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Study on the improvement effect of edaravone combined with Ginkgo biloba extract on neurological function after interventional therapy of cerebral infarction

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ABSTRACT

Objective: To study the effect of edaravone combined with Ginkgo biloba extract on neurological function after interventional therapy of cerebral infarction. **Methods:** A total of 152 cases of patients with acute cerebral infarction who received interventional therapy in Mianyang Central Hospital between May 2013 and September 2016 were retrospectively analyzed and divided into intervention group and control group, intervention group received routine treatment combined with edaravone and Ginkgo biloba extract treatment after interventional therapy, and control group received routine medical treatment after interventional therapy. 3 d, 7 d, 14 d after therapy, serum was separated, and the levels of neural function injury markers, oxidative stress products, antioxidant enzymes and platelet activation indexes were determined. **Results:** 3 d, 7 d and 14 d after treatment, serum UCH-L1, GFAP, NSE, S100B, ROS, GMP-140, PAC-1 and CD62p contents of intervention group were significantly lower than those of control group while CAT, SOD and GSH-PX contents were significantly higher than those of control group. **Conclusion:** Edaravone combined with Ginkgo biloba extract can reduce neurological injury and promote neurological function recovery after interventional therapy of cerebral infarction, and this effect is related to the reduction of oxidative stress and inhibition of platelet activation.

1. Introduction

Acute cerebral infarction is a clinical emergency with high morbidity and mortality rates, and effective intervention can recover the blood perfusion of ischemic brain tissue in time and furthest reduce ischemia hypoxia damage to nerve function. There is different degree of cerebral ischemia hypoxia injury in cerebral infarction patients before interventional therapy, and also the ischemia-reperfusion injury caused by intervention treatment, so there is still different degree of nerve function defect in patients with cerebral infarction in convalescence stage after interventional therapy, and the medical assistance and exercise are needed to promote the recovery and reconstruction of neural function[1,2]. Edaravone is an effective oxygen free radical scavenger that can effectively remove the excessively generated oxygen free radicals in the course of cerebral infarction and reduce oxidative stress damage to nerve function[3]; Ginkgo biloba extract includes ginkgo flavone glycosides, ginkgolide and other compositions, and it not only has antioxidant properties, but can also inhibit platelet activation and improve the blood perfusion of ischemic brain tissue[4,5]. In the following study, the improvement of edaravone combined with ginkgo biloba extract application after interventional therapy of cerebral infarction on the neurological function was analyzed.

2. Information and methods

2.1 Case information and grouping

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A total 152 cases of patients with acute cerebral infarction who received interventional therapy in Mianyang Central Hospital between May 2013 and September 2016 were selected as the research subjects, the medical records of all the patients were reviewed, and according to the application of edaravone combined with ginkgo biloba extract therapy after interventional treatment, the patients were divided into intervention group and control group. Intervention group, a total of 68 cases, received routine treatment combined with edaravone and Ginkgo biloba extract treatment after interventional therapy, including 42 male cases and 26 female cases that were 42-68 years old; the control group, a total of 84 cases, received routine medical treatment after interventional therapy, including 52 female cases and 32 female cases that were 45-70 years old. The two groups of patients were not significantly different in general data (P>0.05).

2.2 Therapy

Both groups of patients received routine drug treatment and rehabilitation exercise after interventional therapy, and drug treatment included lowering lipid, lowering blood pressure, reducing blood glucose as well as improving circulation, neurotrophy and anti-platelet aggregation. Intervention group, based on conventional drug treatment, received edaravone combined with ginkgo biloba extract therapy, which was as follows: 30 mg edaravone injection in 250 mL saline injection, by intravenous drip, 1 time/d; 20 mL Ginkgo biloba injection in 250 mL saline injection, by intravenous drip, 1 time/d. Both groups of patients received treatment for 14 consecutive days.

2.3 Serum index detection methods

3 d, 7 d and 14 d after treatment, 5 mL peripheral venous blood was collected from two groups of patients, anti-coagulated with EDTA and centrifuged to separate serum, then enzyme-linked immunosorbent assay kits were used to determine UCH-L1, GFAP, NSE, S100B, GMP-140, PAC-1 and CD62p levels, and the ROS, CAT, SOD and GSH-PX levels were determined by radioimmunoprecipitation kits.

