CLINICAL RESEAPCH

**Therapeutic Effect of lipoic Acid Injection Intointo Patients with Cerebral Infarction and its Effects on Inflammatory Factors and Oxidative Stress**

Yuting Lu1 and Xibin Zhao1,\*

1Jiaxing Hospital of Traditional Chinese Medicine

**Keywords**

Lipoic acid,Cerebral infarction, Inflammatory factors, Oxidative stress

**Correspondence**

Xibin Zhao, Jiaxing Traditional Chinese Medicine Hospital, No. 1501, Zhongshan East Road, Xinxing Street, Nanhu District, Jiaxing City, Zhejiang Province.

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**Abstract**

**Objective** To analyze thetherapeutic effect of lipoic acid injection on patients with cerebral infarction and its effects on inflammatory factors and oxidative stress. **Methods** A total of 110 patients with cerebral infarction who were treated in our hospital from June 2018 to June 2020 were selected as the research subjects. All the 110 patients were randomly divided into observation group (n=55) and control group (n=55) according to the random number table method. The patients in the control group were treated with routine therapy, while those in the observation group were treated with lipoic acid injection on the basis of the control group. The clinical efficacy, levels of inflammatory factors [interleukin-6 (IL-6), interleukin-8 (IL-8), soluble intercellular adhesion molecule-1 (sICAM-1)] and oxidative stress indexes [total antioxidant capacity (T-AOC), malondialdehyde (MDA)] were compared between the two groups. **Results** The total effective rate of the observation group was significantly higher than that of the control group (*P*<0.05). After treatment, the levels of IL-6, IL-8 and sICAM-1 in the two groups were significantly lower than those before treatment (*P*<0.05), and the levels of IL-6, IL-8 and sICAM-1 were greatly lower in the observation group than those in the control group (*P*<0.05). Also, after treatment, the level of T-AOC (*P*<0.05) and MAD (*P*<0.05) in the two groups were significantly higher and lower than those before treatment (*P*<0.05), respectively. Noticeably, the levels of T-AOC (*P*<0.05) and MDA (*P*<0.05) were greatly higher and lower in the observation group than those in the control group, respectively. **Conclusion** Lipoic acid injection was effective in treating patients with cerebral infarction, as it could not only reduce the release of inflammatory factors, but also improve the oxidative stress response of the body and promote the recovery of brain tissues.

**Introduction**

Cerebral infarction, also known as ischemic stroke, will result in brain blood circulation disorders, causing brain tissue ischemia, hypoxic necrosis or softening. Patients with cerebral infarction may appear coma, hemiplegia, language difficulties, and other nervous system functions that seriously affect the life quality of patients [1]. At present, the clinical treatments of patients with cerebral infarction are mainly conventional treatments such as improvement of cerebral blood circulation and anti-infection. Although these methods have shown great effect during clinical practice, the incidence of adverse drug reactions is still high [2], thus, it is necessary to explore more effective therapeutic drugs for the management of patients with cerebral infarction. As a strong antioxidant, lipoic acid can significantly attenuate the symptoms of cerebral edema in rats and the apoptosis of nerve cells to improve the nerve function of the rats [3]. In order to further explore the role of lipoic acid in patients with cerebral infarction, this study applied lipoic acid injection therapy on the basis of conventional treatment, aiming to improve the quality of clinical treatment and the prognosis of patients with cerebral infraction. The results of the study are reported as follows.

**Materials and methods**

**General information**

**The research subjects**

The 110 patients with cerebral infarction who were treated in our hospital from June 2018 to June 2020 were selected as the research objects, and they were divided into observation group and control group by random number table method, with each group containing 55 cases. In the control group, there were 27 male cases and 28 female cases aged 50-75 years old, with an average age of 63.24±7.55 years old and time from onset to consultation of 2-18 hours (average time of 12.30±4.16 hours). In observation group, there were 29 male patients and 26 female patients aged between 50 and 75 years old, with an average age of 62.78±7.38 years old and time from onset to consultation of 3-20 hours (average time of 12.98±4.72 hours). This study was approved by the Medical Rthics Committee of our hospital. All the patients volunteered to participate in the study and signed informed consent. The two groups of patients were not statistically different in gender, age, or time from onset to consultation (P>0.05), thus, the data of the patients were comparable.

**Inclusion and exclusion criteria**

Inclusion criteria: patients diagnosed with cerebral infarction after clinical diagnosis [4]. Exclusion criteria: those who fall into a coma and cannot cooperate with treatment; those who have serious diseases in important organs such as heart, liver, and kidney; those who have had brain diseases such as brain tumors, brain trauma, and cerebral hemorrhage; those who were allergic to the drugs used in this study.

**Methods**

① Control group: application of conventional treatments such as lowering intracranial pressure, regulating blood pressure, maintaining water and electrolyte balance, antiplatelet, improving blood circulation and anti-infection; ② observation group: application of intravenous infusion of lipoic acid on the basis of control group (250 mg of lipoic acid mixed with 100 ml of normal saline). The injection was performed once a day for a total of 4 weeks of treatment.

