Effect of monosialotetrahexosyl ganglioside sodium on inflammatory reaction, stress response and humoral immunity in patients with traumatic brain injury

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ABSTRACT

Objective: To investigate the effects of monosialotetrahexosyl ganglioside sodium on inflammatory response, stress response and humoral immunity in patients with traumatic brain injury.

Methods: A total of 100 patients with traumatic brain injury treated in our hospital from January 2015 to August 2017 were selected as the research object and divided into observation group and control group according to the random number table, each with 50 cases. The control group was given routine treatment while the observation group was given monosialotetrahexosyl ganglioside sodium on the basis of the control group. The changes of inflammatory response, stress response and humoral immunity were compared between the two groups.

Results: Before treatment, there was no significant difference in inflammatory factors CRP, TNF-alpha, NPY level, stress response index MAP, HR, NE, Cor level, humoral immune index IgG, IgM and IgA levels between the two groups. After treatment, the levels of CRP, TNF-α and NPY in the two groups were significantly lower than those before treatment, and CRP level (9.31±2.04) mg/L, TNF-α level (1.47±0.14) ng/L, NPY level (70.02±5.28) ng/L were significantly lower than the corresponding levels of the control group. After treatment, the levels of MAP, NE and Cor in the two groups were significantly lower than those before treatment, HR was significantly higher than before treatment. After treatment, the MAP level (112.07±14.58) mmHg, NE (404.73±105.79) pmol/L and Cor (201.31±42.34) ng/L in observation group were significantly lower than those in control group; HR level (76.34±5.11) times/min was significantly higher than that of the control group. After treatment, the levels of IgG, IgM and IgA in both groups were significantly higher than those before treatment, and the IgG level (19.02±2.28) g/L, IgM level (2.64±0.42) g/L, IgA level (4.31±0.48) g/L in the observation group were significantly higher than the corresponding levels in the control group.

Conclusions: Sodium monosialotetrahexosyl ganglioside treatment of patients with traumatic brain injury can significantly improve the body’s inflammatory response, control the level of postoperative stress response, and improve the level of humoral immunity in patients. It is worthy of clinical promotion.

1. Introduction

Craniocerebral injury is common neurosurgical diseases, severe craniocerebral injury of which have high morbidity and mortality, and more need for craniotomy[1]. Patients with craniocerebral injury have different degrees of inflammation and stress response, and easily lead to secondary injury, affecting the surgical efficacy and prognosis[2]. Monosialotetrahexosyl ganglioside sodium (GM-1) in recent years attracts much attention, and in the early application has a better effect[3]. GM-1 has the function of nerve repair, which can promote the formation of synapse structure and axon growth, and has a positive value for the repair of craniocerebral injury[4]. This
2. Materials and methods

2.1. General Data

A total of 100 patients with craniocerebral injury in our hospital from January 2015 to August 2017 were selected as the research object and divided into observation group and control group according to random number table method. The observation group: 25-38 years old; 29 males and 21 females; 14 cases of falling injury, 28 cases of car accident injury, 8 cases of strikes injury; 26 cases of epidural hematoma, 19 cases of subdural hematoma, 5 cases of subdural hematoma combined with brain contusion. Control group: 26-40 years old; 27 males and 23 females; falling injury in 17 cases, car accident injury in 21 cases, strikes injury in 12 cases; epidural hematoma in 21 cases, subdural hematoma in 23 cases, subdural hematoma combined with brain contusion in 6 cases. There was no significant difference between the two groups in general information (P>0.05). The study was approved by the medical ethics committee of our hospital, the patients were informed and signed the informed consent.

Inclusion criteria: (1) brain injury diagnosed by CT, MRI imaging diagnosis, in line with surgical indications. (2) American Society of Anesthesiologists ASA grading[5] grade II-III. (3) Glasgow coma score[6] 8 points or more. (4) time from injured to admission within 12 h. Exclusion criteria: (1) critical and serious patients, threatening life. (2) merged with other serious traumas. (3) liver, spleen, kidney damaged seriously, with hemorrhagic shock symptoms. (4) accompanied by cardiovascular, endocrine diseases, infections or malignant tumors.

