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Effectiveness of cefotaxime sodium in combination with penicillin in the treatment of neonatal sepsis and its effect on the level of immunity in pediatric patients

Peini Wu* and Zhengzheng Huang
Department of Neonatology, The Affiliated People's Hospital of Ningbo University

Abstract: Neonatal septicemia seriously threatening the lives of pediatric patients and currently facing certain challenges in clinical treatment. This study analyzed the effectiveness of cefotaxime sodium combined with penicillin in the treatment of neonatal sepsis and the effect on immunity levels. 101 septic neonates from the Affiliated People's Hospital of Ningbo University between October 2020 and December 2023 were divided into CS and CP groups; both groups were treated with cefotaxime sodium and penicillin was added to CP group. The primary assessment was the clinical efficacy, inflammatory and immune indices of both groups. Secondary outcomes included symptom improvement time, serum procalcitonin levels and white blood cell (WBC) counts, recurrence rate, complication status and adverse reaction incidences. After treatment, the indices of both groups were compared for any significant difference with pre-treatment. The clinical efficacy, immunity indices, symptom improvement of CP group were significantly higher than CS group and inflammatory indices, serum procalcitonin levels and WBC counts, complication conditions and adverse reaction incidences were significantly lower than the CS group (P<0.05). No obvious differences of recurrence rate among both groups (P>0.05) were found. This combined therapy has a remarkable curative effect, which is worthy of popularization and use in the clinic.

Keywords: Cefotaxime sodium; Immune indices; Inflammatory indices; Neonatal sepsis; Penicillin

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INTRODUCTION

Sepsis is a common and serious infectious disease of the newborn, which is highly prevalent in low-birth-weight and preterm infants and usually occurs within 1 week of birth. Neonatal sepsis is one of the leading causes of neonatal mortality. The definition of neonatal sepsis is still controversial because the clinical presentation and laboratory tests are often nonspecific (Popescu *et al.*, 2020). In most cases, neonatal sepsis can be diagnosed clinically by the presence of at least two clinical signs and at least two nonspecific laboratory findings or a positive blood specimen for pathogenic bacterial antigens or DNA; or the diagnosis can be confirmed by the clinical signs and bacterial cultures (derived from blood or sterile body cavities) for the causative organisms (Glaser *et al.*, 2021). The main pathogens of sepsis are Staphylococcus spp. and Escherichia coli, which are infected through the umbilical cord, skin and other parts of the body. The initial stage of infection does not have obvious symptoms, but the disease progresses rapidly and with the development of the disease, it can involve multiple systems, which is a serious threat to the safety of the lives of pediatric patients (Eichberger *et al.*, 2022). The mechanism of sepsis is complex, mainly due to poor immune barrier function, pathogenic bacteria invade the body's blood circulation and multiply, generate toxins, inducing systemic inflammatory reaction, clinical characteristics of the condition is acute and severe, high lethality (Kim *et al.*, 2020). The systemic symptoms of neonatal sepsis usually include abnormal body temperature, poor feeding or edema, etc. In addition, digestive symptoms such as abdominal distension and vomiting, respiratory symptoms such as shortness of breath and respiratory distress, neurological symptoms such as irritability, somnolence, tremor, hematological abnormalities such as jaundice and purpura and, secondly, urinary abnormalities and low blood pressure may also occur from time to time. However, these early clinical manifestations are very atypical and have poor specificity, making it difficult to perform effective typing based on symptoms. Due to the imperfect immune function of neonates, sepsis leads to rapid development and deterioration in the late stage, which can easily lead to multifunctional organ failure and even shock and death (Procianoy and Silveira, 2020).

As soon as a neonate shows signs of infection, a variety of specimens should be collected to refine bacterial cultures, which often require a wait of 48 hours or more for results. Due to the immune deficiency of the neonatal organism and the rapid spread of infection-causing organisms, clinicians must initiate empirical antibiotic therapy immediately after specimen collection without waiting for culture results in order to reduce morbidity and mortality (Fleischmann *et al.*, 2021). Initial treatment should be based on empirical selection of antibiotics based on the clinical presentation of pediatric patients, the local spectrum of predominantly pathogenic bacteria at different times and the spectrum of drug resistance. The causative organisms and drug

**Corresponding author:* e-mail: YZRMWPN76@hotmail.com

sensitivities are unknown at the beginning of treatment and the antibiotics selected should cover as many causative organisms as possible and a regimen that targets both gram-positive and gram-negative organisms should be chosen (Al Bakoush *et al.*, 2023). The common first-line empirical treatment is penicillins in combination with aminoglycoside antibiotics, with third-generation cephalosporins often used as an alternative to aminoglycoside antibiotics (Fuchs *et al.*, 2018).

