



The influence of ganglioside on the blood gas analysis and serum inflammatory cytokines in newborns with anoxic ischemic encephalopathy

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ABSTRACT

Objective: To observe the influence of ganglioside on the blood gas analysis and serum levels of inflammatory cytokines in newborns with anoxic ischemic encephalopathy. **Method:** A total of 100 newborns with anoxic ischemic encephalopathy in our hospital were selected and randomly divided into 2 groups: the control group and the observation group. Conventional oxygen inhalation, reducing intracranial pressure, controlling eclampsia and neurotrophic drug treatment were given to the observation group. Treatment of ganglioside was given to the control group on the basis of observation group. Blood gas analysis and serum levels of inflammatory cytokines were detected before treatment (T0), 3 d after treatment (T1), and 7 d after treatment (T2). **Result:** (1) The comparison of pH, PaO₂, PaCO₂, SaO₂ in the two groups in T0 was not statistically significant. The comparison of pH, PaO₂, PaCO₂, SaO₂ in T0, T1, T2 was considered to be statistically significant. Among these, the result of comparison of pH, PaO₂, SaO₂: T0<T1<T2. comparison of PaCO₂: T0>T1>T2. The pH, PaO₂, SaO₂ in observation group were higher, PaCO₂ in observation group was lower compared with that in control group in T1 and T2. The difference was considered to be statistically significant. (2) The comparison of IL-2, IL-6, hs-CRP, TNF- α in the two groups in T0 was not statistically significant. IL-2 in the observation in T1 and T2 was higher than that in the control group, IL-6, hs-CRP, TNF- α in the observation in T1 and T2 was lower than that in the control group. The difference was considered to be statistically significant. **Conclusion:** Ganglioside can improve blood gas analysis indexes, decrease the serum inflammatory cytokines in newborns with anoxic ischemic encephalopathy.

1. Introduction

Hypoxic-ischemic encephalopathy of newborn is a common brain injury disease caused by perinatal asphyxia. In recent years, the domestic and foreign research found that children with HIE has abnormal blood gas analysis indexes in different degrees. The release of a large number of serum inflammatory factors has a correlation with the patient's condition. And the improvement of the situation has an important reference value for the assessment of the treatment effect[1,2]. Ganglioside is a new type of nerve injury therapeutics, which has a certain effect in improving the brain nerve

function in the clinical research. In this study, we have received good results in the treatment of HIE by using the ganglioside. The results are as follows.

2. Materials and methods

2.1. General information

A total of 100 cases of HIE patients in the department of neurological rehabilitation of our hospital from January 2014 to June 2016 were selected according to the method of continuous enrollment. According to the random number table method, all patients were divided into two groups, the control group (50 patients) and the observation group (50 patients). In the observation group, there were 26 males and 24 females, gestational age was 35-41 weeks and the average gestational age was (38.25±1.75)

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weeks. Birth weight was 2.85-4.55 kg, and the average weight was (3.51±0.46) kg. Apgar score was 4-7 points, and the average score was (6.25±0.55) points. In the control group, there were 27 males and 23 females, gestational age was 35-42 weeks and the average gestational age was (38.55±2.25) weeks. Birth weight was 2.72-4.72 kg, and the average weight was (3.55±0.55) kg. Apgar score was 4-8 points, and the average score was (6.22±0.68) points. There no differences in the sex, age, gestational age, weight, Apgar score and there was no statistical significance, which were comparable ($P>0.05$).

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) Meet the criterion of "Criteria for diagnosis of neonatal hypoxic ischemic encephalopathy" instituted by The Subspecialty Groups of neonatology, The Society of Pediatrics, Chinese Medical Association. The appearance of EEG, imaging examination conformed to the HIE. (2) Apgar 4 points. (3) Parents can follow the doctors' advice well and signed the informed consent. Exclusion criteria: (1) with massive cerebral hemorrhage. (2) Endangered babies. (3) with brain injury, congenital malformation and metabolic diseases.

