



Original Research

Efficacy of cefotaxime combined with gamma globulins on C-reactive protein and procalcitonin in neonatal sepsis

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Abstract: C-reactive protein (CRP) is encoded by *CRP* or *PTX1* gene and procalcitonin (PCT) is produced by the *CALC-1* gene induction. Both PCT and CRP are known as valued biomarkers markers in prediction of Serious Bacterial Infections (SBI) in children. This experiment carried out to analyze the efficacy of cefotaxime combined with gamma globulins on neonatal sepsis and the effect on CRP and PCT. For this purpose, a total of 120 sepsis children were selected and randomly divided into observation and control groups. Children in the control group were treated with cefotaxime, while children in the observation group were treated with cefotaxime combined with gamma globulins. The two groups were compared in terms of the relative measures of efficacy, the total effective rate of treatment, the incidence of complications and serum CRP and PCT levels before and after treatment. The clinical measures of the observation group were all lower than those of the control group, and the total effective rate of the treatment was higher than that of the control group, while the incidence of complications was lower than that of the control group. In addition, before treatment, there was no difference in CRP and PCT between the two groups; after treatment, the above measures in the observation group were lower than those in the control group. It is concluded that Cefotaxime combined with gamma globulins in the treatment of neonatal sepsis has significant efficacy and is clinically more effective than cefotaxime monotherapy. This combination can shorten clinical symptom remission time and hospital stay, improve serum CRP and PCT levels and promote the recovery of children, worthy of promotion.

Key words: Cefotaxime; Gamma globulins; Neonatal sepsis; C-reactive protein; Procalcitonin.

Introduction

C-reactive protein (CRP) is the name of a protein that is synthesized in the liver in response to factors released from macrophages and fat cells, which in cases of inflammation and rheumatism in the blood increases. procalcitonin (PCT) is a precursor to the hormone calcitonin, which is produced in the C-cells of the thyroid gland. The hormone is also produced in liver cells and fat cells under certain conditions, such as bacterial infections and surgery. Therefore, the PCT test can be used to diagnose severe bacterial and septic infections and to prevent wasting treatment time. CRP and PCT are known as biomarkers used to neonatal sepsis diagnose (1-5).

Neonatal sepsis is a kind of systemic inflammatory reaction syndrome caused by the immature immune barrier of the newborn, which leads to the invasion of bacteria into the blood circulation and the production of a large number of toxins (1). Sepsis is a clinically common disease in neonates, and the incidence is higher in premature and low birth weight neonates. Most neonates develop the disease 1 week after birth. Premature babies are infected through the respiratory system and full-term babies are infected through the skin and navel. The disease often affects multiple organs and the positive rate of blood culture is up to 75% (2,3). As the most common neonatal infectious disease, Escherichia coli

and Staphylococcus are the most common pathogens of neonatal sepsis. Anti-infective methods are often used for clinical treatment. However, due to the increasing number of drug-resistant strains and the non-specific and specific immune function defects in the body of the children, pathogenic bacteria rapidly spread in the body after infection. Conventional antibiotics cannot achieve good therapeutic effects and the case fatality rate of neonatal sepsis increases year by year (4,5). Therefore, it is of great clinical significance to find a more effective and safer treatment for improving the quality of life of the children. In this research, clinical data of 120 cases of neonatal sepsis in our hospital were collected as the subjects of the study, and the application value of cefotaxime combined with gamma globulins in the treatment of neonatal sepsis was retrospectively analyzed.

Materials and Methods

Clinical Data

A total of 120 children with sepsis admitted to our hospital from December 2017 to November 2018 were selected as observation subjects. All the selected children were diagnosed with sepsis and met the diagnostic criteria of neonatal sepsis in Practical Neonatology: (A) pathogenic bacteria were found in blood culture; (B) If opportunistic pathogenic bacteria were found in blood culture, then the same bacteria should be found in ste-

Table 1. General data of the two groups of studied children.

	Observation group	Control group
Number of cases	60	60
Male/female (case)	32/28	33/27
Age (day)	15.86±1.65	15.83±1.58
Weight (kg)	2.88±0.99	2.93±1.02
Natural delivery/cesarean section (case)	38/22	40/20
Pathogenic bacteria:		
<i>Staphylococcus viridans</i>	16	17
<i>Staphylococcus epidermidis</i>	11	10
<i>Staphylococcus aureus</i>	13	9
<i>Group B streptococcus</i>	7	11
<i>Escherichia coli</i>	6	9
<i>Klebsiella pneumonia</i>	6	3
<i>Enterococcus sp.</i>	1	1

rile coeloms, other blood samples or on the tip of the catheter. Cases meeting either item of the above criteria can be diagnosed as neonatal sepsis. Children with severe congenital cardiac, hepatic, and renal insufficiency, children with autoimmune diseases, children with trauma or viral infections, and children who had received antibiotics before admission were excluded. Children were divided into an observation group and a control group according to the random number table, with 60 cases in each group. The general data of the two groups (Table 1) had no statistically significant differences ($P > 0.05$) and the two groups were comparable. All the parents of the children had given informed consent and voluntarily participated in this study.