**Clinical efficacy**

The National Institutes of Health Stroke Scale (NIHSS) was employed to evaluate the degree of neurological deficits [5]. According to the degree of decrease in the NIHSS scores before and after treatment, the clinical efficacy was divided into four categories, namely, cured (the patient’s NIHSS score drops >90%), markedly effective (the patient’s NIHSS score drops between 46~91%), effective (the patient’s NIHSS score drops between 18~45%) and ineffective (the patient’s NIHSS score drops <18%). The total Effective rate = (cured + markedly effective + effective) number of cases / total number of cases × 100%.

**Observation indicators**

Before and after treatment, 5 ml of venous blood was collected from all the patients in a fasting state in the early morning, and the serum was separated after centrifugation to detect the level of inflammatory factors and evaluate the antioxidant capacity of the patients. For inflammatory factors, enzyme-linked immunosorbent method assay (ELISA) was performed to detect the serum levels of interleukin-6 (IL-6), interleukin-8 (IL-8), and soluble intercellular adhesion molecule-1 (sICAM-1). For oxidative stress indicators, O-phenanthroline colorimetry and the thiobarbituric acid colorimetric method were used to determine the serum levels of total antioxidant capacity (T-AOC) and malondialdehyde (MDA).

**Statistical methods**

SPSS 20.0 was used for statistical analysis. The count data were compared by 2 test, and the measurement data were expressed by mean ± standard deviation (¯x±s). The data comparison was conducted using t test, and P<0.05 was considered as statistically significant.

**Results**

**Comparison of clinical efficacy between the two groups** The total effective rate of the observation group was 94.55%, and that of the control group was 72.73%. The total effective rate of the observation group was significantly higher than that of the control group (P<0.05), see Table 1.

Table 1 Comparison of clinical efficacy between the two groups [n(%)]

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Groups | Cases | Cured | Markedly effective | Effective | Ineffective | Total effective rate |
| Observation group | 55 | 24（43.64） | 15（27.27） | 13（18.18） | 3（5.45） | 52（94.55） |
| Control Group | 55 | 12（21.82） | 20（36.36） | 8（14.55） | 15（27.27） | 40（72.73） |
| *c2* |  |  |  |  |  | 9.565 |
| *P* |  |  |  |  |  | 0.002 |

**Comparison of the levels of inflammatory factors between the two groups before and after treatment**

Before treatment, there was no significant difference in the levels of IL-6, IL-8 and sICAM-1 between the two groups (P>0.05). However, after treatment, the levels of IL-6, IL-8 and sICAM-1 in the two groups were significantly lower than those before treatment (P<0.05), and the levels of IL-6, IL-8 and sICAM-1 in the observation group were noticeably lower than those in the control group (P<0.05), see Table 2.

Table 2 Comparison of the levels of inflammatory factors between the two groups before and after treatment（¯x±s）

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Groups | Cases | IL-6 (ng/L) | *t* | *P* | IL-8 (ng/L) | *t* | *P* | sICAM-1 (ng/mL) | *t* | *P* |
| Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Observation group | 55 | 107.39±12.57 | 58.42±8.34 | 24.075 | 0.000 | 154.61±21.73 | 75.53±13.47 | 22.939 | 0.000 | 285.78±26.45 | 213.65±17.64 | 16.826 | 0.000 |
| Control Group | 55 | 105.48±12.16 | 74.67±10.28 | 14.350 | 0.000 | 156.14±22.14 | 121.74±17.34 | 9.072 | 0.000 | 286.57±26.95 | 245.27±21.75 | 8.844 | 0.000 |
| *t* |  | 0.810 | -9.104 |  |  | -0.366 | -15.608 |  |  | -0.155 | -8.374 |  |  |
| *P* |  | 0.420 | 0.000 |  |  | 0.715 | 0.000 |  |  | 0.877 | 0.000 |  |  |

**Comparison of the oxidative stress indexes between the two groups before and after treatment**

Before treatment, there was no significant difference in T-AOC and MDA levels between the two groups (P>0.05). However, after treatment, the T-AOC levels in the two groups were greatly higher than before treatment (P<0.05), and the MDA levels were significantly lower than before treatment (P<0.05). Moreover, the T-AOC level of the observation group was significantly higher than that of the control group (P<0.05), and the MDA level was noticeably lower than that of the control group (P<0.05), see Table 3.

