



Effect of edaravone torasemide treatment on elderly patients with acute cerebral hemorrhage

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ABSTRACT

Objective: To observe the effect of edaravone torasemide treatment on acute cerebral hemorrhage in elderly patients. **Methods:** A total of 100 patient with acute intracerebral hemorrhage senile patient were selected and randomly divided into groups: the combined group (50 people) and the control group (50 people). The senile patients in the control group were treated with conventional therapy and the senile patients in the combined group were treated with edaravone combined with torasemide and conventional therapy. Inflammatory, coagulation function and hemorheology were compared before and after seven days therapy. **Results:** Before treatment, inflammatory, coagulation function and hemorheology of two groups showed no statistically significant difference. Inflammatory (IL-6, IL-8, CRP, and TNF- α) and hemorheology (WLV, WMV, WHV, PV, and PCV) of two groups decreased significantly than before treatment ($P<0.05$), coagulation function (PT, APPT) of two groups increased significantly than before treatment ($P<0.05$); Coagulation function (PT, APPT) and hemorheology (WLV, WMV, WHV, PV, and PCV) of the combined groups after treatment increased significantly than control group after treatment ($P<0.05$), inflammatory (IL-6, IL-8, CRP, and TNF- α) and FIB of the combined groups after treatment decreased significantly than control group after treatment ($P<0.05$). **Conclusions:** Edaravone combined with torasemide can perfect effectively inflammatory, coagulation function and hemorheology on senile patient acute intracerebral hemorrhage, it has important clinical significance for senile patient acute intracerebral hemorrhage treatment.

1. Introduction

Acute cerebral hemorrhage is a serious brain disorder, the mortality rate is as high as 40%, survivors after treatment are often stay in some degree of cognitive impairment, movement disorders, language disorders and other complications, which impact the patients' daily life and health seriously[1,2]. The subsided physical function, lowered immunity and weak physical recovery in elderly patients make the acute cerebral hemorrhage clinical treatment more difficult in older patients. Looking for the right clinical treatment of elderly patients with acute cerebral hemorrhage becomes

particularly important[3,4]. This study explored the influence of edaravone torasemide on the inflammatory factors, blood rheology and coagulation levels in elderly patients with acute cerebral hemorrhage to provide help for the treatment of acute cerebral hemorrhage.

2. Materials and methods

2.1. General information

This study was approved by the hospital ethics committee agreed and signed by the patient after informed consent in their implementation. A total of 100 elderly patients with acute cerebral hemorrhage treated in our hospital from May 2014 to March 2016 were selected, and divided into two groups with random number

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table: the combination group and the control group, of which 50 patients in the combined group (30 males, 20 females), aged 60 to 75 years, mean ages (68.6±8.1) years, 20 patients with the base section bleeding, 15 patients with cerebellar hemorrhage and 15 patients with thalamic hemorrhage; And 50 patients in the control group (28 males, 22 females), aged 61 to 75 years, mean ages (69.0±7.7) years, 24 patients with the base section bleeding, 13 patients with cerebellar hemorrhage and 13 cases with thalamic hemorrhage.

2.2. Inclusion and exclusion criteria

All patients were confirmed by CT or MRI and were in line with diagnostic criteria of cerebral hemorrhage and conscious; There was no difference in the age, sex aspect, the amount of bleeding, post time, the severity of the surgery, the physical condition and other aspects of the two groups ($P>0.05$), so the patients had no other heart, intestine, kidney, liver, lung, endocrine disease, and all patients could actively cooperate with related treatment and no treatment related allergies; There were detailed information before treatment. This study was approved by the hospital ethics committee agreed, and signed by the patient or their families after informed consent in their implementation.

2.3. Therapeutic method

Two groups of older patients with acute cerebral hemorrhage were both implemented; The control group were treated with minimally invasive hematoma while giving oxygen, brain-protecting agent to control blood pressure and other conventional treatments. Joint group of patients were treated with intravenous injection of edaravone (Zhunzi: H20031342, Nanjing Pharmaceutical Co., Ltd. Harbinger TECO) 30 mg/times, 2 times/day and torasemide (Zhunzi: H20052493, Nanjing pharmaceutical Co., Ltd.) orally 10 mg/times, 1 time/day based on the treatment in the control group, the two groups of patients were treated for 1 week.

2.4. Blood sample collection

A total of 5 mL peripheral blood were extracting before and after 7 days of treatment in the control group and the combined group of patients, and related indicators were detected.

2.5. Inflammation factors detection

Interleukin-6 (IL-6), interleukin-8 (IL-8), C-reactive protein

(CRP) and tumor necrosis factor- α (TNF- α) were measured by enzyme-linked immunosorbent assay. The enzyme-linked kits provided by the Shanghai biological technology Co., Ltd, Jiangsu crystal biotechnology Co., Ltd and Shanghai Institute enzyme biotechnology Co., Ltd.

