Mechanism of Sodium aescinate combined with Torasemide for cerebral hemorrhage treatment

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Objective: To observe the mechanism of Sodium aescinate combined with Torasemide for cerebral hemorrhage treatment and offer clinical help to cerebral hemorrhage treatment.

Methods: 86 patients with cerebral hemorrhage were selected and randomly divided into groups: the observation group (43 people) and the control group (43 people). The patient in the control group were treated with conventional therapy and the patients in the observation group were treated with Sodium aescinate combined with Torasemide on the basis of conventional therapy. Oxidative stress indexes [Glutathione peroxidase (GSH-Px), catalase (CAT), malondialdehyde (MDA), superoxide dismutase (SOD)], serum inflammatory factors [interleukin-6 (IL-6), interleukin-2 (IL-2), C reactive protein (CRP) and tumor necrosis factor-α (TNF-α)] and hemorheology indexes [Hematokrit (PCV), plasma viscosity (PV), erythrocyte aggregation index (PAdT) and whole blood viscosity at high shear rate (WHV)] were detected and analyzed before and after treatment.

Results: The comparison of oxidative stress indexes, serum inflammatory factors and hemorheology indexes in the two groups before treatment were not statistically significant (P>0.05). Serum inflammatory factors (TNF-α, IL-6, CRP), MDA and hemorheology indexes (WHV, PV, PCV and PAdT) in both groups after treatment significantly decreased compared with that before treatment (P<0.05); Oxidative stress index (GSH-Px, CAT, SOD and MDA) and IL-2 in both groups after treatment significantly increased compared with that before treatment (P<0.05). Serum inflammatory factors (TNF-α, IL-6, CRP), MDA and hemorheology indexes (WHV, PV, PCV and PAdT) in observation group after treatment decreased more significantly than that in control group (P<0.05), and oxidative stress index (GSH-Px, CAT, SOD and MDA) and IL-2 increased more significantly than that in control group (P<0.05). Conclusions: Sodium aescinate combined with Torasemide could decrease the oxidative stress and inflammatory reaction in patients with cerebral hemorrhage, which is beneficial to improving the condition of circulating blood stasis, accelerating microcirculation. So it has a very important clinical significance of the treatment to cerebral hemorrhage.

1. Introduction

Cerebral hemorrhage is a common acute neurosurgical instance[1]. Brain edema will appear after cerebral hemorrhage, producing a large number of toxins and constricting the brain nerves. Then, the changes of inflammatory reaction, oxidative stress reaction and hemorheology indexes will occur[2]. With the aging of our population, the incidence of cerebral hemorrhage increases year by year. So, the clinical treatment of cerebral hemorrhage plays an important role[3]. In this research, through studying the influences of Sodium aescinate combined with Torasemide on oxidative stress indexes, serum inflammatory factors and hemorheology indexes, we aimed to provide help for the clinical treatment of cerebral hemorrhage.
2. Materials and methods

2.1. General information

86 cases of cerebral hemorrhage from September 2013 to June 2016 in our hospital were selected. According to the random number table method, 86 cases patients were divided into two groups, the observation group and the control group. In the observation group, there were 43 patients (25 males and 18 females), aged from 55 to 70 years old. The duration from onset of symptoms to admission was 1–12 h, with an average of (4.4±1.8) h. Arterial pressure on admission was 85–160 mmHg, with an average of (132±25) mmHg. Hematoma volume of the patients were 15–60 mL, which was detected by Cranial CT, with an average of (29±17) mL. In the control group, there were 43 patients (23 males and 20 females), aged from 55 to 70 years old. The duration from onset of symptoms to admission was 1–12 h, with an average of (4.2±2.0) h. Arterial pressure on admission was 85–160 mmhg, with an average of (137±19) mmHg. Hematoma volume of the patients were 15–60 mL, which was detected by Cranial CT, with an average of (31±19) mL.

2.2. Exclusion and inclusion criteria

All patients were consistent with the diagnosis standard of the “Guidelines for the Diagnosis of Cerebral Hemorrhage” published in 2006 and all the patients were entirely awake. There was no difference in the age, sex, disease duration, severity of illness and physical condition between two groups (P>0.05). All patients had no diseases of heart, liver, lung, immune system, blood and endocrine system. Cerebral hemorrhage caused by cardiogenic, trauma, arteritis and blood diseases were excluded. Every patients could cooperate with relevant treatment actively, and were not allergic to related drugs. This study was approved by the ethics committee of our hospital, and the patients or their families signed the informed consent.

