Effects of Ginaton combined with batroxobin on oxidative stress, hemodynamics and coagulation in SHL patients

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Abstract

Objective: To investigate the effects of ginaton combined with batroxobin on oxidative stress, hemodynamics and coagulation in patients with sudden hearing loss. Methods: According to random data table method, 100 cases of sudden hearing loss were randomly divided into the control group (n=50) and observation group (n=50), patients in the control group were given batroxobin treatment, the observation group received ginaton combined with batroxobin therapy. The levels of oxidative stress, hemodynamics and coagulation were compared between the two groups before and after treatment. Results: The levels of WBV, HCT, PV, APTT, PT, TT, PF, SOD, LPO in the two groups before treatment were not statistically significant. After treatment, the levels of WBV, PV in the control group and observation group were respectively (5.33±0.62) mPa•s, (1.73±0.59) mPa•s and (4.07±0.55) mPa•s, (1.32±0.41) mPa•s, which were significantly lower than those before treatment, and after treatment in the observation group the levels of WBV, PV were significantly lower than the control group; After treatment, the levels of APTT, PT, TT, PF in the control group and observation group were respectively (43.75±6.15) s, (18.23±2.02) s, (15.38±2.51) s, (58.61±12.96) µg/L and (53.68±7.16) s, (24.67±4.35) s, (22.51±4.85) s, (41.47±8.63) µg/L, compared with those in the same group before treatment, the levels of APTT, PT and TT were significantly increased, PF level was significantly decreased, and in the observation group APTT, PT and TT levels were significantly higher and PF level was significantly lower than that in the control group. After treatment, the levels of SOD, LPO in the control group and observation group were respectively (101.78±10.53) nM/L, (5.91±0.95) mmol/L and (110.07±12.62) nM/L, (4.68±1.02) mmol/L, compared with those in the same group before treatment, the level of SOD were significantly increased, the level of LPO level was significantly decreased, and in the observation group LPO level was significantly lower and SOD level was significantly higher than that in the control group. Conclusion: Compared with the use of batroxobin alone, Ginaton combined with batroxobin can better reduce the stress response, improve hemodynamics and coagulation in patients with sudden hearing loss.

1. Introduction

Sudden hearing loss (SHL) refers to a sudden, unexplained sensorineural hearing loss. Its clinical features is mainly unilateral hearing loss, may be associated with tinnitus, dizziness and other symptoms[1,2]. Its incidence may be related to blood circulation disorders, autoimmune diseases and labyrinthine membrane rupture. At this stage, there is no recognized drugs for clinical treatment of SHL, but the disease could be treated by improving the inner ear circulation[3,4]. Ginaton has the function of improving blood vessel function and promoting blood circulation, which is widely used in the treatment of blood circulation disorder[5,6]. Batroxobin, as a drug that can improve circulation, has been shown to be effective in combination therapy for deafness[7]. This study was designed to investigate the effects of Ginaton combined with batroxobin on oxidative stress, hemodynamics and coagulation in SHL patients.
2. Research objects and methods

2.1 Research object

A total of 100 patients with sudden hearing loss from Nov. 2016 to June 2017 in our hospital were selected as research object, all of them were fully in accord with Sudden deaf diagnosis and treatment guidelines (Chinese Medical Association Otolaryngology Head and Neck Surgery Branch 2015 revised). Inclusion criteria: (1) no allergy history of Kinnara and Batroxobin; (2) other middle ear lesions did not occur. (3) a sudden occurrence within a few minutes, a few hours or less than 3 d. (4) The main clinical manifestations is unilateral hearing loss, may be associated with tinnitus, ear blockage, nausea, vomiting, dizziness and so on. Exclusion criteria: (1) having taken drugs that affect the blood system nearly 30 d; (2) suffering from acute and chronic inflammation, severe liver and kidney dysfunction; (3) accompanied with brain stem injury and acoustic neuroma patients; (4) suffering from endocrine diseases; (5) failed to complete the treatment according to the course of treatment, half-way off cases, and with incomplete clinical data.

Patients were divided into observation group and control group according to random data table method. There were 28 males and 22 females in the control group (a totally 50 patients); with ages of 33-61 years; the patient in control group was treated by ginaton. There were 23 males and 27 females in the observation group; with ages of 34-59 years, the patient in observation group was treated ginaton combined with batroxobin; there is no significant difference on the general information between two groups ($P>0.05$).

