mental illness or history of a similar genetic disease.

Treatments

Control group received 20 mg betahistine alone in 250 mL normal saline administered intravenously for 1 week. The study group received 25 mg DGMI (National Drug approval no Z20120024) in 250 mL normal saline administered intravenously for 1 week. During this period, both groups received appropriate rehabilitation treatment, stopped vasodilators and anticoagulants, and were given antihypertensive and hypoglycemic drugs as appropriate

Evaluation of parameters/indices

Clinical efficacy

Clinical efficacy was classified as *Markedly Effective* (ME): All relevant clinical symptoms disappear, which may last for 5 weeks; Effective (E): Related clinical symptoms improved, and may last for 5 weeks, and *Ineffective* (I): Clinical symptoms do not change, but the disease tends to worsen. The clinical effective rate (ER) was chosen using Eq 1.

$$ER = (ME+E/N)100 \quad \ldots\ldots\ldots\ldots\ldots (1)$$

Where N is total cases

National Institute of Health Stroke Scale (NIHSS) score

The National Institute of Health Stroke Scale (NIHSS) was used to assess neurological functions such as consciousness, speech, gaze, facial paralysis, limb movement, sensation and vision with a full score of 42 points. The scores were directly proportional to the degree of defect. A score < 1 was normal, 1 – 4 (mild neurological impairment), 5 – 15 (moderate neurological impairment), 16 – 20 (moderately severe neurological impairment) and > 20 (severe neurological impairment).

Hemorheology

Plasma viscosity (PV), whole blood reduced viscosity, fibrinogen (FIB), and erythrocyte aggregation index (EAI) were evaluated before and after treatment.

Adverse effects

The adverse events in all patients (such as nausea, vomiting, dry mouth, dizziness, fatigue, and palpitations) were recorded in detail and compared between groups.

Data analysis

Data was analyzed using Statistical Packages for Social Sciences (SPSS 26.0 IBM, Armonk, NY, USA). Categorical data were presented in mean ± standard deviation (SD) and compared using

the student t-test. Count data were expressed as percentage (%), and compared using the chi-square test (χ^2). $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

There was no statistical difference in baseline characteristics of the participants in both control and study groups ($p > 0.05$; Table 1).

Clinical efficacy

The total effective rate in study group was significantly higher compared to control group ($p < 0.05$) (Table 2).

Neurological deficit

There was no statistical difference in NIHSS scores of the two groups before treatment ($p > 0.05$). However, the NIHSS score was significantly lower in study group compared to control group ($p < 0.05$) (Table 3).

Hemorheology

There was no significant difference in PV, FIB, and EAI in both groups before treatment ($p > 0.05$). However, after treatment, PV, FIB, and EAI significantly reduced in study group compared to control group ($p < 0.05$; Table 4).

Table 1: Baseline characteristics (%, mean ± SD) (n = 40 in each group)

Characteristic	Sub-characteristic	Study	Control	χ^2/t	*P*-value
Sex	Male	24	23	0.202	0.653
	Female	16	17		
Age (years)	Range	47-81	40-85		
	Average	61.40±10.68	61.08±10.71	0.134	0.894
The course of disease (weeks)	Range	2-11 years	15-188		
	Average	35.98±21.48	34.58±19.56	0.305	0.761
Hospital stays	Range	6-14	6-14		
	Average	8.29±1.88	9.14±2.13	1.892	0.062
Complications	Hypertension	34	16	0.984	0.805
	Hyperlipidemia	9	6		
	Diabetes	28	12		
	Coronary heart Disease	1	0		

Table 2: Clinical efficacy (%)

Class	Study	Control	χ^2	*P*-value
Markedly effective	15	11		
Effective	23	20		
Ineffective	2	9		
Total effective rate	95.00	77.50	5.165	0.023

Table 3: NIHSS scores (mean ± SD, n = 40 in each group)

Category	Study	Control	*T*-value	*P*-value
Before treatment	15.52±3.51	15.12±3.45	0.514	0.609
After treatment	6.15±1.86	9.56±2.14	7.606	<0.001

Table 4: Hemorheology indices before and after treatment (mean ± SD)

Category		Study	Control	*T*-value	*P*-value
Before treatment	PV (mPa/s)	2.41±0.63	2.38±0.59	0.220	0.826
	Whole blood reduced viscosity (mPa/s)	12.45±1.83	12.57±1.94	0.285	0.776
	FIB (g/L)	3.12±0.67	3.18±0.85	0.588	0.558
	EAI (%)	3.23±0.81	3.17±0.99	0.297	0.767
After treatment	PV (mPa/s)	1.18±0.23	1.89±0.48	8.437	<0.001
	Whole blood reduced viscosity (mPa/s)	9.01±1.73	10.68±2.44	3.531	0.001
	FIB (g/L)	2.27±0.51	2.98±0.72	7.601	<0.001
	EAI (%)	2.18±0.37	2.91±0.65	6.173	<0.001

Adverse effects

The incidence of adverse effects was significantly lower in study group compared to control group ($p < 0.05$) (Table 5).