2.3. Treatment method

The control group was performed micro invasive removal of intracranial hematoma. At the same time they were given decreasing intracranial pressure, blood control, brain protective agent, dehydration, maintaining electrolyte balance, and other routine treatment. The observation group was given β-Sodium aescinate injection (Chinese medicine standard word: H20023112, Shandong City Lyve Pharmaceutical Co. Ltd.), 15 mg β-Sodium aescinate+0.9% sodium chloride, 1 time a day, intravenous injection. And Torasemide (Chinese medicine standard word: H20052493, Nanjing City Zhengke Pharmaceutical Co. Ltd), taken orally, 20 mg per time, 1 time a day, which was on the basis of conventional therapy. The treatment period of the 2 groups was 4 weeks.

2.4. Blood sample collection

5 mL of fasting peripheral venous blood of cerebral hemorrhage patients in two groups were collected before treatment and 4 weeks after treatment. And then the related indexes were detected by clinical laboratory.

2.5. Detection of related factors

Glutathione peroxidase (GSH-Px), catalase (CAT), malondialdehyde (MDA), superoxide dismutase (SOD) and interleukin-6 (IL-6), interleukin-2 (IL-2), C reactive protein (CRP) and tumor necrosis factor-α (TNF-α) were detected by ELISA kits. The kits were purchased from Hangzhou Hua'an Biological Technology Co., Ltd.; Becton, Dickinson and Company of America; Jiangsu Jingmei Biological Technology Co., Ltd; Thermo Fisher Scientific company and Merck Drugs & Biotechnology of Germany. Enzyme standard instrument (Experimental Equipment Co., Ltd. Nanjing Germany iron, model number: HBS-1096A) was used to detect the absorbance OD value at 450 nm. And then, the corresponding concentration value was calculated by the standard curve. The operation process was performed according to the instruction strictly.

2.6. Detection of hemorheology

Hematokrit (PCV), plasma viscosity (PV), erythrocyte aggregation index (PAdT) and whole blood viscosity at high shear rate (WHV) were detected using full automatic blood rheology detector (Beckman Coulter, model number: DxA 800). The operation process was performed according to the instruction strictly.

2.7. Statistical analysis

SPSS 21.0 statistical package was conducted for statistical analysis. Oxidative stress indexes, hemorheology indexes and inflammatory factors were described as mean ± standard deviation. Intergroup comparison was conducted by t test. Values of P<0.05 were considered to be statistically significant.

3. Results

3.1. Comparison of hemorheology in the two groups before and after treatment

Analysis and comparison of hemorheology indexes, WHV, PV, PCV and PAdT in cerebral hemorrhage patients were conducted. The comparison of hemorheology in the two groups before treatment was not statistically significant (P>0.05). Hemorheology indexes, WHV, PV, PCV and PAdT, though the treatment of Sodium aescinate combined with Torasemide, in observation group after treatment significantly decreased compared with that before treatment (P<0.05). Hemorheology indexes (WHV, PV, PCV and PAdT) in control group after treatment significantly decreased (P<0.05). Hemorheology indexes (WHV, PV, PCV and PAdT) in observation group after treatment decreased more significantly than that in control group (P<0.05) (Table 1).

3.2. Comparison of inflammatory factors in the two groups before and after treatment
Analysis and comparison of inflammatory factors, TNF-α, IL-6, CRP and IL-2 in cerebral hemorrhage patients were conducted. The comparison of inflammatory factors in the two groups before treatment was not statistically significant (p>0.05). Inflammatory factors, TNF-α, IL-6, CRP significantly increased, while IL-2 significantly increased in observation group though the treatment of Sodium aescinate combined with Torasemide (p<0.05). Inflammatory factors, TNF-α, IL-6, and CRP in observation group after treatment decreased more significantly than that in control group, while IL-2 in observation group after treatment increased more significantly than that in control group (p<0.05) (Table 2).

3.3. Comparison of oxidative stress indexes in the two groups before and after treatment

Analysis and comparison of oxidative stress indexes (GSH-Px, CAT, SOD and MDA), in cerebral hemorrhage patients were conducted. The comparison of oxidative stress indexes in the two groups before treatment was not statistically significant (p>0.05). Oxidative stress indexes, GSH-Px, CAT, SOD significantly increased, while MDA significantly decreased in observation group though the treatment of Sodium aescinate combined with Torasemide (p<0.05). Oxidative stress indexes, GSH-Px, CAT, and SOD significantly increased, while MDA significantly decreased in control group after treatment (p<0.05). Oxidative stress indexes, GSH-Px, CAT, and SOD in observation group after treatment increased more significantly than that in control group, while MDA in observation group after treatment decreased more significantly than that in control group (p<0.05) (Table 3).