The combination of aminoglycosides and penicillins (such as the commonly used penicillin and ampicillin) can cover a broad antimicrobial spectrum. Moreover, aminoglycosides produce relatively little resistance and their combination with penicillins has long been used by clinicians as a first-line empirical antimicrobial regimen for the treatment of neonatal sepsis (Garrido *et al.*, 2021). Aminoglycoside antibiotics mainly act on aerobic gram-negative bacilli and achieve antibacterial effects by inhibiting bacterial protein synthesis and destroying the integrity of the bacterial plasma membrane (Mukhopadhyay *et al.*, 2019). Penicillins, on the other hand, mainly inhibit bacterial cell wall synthesis by acting on penicillin-binding proteins (PBPs) in the bacterial body and at the same time produce antibacterial effects with the help of bacterial autolytic enzymes (Korang *et al.*, 2021). These two classes of antibiotics have synergistic antibacterial effects due to the different antibacterial mechanisms and the expansion of the antibacterial spectrum to enhance antibacterial activity when used in combination. Aminoglycoside antibiotics have some disadvantages that are difficult to avoid in the process of application. Their bactericidal rate and duration are concentration-dependent and their half-life varies greatly among neonates of different birth weights, requiring dynamic monitoring of blood concentrations (Korang *et al.*, 2019). Aminoglycosides have a high affinity for the renal cortex and accumulate in the renal cortex through cell membrane swallowing; they also accumulate in high concentrations in the inner and outer lymphatic fluids of the inner ear and the concentration in the inner ear lymphatic fluid decreases very slowly, so they are prone to ototoxicity and nephrotoxicity and the use of drugs should be monitored to check the renal function and screening of hearing. Aminoglycosides are also unable to cross the blood-brain barrier and even when the meninges are inflamed, it is difficult to reach effective concentrations in the cerebrospinal fluid (Weissman and Stoll, 2021).

Third-generation cephalosporins are more potent against gram-negative bacteria, including Enterobacteriaceae, Pseudomonas aeruginosa and anaerobes. With the exception of enterococci and Listeria monocytogenes, third-generation cephalosporins have a more favorable antimicrobial spectrum than aminoglycosides and are more advantageous in eliminating gram-negative bacterial infections (Dudeja, 2020). Third-generation cephalosporins can also cross the blood-brain barrier and their advantage in practice is that they do not require dynamic monitoring of blood concentrations, considering that many developing countries do not have the conditions for monitoring blood concentrations in clinical applications, so third-generation cephalosporins alone or in combination with penicillins are often used as the preferred empirical therapeutic regimen in developing countries (Longardt *et al.*, 2020).

Cefotaxime sodium belongs to the third-generation cephalosporins, which has the advantages of broad antibacterial spectrum and strong effect and is used as a commonly used therapeutic drug for neonatal infectious diseases in the clinic but the treatment time is longer, which is prone to lead to adverse reactions (Darlow *et al.*, 2021). Penicillin belongs to β-lactam antibiotics, which can destroy the cell wall of bacteria and has a better bactericidal effect, but the degree of improvement of immune function in pediatric patients is general (Rallis *et al.*, 2023). Therefore, in view of the two in the treatment of septic neonates, this study observed the clinical efficacy of cefotaxime sodium in combination with penicillin in the treatment of neonatal sepsis, analyzed the inflammatory indexes and immune levels after treatment and clarified the efficacy and safety of the combination of the two in the treatment of sepsis, so as to provide more therapeutic options for the clinic.

MATERIALS AND METHODS

Study design and participants

The present study is a systematic evaluation and integration aiming to comparatively analyze the clinical efficacy of cefotaxime sodium in combination with penicillin in the treatment of sepsis in neonates and to further assess its effect on inflammatory markers and immune levels in pediatric patients. This is a retrospective study, 101 cases of septic neonates from the Affiliated People's Hospital of Ningbo University between October 2020 and December 2023 were selected, which were divided into two groups according to the different interventions, CS group and CP group. The flow chart of this study is presented in fig. 1.

Inclusion and exclusion criteria

Inclusion criteria

Meeting the diagnostic criteria of the Expert Consensus on the Diagnosis and Treatment of Neonatal Sepsis (Taneri *et al.*, 2025); (2) Day old ≥1d; (3) Positive blood bacterial culture results; (4) Milk refusal, fever and abnormal skin color; (5) Completeness of clinical data; (6) Tolerance to the medications involved in this study; (7) Informed and consenting family members who signed an informed consent form.