Table 5: Incidence of adverse events (%)

Adverse effect	Study	Control	χ^2	P-value
Nausea	1	2		
Vomit	0	3		
Dry mouth	0	1		
Dizziness and Fatigue	0	1		
Heart palpitations	1	2		
Total incidence	5.00	22.50	5.165	0.023

DISCUSSION

Since the 21st century, the clinical incidence of CI has been rising. Atherosclerosis and thrombosis are the pathological causes of CI, with increasing morbidity and mortality rates. A large number of microthrombi appear in the brains of CI patients. Western medical treatment of CI includes promoting the repair of cerebral vascular endothelial cells, improving local tissue blood supply using antioxidants, anticoagulants, and antithrombotic drugs, reducing blood viscosity, and stabilizing plaques. Traditional Chinese medicine believes that CI belongs to the category of stroke. Due to emotional disturbance, smoking, drinking, fatigue, internal injury, and other stimuli may occur outside the cerebral arteries [10,11]. Therefore, this study investigated the effect of diterpene ginkgolides meglumine injection (DGMI) compared to betahistine in convalescent cerebral infarction (CI). The results revealed that the total effective rate in study group was higher, and NIHSS score and incidence of adverse reactions were lower.

Brain tissue necrosis occurs in patients with cerebral ischemia, and the disease will continue to deteriorate the brain tissue over time, leading to dysphagia and cognitive impairment. Betahistine has a high-quality curative effect on CI, improves clinical symptoms, promotes neurological function recovery, and helps patients recover their activities and self-care ability. It is commonly used in Western medicine for treating CI, improving microcirculation, promoting blood reperfusion in cerebral ischemic regions, and preventing thrombosis and cerebral edema by inhibiting plasma coagulation and platelet inhibition [12,13]. Diterpene ginkgolides meglumine injection (DGMI) is a new type of synthetic preparation in traditional Chinese medicine. The solution is yellow or colorless and it activates blood circulation. The main component is ginkgolide, which has antithrombotic and antiplatelet aggregation effects. After drug administration, there is an improvement in brain tissue hypoxia and ischemia, local cerebral blood vessels, and blood circulation [14,15]. Furthermore, it inhibits platelet activity, protects platelet endothelial function, reduces inflammatory mediators, inhibits lipid peroxidation, removes free radicals, and protects brain cells [16]. Some scholars have also highlighted that betahistine is an H1 receptor agonist [17], which not only causes heart and cerebral blood vessels, but also reduces blood viscosity, prevents excessive platelet aggregation, and improves blood flow. Kinetic indicators need to be monitored to avoid the formation of thrombus due to poor blood flow or too viscous blood. Combined treatment of ginkgo biloba extract improves therapeutic effect with minimal incidence of adverse effects. Blood viscosity also improved significantly, thus a change in blood viscosity is employed as a therapeutic evaluation parameter in clinical treatment. According to the theory of traditional Chinese medicine, deficiency of *qi* and blood is the pathological basis of CI, and mucus and blood stasis are intertwined during the development of the disease. Clinical treatment should focus on dispelling blood stasis, dredging collaterals, and resuscitating phlegm. Diterpene ginkgolides meglumine injection (DGMI) is rich in ginkgo biloba components, which promote blood circulation, remove blood stasis, and dredge meridians in patients with central CI [18]. At the same time, modern pharmacological studies have shown that the drug is rich in ginkgolides A, B, C, and K and has a good anti-platelet aggregation effect [19]. In addition, the drug inhibits mitochondrial apoptosis and affects NF-κB. Down-regulation of B cell receptor signaling pathway effectively inhibits oxidative stress response, thereby inhibiting neuronal apoptosis, which plays a role in neuronal protection [20]. The results indicated that PV, whole blood reduced viscosity, FIB, and EAI of group B after treatment were lower, similar to previous study results [21].

Limitations of this study

This study had some limitations which include a small sample size and insufficient diversity.

CONCLUSION

Administration of DGMI improves neurological deficit, and average blood flow velocity in the

brain, promotes physical recovery, and improves treatment effectiveness with minimal adverse effects. Further studies with larger sample sizes and a multi-center approach will be required to validate these findings.

DECLARATIONS

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Ethical approval

This study was approved by the Ethics Committee of Anhui Second People's Hospital, China (approval no. R-2024-032).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We certify that the work in question was performed by the author(s) identified in this article. All claims referring to claims related to the material in this paper will have to be borne by the writers.

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