2.3 Treatment method

Control group: Conventional therapy and symptomatic treatment were given, including low flow oxygen inhalation, constant temperature cabinet method, reducing intracranial pressure by mannitol or/and diuretics, controlling eclampsia by phenobarbitone, giving neurotrophic drugs such as cerebrolysin and so on. At the same time, energy mixture was given; acid-base imbalance was corrected; hypopnea was controlled by hemorheologic agent.

Observation group: Treatment of ganglioside (Beijing SaiShen Pharmaceutical Group Co., Ltd. standard: 20 mg/branch, Chinese medicine standard word H20093980) was given to the control group on the basis of observation group. Detailed usage: 100 mg were added to 100 mL of 5% glucose solution, intravenous drip, 1 time a day, for 7 d as a course.

2.4 Observation indexes

(1) Blood gas analysis indexes, including pH, arterial partial

pressure of oxygen (PaO_2), arterial carbon dioxide partial pressure (PaCO_2), arterial oxygen saturation (SaO_2) were detected in the 2 groups before treatment (T0), 3 d after treatment (T1) and 7 d after treatment (T2). Among these, pH, PaO_2 and PaCO_2 were detected by blood gas analyzer of Ruifeng type PL2200 of Nanjing per-long Medical Equipment Co., Ltd. SaO_2 was revealed by monitor. (2) Serum inflammatory factor indexes, including Interleukin-2 (IL-2), interleukin-6 (IL-6), high sensitive C reactive protein (hs-CRP) and tumor necrosis factor - α (TNF- α) were detected by ELISA kits in the T0, T1 and T2. The kits were purchased by Shanghai Hengyuan Biological Technology Co. Ltd.

2.5 Statistical methods

SPSS 19.0 statistical package was conducted for statistical analysis. Measurement data were described as Mean \pm SD with variance analysis, multi time period comparison was conducted by t test, values of $P<0.05$ were considered to be statistically significant.

3. Results

3.1 Comparison of blood gas analysis indexes in the two groups

The comparison of pH, PaO_2 , PaCO_2 , SaO_2 in the two groups in T0 was not statistically significant ($P>0.05$). The comparison of pH, PaO_2 , PaCO_2 , SaO_2 in the two groups in T0, T1, T2 was statistically significant ($F_{\text{observation group}}=13.263$, $F_{\text{observation group}}=22.658$, $F_{\text{observation group}}=21.658$, $F_{\text{observation group}}=52.639$, $F_{\text{control group}}=10.365$, $F_{\text{control group}}=15.635$, $F_{\text{control group}}=15.286$, $F_{\text{control group}}=35.024$, $P<0.05$). The comparison of pH, PaO_2 , PaCO_2 , SaO_2 in the two groups in T0 was not statistically significant ($P>0.05$). The comparison of pH, PaO_2 , PaCO_2 , SaO_2 in T0, T1, T2 was considered to be statistically significant ($P<0.05$). Among these, the result of comparison of pH, PaO_2 , SaO_2 : T0<T1<T2. Comparison of PaCO_2 : T0>T1>T2. The pH, PaO_2 , SaO_2 in observation group were higher, PaCO_2 in observation group was lower compared with that in control group in T1 and T2. The difference was considered to be statistically significant (${}^{\text{T1}}t_{\text{pH}}=7.021$, ${}^{\text{T1}}t_{\text{PaO}_2}=9.036$, ${}^{\text{T1}}t_{\text{PaCO}_2}=11.052$, ${}^{\text{T1}}t_{\text{SaO}_2}=42.315$, ${}^{\text{T2}}t_{\text{pH}}=6.332$, ${}^{\text{T2}}t_{\text{PaO}_2}=8.652$, ${}^{\text{T2}}t_{\text{PaCO}_2}=10.172$, ${}^{\text{T2}}t_{\text{SaO}_2}=35.412$, $P<0.05$). See table 1.