Exclusion criteria

(1) Combination of other congenital diseases; (2)

Combination of hematologic diseases; (3) Pulmonary, cardiac, renal and hepatic defects and severe cardiovascular diseases; (4) Combination of chronic infectious diseases; (5) Combination of neurological diseases; (6) Combination of neonatal respiratory distress syndrome; (7) Request to stop treatment or automatic discharge for personal or family reasons; (8) Allergy to the medication used in this study; (9) Other conditions that the study physician believes should not be included; (10) Other conditions that affect the indicators of subsequent observation.

Interventions

Both groups were given routine treatments such as nutritional support, warmth preservation, anti-infection, correction of electrolyte disorders, improvement of microcirculation, etc. The vital signs of pediatric patients were closely monitored to prevent the occurrence of cerebral edema, hypoxemia and other related complications. At the same time, all of them were given intravenous injection of cefotaxime sodium (Huabei Pharmaceutical Hebei Huamin Pharmaceutical Co., Ltd; National Drug License: H20054822; Specification 2.0g), 12 h/times, 50 mg/kg once and treated continuously for 7 d (Shang *et al.*, 2022).

In the CP group, penicillin sodium treatment was added on this basis. Penicillin sodium for injection (Jiangxi Dongfeng Pharmaceutical Co., Ltd; National Drug License: H36020261; Specification 800, 000U/ 0.48 g (per dose) and 5mL of 0.9% sodium chloride injection were mixed thoroughly and intravenous injection for 12 hours/time, 50, 000 U/kg, continuous treatment for 7 d (Rohatgi *et al.*, 2017).

Observational indicators

Primary indicators

Clinical efficacy

Compare the clinical efficacy of the pediatric patients in both groups. Criteria for judging the efficacy: Obvious effect: the symptoms of pediatric patients improved significantly after treatment, body temperature returned to normal, mental state was good, vital signs returned to normal and the blood bacterial culture results turned negative; Effective: the symptoms improved after treatment, body temperature basically returned to normal, vital signs improved and the blood bacterial culture results turned negative; Ineffective: The above criteria were not met (Hayes *et al.*, 2023). Total effective rate = (Obvious effect + Effective) / Total × 100%.

Inflammatory factors

Fasting peripheral venous blood of 3 mL was drawn from pediatric patients before and after treatment, centrifuged and processed and then kept refrigerated for testing and the levels of tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-8 (IL-8) and ultrasensitive C-reactive protein (hs-CRP) were determined and calculated in serum samples using enzyme-linked immunosorbent assays (Bakhsh *et al.*, 2022).

The kits used were Human TNF-α ELISA kit (Item No.: ml077385, Shanghai Enzyme-linked Biotechnology Co., Ltd.), Human IL-6 ELISA kit (Item No.: ml027379, Shanghai Enzyme-linked Biotechnology Co., Ltd.), Human IL-8 ELISA kit (Item No.: ml103387, Shanghai Enzyme-linked Biotechnology Co., Ltd.) and Human hs-CRP ELISA kit (Item No.: ml106583, Shanghai Enzyme-linked Biotechnology Co., Ltd.).

Immunological indicators

Before and after treatment, 3 mL of fasting venous blood was drawn from pediatric patients in the morning and immunoglobulin A (IgA), immunoglobulin G (IgG) and immunoglobulin M (IgM) levels were detected by an automatic biochemical analyzer (Beckman Coulter K.K., AU5800, China National Instrument Imprint 20152401623) (Qian *et al.*, 2020).

Secondary indicators

Improvement of symptoms

Recording of milk refusal, normalization of body temperature, neurological symptoms and hospitalization time of pediatric patients in both groups.

Serum procalcitonin levels and white blood cell counts

Peripheral venous blood was collected from pediatric patients and serum procalcitonin (PCT) levels were detected using a fully automated biochemical analyzer (Yuan *et al.*, 2021). White blood cell (WBC) count was performed by applying a fully automatic blood cell analyzer (BC-5000, Shenzhen Myriad Bio-Medical Electronics Co., Ltd.) (Luo *et al.*, 2020).

Recurrence rate

Record the recurrence of sepsis in pediatric patients in both groups. After the initial treatment is completed and the clinical symptoms are completely relieved, the recurrence of infection symptoms requires hospitalization.