4. Discussion

Cerebral hemorrhage, a common acute neurosurgical instance, common in elderly, is caused by rupture of the blood vessels in the non-traumatic brain parenchyma[4]. Forcing, emotion will cause the disease, which has the features of high mortality, poor prognosis and high disability rate[5]. Brain parenchyma of the patients will be compressed by hematoma after cerebral hemorrhage, which cause the ischemia and edema response. Then cytotoxic edema, blood brain barrier damage, cell gap osmotic pressure change occur[6], which lead to the change of inflammation, oxidative stress, and hemorheology. Survivors often left different levels of cognitive impairment, movement disorders, speech disorders and other sequelae. This disease endangers the life and health, social communication of patients seriously[7]. Reducing the incidence of edema and mortality in patients with cerebral hemorrhage and controlling the development of this disease are of important clinical significance[8]. With the aging of our population and the development of our society, the number of patients with high blood lipids, hypertension, diabetes, and vascular aging increases rapidly, which makes the incidence of cerebral hemorrhage increasing year by year. So, the timely and effective treatment of cerebral hemorrhage plays an important role[9].

This study found that Sodium aescinate combined with Torasemide can improve effectively serum inflammatory factors (TNF-α, IL-6, CRP and IL-2), hemorheology indexes (WHV, PV, PCV and PAdT).

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<th>Table 1</th>
<th>Comparison of hemorheology in the two groups before and after treatment (n=43, t±s)</th>
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Compared with control group before treatment, *p<0.05; compared with control group after treatment, *p<0.05.

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<th>Comparison of inflammatory factors in the two groups before and after treatment (n=43, t±s)</th>
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Compared with control group before treatment, *p<0.05; compared with control group after treatment, *p<0.05.

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Compared with control group before treatment, *p<0.05; compared with control group after treatment, *p<0.05.
and oxidative stress indexes (GSH-Px, CAT, SOD and MDA) on patients with cerebral hemorrhage. And the effect of observation group is superior to the effect of control group[10]. TNF-α, IL-6 and CRP are the important pro-inflammatory factors[11]. IL-2 is the important anti-inflammatory factor, which can inhibit the aggravation of inflammatory reaction[12]. After cerebral hemorrhage, related inflammatory cells will be activated. And then, a large number of free radicals will be produced by reduced coenzyme II oxidase, which causes the death of brain cells, promotes the occurrence of edema and destruction of blood brain barrier[13]. SOD can promote the oxidation of cell membrane, which produces the promotion of MDA. GSH-Px, CAT and SOD will be consumed because of the excessive free radical production[14]. Torasemide is a new effect loop diuretics, which has an effect on diuresis and the discharge of Na⁺ and Cl⁻. And then, brain osmotic pressure can be relieved; Brain edema can be improved[15]; and the severity of the disease can be reduced. All these fundamentally improve the inflammatory reaction and oxidative stress reaction. Sodium aescinate, with anti-permeability effect, can prevent the aggravation of brain edema and can resist the decrease of ATP content[16]. And then, the production of TNF-α will be inhibited, and the release of phospholipase A2 will be reduced, which prevents the expression of IL-6 and CRP. Sodium aescinate can stimulate anterior pituitary and adrenal cortex, then sodium aescinate combined with Torasemide were detected in the research. Also the mechanism of Sodium aescinate combined with Torasemide for the treatment of mycoplasm pneumonia in patients was discussed. This study provides help for the clinical treatment of cerebral hemorrhage.

In conclusion, the influence on hemorheology indexes (WHV, PV, PCV and PAdT), oxidative stress indexes (GSH-Px, CAT, SOD and MDA), and the serum inflammatory factors (TNF-α, IL-6, CRP and IL-2) in cerebral hemorrhage patients with the treatment of sodium aescinate combined with Torasemide were detected in the research. The also mechanism of Sodium aescinate combined with Torasemide for the treatment of mycoplasma pneumonia in patients was discussed. This study provides help for the clinical treatment of cerebral hemorrhage.

References