2.4 Statistical methods

SPSS 19.0 software was used to input and process data, measurement data analysis between two groups at the same point in time was by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1 Postoperative serum nerve injury marker molecule levels

3 d, 7 d and 14 d after treatment, analysis of serum nerve injury marker molecules UCH-L1 (ng/L), GFAP (ng/L), NSE (pg/L) and S100B (pg/L) levels between two groups of patients was as follows: serum UCH-L1, GFAP, NSE and S100B contents of intervention group were significantly lower than those of control group. Differences in serum UCH-L1, GFAP, NSE and S100B contents were statistically significant between two groups of patients 3 d, 7 d and 14 d after treatment (P<0.05). Specific data were shown in Table 1.

3.2 Postoperative serum oxidative stress product and antioxidant enzyme levels

3 d, 7 d and 14 d after treatment, analysis of serum oxidative stress product ROS (μmol/L) as well as antioxidant enzymes CAT (U/L), SOD (U/L) and GSH-PX (U/L) between two groups of patients was as follows: serum ROS contents of intervention group were significantly lower than those of control group while CAT, SOD and GSH-PX contents were significantly higher than those of control group. Differences in serum ROS, CAT, SOD and GSH-PX contents were statistically significant between two groups of patients 3 d, 7 d and 14d after treatment (P<0.05). Specific data were shown in Table 2.

3.3 Postoperative serum platelet activation index levels

3 d, 7 d and 14 d after treatment, analysis of serum platelet

Table 1.

Postoperative serum nerve injury marker molecule levels of two groups of patients.

Groups	n	Time point (d)	UCH-L1	GFAP	NSE	S100B
Intervention group	68	3	85.52±9.34*	21.34±3.52*	15.62±2.25*	0.93±0.12*
		7	71.24±8.38*	14.58±1.94*	10.28±1.89*	0.77±0.08*
		14	64.52±8.91*	10.24±1.32*	7.32±0.93*	0.53±0.07*
Control group	84	3	110.32±14.56	29.65±4.58	22.28±3.28	1.35±0.18
		7	102.54±12.49	24.52±3.24	17.71±2.59	1.14±0.16
		14	88.44±10.38	20.12±2.94	12.55±1.95	0.89±0.11

*: comparison between intervention group and control group at the same point in time, P<0.05.

Table 2.

Postoperative serum oxidative stress product and antioxidant enzyme levels of two groups of patients.

Groups	*n*	Time point (d)	ROS	CAT	SOD	GSH-PX
Intervention group	68	3	5.62±0.89*	26.48±4.51*	40.29±7.76*	52.49±6.74*
		7	3.02±0.44*	36.79±5.12*	55.62±7.91*	67.39±8.31*
		14	1.69±0.24*	58.68±7.39*	72.49±9.34*	80.33±10.25*
Control group	84	3	8.21±1.04	19.38±2.16	28.75±4.16	37.58±5.62
		7	5.68±0.84	25.25±3.58	37.54±6.02	46.49±7.13
		14	4.26±0.56	40.21±5.74	48.49±7.29	56.59±7.39

*: comparison between intervention group and control group at the same point in time, $P<0.05$.

activation indexes GMP-140 (μg/L), PAC-1 (mg/L) and CD62p (mg/L) levels between two groups of patients was as follows: serum GMP-140, PAC-1 and CD62p contents of intervention group were significantly lower than those of control group. Differences in serum GMP-140, PAC-1 and CD62p contents were statistically significant between two groups of patients 3 days, 7 days and 14 days after treatment ($P<0.05$). Specific data were shown in Table 3.

4. Discussion

The significance of adjuvant drug therapy after interventional therapy of cerebral infarction is to promote the neural functional recovery. In the study, edaravone combined with ginkgo biloba extract was applied for adjuvant treatment after interventional therapy of cerebral infarction, and in order to specify the value of the auxiliary solution for treatment of cerebral infarction, serum contents of nerve injury marker molecules were analyzed after treatment so as to reflect the recovery of neural function. UCH-L1 is a type of cysteine hydrolase in neuronal cytoplasm, and NSE is metabolic enzymes involved in glycolysis in neuronal cytoplasm[6]; GFAP is the filamentous protein in astrocytes and participates in the composition of the cytoskeleton, and S100B is the protein adjusting the calcium ion homeostasis in astrocytes, microglia and other cells[7,8]. In the course of cerebral infarction, ischemic injury can cause UCH-L1, GFAP, NSE and S100B release from neurons and glial cells into the blood circulation and become the symbol to reflect nerve function damage. Comparison of serum nerve injury marker molecules between the two groups showed that 3 d, 7 d and 14 d after treatment, serum UCH-L1, GFAP, NSE and S100B contents of intervention group were significantly lower than those of control group. This means that after interventional therapy of cerebral infarction, the application of edaravone combined with ginkgo biloba extract for auxiliary treatment has improving effect on the neural function, and can promote neural functional recovery and reduce nerve injury.