Complications

To record the complications, including shock, hypoxemia, acidosis, septic meningitis and necrotizing small bowel colitis in both groups of pediatric patients

Adverse reaction

Record the occurrence of adverse reactions, including hypotension, vomiting and diarrhea, etc. during the treatment of pediatric patients in both groups.

Follow-up visits

Follow-up visits at 3 months after treatment were mainly arranged in this study to assess the durability of the effect and to deal with any potential adverse reactions or problems.

Sample size calculation

Sample size was calculated by performing a power analysis according to the G*Power 3.1.9.7 computer software to determine the sample size required to detect a statistically significant difference. Based on the primary outcome of clinical efficacy, considering an α level of 0.05 and 85% efficacy, we calculated that a sample size of 41 pediatric patients would be required in each group. Considering the potential uncertainties, the sample sizes chosen for this study were the CS group (n=50) and the CP group (n=51) and we believe that the sample sizes in this study allow for reliable conclusions to be drawn.

Statistical analysis

SPSS27.0 statistics software was applied for analysis of the data. Lucidchart is used to draw flowcharts. The data in this study were subjected to a normal distribution test. The baseline features are described as the number of people and variables (represented by $\bar{x}$±s). The inflammatory indicators, immune function indicators, symptom improvement, PCT levels and WBC count in the results are all expressed as $\bar{x}$±s. Independent sample t-test was used to compare the two groups. The clinical efficacy, recurrence rate, incidence of complications and adverse reactions in the results are expressed as percentages (%). Compare the two groups using the x^2 test for analysis. All statistical tests were bilateral, with P<0.05 indicating statistically significant differences.

RESULTS

Basic information

In this study, 101 septic neonates from the Affiliated People's Hospital of Ningbo University between October 2020 and December 2023 were divided into CS group (n=50) and CP group (n=51) based on different treatment modalities. The baseline demographic and baseline characteristics of the pediatric patients in both groups are demonstrated in table 1, these characteristics showed no remarkable differences among both groups (P>0.05). Thus, the randomization process achieved the important goal of randomly assigning participants to both groups, both groups were comparable at the pre-treatment level and the confounding of demographic/clinical factors did not affect the analysis of the results.

Primary results

Clinical efficacy

Combining the drug treatment effects of the pediatric patients in both groups we analyzed the clinical efficacy and the results are displayed in table 2. The total efficacy rate of treatment in CS group pediatric patients was 80.00% (40/50) and 90.20% (46/51) in CP group, which was statistical significance between the groups (P<0.05). The results showed better efficacy in CP group, indicating that the clinical efficacy of cefotaxime sodium in combination with penicillin in the treatment of neonatal sepsis is better than cefotaxime sodium alone.

Inflammatory indicators

The results of the comparison of inflammatory indicators among the two groups of pediatric patients are demonstrated in table 3. Pre-treatment, the TNF-α, IL-6, IL-8 and hs-CRP levels in both groups were not significantly different among groups as compared to each other (P>0.05). Post-treatment, the inflammatory indicators levels were 16.19±4.41 pg/mL, 20.76±5.81 pg/mL, 42.46±9.09 pg/mL and 55.86±9.97 mg/L in CS group and 10.29±1.87 pg/mL, 11.28±5.02 pg/mL, 28.49±8.35 pg/mL and 32.20±6.56 mg/L in CP group, respectively, all of which were significantly reduced versus pre-treatment and the CP group was significantly lower than the CS group (P<0.05). It indicated that the inflammatory indicators levels of both groups of pediatric patients were significantly decreased post-treatment and the CP group showed better improvement.

Immune indicators

We analyzed and compared the results of the immune function indicators of both groups and the results are presented in table 4. No remarkable differences were found in the immune indicators of both groups of pediatric patients at pre-treatment (P>0.05). Post-treatment, the IgA, IgG and IgM levels were 3.57±1.06 g/L, 9.19±1.50 g/L and 1.16±0.20 g/L, respectively, in the CS group and 4.53±1.06 g/L, 10.90±1.71 g/L and 1.48±0.21 g/L, respectively, in the CP group, which were all increased significantly higher than pre-treatment. CP group was significantly higher than CS group (P<0.05). It indicated that the immunity indicators of both groups improved significantly after treatment and the improvement of immune function was more obvious in the CP group.

