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Efficacy of mild hypothermia combined with monosialotetrahexosyl ganglioside in the treatment of neonatal hypoxic-ischemic encephalopathy and its effect on serum inflammation, GFAP and NSE levels

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Abstract: *Background and purpose Analyze the efficacy of mild hypothermia combined with monosialotetrahexosyl ganglioside in the treatment of neonatal hypoxic ischemic encephalopathy (HIE) and its effect on serum inflammation and serum glial fibrillary acidic protein (GFAP),effect of neuron specific enolase (NSE) levels. 98 children with HIE admitted to our hospital from June 2020 to June 2024 were randomly divided into a control group and an observation group with 49 cases in each group. On the basis of routine oxygen inhalation treatment, the control group was treated with monosialotetrahexosyl ganglioside, and the observation group was treated with mild hypothermia on the basis of the control group. After 14 days of treatment, the treatment efficacy and functional recovery time [muscle tone, sucking ability, primitive reflexes] were compared between the two groups. The levels of serum inflammation-related indicators [high-sensitivity C-reactive protein (hs-CRP), micro-molecule ribonucleic acid-384 (miR-384)] and nerve damage markers [GFAP, NSE, B lymphomas-2 (Bcl-2)] were compared between the two groups before and after treatment. After 14 days of treatment, compared with the control group, the total effective rate of treatment in the observation group was significantly higher (P<0.05). The recovery time of muscle tension, sucking ability, and original reflexes was significantly shorter (P<0.05). After 14 days of treatment, hs-CRP, GFAP, NSE, and Bcl-2 decreased in both groups, and compared with the control group, the levels in the observation group were lower (P<0.05) . The levels of miR-384 increased, and compared with the control group, the levels in the observation group were higher (P<0.05). Mild hypothermia combined with monosialotetrahexosyl ganglioside is effective in treating children with HIE. It can reduce their inflammation level, relieve nerve damage, and be conducive to the recovery of muscle tone and other functions.*

Keywords: *Mild hypothermia; Monosialotetrahexosyl ganglioside; Neonatal hypoxic-ischemic encephalopathy*

1. Introduction

Neonatal hypoxic-ischemic encephalopathy (HIE) is a disease that causes brain damage in newborns due to insufficient blood and oxygen supply during or after birth. It is mostly caused by factors such as placental abruption and uterine rupture. It is the main cause of neurological disability and death in newborns. More than 1 million newborns die every year due to HIE[1]. HIE is divided into mild, moderate and severe categories according to the degree of brain damage and the resulting nervous system problems. There are also different stages of change in its condition, including primary, latency, secondary and tertiary stages. The primary and secondary stages are characterized by failure of energy and cell metabolism, increased cytotoxicity and apoptosis, and activation of microglia and inflammation in the brain. If brain damage persists, it will progress to the third stage. It is characterized by reduced neural plasticity and loss of neurons, which in turn leads to serious neurodevelopmental sequelae such as epilepsy and cerebral palsy, and even death. Therefore, early active and effective treatment measures are of great significance for improving neonatal survival and improving prognosis[2]. Monosialotetrahexosyl ganglioside is a commonly used drug for the clinical treatment of

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HIE. It can promote the recovery and regeneration of nerve cells and achieve good therapeutic effects in various vascular nerve injury diseases. However, the pathological process of HIE is complex, and the treatment effect of single neuroprotective drugs has certain limitations, and multiple treatment measures are usually needed in combination[3]. Studies have shown that mild hypothermia can achieve good results in children with HIE[4]. In this regard, this study analyzed the efficacy of mild hypothermia combined with monosialotetrahexosyl ganglioside in the treatment of HIE and its impact on inflammation-related indicators and nerve damage-related indicators. The results are now reported as follows.

2. Materials and methods

2.1. General information

98 children with HIE admitted to our hospital from June 2020 to June 2024 were selected and randomly divided into a control group and an observation group with 49 cases in each group. Inclusion criteria: confirmed diagnosis of HIE[5]. Continuous ventilation time after birth>10 minutes, informed consent from family members. Exclusion criteria: children with congenital nervous system disease. congenital heart disease, spontaneous bleeding tendency, concomitant bacterial and viral infections, critically ill patients with estimated survival time of less than 14 days. Sex (male/female) in the control group: 25/24 cases; average gestational age (38.79±0.86) weeks; average birth weight (3415.87±150.94) g; delivery method: 16 cases had natural labor and 33 cases had cesarean section. Gender (male/female) in the observation group: 27/22 cases, average gestational age (38.51±0.82) weeks; average birth weight (3436.91±160.88) g, delivery method: 18 cases had natural labor and 31 cases had cesarean section. This study was approved by the Medical Ethics Committee.

