

# Effects of Ginkgo Biloba Extract Inhaled with Oxygen on Serum VEGF, SOD and MDA Levels in Patients with Acute Cerebral Infarction

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**Abstract:** Purpose To investigate the effects of levels of vascular endothelial growth factor (VEGF), superoxide dismutase (SOD) and malondialdehyde (MDA) in the serum of acute cerebral infarction by fibrinolytic enzyme combined with ginkgo biloba extract with oxygen inhalation. Methods It were selected that 106 patients with acute cerebral infarction who visited the hospital from January 2014 to December 2015, All the patients were divided into study group and control group according to the treatment method and 53 cases in each group. Both groups were treated with conventional therapy and fibrinolytic enzyme therapy. The study group was given ginkgo biloba extract inhaled with oxygen while the control group was given pure oxygen inhalation. It was detected that the levels of VEGF, SOD and MDA in Serum before and after treatment. Results It was no significant difference that the levels of VEGF, SOD and MDA in serum before treatment in two groups ( $P > 0.05$ ). It was higher that levels of VEGF and SOD in Serum after treatment than before in the two groups, and MDA levels were lower than before ( $P < 0.05$ ). After treatment, it was higher that VEGF and SOD levels in the study group than those in the control group, and MDA levels were lower than in the control group ( $P < 0.05$ ). Conclusion It can effectively increase the levels of VEGF and SOD, and reduce the level of serum MDA via fibrinolytic enzyme combined with ginkgo biloba extract ad-jointed oxygen inhalation in the treatment of acute cerebral infarction

**Keywords:** Cerebral infarction; Fibrinolytic enzyme; Ginkgo biloba extract; Vascular endothelial growth factor subclass; Superoxide dismutase; Malondialdehyde

## 1. Introduction

It was increasing year by year that the clinical incidence of acute cerebral infarction due to the increasing of the aged population in China. Studies have shown that a high rate of disability and death of cerebral infarction and about 50% patients is caused by the cerebral artery lumen of the patients narrow or occluded due to the thrombosis or atherosclerosis in the blood supply artery of the brain [1]. on account of insufficient blood supply and oxygen supply to the local brain and brain tissue necrosis. The therapies are to reduce intracranial pressure, vascular recanalization, prevention stop thrombosis regeneration. At present, it is Ultra early intravenous thrombolysis which effective method for the treatment of cerebral infarction, but this method has strict contraindication and suitable. Fibrinolytic enzyme has strong antithrombotic function and can prevent the aggravation of cerebral infarction. Ginkgo biloba extract is medicine which often used in clinical treatment of coronary atherosclerosis. In

this study, It observed the effects of serum vascular endothelial growth factor (VEGF), superoxide dismutase (SOD) and malondialdehyde (MDA) levels on patients with acute cerebral infarction treated that patients were treated with fibrinolytic enzyme combined with ginkgo biloba extract with oxygen inhalation.

## 2. Materials and Methods

### 2.1. Clinical data

It is selected 106 cases of acute cerebral infarction treated in Handan central hospital from January 2014 to December 2015. All patients were divided into study group and control group and 53 cases in each group according to the treatment method. There were 29 male and 24 female cases, aged (49 ~ 72 (58) 3 + 8.5); There were 31 cases of basal ganglia infarction. 11 cases of Lacunar cerebral infarction, 11 cases multiple cerebral infarction. The control group included 28 males and 25 females, aged 48 ~ 73(58.8 + 8.1), There were 30 cases

of basal ganglia infarction, 12 cases of cerebral infarction and 11 cases of multiple cerebral infarction. There was no significant difference between the two groups in gender, age, infarct type and other aspects ( $P > 0.05$ ).

## 2.2. Criteria for case selection

**Inclusion criteria** all patients were in line with the "diagnosis of various cerebrovascular diseases" in urgency Diagnostic criteria for cerebral infarction and CT /MRI imaging examination confirmed cerebral infarction lesions .the onset time was less than 24 h at the time of visit; they did not receive treatment related to cerebral infarction at first onset and recently. all patients signed by myself or my family members and had the informed consent approved by the ethics committee.