The ginkgo flavone glycosides in edaravone and ginkgo biloba extract have oxygen free radical scavenging and anti-oxidative injury effect[9,10]. Oxidative stress reaction is an important factor causing neural function injury after cerebral infarction, and both ischemia hypoxia and hypoxia reoxygenation processes will result in increased formation of oxygen free radical, cause oxidation reaction of lipid, protein, nucleic acid and other compositions in nerve tissue, and thus cause neurological damage[11]. CAT, SOD and GSH-PX are the important antioxidant enzymes in local tissue, SOD and GSH-PX can reduce ROS into H_2O_2, the latter is reduced into water under the action of the CAT and discharged out of the body[12]. In the pathological conditions of massive ROS generation in patients with cerebral infarction, the antioxidant enzymes in the local tissue will be continuously consumed, the content reduces, and the oxygen radical scavenging ability is weakened[13,14]. In the study, the analysis of the content of above oxidative stress product and antioxidant enzymes showed that 3 d, 7 d and 14 d after treatment, serum ROS contents of intervention group were significantly lower than those of control group while CAT, SOD and GSH-PX contents were significantly higher than those of control group. This means that after interventional therapy of cerebral infarction, the application of edaravone combined with ginkgo biloba extract for auxiliary treatment can effectively remove oxygen free radicals, reduce the consumption of antioxidant enzymes, and thus alleviate oxidative

Table 3.

Postoperative serum platelet activation index levels of two groups of patients.

Groups	*n*	Time point (d)	GMP-140	PAC-1	CD62p
Intervention group	68	3	104.61±14.48*	43.56±6.72*	29.33±4.52*
		7	78.45±9.35*	27.83±4.15*	10.12±1.63*
		14	35.51±5.52*	16.20±2.27*	7.64±0.94*
Control group	84	3	157.52±22.17	58.75±8.12	36.66±5.27
		7	114.25±14.86	40.36±6.25	21.24±3.52
		14	83.15±10.25	24.51±3.58	16.53±2.18

*: comparison between intervention group and control group at the same point in time, $P<0.05$.

stress injury to nerve function.

The ginkgolide in ginkgo biloba extract has antiplatelet effect, which antagonizes the platelet-activating factors to inhibit platelet aggregation, and then improve the blood perfusion of ischemic brain tissue[15,16]. In the progression of cerebral infarction, platelet activation and aggregation are the important pathological links causing arterial occlusion and blood flow interruption, and a variety of molecules on the platelet surface are closely related to its activation process. GMP-140 is the membrane protein specifically expressed on the surface of activated platelet, and can mediate inflammatory cells and platelet adhesion, and promote platelet aggregation and thrombosis[17]; PAC-1 is the glycoprotein epitope exposed in the process of platelet activation and conformation change, and it can promote the formation of platelet-fibrinogen complex[18]; CD62p is the membrane receptor located on the platelet surface, and it promotes platelet and endothelium adhesion through interaction with ligands CD24 and PSGL1[19]. In the study, analysis of the contents of the platelet activation indexes showed that 3 d, 7 d and 14 d after treatment, serum GMP-140, PAC-1 and CD62p contents of intervention group were significantly lower than those of control group. This means that after interventional therapy of cerebral infarction, the application of edaravone combined with ginkgo biloba extract for auxiliary treatment can effectively inhibit platelet activation, thereby inhibit thrombosis and improve the blood perfusion of ischemic brain tissue.

In conclusion, edaravone combined with Ginkgo biloba extract can reduce neurological injury and promote neurological function recovery after interventional therapy of cerebral infarction; this effect of edaravone combined with Ginkgo biloba extract is related to reducing oxidative stress, enhancing antioxidant capacity and inhibiting platelet activation.

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