Table 3 Comparison of oxidative stress indexes between the two groups before and after treatment（¯x±s）

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Groups | Cases | T-AOC（U/mL） | *t* | *P* | MDA(mmol/L) | *t* | *P* |
| Before treatment | After treatment | Before treatment | After treatment |
| Observation group | 55 | 9.72±3.13 | 21.78±4.02 | -17.555 | 0.000 | 3.75±0.63 | 2.38±0.38 | 13.810 | 0.000 |
| Control Group | 55 | 10.15±3.26 | 15.82±3.91 | -8.260 | 0.000 | 3.63±0.61 | 3.08±0.43 | 5.465 | 0.000 |
| *t* |  | -0.706 | 7.882 |  |  | 1.015 | -9.047 |  |  |
| *P* |  | 0.482 | 0.000 |  |  | 0.312 | 0.000 |  |  |

**Discussion**

Cerebral infarction accounts for about 70% of all stroke cases, with high morbidity and disability, and it is also an important cause of death to patients. It has been reported [6] that the pathological process of brain injury in patients with cerebral infarction is related to inflammation and oxidative stress. Cerebral infarction will promote the release of inflammatory cytokines, accompanied with the induced production of chemokines and adhesion molecules, to activate white blood cells, causing inflammatory immune cells to invade brain injury tissues, thereby triggering inflammatory response. In addition, a large amount of oxygen free radicals will be produced after cerebral infarction and result in overload of calcium ions in nerve cells, triggering acidosis and promoting cell apoptosis, thus further aggravating brain damage. The interaction of inflammation and oxidative stress together will seriously affects the prognosis of patients. Therefore, controlling inflammation and anti-oxidative stress is the key for clinical treatment of cerebral infarction.

Lipoic acid is a coenzyme existing in the mitochondria, with a high electrophilicity and strong ability to scavenge oxygen free radicals. Lipoic acid has been widely used in the clinical treatment of diabetes and its chronic complications. Evangelos Agathos et al [7] used lipoic acid to treat patients with diabetic neuropathy, and found that it can effectively reduce neuropathy symptoms and improve patients’ quality of life. In an animal study, Yang Liu et al [8] treated brain-injured mice with lipoic acid, and observed that the drug can inhibit oxidative stress and inflammation, showing a better protective effect on the mouse brain tissues. To further expand the scope of clinical treatment of lipoic acid, this study applied lipoic acid injection in the clinical treatment of patients with cerebral infarction. It was found that the therapeutic effect of the drug on the cerebral infarction patients was noticeably better than the conventional treatment of using cerebral infarction alone. This may be related to the functions that lipoic acid could relieve oxidative stress and controlling inflammation.

In order to explore the mechanism of lipoic acid in the oxidative stress response of patients with cerebral infarction, we measured the patient's T-AOC and MDA levels to assess oxidative stress response in patients’ bodies. T-AOC is a clinical indicator that reflects the body's total antioxidant capacity. MDA, which is the final product of lipid peroxides and an important factor leading to cell senescence and death, is often used to assess the degree of damage to tissue cells. The results of this study showed that lipoic acid injection can increase the level of T-AOC in patients with cerebral infarction and reduce the level of MDA, with a degree of improvement significantly better than that of using conventional treatment alone. This indicated that lipoic acid injection has good antioxidant properties in protecting brain tissues. According to previous reports [9], lipoic acid can easily penetrate the blood-brain barrier, effectively remove active oxygen free radicals, can also chelate metal ions, repair oxidized proteins, and promote endogenous and exogenous antioxidants such as vitamin C, and regenerate glutathione, thereby alleviating oxidative stress and reducing brain damage.

A number of studies have shown [10,11] that due to increased oxidative stress response in patients with cerebral infarction, the serum levels of IL-6, IL-8, and sICAM-1 in patients also increase correspondingly, and this is related to certain neurological deficits in patients to some extent. IL-6, IL-8, and sICAM-1 play important roles in the body's inflammatory response. Among them, IL-6 has a variety of biological activities and is an important pro-inflammatory factor that induces the body's inflammatory response. sICAM-1 is a kind of adhesion molecule that promote the aggregation and adhesion of white blood cells. IL-8, which is mainly produced by T lymphocytes and macrophages, participates in inflammation and also regulates adhesion molecules, promote the adhesion between endothelial cells and white blood cells, thus further enhancing inflammation reaction. After treatment with lipoic acid injection, the levels of IL-6, IL-8, and sICAM-1 in the patients with cerebral infarction were significantly reduced. This is similar to the results of Shaafi S et al [12] who indicated that lipoic acid injection has a better anti-inflammatory effect. Lipoic acid can not only improve inflammation by reducing oxidative stress, but also restore blood perfusion disorders in neurotrophic blood vessels, improve nerve conduction velocity, reduce endothelial vascular damage, accumulation and adhesion of white blood cells, inflammatory factors and adhesion molecules, thereby further improving the inflammatory response and promoting the recovery of brain tissues.

In summary, lipoic acid injection is effective in treating patients with cerebral infarction, as it could reduce the release of inflammatory factors improve the body's oxidative stress response and promote brain tissue recovery.

**Declaration of conflict-of-interest**

The authors declare no conflict-of –interest.

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