Treatment methods

Nutritional support, warmth, correction of acid-alkali-electrolyte disorder, shock, strict monitoring of vital signs and other conventional symptomatic treatments were given to the children in both groups to prevent the occurrence of brain edema, DIC, hypoxemia, etc. Control group: on the basis of conventional symptomatic treatments, Cefotaxime Sodium for Injection (Qilu Pharmaceutical Co., Ltd., SFDA Approval No. H37020571, specification 1 g × 10 vials/box) was given 100 mg/(kg·d), IV drip, 2 times/d. Observation group: on the basis of treatments in the control group, gamma immunoglobulin (Shanxi Kangbao Biological Products Co., Ltd., SFDA Approval No. S19994004, specification 5%, 50 ml (2.5 g/vial) was given 400 mg/(kg·d), IV drip, with an initial rate of 5 drops/min. The children were observed for 30 min. If there was no adverse reaction, the drip would be accelerated and finished within 2 hours. Both groups were treated for 5 consecutive days.

Observation measures

Measures related to efficacy (hospital stay, body temperature improvement time, neurological symptom improvement time, nursing strike improvement time), the total effective rate of treatment, incidence of complications (skin exanthematous pustulosis, purulent meningitis and infectious diarrhea, etc.) in the two groups were recorded. Five ml of venous fasting blood was extracted

in the morning before and after treatment. After agglutination for 30min, the serum was separated by centrifugation and was placed at -8°C for the test. The levels of procalcitonin (PCT) and C-reactive protein (CRP) in children were detected by an immunoquantitative analyzer produced by Wuhan EasyDiagnosis Biomedicine Co., Ltd.

Efficacy evaluation criteria

Excellent: after 7 days of treatment, the child's clinical symptoms were significantly improved, the body temperature was stable, the skin was ruddy and normal feeding was restored; the results of the second bacterial culture were negative, and the cerebrospinal fluid was normal in examinations. Effective: the child's clinical symptoms were improved to some extent, the cerebrospinal fluid or bacterial culture examinations showed improvement. Ineffective: the child's clinical symptoms didn't show any signs of improvement or even worsened, and the results of the bacterial culture test were still positive.

Statistical analysis

The results of this study were processed by SPSS18.0 software. Count data were expressed as percentages and analyzed with the χ^2 test. Measurement data were expressed in the form of mean±standard deviation, and the t-test was performed after the analysis of variance. $P < 0.05$ was considered statistically significant.

Results

Comparison of clinical measures between the two groups

After treatment, clinical measures (hospital stay, body temperature improvement time, neurological symptom improvement time, nursing strike improvement time) of the observation group were lower than the control group ($p < 0.05$) (Table 2).

Comparison of treatment efficacy between the two groups.

The total effective rate in the observation group was significantly higher than that in the control group, and

Table 2. Comparison of clinical measures between the two groups (day).

Group	n	Hospital stay	Body temperature improvement time	Neurological symptom improvement time	Nursing strike improvement time
Observation group	60	7.12±1.23	3.24±1.55	6.75±1.44	5.75±1.26
Control group	60	10.35±2.63	6.44±1.96	8.93±1.84	7.33±1.75
t		8.001	9.383	6.850	5.266
p		0.000	0.000	0.000	0.000

Table 3. Comparison of treatment efficacy between the two groups (case).

Group	n	Excellent	Effective	Ineffective	Total effective rate
Observation group	60	26	28	6	90.00%
Control group	60	19	24	17	71.67%
χ^2					6.327
p					0.043

the difference was statistically significant ($p < 0.05$) (Table 3).

Comparison of complications between the two groups

In terms of complications (skin exanthematous pustulosis, purulent meningitis and infectious diarrhea, etc.), the incidence of complications in the observation group was significantly lower than that in the control group. And statistical results showed that the above difference was significant ($p < 0.05$) (Table 4).

Comparison of serum CRP and PCT between the two groups before and after treatment

There were no significant differences in serum CRP and PCT between the two groups before treatment ($p > 0.05$). After treatment, the serum CRP and PCT were significantly decreased in the two groups, and the serum CRP and PCT levels in the observation group were significantly lower than the control group, with statistically significant differences ($p < 0.05$) (Table 5).