Secondary results

Improvement of symptoms

We recorded the improvement of symptoms in the neonates of both groups as presented in table 5. Improvement in times of milk refusal, return to normal temperature, neurological symptoms and hospitalization in the CP group were 3.02±0.83 d, 3.25±0.65 d, 4.32±0.44 d and 6.79±0.83 d, respectively, which were significantly lower than the CS group's 4.89±1.05 d, 5.58±1.05 d, 6.33±0.46 d and 8.72±0.49 d (P<0.05). It indicates that the CP group had better clinical symptom improvement.

PCT levels and WBC counts

The results of serum PCT levels and WBC counts of neonates in both groups are demonstrated in table 6. Pre-treatment, no remarkable discrepancy was found among the PCT levels and WBC counts of the groups (P>0.05). Post-treatment, the PCT levels and WBC counts were 3.28±0.78 ng/mL and 19.92±3.60 $\times 10^8$/L in the CS group and 1.51±0.43 ng/mL and 15.63±2.56 $\times 10^8$/L in the CP group, respectively and the CP group was significantly lower than the CS group. It showed that the two neonates recovered well after treatment and the CP group had a better recovery.

Recurrence rate

No recurrence was seen in both groups. It indicates that both treatment modalities have some efficacy.

Complications

Neonatal sepsis is a serious infectious disease in the neonatal period, which is prone to complications and the complications in both groups are presented in table 7. No remarkable discrepancy was found in the incidence of shock, hypoxemia, acidosis and septic meningitis among the CS group and the CP group (P>0.05) and the incidence of necrotizing small bowel colitis in the CS group was greater the CP group (P<0.05). The total complication rate of 20.00% (10/50) was significantly greater in the CS group than the CP group, which was 7.84% (4/51) (P<0.05). It shows that the treatment used in CP group had better therapeutic effect and effectively reduced the complication rate.

Adverse reaction incidence

We followed up the pediatric patients to observe the adverse reactions. The occurrence of adverse reactions of varying degrees, such as hypotension, during treatment in both groups is demonstrated in table 8. The total incidence of adverse reactions in CS group pediatric patients was 16.00% (8/50), which was significantly greater than the CP group's 5.88% (3/51) (P<0.05). It indicates that the therapeutic efficacy of the treatment used in the CP group was better and safer.

DISCUSSION

In-depth analysis of the pathogenesis of neonatal sepsis reveals that the disease is mainly caused by various pathogenic bacteria that invade the circulatory system of neonates through various ways and the toxins produced by the reproduction and metabolism of the pathogenic bacteria cause systemic infections and it is prone to occur in neonates under 28 d of age, with the most important causative organisms being group B Streptococcus, Escherichia coli, Klebsiella pneumoniae and Staphylococcus (Shane *et al.*, 2017). Neonatal sepsis can be categorized into early-onset and late-onset according to the cause of the disease, in which late-onset sepsis is usually caused by postnatal infections, mostly due to nosocomial infections and environmental factors of life, with staphylococci as the main causative agent and with a low mortality rate.

Early-onset sepsis is usually caused by prenatal or intrapartum infections, with Escherichia coli and group B streptococci as the main causative organisms and is usually caused by factors in the mothers of the pediatric patients (premature rupture of membranes, intra-amniotic infections, etc.) and the onset of sepsis in the patients is often accompanied by pneumonia and multi-organ damage, with high mortality rates, which is a serious threat to the lives of the pediatric patients (Mariani *et al.*, 2022; Ogundare *et al.*, 2019).

For neonatal sepsis, pediatric patients are routinely given basic treatment such as nutritional support, warmth and correction of electrolyte disorders in the clinic to stabilize the clinical symptoms with the help of basic information (Nyenga *et al.*, 2021). After stabilization of pediatric patients, cefotaxime is usually given to pediatric patients. Cefotaxime belongs to a third-generation cephalosporin drug, which has antimicrobial effects and is effective against both gram-positive and gram-negative bacteria and can rapidly improve the clinical symptoms of septic pediatric patients. Although the use of cefotaxime in the treatment of neonatal sepsis is significant, it is not effective in the enhancement of immunity in pediatric patients (Hile *et al.*, 2020). Penicillin is a peptidoglycan antibiotic that interferes with the peptidoglycan of the cell wall of pathogenic bacteria, reduces the synthesis of phospholipids and peptides in the cell wall, inhibits the synthesis of the cell wall and then inhibits the growth of bacteria as well as their proliferation and ultimately plays an effective role in the killing of bacteria. Its half-life is relatively short and it can be rapidly absorbed and distributed to various tissues of the body after intravenous infusion, which can change the permeability of the cell membrane of the pathogenic bacteria and inhibit their RNA synthesis and has a strong bactericidal effect (Boscarino *et al.*, 2024). Therefore, cefotaxime sodium in combination with penicillin was selected for the treatment of neonatal sepsis in this study to observe the clinical efficacy.