Table 1.

Comparison of blood gas analysis indexes in the two groups ($n=50$).

Group	time	pH	PaO_2 (kPa)	PaCO_2 (kPa)	SaO_2 (%)
Observation	T0	7.28±0.11	9.68±1.36	6.56±1.05	89.05±8.73
	T1	7.35±0.14 [▲]	10.44±2.07 [▲]	6.21±1.26 [▲]	92.85±6.15 [▲]
	T2	7.40±0.09 [▲]	12.47±2.36 [▲]	5.73±1.37 [▲]	95.98±3.84 [▲]
	<i>F value</i>	13.263	22.658	21.658	52.639
	<i>P value</i>	0.003	0.000	0.000	0.000
Control	T0	7.27±0.09	9.71±1.38	6.61±1.09	89.22±8.62
	T1	7.32±0.13	10.06±2.11	6.37±1.27	91.36±6.05
	T2	7.35±0.10	11.85±2.28	6.01±1.22	93.77±3.65
	<i>F value</i>	10.365	15.635	15.286	35.024
	<i>P value</i>	0.005	0.002	0.002	0.000

Note: compared with observation group : [▲] $P<0.05$.

Table 2.

Comparison of serum inflammatory cytokines in the two groups (n=50).

Group	time	IL-2 (pg/mL)	IL-6 (pg/mL)	hs-CRP (ng/L)	TNF- α (ng/mL)
Observation	T0	1.53±0.25	226.31±61.44	26.38±6.44	89.26±23.59
	T1	1.82±0.61 [▲]	111.36±21.05 [▲]	16.38±2.05 [▲]	69.21±15.51 [▲]
	T2	2.26±0.71 [▲]	52.37±12.38 [▲]	8.37±1.38 [▲]	42.73±12.38 [▲]
	<i>F value</i>	11.352	56.384	23.361	74.112
	<i>P value</i>	0.006	0.000	0.000	0.000
Control	T0	1.56±0.27	233.59±55.21	26.59±6.18	91.25±24.17
	T1	1.76±0.58	161.35±23.19	21.28±3.08	75.71±15.73
	T2	2.03±0.66	72.06±15.32	12.06±2.26	52.44±11.38
	<i>F value</i>	9.352	41.235	20.012	52.384
	<i>P value</i>	0.009	0.000	0.000	0.000

Note: compared with observation group : [▲] $P < 0.05$.

3.2 Comparison of serum inflammatory cytokines in the two groups

The comparison of IL-2, IL-6, hs-CRP, TNF- α in the two groups in T0 was not statistically significant ($P > 0.05$). The comparison of IL-2, IL-6, hs-CRP, TNF- α in the two groups in T0, T1, T2 was statistically significant ($P > 0.05$). (^{observation group} $F_{IL-2} = 11.352$, ^{observation group} $F_{IL-6} = 56.384$, ^{observation group} $F_{hs-CRP} = 23.361$, ^{observation group} $F_{TNF-\alpha} = 74.112$, ^{control group} $F_{IL-2} = 9.352$, ^{control group} $F_{IL-6} = 41.235$, ^{control group} $F_{hs-CRP} = 20.012$, ^{control group} $F_{TNF-\alpha} = 52.384$, $P < 0.05$). IL-2 in the observation in T1 and T2 was higher than that in the control group, IL-6, hs-CRP, TNF- α in the observation in T1 and T2 was lower than that in the control group. The difference was considered to be statistically significant (^{T1} $t_{IL-2} = 6.355$, ^{T1} $t_{IL-6} = 35.685$, ^{T1} $t_{hs-CRP} = 13.114$, ^{T1} $t_{TNF-\alpha} = 21.065$, ^{T2} $t_{IL-2} = 7.083$, ^{T2} $t_{IL-6} = 46.372$, ^{T2} $t_{hs-CRP} = 14.385$, ^{T2} $t_{TNF-\alpha} = 29.384$, $P < 0.05$). See table 2.