2.2 Treatment process

The two groups of patients received the corresponding basic treatment after hospitalization, in which the control group was given intravenous drip batroxobin injection (Jiangsu Chia Tai Pharmaceutical Co., Ltd., byua powerfulfuo H20031074) the amount of 10 BU was given for the first time, followed by the next day’s dosage of 5 BU. On the basis of the control group, the observation group was given intravenous infusion of ginaton injection (Yue Kang Pharmaceutical Group Co., Ltd., Zhunzi H20070226) 105 mg/times. Both groups were treated for 10 d to observe the improvement of each index.

2.3 Observed indicators

Blood flow dynamics, coagulation function and oxidative stress were measured before treatment and after treatment respectively. Patients were taken 10 mL venous blood in the early morning, and placed at ordinary tube set aside for a few minutes, and then centrifuged 10 min at 3 000 r/min. The supernatant was collected in the EP tube, placed in -20 ℃ refrigerator to be measured. (1) Hemodynamic parameters: plasma viscosity (PV), whole blood viscosity (WBV) and hematocrit (HCT) were detected by USCOM noninvasive hemodynamic monitor; The coagulation function: The detection of APTT, PT, PF and TT was detected by the German MC-2000 dual-channel hemagglutination assay. Test kits were purchased from Shanghai Fuxing Changzheng Medical Science Co., Ltd., the operating steps in strict accordance with the kit. (3) Oxidative stress index: The levels of lipid peroxide (LPO) and superoxide dismutase (SOD) were measured by thiobarbituric acid (TBA) colorimetric assay and xanthine oxidase colorimetric assay

2.4 Statistical analysis

SPSS 17.0 software was used for data statistical analysis. In the study, hemodynamics, coagulation function, oxidative stress and other indicators were in line with the normal distribution, and described as Mean ± SD, independent-samples t test was conducted, values of $P<0.05$ were considered to be statistically significant.

3. Results

3.1 Comparison of hemodynamic between the two groups

Hemodynamic levels in both groups before and after treatment are shown in Table 1. Before treatment, the WBV, PV and HCT levels in both groups were similar, and there was no significant difference ($P>0.05$). After treatment, the levels of WBV and PV in the control group and the observation group were (5.33 ± 0.62) mPa·s, (1.73 ± 0.59) mPa·s and (4.07 ± 0.55) mPa·s, (1.32 ± 0.41) mPa·s, respectively. The levels of WBV and PV in both groups were significantly lower than those in the same group before treatment, and the levels of WBV and PV in observation group were significantly lower than those in control group (all $P<0.05$) after treatment. Compared with those before treatment, the levels of HCT in both groups decreased after treatment, but the reduction was not significant, with no significant difference ($P>0.05$).

Table 1.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>WBV (mPa·s)</th>
<th>HCT (%)</th>
<th>PV (mPa·s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before</td>
<td>6.36±0.91</td>
<td>47.90±6.69</td>
<td>2.68±0.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Treatment</td>
<td>5.33±0.62*</td>
<td>46.82±6.25</td>
<td>1.73±0.59*</td>
</tr>
<tr>
<td>Observation group</td>
<td>50</td>
<td>Before</td>
<td>6.39±0.89</td>
<td>48.69±6.73</td>
<td>2.83±0.63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Treatment</td>
<td>4.07±0.55**</td>
<td>46.18±5.86</td>
<td>1.32±0.41**</td>
</tr>
</tbody>
</table>

Note: Compared with pre-treatment levels in the group, *$P<0.05$; Compared to post-treatment levels in the control group, **$P<0.05$. 

* Yan Zhao et al./ Journal of Hainan Medical University 2017; 23(21): 143–146
Patient’s coagulation function in two groups as shown in Table 2. Before treatment, the levels of APTT, TF, PT and PF in both groups were similar, with no significant difference ($P>0.05$). The levels of APTT, PT, TT and PF in the control group and the observation group were (43.75 ± 6.15) s, (18.23 ± 2.02) s, (15.38 ± 2.51) s, (58.61 ± 12.96) µg/L and (53.68 ± 12.62) nmol/L, respectively. Compared with the same group before treatment, the APTT, PT, TT levels in both control group and the observation group were significantly higher than those in the control group ($P<0.05$), and the PF levels were significantly lower than before treatment after treatment, the levels of APTT, TT, PT and PF in both groups were significantly decreased, and the decrease compared with the same group before treatment ($P<0.05$).