Discussion

The immune system of the newborn is not fully developed. Although maternal immunoglobulins can be

transmitted to the newborn through the placenta, once bacterial infection occurs, the consumption of immunoglobulin G (IgG) will increase. If the newborn cannot produce enough immunoglobulins by himself, he will become immunocompromised. Neonatal infection is clinically difficult to control, and bacteria are easy to enter the neonatal blood circulation and proliferate, causing sepsis (6,7). Anti-infective treatment with broad-spectrum antibiotics is the main method used clinically to treat neonatal sepsis. However, with the massive abuse of antibiotics, the drug resistance of bacteria becomes increasingly serious, leading to the poor effect of traditional broad-spectrum antibiotics in the treatment of neonatal sepsis.

Cefotaxime is a third-generation cephalosporin drug, characterized by strong effects and a wide antibacterial spectrum, powerful against Gram-positive and Gram-negative bacteria; especially in the treatment of pathogens resistant to penicillin and aminoglycosides, its efficacy is still significant. Therefore, it has become a commonly used preferred drug in the clinical treatment of neonatal infectious diseases (8,9). The results of this study showed that the clinical measures of the observation group were all lower than those of the control group, and the total effective rate of the treatment was higher than that of the control group, while

Table 4. Comparison of complications between the two groups (case).

Group	n	Skin exanthematous pustulosis	Purulent meningitis	Infectious diarrhea	Complication rate
Observation group	60	1	1	0	3.33%
Control group	60	4	4	7	25.00%
χ^2					10.374
p					0.013

Table 5. Comparison of serum CRP and PCT between the two groups before and after treatment.

Group	n	CRP (mg/L)		PCT (ng/L)	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	60	22.42±2.52	10.64±4.27 ^a	7.87±2.16	1.59±0.55 ^a
Control group	60	23.03±3.35	15.36±3.16 ^a	7.66±2.38	3.27±0.99 ^a
t		1.037	6.257	0.465	4.976
p		0.302	0.000	0.643	0.000

the incidence of complications was lower than that of the control group. C-reactive protein and procalcitonin are two common biomarkers of neonatal infection. C-reactive protein is a marker of acute-phase pathogenic infection and has important clinical application value in inflammatory responses and tissue damage repair, and is one of the important measures for the diagnosis of infectious diseases in clinical practice (10,11). Clinically, procalcitonin concentration exceeding 0.5 ng/L indicates the existence of an acute bacterial infection. Children with systemic bacterial infection have higher and more significantly elevated procalcitonin levels (12). In addition, procalcitonin is also one of the markers of pathogenic infection. During infection, plasma procalcitonin significantly increases and becomes relatively stable, and it only increases with the aggravation of the disease. In this article, before treatment, there was no significant difference in C-reactive protein and procalcitonin between the two groups; after treatment, the measures in the combination group were significantly better than the cefotaxime monotherapy group.

Human blood immunoglobulin for injection is isolated from mixed plasma, and its IgG ratio is appropriate to prevent allergic reactions caused by IgG aggregation in children after injection. At the same time, IgA and IgM, powerful against viruses, are main immunoglobulins that start immune responses in the early stage; they appear at the earliest time and can improve clinical efficacy. They can bind to pathogens or toxins and fuse with bacteria, then developing antibody-dependent cell-mediated cytotoxicity. The antibody complex is formed and the complement is activated; the IgG level in the body is elevated. The FC segment is bound to the FC receptor of phagocytes, and the phagocytosis of the cells is improved, and then the cells are dissolved. The specificity of the antigen is enhanced, and the immune response of the newborn is improved. Central granulocytes are constantly released from the bone marrow and move to the infected lesion, and the phagocytosis of central granulocytes is improved. Therefore, cefotaxime combined with gamma globulins in the treatment of neonatal sepsis not only directly kill bacteria with antibiotics, but also kill bacteria by improving the immune function of neonates (13,14).

C-reactive protein (CRP) is encoded by CRP or PTX1 gene. The protein encoded by this gene belongs to the pentaxin family. It is involved in numerous host defense related functions according to its capability to recognize foreign pathogens and damaged cells of the host and to initiate their removal by interacting with humoral and cellular effector systems in the blood. So, the level of this protein in plasma increases significantly during acute phase response to tissue injury, infection, or other inflammatory stimuli (15).

The procalcitonin (PCT) is produced by the *CALC-1* gene induction. Through inflammation, LPS, microbial toxin, and inflammatory mediators, for example IL-6 or TNF- α , induce the *CALC-1* gene in adipocytes, but PCT never gets cleaved to produce CT. [9] In a healthy individual, PCT in endocrine cells is created with *CALC-1* by elevated calcium levels, CGRP, glucocorticoids, glucagon or gastrin, and is cleaved to produce CT, that is released to the blood (16).

In summary, cefotaxime combined with gamma glo-

bulins in the treatment of neonatal sepsis has significant efficacy and is clinically more effective than cefotaxime monotherapy. This combination can shorten clinical symptom remission time and hospital stay, improve serum CRP and PCT levels and promote the recovery of children, worthy of promotion.

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