4. Discussion

HIE is an important cause of neonatal central nervous system dysfunction, which has a serious impact on the mental and physiological function of the children. In recent years, domestic and foreign research found that the early onset of HIE in children often has different degrees of blood gas function abnormalities, such as SaO₂, PaO₂ decreased, PaCO₂ increased. It has a certain effect on brain cell hypoxia and acidosis[4]. In addition, IL-2, IL-6, hs-CRP, TNF- α and other inflammatory factors are involved in the pathogenesis of HIE, and it has important effects of progression and prognosis. IL-2 mainly composed and secreted by CD4T lymphocytes, which can promote the activation and proliferation of T lymphocytes, improve the level of cytokine in the body. At the same time, the natural killer cells can be activated to improve the immune function, which plays an important role in HIE immune

response and immune regulation. Also, it has important effects on the inhibition of the release of several inflammatory factors[5]. Hs-CRP, IL-6 and TNF- α are all with multi efficiency, which were increased in varying degrees in HIE children. The plasma IL-6 and TNF- α can aggravate the inflammatory reaction of the brain nerve cells and induce the apoptosis of the brain cells by penetrating the blood brain barrier, leading to the injury of the central nervous system[6,7].

Ganglioside is a new type of drug used in the treatment of brain nerve injury in recent years, which has obvious effect in the treatment of HIE. At home, Yu Zongjun[8] apply ganglioside to treat neonatal HIE, which can reduce the brain edema effectively, control brain damage and improve clinical symptoms. In foreign, Ohmi[9] and other studies confirmed that ganglioside is helpful to repair nerve fiber and improve the nerve function. This study shows that the pH, PaO₂, SaO₂ increased more significantly, and the PaCO₂ decreased more significant in children with HIE treated by ganglioside in the 3 d and 7 d compared with that in the patients with conventional therapy. It is suggested that the blood gas indexes of HIE can be improved by the help of the ganglioside. Further to observe the changes of serum levels of inflammatory factors, we found that IL-2 increased more significantly, and IL-6, hs-CRP, TNF- α decreased more significantly in the patients treated by ganglioside compared with that in the patients with conventional therapy. The result showed that ganglioside has a certain effect in regulating the level of inflammatory factors and reducing inflammatory reaction of HIE.

Ganglioside is a kind of sialic acid-containing sphingoglycolipid which widely existed in most cell membranes of mammalian. It is rich in the central nervous system and gangliosidethe is the only ganglioside which can cross the blood-brain barrier[10-15]. On the one hand, it is involved in the process of nerve cell growth and differentiation. Also, it can gather to the damaged brain tissue area and is with high affinity to damaged brain tissue. So, it is helpful to nerve cell regeneration. Also, it can protect and repair the brain damage caused by hypoxia and ischemia[16-19]. On the other hand, gangliosides can protect Ca²⁺-ATP enzyme and Na⁺-K⁺-ATP

enzyme on the cell membrane, which helps to protect the cerebral energy metabolism, ensure the function of brain cells, prevent ion imbalance, reduce cells edema, effectively remove free radicals, inhibit lipid peroxidation, reduce body and brain inflammation. All these helps to promote the recovery of neurological function[20,21]. In addition, the domestic Chen Jun study[22] found that treating severe brain injury by ganglion glycosides can regulate the level of neuron specific level, and improve the level of serum inflammatory factors. Improvement of blood gas analysis in children with HIE by ganglion is considered to be involved in repairing the brain nerve effectively, improving the function of the brain, and stabilizing the respiratory function.

In conclusion, treating neonatal HIE by ganglioside can improve the blood gas analysis indexes, regulate serum levels of inflammatory factors. It is showed that ganglioside has significant clinical significance to improve the effect of neonatal HIE treatment. It is worthy of clinical application.

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