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Clinical analysis of immunoglobulin in the treatment of neonatal hemolytic disease

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Abstract: *To study the clinical effect of immunoglobulin in the treatment of neonatal hemolytic disease. From January 2019 to January 2023, 45 children with hemolytic disease of newborns were selected and divided into two groups. The reference group was treated with blue light, while the experimental group was treated with immunoglobulin. The serum TBIL level, treatment situation, NBNA score, serum factor level and treatment effect were compared between the two groups. After treatment, the TBIL level of children in the experimental group decreased significantly and was lower than that in the reference group. Phototherapy time, jaundice regression time and hospitalization time of children in experimental group were shorter. After treatment, the NBNA scores of children in the experimental group were higher. After treatment, the serum factor level of the experimental group was lower. The therapeutic effect of children in the experimental group was better ($p < 0.05$). Immune immunoglobulin can effectively reduce the level of TBIL, accelerate the regression of jaundice and improve the therapeutic effect of neonatal hemolytic disease.*

Keywords: *Immune gamma globulin; Newborns; Hemolytic disease*

1. Introduction

Hemolytic disease of newborn is a common neonatal disease, which is mainly caused by the incompatibility of blood types between fetus and mother. In this case, the mother's immune system will produce antibodies to attack the fetal red blood cells, which will cause the fetal red blood cells to rupture and release a large amount of bilirubin [1]. The accumulation of bilirubin leads to jaundice in newborns, and in severe cases, it may cause nuclear jaundice, which has toxic effects on the central nervous system of newborns. At present, the common treatment method of neonatal hemolytic disease is blue light therapy, which irradiates the skin of newborns with blue light of specific wavelength, and promotes bilirubin to be transformed into soluble form, which is excreted out of the body through urine and feces [2]. However, although blue light therapy can relieve neonatal jaundice and reduce bilirubin level to a certain extent, its effect is limited for severe neonatal hemolytic disease, and it cannot completely remove bilirubin accumulated in the body. Sometimes exchange transfusion therapy is still needed to quickly reduce bilirubin level [3]. Immunoglobulin therapy has the potential to slow down immune response, reduce erythrocyte destruction, reduce bilirubin production, and slow down or avoid the occurrence of nuclear jaundice. Compared with traditional blue light therapy, immunoglobulin can not only relieve bilirubin accumulation, but also intervene the root of hemolysis. Based on this, this article will study the clinical effect of immunoglobulin in the treatment of neonatal hemolytic disease, which is reported as follows.

2. Data and Methods

2.1. General information

From January 2019 to January 2023, 45 children with hemolytic disease of newborn were selected as the research target, and were divided into experimental group (22 cases) and reference group (23 cases) according to odd-even method. Experimental group: 12 males and 10 females, aged 1-9 days, with an average of (2.38 0.64) days; Reference group: 13 males and 10 females, aged from 1 to 8 days, with an average of (2.26 ± 09.42) days. There was no significant difference in general data between the two groups ($p > 0.05$). Inclusion criteria: (1) Meet the clinical diagnostic criteria of neonatal hemolytic disease; (2) Complete clinical data. Exclusion criteria: (1) gestational age less than 35 weeks; (2) Complicated with severe organ failure.

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2.2. Methods

Children in the reference group were treated with blue light. Naked children were placed in a blue light box, and the temperature and humidity of the blue light box were adjusted to 30-32 ℃ and 55%-65%. In order to protect the eyes and perineum of children, these two parts were covered with cloth. The distance between the light of the blue light box and the child is set to 20-25cm, so as to ensure that the light can evenly irradiate the child's body. The main peak of blue light wavelength is set to 420-470 nm, so that the front and back bodies of children can get illumination and ensure uniform light reception. After continuous blue light irradiation for 8 ~ 12 hours, stop for 12 hours, and the medical staff will regularly check the jaundice of the children. If the yellow skin subsides, suspend blue light treatment. If jaundice occurs repeatedly, take blue light treatment again. The whole blue light treatment lasted for 5 ~ 7 days.

On this basis, the children in the experimental group were treated with immunoglobulin (Shanxi Kangbao Biological Products Co., Ltd., Sinopharm Zhunzi S19994004), and the injection dose was 0.5 g ~ 1kg/kg, once a day according to the weight of the children. The treatment time was 7 days.

2.3. Observation indicators

1) Serum TBIL level: The serum total bilirubin level of children was measured before treatment, 24h after treatment, 48h after treatment and 72h after treatment [4].

2) Treatment: including phototherapy time, jaundice regression time and hospitalization time.

3) NBNA score: NBNA score was used to evaluate children's neurological behavior, including behavioral ability, passive muscle tension, active muscle tension and primitive reflex. The total score of each dimension was 40 points, and the higher the score, the better [5].

4) Serum factor level: including hemoglobin and hematocrit.