Corresponding concentration of the standard curve was calculated. Absorbance OD values were measured at 450 nm by ELISA analyzer (German Rail Nanjing experimental equipment Co., Model: HBS-1096A).

2.6. Blood rheology detection

Automatic blood rheology detector (beckman coulter, models: DxH 800) was used to detect patients' packed cell volume (pcv), plasma viscosity (PV), high shear whole blood viscosity (WHV), whole blood viscosity cut (WMV) and whole blood viscosity at low shear (WLV).

2.7. Test of blood coagulation function

Automated coagulation analyzer (Sysmex, Japan, Model: CA-510) was used to detect prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen concentration (FIB).

2.8. Statistical Methods

SPSS18.0 statistical software was used for statistical relevant analysis, data were expressed as mean±standard deviation. The comparison between groups and within groups of the combination group and the control group was conducted by *t*-test. There were significant differences when $P<0.05$.

3. Results

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

Before treatment, there was no significant difference in hemorheological indexes of two groups ($P>0.05$); the hemorheology WLV, WMV, WHV, PV and PCV levels of combined group after combined treatment were significantly reduced ($P<0.05$); the hemorheology WLV, WMV, WHV, PV and PCV levels of the control group after treatment were significantly reduced ($P<0.05$); Compared with the control group after treatment, the hemorheology

Table 1

Comparison of hemorheology of two groups before and after treatment.

Groups	Time	WLV(η /mPa·s ⁻¹)	WMV(η /mPa·s ⁻¹)	WHV(η /mPa·s ⁻¹)	PV(η /mPa·s ⁻¹)	PCV(%)
Combination group	before treatment	11.55±1.21	7.83±0.77	7.31±0.35	2.16±0.24	44.83±3.17
	after treatment	7.23±0.74 [#]	4.13±0.48 [#]	4.04±0.22 [#]	1.09±0.17 [#]	29.77±2.95 [#]
Control group	before treatment	11.48±1.16	7.80±0.69	7.34±0.37	2.14±0.22	44.45±3.41
	after treatment	9.81±0.95 [*]	5.81±0.57 [*]	5.88±0.30 [*]	1.55±0.20 [*]	36.52±3.22 [*]

Note: compare with this group before treatment, * $P<0.05$; compare with the control group after treatment, # $P<0.05$.

WLV, WMV, WHV, PV and PCV levels of combination group after treatment were significantly reduced ($P<0.05$), as shown in Table 1.

3.2. Comparison of coagulation function of two groups before and after treatment

Before treatment, the difference of coagulation parameters in was not statistically significant ($P>0.05$); the coagulation parameters PT and APPT of combination group after combination therapy were increased significantly, while FIB reduced significantly ($P<0.05$); the coagulation parameters PT and APPT of control group after treatment was increased significantly, while FIB reduced significantly ($P<0.05$); compared with the control group after treatment, the coagulation parameters PT and APPT of the combined group patients after treatment increased significantly, the FIB reduced significantly ($P<0.05$), as shown in Table 2.

3.3. Comparison of inflammatory cytokines of two groups before and after treatment

Before treatment, the difference of inflammatory cytokines was not statistically significant ($P>0.05$); the inflammatory cytokines IL-6, IL-8, CRP and TNF- α levels of combined group after combination therapy were significantly reduced ($P<0.05$); the inflammatory cytokines IL-6, IL-8, CRP and TNF- α levels of the control group after treatment were significantly reduced ($P<0.05$); Compared with the control group after treatment, the inflammatory cytokines IL-6, IL-8, CRP and TNF- α levels of the combined group of patients reduced significantly ($P<0.05$), as shown in Table 3.

4. Discussion

Cerebral hemorrhage is the essence of the site due to non-traumatic brain caused by ruptured blood vessels and cause bleeding[5], the incidence ratio raise up to 30% in total stroke[6]. Acute cerebral hemorrhage is often associated with high cholesterol, hypertension, smoking, vascular aging and other closely related, emotional, stay up

late, excessive force and so often leads to acute cerebral hemorrhage, the mortality rate of acute cerebral hemorrhage can be as high as 40%[7], The survivors often leave some degree of cognitive disorders, movement disorders and language disorders and other complications, seriously affecting the patient's daily life and health[8,9]. Acute cerebral hemorrhage has been mainly happened in elderly patients, the subsided serious bodily functions, lowered immunity and weak sensitivity to inflammation and weak recovery ability of the body in elderly patients with acute cerebral hemorrhage make the treatment of elderly patients with acute cerebral hemorrhage more urgent, the more serious situation is that elderly patients with acute cerebral hemorrhage patients are often accompanied by the occurrence of a variety of complications, further exacerbating the suffering of patients, and posed a serious threat to patients' safety[10,11]. The treatment of elderly patients with acute cerebral hemorrhage patient has become a top priority for the majority of health workers.