IL-6 is an inflammatory mediator involved in the acute inflammatory response, IL-8 and TNF-α are common pro-inflammatory cytokines and hs-CRP is closely related to acute bacterial infections and all four of them are commonly used as indicators of the severity of infectious diseases (Zwiri *et al.*, 2022). The higher the level of inflammatory factors, the more serious the inflammatory reaction of the body and the detection of changes in inflammatory indexes has a certain guiding role in the assessment of the condition of neonatal sepsis and the effectiveness of treatment (Li *et al.*, 2020). Changes in immunoglobulin levels (IgA, IgG, IgM) can reflect the immune status of newborns. In this study, both groups showed a significant increase in the above indicators after treatment, with the CP group showing better results, suggesting that treatment may promote infection control by regulating immunity. This elevation is related to both the resolution of infection and immune maturation: after the resolution of infection, the stimulation of pathogens decreases, the synthesis function of plasma cells is restored and especially the recovery of IgM reflects the normalization of immune response.

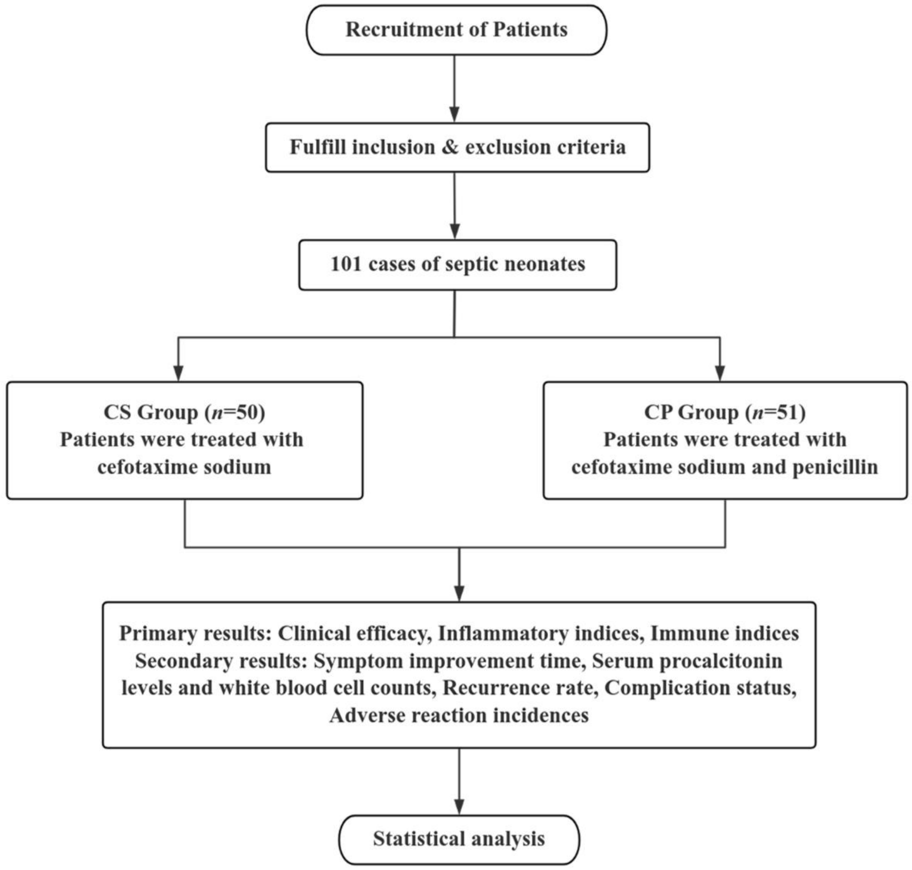

Fig. 1: The flow chart

Table 1: Patient demographics and baseline disease characteristics

Parameter	CS group (*n*=50)	CP group (*n*=51)	t/x^2	*P*
Age (d)	5.45±2.04	5.47±2.36	0.046	0.964
Sex (male/female)	29/21	30/21	0.021	0.886
Weight (kg)	3.21±0.37	3.26±0.42	0.634	0.527
Normal birth / Cesarean section	38/12	40/11	0.113	0.737
Gestational age (week)	33.82±1.10	33.96±1.26	0.594	0.554
Full term/premature	21/29	22/29	0.020	0.886
Preterm/ Late term	26/24	28/23	0.181	0.671
Birth asphyxia (yes/no)	7/43	8/43	0.157	0.692
Premature rupture of membranes (yes/no)	16/34	16/35	0.023	0.879
Amniotic fluid contamination (yes/no)	8/42	7/44	0.157	0.692
Prenatal infection in mother (yes/no)	9/41	10/41	0.130	0.718