5) Therapeutic effect: Significant effect: After 2 days of treatment, the symptoms of jaundice basically subsided and the level of TBIL returned to normal; Effective: After 1 week of treatment, jaundice symptoms basically subsided and TBIL level basically normal; Ineffective: The disease is aggravated, and the effective rate = (markedly effective + effective)/total cases × 100% [6].

2.4. Statistical analysis

The data were analyzed by SPSS 24.0 statistical software. The measurement data were expressed by (` x ± s), row t test, count data by (%), row x2 test. When $P < 0.05$, the difference was statistically significant.

3. Results

3.1. Serum TBIL level

The level of TBIL in the experimental group was significantly lower than that in the reference group ($p < 0.05$). See Table 1.

Table 1: Serum TBIL level (` x ± s; μ mol/L)

Group	TBIL			
	Before treatment	24 hours after treatment	48 H after treatment	72h after treatment
Experimental group (n=22)	320.58 ± 60.37	267.15 ± 53.72	208.64 ± 38.62	172.64 ± 20.58
Reference group (n=23)	320.48 ± 60.72	301.26 ± 60.37	255.48 ± 42.68	217.64 ± 25.67
t	0.068	2.367	4.267	7.628
p	> 0.05	< 0.05	< 0.05	< 0.05

3.2. Status of treatment

Phototherapy time, jaundice fading time and hospitalization time were shorter in the experimental group ($p < 0.05$). See Table 2.

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Table 2: Treatment status (` x ± s)

Group	Phototherapy time (h)	Jaundice regression time (d)	Duration of stay (d)
Experimental group (n=22)	55.48 ± 3.48	5.48 ± 0.34	7.52 ± 1.47
Reference group (n=23)	70.34 ± 5.34	7.26 ± 1.48	9.81 ± 2.47
t	11.005	5.501	8.324
p	< 0.05	< 0.05	< 0.05

3.3. NBNA score

After treatment, the NBNA scores of children in the experimental group were higher ($p < 0.05$). See table 3.

Table 3: NBNA score (` x ± s; Score)

Group	Behavior ability		Passive muscular tension	
	Before treatment	After treatment	Before treatment	After treatment
Experimental group (n=22)	18.34 ± 3.56	34.26 ± 3.27	20.16 ± 2.09	33.58 ± 3.18
Reference group (n=23)	18.42 ± 2.88	25.48 ± 3.18	20.42 ± 2.29	24.19 ± 3.48
t	0.083	9.131	0.397	9.436
p	> 0.05	< 0.05	> 0.05	< 0.05
Group	Active muscle tension		Primitive reflection	
	Before treatment	After treatment	Before treatment	After treatment
Experimental group (n=22)	21.42 ± 2.72	36.58 ± 3.42	23.64 ± 2.35	35.49 ± 3.26
Reference group (n=23)	21.36 ± 2.42	27.42 ± 3.46	23.48 ± 2.34	29.64 ± 3.15
t	0.078	8.928	0.229	6.122
p	> 0.05	< 0.05	> 0.05	< 0.05

3.4. Serum Factor Levels

After treatment, the serum factor level of the experimental group was lower ($p < 0.05$). See Table 4.

Table 4: Serum factor levels (` x ± s)

Group	Hemoglobin (g · L-1)		Hematocrit (%)	
	Before treatment	After treatment	Before treatment	After treatment
Experimental group (n=22)	152.34 ± 10.34	142.62 ± 5.26	60.34 ± 3.33	40.38 ± 3.52
Reference group (n=23)	152.62 ± 10.48	131.28 ± 6.32	60.28 ± 3.29	36.52 ± 3.48
t	0.090	6.526	0.061	3.699
p	> 0.05	< 0.05	> 0.05	< 0.05

3.5. Therapeutic effect

The therapeutic effect of children in the experimental group was better ($p < 0.05$). See table 5.

Table 5: Therapeutic effect [n (%)]

Group	Significant effect	Effective	Invalid	Total effective rate
Experimental group (n=22)	13 (59.09)	9 (40.91)	0 (0.00)	22 (100.00)
Reference group (n=23)	9 (39.13)	9 (39.13)	5 (21.74)	18 (78.26)
x2				5.380
p				< 0.05