Edaravone is a common antioxidant and free radical scavenging class of drugs[12], which has caused a wide attention since the list in Japan in 2014 for the first time. Edaravone can effectively remove free radicals, has a significant inhibition on lipid peroxidation, at the same time, which can protect reperfusion and prevent brain cell damage by peroxidation to delay brain cell death[13,14]. Edaravone can significantly improve the N-acetyl aspartate content of the brain, to protect the role of the brain[15]. Torasemide is a loop diuretic potent new class of sulfonil urinary ding, which obtained widespread attention after appearing on the market for the first time in 1993 in Belgium. Torasemide officially enter our the country in 2003, renal medullary loop of the ascending support is the main site of action of torasemide, which can effectively suppress the relevant vector system for Na⁺, K⁺ and Cl⁻ reabsorption of plasma, resulting in a concentration of NaCl in the tubular fluid increases, thus affecting the concentration process urine, playing its diuretic effect[16,17]. Compared with traditional diuretic furosemide, torasemide companion with longer duration ,stronger bioavailability a, stronger diuretic effect and electrolyte disorder occurs in a lower probability[18]. Tuo *et al* has been widely used in the treatment of various diseases and achieved a satisfactory therapeutic effect. Edaravone and torasemide have different effects; the combination of

Table 2
Comparison of coagulation function of two groups before and after treatment.

Groups	Time	PT(s)	APPT(s)	FIB(g/L)
Combination group	before treatment	12.47±1.31	32.68±3.45	4.44±0.71
	after treatment	13.55±1.28 [#]	38.40±3.78 [#]	3.38±0.58 [#]
Control group	before treatment	12.44±1.24	32.94±3.69	4.50±0.76
	after treatment	13.05±1.30 [*]	35.70±4.02 [*]	3.97±0.63 [*]

Note: compare with this group before treatment, * $P<0.05$; compare with the control group after treatment, # $P<0.05$.

Table 3
Comparison of inflammatory cytokines of two groups before and after treatment.

Groups	Time	IL-6(ng/mL)	IL-8(pg/mL)	CRP(mg/L)	TNF- α (μ g/L)
Combination group	before treatment	64.62±6.17	459.19±12.73	32.43±3.74	3.11±0.41
	after treatment	28.24±4.94 [#]	147.21±10.51 [#]	8.69±2.66 [#]	1.80±0.28 [#]
Control group	before treatment	64.51±6.08	460.55±13.28	32.58±3.58	3.18±0.44
	after treatment	40.95±5.22 [*]	191.53±11.11 [*]	15.46±3.08 [*]	2.06±0.35 [*]

Note: compare with this group before treatment, * $P<0.05$; compare with the control group after treatment, # $P<0.05$.

the two would be more conducive in the treatment of acute cerebral hemorrhage.

The study found that edaravone torasemide significantly improved the serum inflammatory cytokines (IL-6, IL-8, CRP and TNF- α), hemorheology (WLV, WMV, WHV, PV and PCV) and coagulation levels (PT, APPT and FIB) in elderly patients with acute cerebral hemorrhage and have great clinical significance in patients with acute cerebral hemorrhage in elderly patients. Acute cerebral hemorrhage often lead to inflammatory reactions, CRP is an acute inflammatory protein, which can promote neutrophil secretion of inflammatory cytokines and activate complement while; IL-6 and CRP have a synergistic effect, while IL-8 has an enhancement function in neutral neutrophils and inflammatory factors, resulting in damage to brain tissue; TNF- α can promote the synthesis and release of vasoactive related activity substances, increase the permeability of blood vessels and the release of blood[19,20]. Edaravone can eliminate free radicals caused in the blood to reduce tissue damage, thereby reducing the release of inflammatory factors. The protection of edaravone on brain tissue also reduces the release of inflammatory factors. The increased blood viscosity and enhanced coagulation function in patients with acute cerebral hemorrhage are in favor of blood clotting and reduced blood loss. Torasemide has a diuretic effect, which can reduce the water content in the blood, improve blood rheology, reduce blood pressure and reduce brain hemorrhage; Torasemide can increase sympathetic - adrenal medulla system excitability, making the catecholamine levels in blood increased and improve blood coagulation. Edaravone joint torasemide to improve inflammation and blood circulation system in elderly patients with acute cerebral hemorrhage are in favor of the treatment of acute cerebral hemorrhage.

In summary, the study examined the impact of torasemide edaravone on the influence of inflammatory cytokines (IL-6, IL-8, CRP and TNF- α), hemorheology (WLV, WMV, WHV, PV and PCV) and coagulation levels (PT, APPT and FIB) in elderly patients with acute cerebral hemorrhage and explored the mechanism of edaravone torasemide on elderly patients with acute cerebral hemorrhage, which provides important help on the treatment of acute cerebral hemorrhage.

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