2.2. Treatment methods

On the basis of routine oxygen inhalation treatment, the control group was treated with monosialotetrahexosyl ganglioside (Southwest Pharmaceutical Co., Ltd., Sinopharm Approval No. H20093712, 2mL:20mg), 20mg added to 20mL of glucose injection intravenously, once a day. The observation group received mild hypothermia treatment on the basis of the control group. A 6 - 12℃ cooling cap was used to wrap the head of the child with HIE, and the temperature was monitored on the forehead. The child's body surface temperature was monitored and maintained at about 33℃. The treatment was maintained for 3 days. After the end, the child was allowed to rewarm naturally for 6 hours. Thermal radiation may also be used to assist rewarm. All children were treated for 14 days.

2.3. Observation indicators

The treatment efficacy of the two groups was compared: excellence: clinical symptoms of HIE completely disappeared and vital signs returned to normal, effective: vital signs were significantly improved and HIE symptoms were relieved, invalid: vital signs and symptoms were not significantly improved or even deteriorated. Total effective rate =(excellence + effective)/total number of cases ×100%.

The functional recovery time of the two groups was compared: the recovery time of muscle tension, sucking ability, and original reflexes were recorded in the two groups.

The levels of serum inflammation-related indicators before and after treatment were compared between the two groups: fasting venous blood was taken from the children, and the level of high-sensitivity C-reactive protein (hs-CRP) was detected by enzyme-linked immunosorbent assay, and the level of micro-molecule ribonucleic acid-384 (miR-384) was detected by real-time reverse transcription polymerase chain reaction.

The levels of nerve injury markers were compared between the two groups of children before and after treatment: Fasting venous blood was taken from children, and serum glial fibrillary acidic protein (GFAP), neuron specific enolase (NSE), and B lymphomas-2 (Bcl-2) levels were measured by reflex immunoassay.

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2.4. Statistical methods

The above data were analyzed by SPSS22.0,and counting data were described as $\bar{x} \pm s$, and differences between groups were evaluated by t test; Counting data were described as %, differences between groups were evaluated by $\chi 2$ test, and differences in grade data were evaluated by rank sum test. P<0.05 was the test standard.

3. Results

3.1. Comparison of treatment efficacy between the two groups of children

After 14 days of treatment, compared with the control group, the total effective rate of treatment in the observation group was significantly higher (*P*<0.05), as shown in Table 1.

Table 1 Comparison of treatment efficacy in children between the two groups [n=49, n (%)]

Group	Excellence	Effective	Invalid	Total Effective Rate
Observation Group	20(40.82)	25(51.02)	4(8.16)	45(91.84)
Control Group	12(24.49)	20(40.82)	17(34.69)	32(65.31)
$\chi 2$				10.242
P				0.001

3.2. Comparison of functional recovery time between the two groups

After 14 days of treatment, compared with the control group, the recovery time of muscle tension, sucking ability, and original reflexes in the observation group was significantly shorter (*P*<0.05), as shown in Table 2.

Table 2 Comparison of functional recovery time between the two groups (n=49, d, $\bar{x} \pm s$)

Group	Dystonia	Sucking Ability	Primitive Rreflexes
Observation Group	4.91±1.35	5.39±1.54	3.62±1.12
Control Group	6.24±1.68	6.77±1.73	4.65±1.40
t	4.320	4.171	4.021
P	<0.001	<0.001	<0.001

3.3. Comparison of serum inflammation-related indicators levels between the two groups before and after treatment

After 14 days of treatment, the hs-CRP levels in both groups decreased, and compared with the control group, the level in the observation group was lower (*P*<0.05); the level of miR-384 increased, and compared with the control group, the level in the observation group was higher (*P*<0.05), as shown in Table 3.

Table 3 Comparison of the levels of serum inflammation-related indicators between the two groups before and after treatment (n=49, $\bar{x} \pm s$)

Group	Hs-CRP(ng/mL)		MiR-384	
	Before Treatment	After Treatment	Before Treatment	After Treatment
Observation Group	20.15±3.39	6.33±0.85*	0.56±0.23	1.13±0.34*
Control Group	20.67±3.56	9.34±1.12*	0.54±0.21	0.88±0.30*
t	0.740	14.986	0.450	3.859
P	0.461	<0.001	0.654	<0.001

Note:*Compared with before treatment, *P* < 0.05

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3.4. Comparison of nerve injury markers levels between the two groups of children before and after treatment.

