Clinical efficacy and effect of mNGF on inflammatory factor and oxidative stress in patients with severe intracerebral hemorrhage

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ABSTRACT

Objective: To investigate the effect of mouse nerve growth factor (mNGF) on inflammatory factors and oxidative stress in patients with severe intracerebral hemorrhage. Methods: A total of 84 severe intracerebral hemorrhage patients were randomly divided into observation group (42 cases) and control group (42 cases). The two groups were given the conventional therapy of controlling intracranial pressure and glucose, and the observation group was additionally given mNGF. The efficacy in the two groups was observed. The levels of inflammatory factors including hs-CRP, IL-8 and TNF-α and oxidative stress indicators including malondialdehyde (MDA) and superoxide dismutase (SOD) were tested before and after treatment and compared in the two groups. Results: Total effective rate was significantly increased after treatment in observation group; compared with before treatment, the levels of hs-CRP, IL-8 and TNF-α were significantly reduced after treatment in the two groups, and more significantly decreased in the observation group; compared with before treatment, the levels of MDA and SOD were significantly reduced after treatment in the two groups, and more significantly decreased in the observation group. Conclusion: The mNGF treatment has reliable curative effect in severe intracerebral hemorrhage patients, which can improve inflammatory response and oxidative stress.

1. Introduction

Intracerebral hemorrhage is non-traumatic spontaneous bleeding inside the brain parenchyma with various pathogenic factors, mainly caused by caused ruptured vessels of hypertensive arteriolar sclerosis, which has high mortality and morbidity. Although conventional treatment methods of reducing the intracranial pressure and blood pressure help to stable the condition of disease, long-term effect is not satisfactory. MNGF is a kind of small molecular protein, extracted and purified from mouse submandibular gland, which can effectively inhibit inflammation, remove oxygen free radicals and reduce oxidative damage to nerve cells and vascular endothelial cells, thus enhancing the efficacy of treatment. In this study, on the basis of conventional treatment, mNGF (SuTaiSheng) was used in 84 patients to treat intracerebral hemorrhage to explore the therapeutic effect and influence of it on inflammatory factor and oxidative stress. Details as follows.

2. Materials and methods

2.1 General data

From April 2012 to March 2015, a total of 84 patients from People’s hospital of Xinjiang autonomous region with severe intracerebral hemorrhage were selected and divided into control group and observation group according to the random number table method, with 42 cases in each group. In the control group, there were 25 males and 17 females, who were 47-82 (65.64 ± 11.36) years old. Among them, there were 18 cases with basal ganglia
hemorrhage, 14 cases with putaminal hemorrhage hemorrhage, 6 cases with cerebral lobe hemorrhage and 4 cases thalamus hemorrhage. In the observation group, there were 24 males and 18 females, who were 49.84 (66.83 ± 11.64) years old. Among them, there were 19 cases with basal ganglia hemorrhage, 15 cases with putaminal hemorrhage hemorrhage, 5 cases with cerebral lobe hemorrhage and 3 cases thalamus hemorrhage. Inclusion criteria: in accordance with the fourth session of the national cerebral hemorrhage diagnosis standards; confirmed by the imaging examination; without blood system disease; without immune system disease; without severe liver and kidney damage; without hereditary gluco-lipid metabolic abnormalities; without a history of depression.

2.2 Therapeutic methods

Patients in the two groups were given conventional therapies including discretionary control of intracranial pressure and blood pressure, prevention of bleeding and infection, protection and nutrition for brain cells, and dehydration. On the basis of the control group, the observation group was given mgNOF (SuTaiSheng; approved by the state: z20060023, Beijing ShuTaiShen biological pharmaceutical co., LTD) at a dose of 30 µg each time and once a day. Four weeks were considered as a period of treatment, and the two groups received two courses of treatment.

2.3 Observation indicators

6 mL of fasting venous blood was collected and centrifuged under 4°C at 4,000 r/min for 10 min. Serum was separated and stored at -80°C for further detection. Levels of inflammatory factors including hs-CRP, IL-8 and TNF-α, as well as oxidative stress indicators including MDA and SOD were measured by enzyme-linked immunosorbent (ELISA) method before and after treatment.