**Exclusion criteria** they had Other diseases of the blood system (such as coagulation disorders, etc.). they had diseases related to drug absorption and excretion (such as severe liver and kidney dysfunction, other intestinal diseases); they had allergy of the drug such as fibrinolytic enzyme, ginkgo biloba extract and others; they had other tumor diseases (such as lung cancer, liver cancer, etc.)

**Methods:** both groups were given conventional treatment and fibrinolytic enzyme. Routine treatment: blood pressure adjustment, electrolyte balance maintenance, symptomatic treatment, hypoglycemia. Plasmin therapy: it was intravenously drip for 2 h and continued for 2 weeks that plasmin for injection (sihuan pharmaceutical co, LTD.) 100 U add the 0.9% sodium chloride injection. Study Group administered ginkgo biloba extract with oxygen inhalation. Ginkgo biloba extract drops (German Dr. Willmar Schwabe GmbH & amp; Co) 30ml of drug oxygen solution was dissolved in 150ml distilled water and added to the humidified bottle. The medical oxygen

was combined with the atomizer damper to fully mix the oxygen and drugs. The atomized mouth was contained in the patient's mouth and inhaled at a low oxygen flow rate of 1.5 L/min for 30 min. The control group was given oxygen inhalation alone and all were the same as the study group.

**Serological detection method:** 5ml of elbow venous blood was extracted on an empty stomach in the morning, and centrifuged at 3000 r/min for 20 min after 30 min. The supernatant was taken to measure VEGF, SOD and MDA levels in both groups. it was detected by elisa that Serum VEGF, SOD and MDA levels. VEGF detection kit is provided by Shanghai fengshou industrial co. LTD. SOD detection kit is provided by Shanghai jimian industry co. LTD. MDA testing kits are provided by Beijing bomex technology development co. LTD. Three methods of serological indexes were operated in strict accordance with the manufacturer's instructions.

**1.5 statistical methods** it was used to analyze the data that SPSS 22.0 statistical software. The measurement data were expressed as mean standard deviation ( $\bar{x} \pm s$ ), and t test was used for the comparison between groups.  $\alpha = 0.05$  is the test level.

**Consequence:** there was no statistically significant difference in serum VEGF, SOD and MDA levels between the two groups before treatment ( $P > 0.05$ ). serum VEGF and SOD levels were increased and serum MDA levels were decreased in the two groups after treatment ( $P < 0.05$ ). serum VEGF and SOD levels in the study group were higher than those in the control group, and serum MDA levels were lower than those in the control group After treatment ( $P < 0.05$ ).

**Table 1. Serum index levels ( $\bar{x} \pm s$ ) before and after acute cerebral infarction**

Group	Number of cases	Time	Vegf (pg/ml)	Sod (U/ml)	Mda (nmol/L)
Study Group	53	Before treatment	300.26±30.25	78.12±12.36	7.04±0.72
		After treatment	370.26±56.68 ac	105.26±18.05 ac	4.32±0.52 ac
Control group	53	Before treatment	312.32±28.94	76.42±12.09	6.94±0.71
		After treatment	342.16±39.55 a	92.26±12.05 a	5.36±0.63 a

Note: ginkgo biloba extract was given oxygen inhalation therapy in the study group, and pure oxygen inhalation therapy was given in the control group. compared with before treatment,  $P < 0.05$ ; Compared with the control group after treatment,  $P < 0.05$ .

## 3. Discussion

Fibrinolytic enzyme is an exogenous proteolytic enzyme extracted from snake venom, which can reduce blood viscosity, enhance fibrinolytic activity, and resist platelet aggregation, so as to improve cerebral microcirculation and dissolve arterial thrombosis [2]. Fibrinolytic enzyme is a single-chain zinc metalloproteinase, which belongs to fibrinolytic drugs. It has a high affinity with fibrinogen in arterial thrombosis. it can prevent thrombosis from

forming again By directly degrading fibrinolytic protein, dissolving thrombus and reducing blood viscosity. Fibrinolytic enzyme can also activate fibrinogen to form fibrinolytic enzyme and promote thrombolysis. Fibrinolytic enzyme has enough time to reach the thrombus position and play the role of thrombolysis because it has a long half-life. Fibrinolytic enzyme can avoid hemorrhagic complications to some extent as it does not activate the fibrinolytic system. Foreign studies have reported that a2-antifibrinolytic inhibitor can improve the efficacy of fibrinolytic enzyme, but it has not been confirmed and recognized [3].