After 14 days of treatment, GFAP, NSE, and Bcl-2 decreased in both groups, and compared with the control group, the levels in the observation group were lower (P<0.05), as shown in Table 4.

Table 4 Comparison of nerve injury markers levels between the two groups before and after treatment ($n=49, \bar{x} \pm s$)

Group	GFAP(ng/mL)		NSE(μg/L)		Bcl-2(u/mL)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Observation Group	5.19±1.01	3.46±0.58*	18.43±2.07	7.41±1.06*	15.26±3.01	3.11±0.54*
Control Group	5.02±0.97	3.81±0.62*	18.69±2.09	8.75±1.32*	15.07±2.86	3.82±0.69*
t	0.850	2.886	0.619	5.541	0.320	5.672
P	0.398	0.005	0.538	<0.001	0.749	<0.001

Note:*Compared with before treatment, $P < 0.05$

4. Discussion

The occurrence of HIE is mainly related to perinatal asphyxia. Hypoxia can lead to a variety of conditions, such as neurological dysfunction, reperfusion injury, inflammatory response, and blood-brain barrier damage. Traditional treatment options include oxygen inhalation, maintaining water and electrolyte balance, etc. However, the mortality rate of HIE patients within one year is still high, and surviving children are also at a very high risk of having sequelae of nerve damage such as epilepsy, which causes a certain burden on the children's families and society. Therefore, this study analyzed effective treatment options for children with HIE, In order to improve the curative effect and improve the prognosis of children[6-7].

Monosialotetrahexosyl ganglioside has protective effects on neurons. It can nourish nerves and promote neuron repair by reducing the production of factors such as ammonia oxide[8]. Mild hypothermia treatment can reduce brain tissue oxygen consumption and reduce neurotoxicity[9]. Hs-CRP is an immunoregulation-related protein. Its level will rise rapidly after hypoxia damage occurs in the body. miR-384 is closely related to multiple organ damage. It promotes the secretion of inflammatory factors in organs and other tissues after hypoxia and ischemia. MiR-384 can regulate inflammatory and immune responses. GFAP is a specific acidic protein that causes astrocyte proliferation after brain injury and releases a large amount of GFAP into the blood through the damaged blood-brain barrier. NSE can specifically reflect the severity of neuron damage. Bcl-2 expression is closely related to the survival of nerve cells. In the results of this study, after 14 days of treatment, hs-CRP, GFAP, NSE, and Bcl-2 all decreased in both groups, and compared with the control group, the levels in the observation group were lower , the levels of miR-384 increased, and compared with the control group, the levels in the observation group were higher, indicating that mild hypothermia combined with monosialotetrahexosyl ganglioside treatment in children with HIE can relieve nerve damage and inflammatory response. Analyzing the reasons, mild hypothermia treatment can slow down the metabolism of brain cells, inhibit the anaerobic fermentation process, significantly improve the body's oxidative stress response, reduce cerebral vasospasm, thereby alleviating inflammatory response, and combine monosialotetrahexosyl ganglioside with nourishing nerve effect, can promote the repair of nerve cells, further regulate the growth and differentiation of nerve cells, and improve nerve function[10].

In addition, in the results of this study, after 14 days of treatment, compared with the control group, the total effective rate of treatment in the observation group was significantly higher. The recovery time for muscle tone, sucking ability, and original reflexes was significantly shorter, suggesting that mild hypothermia combined with monosialotetrahexosyl ganglioside has a significant effect on children with HIE and can promote the recovery of neurobehavioral function. The reason is that mild hypothermia combined with monosialotetrahexosyl ganglioside treatment can significantly relieve oxidative stress and inflammatory response in children with HIE, effectively protect children's brain function, promote the proliferation and repair of nerve cells, improve their neurological function, thereby improving

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children with HIE Neuromotor development[11].

In summary, mild hypothermia combined with monosialotetrahexosyl ganglioside has significant effects on children with HIE. It can shorten the recovery time of behavioral neural functions such as muscle tone, reduce inflammatory response, and relieve nerve cell damage, which is conducive to the prognosis of children with HIE, and has clinical promotion and application value.

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