2.4 Efficacy assessment

Almost full recovery: decreased rate of neural function defect score was 91%-100% and the degree of sick was at level 0; obvious efficacy: decreased rate of neural function defect score was 46%-90% and the degree of sick was at level 1-3; effective efficacy: decreased rate of neural function defect score was 18%-45% and the degree of sick was at level 4-6; invalid efficacy: decreased rate of neural function defect score was less than 17% and the degree of sick was at level 7. Total effective rate was made up of the former three.

2.5 Statistics

SPSS 17.0 statistical software was adopted for data analysis. Measurement data were described as mean ± standard deviation, and inter-group comparison was carried out by t test. Enumeration data were compared by χ² test. Values of P<0.05 were considered to be statistically significant.

3. Results

3.1 Comparison of the levels of inflammatory factors before and after treatment

Before treatment, the levels of hs-CRP, IL-8 and TNF-α in the observation group were (24.02 ± 7.01) mg/L, (42.98 ± 6.07) ng/L and (42.52 ± 9.71) ng/L, respectively. After treatment, the levels of hs-CRP, IL-8 and TNF-α in the observation group were (9.31 ± 3.49) mg/L, (21.81 ± 4.88) ng/L and (19.09 ± 4.99) ng/L, respectively. Before treatment, the levels of hs-CRP, IL-8 and TNF-α in the control group were (24.64 ± 7.66) mg/L, (39.87 ± 7.31) ng/L and (43.89 ± 9.82) ng/L, respectively. After treatment, the levels of hs-CRP, IL-8 and TNF-α in the control group were (15.69 ± 4.02) mg/L, (28.31 ± 6.17) ng/L and (30.67 ± 6.87) ng/L, respectively. The levels of inflammatory factors were significantly decreased after treatment in the two groups, and more obviously decreased in the observation group (P<0.05) (See table 1).

3.2 Comparison of oxidative stress indicators before and after treatment

Before treatment, the levels of SOD and MDA in the observation group were (84.17 ± 6.46) U/mL and (5.44 ± 0.67) mmol/mL, respectively. After treatment, the levels of SOD and MDA in the observation group were (60.82 ± 5.15) U/mL and (2.35 ± 0.58) mmol/mL, respectively. Before treatment, the levels of SOD and MDA in the control group were (87.18 ± 7.05) U/mL and (5.56 ± 0.72) mmol/mL, respectively. After treatment, the levels of SOD

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Time point</th>
<th>hs-CRP (mg/L)</th>
<th>IL-8 (ng/L)</th>
<th>TNF-α (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>42</td>
<td>Before treatment</td>
<td>24.02 ± 7.01</td>
<td>42.98 ± 6.07</td>
<td>42.52 ± 9.71</td>
</tr>
<tr>
<td>Control</td>
<td>42</td>
<td>Before treatment</td>
<td>24.64 ± 7.66</td>
<td>39.87 ± 7.31</td>
<td>43.89 ± 9.82</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>15.69 ± 4.02</td>
<td>28.31 ± 6.17</td>
<td>30.67 ± 6.87</td>
</tr>
</tbody>
</table>

Note: compared with before treatment, aP<0.05; compared with control group, bP<0.05.
and MDA in the control group were (73.31 ± 5.94) U/mL and (3.72 ± 0.65) mmol/L, respectively. The levels of MDA and SOD were significantly decreased after treatment in the two groups, and more obviously decreased in the observation group (P<0.05) (See Table 2).

Table 1
Comparison of the levels of inflammatory factors before and after treatment

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Time point</th>
<th>hs-CRP (ng/L)</th>
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<tr>
<td></td>
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</tr>
</tbody>
</table>

Note: compared with before treatment, aP<0.05, compared with control group, bP<0.05.

3.3 Comparison of clinical efficacy

In the observation group, there were 19 cases of almost full recovery, 13 cases of obvious efficacy, 8 cases of efficacy and 2 cases of ineffectiveness, making total effective rate of 95.24%; in the control group, there were 10 cases of almost full recovery, 10 cases of obvious efficacy, 11 cases of efficacy and 11 cases of ineffectiveness, making total effective rate of 73.81%, which was significantly lower than that of the observation group (P<0.05).