2.2. Treatment method

The control group was given conventional treatment on the basis of surgery. The patients were evaluated for disease condition after admission, and real-time monitoring of heart rate (HR) and blood pressure (BP) were performed with a multi-function monitor if conformed to surgical indications. The patients were firstly treated with 1.5-2.0 mg/kg propofol + 0.07-0.15 mg/kg vecuronium induction and then tracheal intubation, anesthesia with 0.1-0.2 mg/kg h remifentanil. Craniotomy was carried out to stop bleeding and remove hematoma according to the patient’s injury site, hematoma size, decompression by mannitol, diuretic intracranial and other treatments, hemostasis by hemostatic acid, using pantoprazole for prevention of stress ulcer, prevention of postoperative infection with antibiotics. The observation group was established second venous access in the preoperative on the basis of the above conventional treatment, dissolved 100 mg of monosialotetrahexosyl ganglioside sodium into 200 mL 5% glucose solution for intravenous drip once a day for 7 d after continuous treatment, dosage changed as 40 mg/time, once a day, continue treatment for 2 weeks.

2.3. Indicators detection and methods

2.3.1. Inflammatory cytokines detection

About 30 mL of fasting venous blood samples of patients in two groups was collected before and after treatment and then centrifuged 3 000 r/min for 10 min. The supernatant was measured. The levels of C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) and neuropeptide Y (NPY) were detected by enzyme-linked immunosorbent assay (ELISA) and kit was purchased from Zhejiang Yilikang Biotech Co., Ltd.

2.3.2. Detection of stress response indicators

Mean arterial pressure (MAP) and heart rate (HR) level in patients of both groups were detected before and after treatment. French Kangpulle central arterial pressure detector was selected as detection equipment. The test supernatants were taken for detect the levels of norepinephrine (NE) and cortisol (Cor) by radioimmunoassay before and after treatment. The kit was purchased from Shanghai Lanpai Bio-Company.

2.3.3. Detection of humoral immunity

The prepared supernatant was taken by using enzyme-linked immunosorbent assay (ELISA) to detect immunoglobulin IgG, IgM, IgA levels. Kits was purchased from Zhejiang Yilikang Biotech Co., Ltd.

2.4. Statistical processing

The results of this study were analyzed using SPSS 18.0 statistical software. In this study, the levels of inflammatory cytokines CRP, TNF-α, NPY level, stress response indexes MAP, HR, NE, Cor and humoral immune function indexes IgA, IgM and IgG all obey the normal distribution, represented as Mean ± SD, comparison of intragroup before and after treatment, comparison of intergroup after treatment adopted t test. P<0.05 indicated the difference was statistically significant.

3. Results

3.1. Comparison of inflammatory cytokines level

Before treatment, the levels of inflammatory cytokines TNF-α, CRP and NPY were not significantly different (P>0.05). After treatment, the levels of CRP, TNF-α and NPY in the two groups significantly decreased than those before treatment (P<0.05), and
Comparison of humoral immunity level in two groups (Table 3).

The levels of IgG, IgM and IgA were significantly higher than those before treatment, and the levels of IgG in the observation group (19.02 ± 2.28) g/L, IgM level (2.64 ± 0.42) g/L and IgA level (4.31 ± 0.48) g/L were significantly higher than the corresponding levels in the control group (p<0.05)(Table 3).

4. Discussion

The conventional treatment of severe cranioencebral injury includes medical treatment of dehydration and reducing intracranial pressure, anti-infection, and surgical treatment of hematoma removal, decompression of bone flap, etc., which can usually reduce intracranial hypertension and reduce the continuous injury caused by toxic metabolites on neurological function[7]. However, irreversible traumatic brain injury caused by external factors often results in the incomplete reconstruction of nerve function. Therefore, other effective adjuvant measurements should be taken during the treatment[8]. Gangliosides are present in the cell membrane of vertebrate tissues and are glycosylphospholipid that contain sialic acids and play a key role in the nervous system[9]. Monosialotetrahexosyl gangliosides (GM-1) is a brain cell repair agent that can enter the central nervous system through the damaged blood-brain barrier and bind to brain cell membranes to increase the local blood flow of brain tissue and promote the injury of brain cells repair, have a higher value on treatment of central nervous system injury diseases, neurodegenerative diseases, hypoxic-ischemic encephalopathy and peripheral neuropathy[10,11]. Studies have shown that[12], in traumatic central nervous system damage and other diseases, GM-1 plays a major role in the mechanism of inhibition or blocking of oxygen free radicals causing body damage, reduce occurrence of cerebrovascular accidents and apoptosis. GM-1 can reduce the incidence of lipid peroxidation by hindering the generation of oxygen free radicals, and promote the synthesis of nitric oxide by improving the activity of brain cell membrane...
thereby reduce the damage of vascular endothelial cells[13].