Inhalation of ginkgo biloba extract with oxygen is a treatment method combining traditional Chinese and western medicine, which belongs to drug oxygen therapy. This method enables drugs to improve blood circulation

and nerve function by being absorbed in the alveoli in the form of sols, rapidly reaching the thrombolytic site with the blood and increasing the blood oxygen content. Ginkgo biloba extract contains terpene, flavonoid glucoside and other components, it mainly through the following ways to play a therapeutic role in patients with acute cerebral infarction. it has reduce cerebral ischemia reperfusion injury, prevent cerebral edema, restore brain cell function. it can improve the brain microcirculation, promote the release of neurotransmitters and functional recovery; it can reduce the cytotoxicity of activated platelets, to prevent its adhesion and aggregation; It can inhibit the inflammatory reaction [4]. Guo qiang [5] found that ginkgo biloba extract has a better neuron protective effect on patients with cerebral infarction and reduce the neurological function score of patients in his study.

VEGF increase vascular permeability and promote angiogenesis. It is significantly higher than that of normal people which the serum VEGF content in patients with acute cerebral infarction, which means that the stress of VEGF in the body increases and promotes the generation of new blood vessels, accompanied by the symptoms of ischemia and hypoxia. Increased stress of VEGF level can maintain the integrity of vascular endothelial cells, protect endothelial cells, and increase collateral circulation blood flow due to the control and improvement of cerebral ischemia in patients after treatment. He jian-ming et al [6]. found that serum VEGF level is still higher, which is more conducive to the recovery of patients with cerebral infarction in their study. SOD is an important antioxidant enzyme to eliminate oxygen free radicals in vivo. MDA is a lipid peroxide product that reflects the degree of damage by oxygen free radicals in body cells. The gradual decrease of SOD content is due to the presence of more oxygen free radicals, the consumption of a large number of antioxidant enzymes, and the increased damage of oxygen free radicals, and the gradual increase of MDA content in patients with acute cerebral infarction [7]. The results of this study showed that there was no significant difference in serum VEGF, SOD and MDA levels between the two groups before treatment. After treatment, it was suggested that both treatment methods had a certain effect on patients, because the serum VEGF and SOD levels were higher than before, and the serum MDA level was lower than it

## References

[1] Kwon J.Y., Kwon S.U., Kang D.W., et al. Isolated lateral thalamic infarction: the role of posterior cerebral artery disease. *Eur J Neurol*. 2012, 19, 265.

[2] Jiang Li, Wang Lijun, Zhao Lan, et al. Effect and significance of plasminase on plasma thromboprecursor protein levels in patients with acute cerebral infarction. *Journal of Clinical Neurology*. 2015, 28, 140-142.

[3] Lee K.N., Jackson K.W., Christensen V.J., et al. Enrichment of property by insigation of nature of publication  $\alpha$ 2-antiplasmin. *Thromb Haemost*. 2011, 9, 987-996.

[4] Zheng Xijie, Xu Yun. Research progress in the treatment of acute cerebral infarction with ginkgo biloba extract. *Journal of Chinese and Western Medicine Combined with Cardio Cerebrovascular Disease*. 2014, 12, 617-618.

[5] Guo Qiang. Effect observation of ginkgo biloba extract combined with alantil in the treatment of 60 cases of acute cerebral infarction. *Journal of Baotou Medical College*. 2015, 31, 60-61.

[6] He Jianming, Li Yurong, Wei Yingxiu, et al. Study on the effect of cerebral heart tong capsule on serum Vegf and Mda levels in patients with acute cerebral infarction. *Chinese and Western Medicine Combined with Cardiovascular Complications*. 2012, 10, 54-56.

[7] Kang Zengjun, Wang Fang, Cui Lei, et al. Breviscapine treatment of 68 cases of acute cerebral infarction and its effect on serum sod and mda content. *Shaanxi Traditional Chinese Medicine*. 2013, 34, 798-799.