4. Discussion

Intracerebral hemorrhage is a common clinical neurology disease. After the occurrence of cerebral hemorrhage, regional cerebral blood flow could be greatly reduced by the structural damage of ischemia in patients, thus the brain damage is increased. Hematoma caused by cerebral hemorrhage can oppress the surrounding brain tissue, so the vascular bed was narrowed. At the same time, vascular active substances released by the hematoma cause vasospasm, resulting in a large volume of ischemia, which is a few times as large as hematoma. The mortality of severe cerebral hemorrhage is high, which can reach more than 65%, and the morbidity is also high. Among survivors, about 75% suffer from varying degrees of dementia, paralysis or aphasia, which brings high tension to the society and family and attracts clinical doctors' attention. Clinical treatment of cerebral hemorrhage is mainly divided into surgery and medical treatment, but surgical risk is bigger, so medical treatment is mainly chosen.

Nerve growth factor (NGF plays) is recognized as a neurotrophic factor, and it is very well studied at present with double biological functions of nerve nutrition and neurite growth promotion. NGF is a kind of small molecule protein extracted and purified from mouse submandibular gland, containing three subunits, and . Its activity area lies in subunit, consisting of two single strand of 118 amino acids by non covalent bond. NGF belongs to the neurotrophic factors, playing an important role in maintaining the function of sympathetic and sensory neurons. NGF can strengthen the neurotransmitter activity and promote the development, differentiation and maturation of neurons, thus promoting the regeneration of damaged nerve fiber and neuron; reducing calcium overload; reducing inflammation, weakening peroxidation, reducing neuron damage; inhibiting neurons apoptosis; promoting angiogenesis. A study showed mNGF is safe and reliable to promote the recovery of nerve injury in the treatment of cerebral hemorrhage reliable.

After cerebral hemorrhage, hematoma oppression can activate the immune system to release a large number of inflammatory mediators, causing inflammation in the brain. hs-CRP is a acute phase protein and an indicator of systemic and local inflammation reaction. At the beginning of the inflammatory response, serum level of hs-CRP is clearly increased. IL-8 has a promoting effect on the accumulation and activation of inflammatory cells around the hematoma, which cause a large amount of oxygen free radical production, leading to the injury of vascular endothelial cells and basement membrane to cause damage to the brain edema and brain cells. TNF-α is mainly produced by activated mononuclear cells and macrophages, is one of the important inflammatory mediators participating in inflammation. TNF-α can increase vascular permeability, improving the responses of target cells to a variety of cytokines, eventually releasing a variety of inflammatory factors to promote inflammation. In this study, the levels of inflammatory factors including hs-CRP, IL-6 and TNF-α were significantly decreased after treatment in the two groups, and more obviously decreased in the observation group (P<0.05). These results indicated that the levels of inflammatory factors were reduced after treatment, and anti-inflammatory effects were enhanced, but mNGF has an obviously more significant efficacy.

Oxidative stress is involved in the pathogenesis of acute cerebral hemorrhage through a variety of mechanisms. Oxidative stress is closely associated with the inflammatory reaction after acute cerebral hemorrhage. Free radical damage and oxidative stress are the main factors of hemorrhagic brain injury, MDA is a product of lipid peroxidation reaction of polyunsaturated fatty acids on cell membrane triggered by oxygen free radicals. The higher the level of MDA, the higher the level of oxygen free radicals, and the heavier the body tissue damage. SOD is an important indicator of eliminating oxygen free radicals in the body and preventing physical damage.
injury induced by oxygen free radicals. The body’s inflammatory response can lead to massive production of nitric oxide (NO) and oxygen free radical, making excessive depletion of SOD, lowering SOD activity and decreasing its synthesis. In this study, the levels of MDA and SOD were significantly decreased after treatment in the two groups, and more obviously decreased in the observation group (P<0.05). These results indicated that oxidative stress is involved in the pathogenesis of cerebral hemorrhage, and the adopted therapies in the two groups can significantly improve oxidative stress, enhance the capacity of clearing oxygen free radical and reduce the oxygen free radical damage in the body, but the observation group treated with mNGF has a more significant curative effect than the control group.

To sum up, mNGF is obviously reliable in the treatment of severe cerebral hemorrhage. It can significantly reduce the levels of inflammatory factors such as hs-CRP, IL-8 and TNF-α, as well as oxidative stress indicators such as MDA and SOD, thus improving inflammation and oxidative stress, which is worthy of clinical promotion and application.

References