Table 2: Clinical efficacy analysis

Group	Obvious effect (*n*)	Effective (*n*)	Ineffective (*n*)	Total effective rate (*n*, %)
CS group	15	25	10	40 (80.00)
CP group	18	28	5	46 (90.20)
x^2		3.922		
P		<0.05		

Table 3: Comparisons of inflammation indicators ($\bar{x}$±s)

norm	time	CS group	CP group	t	P
TNF-α (pg/mL)	Pre-treatment	27.88±7.57	28.10±8.55	0.137	0.892
	Post-treatment	16.19±4.41*	10.29±1.87*	-8.783	<0.001
IL-6 (pg/mL)	Pre-treatment	34.35±7.59	34.56±6.25	0.152	0.880
	Post-treatment	20.76±5.81*	11.28±5.02*	-8.780	<0.001
IL-8 (pg/mL)	Pre-treatment	64.72±10.60	64.89±11.68	0.077	0.939
	Post-treatment	42.46±9.09*	28.49±8.35*	-8.046	<0.001
hs-CRP (mg/L)	Pre-treatment	122.63±18.42	122.31±24.03	-0.075	0.940
	Post-treatment	55.86±9.97*	32.20±6.56*	-14.116	<0.001

Note: "*" represents significantly discrepancy compared with pre-treatment, P<0.05.

Table 4: Immune function indicators ($\bar{x}$±s, g/L)

norm	time	CS group	CP group	t	P
IgA	Pre-treatment	2.01±0.59	2.16±0.57	1.300	0.197
	Post-treatment	3.57±1.06*	4.53±1.06*	4.551	<0.001
IgG	Pre-treatment	7.24±1.40	7.15±1.41	-0.322	0.748
	Post-treatment	9.19±1.50*	10.90±1.71*	5.338	<0.001
IgM	Pre-treatment	0.95±0.25	0.97±0.29	0.371	0.712
	Post-treatment	1.16±0.20*	1.48±0.21*	7.839	<0.001

Note: "*" represents significantly discrepancy compared with pre-treatment, P<0.05.

Table 5: Comparison of symptom improvement time ($\bar{x}$±s, d)

Group	Milk refusal	Return of normal body temperature	Neurological symptoms	Hospitalization
CS group	4.89±1.05	5.58±1.05	6.33±0.46	8.72±0.49
CP group	3.02±0.83	3.25±0.65	4.32±0.44	6.79±0.83
x^2	-9.940	-13.438	-22.443	-14.194
P	<0.001	<0.001	<0.001	<0.001

Table 6: PCT level and WBC count ($\bar{x}$±s)

norm	time	CS group	CP group	t	P
PCT (ng/mL)	Pre-treatment	7.22±1.21	7.44±1.09	0.960	0.339
	Post-treatment	3.28±0.78*	1.51±0.43*	-14.160	<0.001
WBC (×10^8/L)	Pre-treatment	32.32±5.54	32.17±4.91	-0.144	0.886
	Post-treatment	19.92±3.60*	15.63±2.56*	-6.912	<0.001

Note: "*" represents significantly discrepancy compared with pre-treatment, P<0.05.

Table 7: Complications

	CS group	CP group	x^2	P
Shock (n, %)	1 (2.00)	1 (1.96)	0.000	1.000
Hypoxemia (n, %)	2 (4.00)	1 (1.96)	0.687	0.407
Acidosis (n, %)	2 (4.00)	1 (1.96)	0.687	0.407
Septic meningitis (n, %)	3 (6.00)	1 (1.96)	2.083	0.149
Necrotizing small bowel colitis (n, %)	2 (4.00)	0 (0.00)	4.082	0.043
Total incidence (n, %)	10 (20.00)	4 (7.84)	5.980	<0.05

Table 8: Adverse reactions incidence

Group	Hypotension	Vomiting	Diarrhea	Skin reactions	Total incidence (n, %)
CS group	2	3	2	1	8 (16.00)
CP group	1	1	1	0	3 (5.88)
x^2	5.107				
P	<0.05				