The main causes of secondary damage of neurological function in severe cranioencephalic injury include inflammatory reaction and immune disorder. Inflammatory cytokines are important cytokines involved in neurological injury, and their levels are closely related to neurological damage[14,15]. CRP is a common inflammatory response marker, an acute phase reaction protein, involved in activating the inflammatory response, can trigger secondary brain injury, CRP level is higher, the damage is more serious[16]. During the inflammatory reaction, TNF-α is the first to be activated and can cause neurological inflammatory injury. It can also enlarge the inflammatory cascade, causing excessive inflammatory reaction and immune damage in the brain tissue[17]. NPY is a neuropeptide that widely exists in peripheral and central nervous system of mammals and inhibits the excitement of sympathetic nerves. When the level is abnormally elevated, NPY can cause strong vasoconstriction and inhibits the excitement of sympathetic nerves. When the level is abnormally elevated, NPY can cause strong vasoconstriction and worsen dysfunction of brain tissue microcirculation, resulting in further brain tissue injury[18]. In this paper, the levels of CRP, TNF-α and NPY in both groups significantly decreased than those before treatment (P<0.05), and the levels of CRP, TNF-α and NPY in the observation group were significantly lower than those in the control group (P<0.05), the difference was statistically significant (P<0.05). It is indicated that GM-1 can inhibit the secretion of related inflammatory cytokines and reduce the body inflammatory response. The reason may be that GM-1 can directly enter the nerve center, improve blood flow to the brain tissue, repair damaged neurons, reduce the inflammatory response, thereby reducing the level of inflammation-related factors. In addition, the results of this study showed that after treatment, the levels of IgG, IgM and IgA in both groups significantly increased than those before treatment, and the levels of IgG, IgM and IgA in the observation group were significantly higher than those in the control group (P<0.05). This suggested that GM-1 adjuvant therapy can significantly improve the body’s humoral immune response and increase the secretion of immunoglobulin. The reason may be related to GM-1 can inhibit or block the oxygen free radicals causing damage to the body, reduce the incidence of cerebrovascular accidents and apoptosis, and decrease the incidence of lipid peroxidation thereby reducing body damage and inflammatory reaction as well as indirectly enhancing immunity function.

In perioperative period, heart rate of severe traumatic brain injury in patients slowed down, the neuroendocrine system activated to release large amounts of cortisol and catecholamines into the blood, resulting in NE, Cor levels were abnormally increased, indicating that patients with traumatic brain injury appeared strong stress response[19,20]. Excessive stress reactions can cause stress ulcers in patients and result in secondary complications such as cerebral hemorrhage and in severe cases can lead to death[21]. In the present study, MAP, NE and Cor levels in both groups were significantly decreased than those before treatment, HR significantly increased than that before treatment, the difference was statistically significant (P<0.05). After treatment, the levels of MAP, NE and Cor in the observation group were significantly lower than those in the control group, HR was significantly higher than that in the control group (all P<0.05). It showed that GM-1 significantly improved the excessive stress caused by external injury. Brain damage caused by external forces usually leads to nerve cell rupture, leading to increased brain stress response, and GM-1 can repair damaged brain cells through the entering blood-brain barrier, alleviate massive brain cell death that induced by cerebral cell and tissue ischemia, avoiding the loss of much nerve cell membrane fatty acids, which maintain the resistance of neurons to oxygen free radicals injury, to some extent, reduce the release of oxygen free radicals, and thus significantly improve stress response caused by excessive release of oxygen free radicals.

In summary, monosialotetrahexosyl ganglioside sodium treatment of patients with cranioencephalic injury surgery can significantly improve the body’s inflammatory response, control post-operative stress response and enhance patient’s humoral immunity. Thus it is worthy of application.

References

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