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4. Discussion

The occurrence of neonatal hemolytic disease is mainly attributed to the blood group incompatibility between mother and baby, which leads to the mother producing antibodies to attack fetal red blood cells [7]. Clinically, ABO hemolysis and Rh hemolysis are the two most common types. ABO hemolytic disease is caused by maternal and infant ABO blood group incompatibility, which is most common between O mother and A and B fetus. Anti-A and anti-B antibodies naturally exist in O-type mothers. When the fetus is type A or type B, the mother's antibodies can enter the fetus through placenta, attack the red blood cells of the fetus and cause hemolysis. This hemolytic disease is usually characterized by mild to moderate jaundice, which generally does not lead to severe hemolytic reaction. Rh hemolytic disease is caused by Rh blood group incompatibility, which often occurs between Rh negative mothers and Rh positive fetuses [9]. When an Rh-negative mother conceives an Rh-positive fetus, if the Rh-positive red blood cells of the fetus enter the mother, the mother may produce anti-Rh antibodies. There is usually no problem in the first pregnancy, but if the mother is pregnant with an Rh-positive fetus again, the anti-Rh antibody produced by the mother will enter the fetus through the placenta and attack the red blood cells of the fetus, resulting in hemolysis. Rh hemolytic disease can lead to severe fetal jaundice, anemia, heart failure and other serious symptoms, which need timely diagnosis and treatment. The clinical manifestations of hemolytic disease of newborn are diverse, among which jaundice is the most common feature. This is due to the increase of free bilirubin in blood after fetal red blood cells are dissolved, which exceeds the metabolic capacity of neonatal liver. Jaundice usually appears within 24-48 hours after birth, and is characterized by yellow staining of skin, mucous membrane and sclera. The degree of jaundice is related to the rate of hemolysis. Rapid hemolysis can lead to nuclear jaundice and affect the nervous system of newborns. Anemia is another common clinical feature. Maternal antibodies enter the fetus through placenta and attack the red blood cells of the fetus, causing red blood cells to dissolve or destroy, resulting in anemia. Anemia can cause fetal heart rate to increase rapidly, and may develop into congestive heart failure in severe cases [8]. In some cases, hemolytic disease of newborn may also interact with jaundice caused by bacterial infection. Bacterial infection can not only aggravate jaundice of neonatal hemolytic disease, but also trigger neonatal immune response and increase the risk of hemolysis. Therefore, for newborns with jaundice, besides evaluating the risk and severity of hemolytic disease, it is necessary to be alert to the possibility of bacterial infection, diagnose and treat it in time to prevent complications. The choice of treatment plan should be based on the severity of neonatal hemolytic disease, bilirubin level, neonatal weight and physiological conditions. The purpose of treatment is to slow down the accumulation of bilirubin, prevent the occurrence of nuclear jaundice, and solve the problem of anemia. For mild hemolytic disease of newborn, observation and supportive treatment are usually taken. Maintain the body temperature of newborns, ensure adequate nutrition intake, and closely monitor the changes of bilirubin level and the general situation of newborns. In moderate neonatal hemolytic disease, especially when bilirubin level gradually increases but has not yet reached the dangerous level, blue light therapy is the first choice [9]. Blue light can convert bilirubin into a form that is easier to excrete from the body and slow down the accumulation of bilirubin in the body. For severe hemolytic disease of newborn, bilirubin level rises rapidly, or there are signs of nuclear jaundice, which requires immediate and more active treatment measures. Exchange blood transfusion is a common method, which can quickly reduce bilirubin level and prevent or alleviate bilirubin damage to brain. Immunotherapy, such as immunoglobulin, can also be considered. Immunoglobulin is a high-purity and high-concentration immunoglobulin preparation isolated from healthy human plasma, which is often used to treat immunodeficiency, autoimmune diseases and some infectious diseases. In the treatment of neonatal hemolytic disease, immunoglobulin can neutralize the antibody transmitted from mother to fetus, slow down the destruction of fetal red blood cells and reduce the level of bilirubin in blood [10]. It provides a safe and effective treatment option for newborns, which can reduce the occurrence of nuclear jaundice, alleviate the damage of nervous system and lay a foundation for the healthy growth of newborns. The choice of treatment plan should be based on the specific situation of newborns, combined with clinical manifestations and laboratory examination results, and formulate individualized and comprehensive treatment plan, aiming at slowing down bilirubin accumulation to the maximum extent, preventing and treating nuclear jaundice and solving anemia caused by hemolysis.

This study showed that the TBIL level of children in the experimental group decreased significantly after treatment and was lower than that in the reference group. Phototherapy time, jaundice regression time and hospitalization time of children in experimental group were shorter. After treatment, the NBNA scores of children in the experimental group were higher. After treatment, the serum factor level of the experimental group was lower. The therapeutic effect of children in the experimental group was better ($p < 0.05$). Immunoglobulin has immunomodulatory effect, which can slow down the destruction of red blood cells mediated by antibodies, thus reducing the level of serum total bilirubin. Secondly, immunoglobulin can enhance the immune response of children, reduce the risk of bacterial infection

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and further alleviate jaundice caused by bacterial infection. The use of immunoglobulin also shortens the phototherapy time and jaundice regression time, which is due to its ability to inhibit immune-mediated hemolysis, which makes bilirubin level stable rapidly. The rapid regression of jaundice further reduces the hospital stay of newborns and reduces the pressure on medical resources. From the aspect of neurobehavior, immunoglobulin can control and reduce jaundice [11], and reduce the toxic effect of bilirubin on neonatal brain. Immune gamma globulin can effectively reduce inflammatory reaction and release of cytokines in vivo. This anti-inflammatory effect not only helps to control hemolysis and jaundice, but also promotes the recovery and promotion of newborn's general health.

To sum up, immunoglobulin can effectively reduce TBIL level, accelerate the regression of jaundice and improve the therapeutic effect of neonatal hemolytic disease.

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