3.3 Comparison of oxidative stress between the two groups

The levels of oxidative stress before and after treatment in both groups are shown in Table 3. Before treatment, serum SOD and LPO levels in both groups were similar, with no significant difference ($P>0.05$). The levels of SOD in the control group and the observation group were (101.78 ± 10.53) nmol/L and (110.07 ± 12.62) nmol/L, respectively. LPO levels in both groups were significantly lower than those before treatment and SOD levels were significantly increased (all $P<0.05$), and the level of SOD in the observation group was significantly higher than that in the control group ($P<0.05$).

4. Discussion

With the increasing pressure of modern life, the incidence of SHL is gradually increasing clinically. At present the cause of the disease is not yet fully clear. Numerous studies show that this may be due to abnormal coagulation, fibrinolysis and anticoagulation mechanisms in vivo, resulting in patient's blood circulation disorders, lack of blood supply to the inner ear, causing tissue hypoxia, edema and metabolic disorders, and further resulting in hearing loss in the cochlea, eventually deafness[9,10]. At this point, patients should receive timely and effective treatment, otherwise it will lead to lifelong tinnitus, deafness, seriously affecting the quality of life of patients. In view of the etiology of the disease, the clinical use drugs to improve the inner ear circulation and blood coagulation for the treatment of the disease[11,12].

Batroxobin is a kind of enzyme obtained by purification from the subspecies snake venom of Brazil, and its main component is serine protease. Studies have shown that the main role of batroxobin is to disassemble fibrinogen, inhibit thrombus formation, induce the release of tissue plasminogen activator (t-PA), decrease the inhibitory factor activity on plasminogen activator, promote fibrinolysis, enhance blood flow, accelerate blood flow and improve microcirculation[13,14]. In addition batroxobin also plays the role in anti-lipid peroxidation and free radical scavenging[15]. Ginaton is a Ginkgo biloba extract, the main components include ginkgolides, flavonoid glycosides. Modern pharmacology shows that Kimundo has multiple roles (1) remove excessive free radicals, inhibit lipid peroxidation occurring on cell membrane, protect the cell membrane and reduce the damage caused by free radicals to the body; (2) promote the release of catecholamines and inhibit its degradation, stimulate the generation of endothelial relaxin, prostacyclin, resulting in arterial relaxation; (3) reduce the viscosity of whole blood, enhance the plasticity of red and white blood cell, improve blood circulation[16,17].

Therefore, this study selected ginaton combined with batroxobin as the research object, to explore the combination efficacy of them to SHL treatment. The results showed that in the hemodynamics; Compared with the same group before treatment, the WBV and PV levels in both groups were significantly decreased, and the decrease in the observation group was greater than that in the control group ($P<0.05$). After treatment, HCT levels decreased in both groups, but the reduction rate was not obvious, there is no significant difference.
In terms of coagulation function: Compared with the same group before treatment, APTT, PT, TT levels were significantly increased ($P<0.05$). PF level was significantly decreased; after treatment, the levels of APTT, PT and TT in the observation group were significantly higher than those in the control group, and the levels of PF in the observation group were significantly lower than those in the control group ($P<0.05$). These results suggested that ginaton combined with batroxobin can significantly improve coagulation and hemodynamics in patients with SHL, thereby promoting the rehabilitation of patients. The specific reasons may be associated with the combination of Ginaton and Batroxobin contribute to reduce blood viscosity, improve vascular function, and promote blood circulation.

In addition, the study found that free radical damage is closely related to the occurrence and development of SHL[18]. SOD, an antioxidant enzyme, is an important part of the body’s antioxidant defense system. It maintains the body’s oxidation and antioxidant balance by scavenging free radicals. In the pathological state, when the body’s free radical content exceeds the body’s own scavenging capacity, it will lead to the occurrence of a series of free radical reaction chain, and produce large amounts of peroxide such as LPO, so as to damage the inner ear hearing-related cells, causing deafness[19,20]. The results of this study showed that: After treatment, LPO levels were significantly deceased in both groups, the SOD levels were significantly increased, and the observation group improved better than the control group ($P<0.05$). This indicated that the combination of the two drugs has the effect of increasing SOD activity and reducing the content of LPO in patients. This may be related to the pharmacological effects of Ginaton’s inhibition of oxygen free radicals, peroxides, and anti-oxidant ability[20,21].

In summary, compared with the use of batroxobin alone, ginaton combined with batroxobin can better reduce the level of oxidative stress in patients with sudden deafness, and improve hemodynamics, blood coagulation. It is worth promoting vigorously in clinical.

References