At the same time, infection control reduces the inhibition of immune development, coupled with the maturation of neonatal B cell function, which assists in immunoglobulin synthesis. Among them, the increase in IgG may be related to the decrease in maternal IgG consumption and the initiation of self-synthesis, while IgA and IgM more reflect autoimmune activation and maturation. Both factors contributed to the change in indicators. (Beudeker *et al.*, 2022). The total effective rate of treatment of CS group pediatric patients was 80.00% (40/50) was significantly lower than the 90.20% (46/51) of CP group ($P<0.05$) and the inflammatory indicators of CP group were significantly lower than the CS group and the immune indicators were above the CS group ($P<0.05$). The results showed that cefotaxime sodium combined with penicillin was more effective in the treatment of neonatal sepsis, which could accelerate the recovery of pediatric patients, reduce the inflammatory response and improve the immune function. The reason for the analysis is that the combination of two drugs can effectively kill bacteria, enhance neutrophil phagocytosis, help control inflammatory factors in children's bodies and thus improve clinical treatment effectiveness. (Shrivastava *et al.*, 2023).

PCT level and WBC count reflect the degree of infection in the organism and are important in the treatment of neonatal sepsis (Celik *et al.*, 2022). The results of this study showed that post-treatment, milk refusal improved, body temperature returned to normal, neurological symptoms and length of hospitalization, PCT levels and WBC counts and the total incidence of complications and adverse reactions were significantly lower than the CS group in the CP group ($P<0.05$) and no recurrence was seen in either group. Zhang reported similar findings in a study of cefotaxime combined with gamma globulin in the treatment of neonatal sepsis (Zhang, 2020). It showed that both treatments were efficacious and both reduced the degree of physical infection in pediatric patients with good control and no recurrence. It indicates that the treatment modality of cefotaxime sodium in combination with penicillin has better efficacy, better improvement of clinical symptoms, reduces complications and adverse reactions, shortens hospitalization time and is worth clinical promotion. This study has certain limitations. Insufficient analysis of potential confounding factors, such as gestational age, severity of infection and pathogen type, may interfere with the objectivity of the efficacy comparison between the two groups.

Secondly, there are shortcomings in the drug dosage regimen. In this study, the doses of cefotaxime sodium and penicillin were fixed for all newborns without individualized adjustment based on gestational age or renal function indicators, which may lead to the risk of insufficient or excessive dosage in some children, thereby affecting the accuracy of treatment efficacy evaluation. In addition, the relatively small sample size did not cover all different conditions of neonatal sepsis, which may lead to biased research results and affect the extrapolation and reliability of conclusions. The limitation of single center studies is that there may be differences in patients' underlying conditions, which could affect the generalizability of the research results. The follow-up time is relatively short, making it difficult to fully evaluate the long-term effectiveness and safety of treatment. Therefore, future research should further expand the sample size, include multi center data, extend follow-up time and strictly control confounding factors. Individualized dosage regimens based on gestational age and liver and kidney function should be developed to more comprehensively evaluate the efficacy and safety of cefotaxime sodium and penicillin combination therapy for neonatal sepsis.

CONCLUSION

In this study, we analyzed the clinical efficacy of cefotaxime sodium in combination with penicillin on neonatal sepsis and its effect on immune level, in order to provide a new drug pathway for the treatment of this type of disease. The results demonstrated that pre-treatment, no remarkable discrepancy was found among the indicators of both groups. Post-treatment, all indicators of pediatric patients in both groups improved. The total clinical effectiveness and immunity indicators of CP group were above the CS group and the inflammation indicators, symptom improvement time, PCT level and WBC count, total incidence of complications and adverse reactions were significantly lower than the CS group and no recurrence was observed in both groups.

This study shows that cefotaxime sodium combined with penicillin is effective in treating neonatal sepsis, effectively improving the immune function of pediatric patients, reducing inflammatory response, decreasing the time for symptomatic improvement, lowering the total incidence of complications and adverse reactions and no relapse was observed, which provides a new reference method for the clinical treatment of the related diseases. However, this study exists a small sample size and the clinical medication course is short, failed to observe the long-term effectiveness of the method of treatment. Due to the limitation of the conditions, it failed to include more specific indexes such as others. Multi-center, large-sample, high-quality clinical studies can be carried out in the later stage for validation.

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Author's contribution
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Data availability statement
The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Ethical approval
This study was approved by the Ethics Committee of the affiliated people's hospital of Ningbo university (Ethics Approval No.: 2024-093). We secured a signed informed consent form from every participant.

Conflict of interest
The authors declare that they have no financial conflicts of interest.

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