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Original Article

Clinical efficacy and safety of meropenem in the treatment of severe neonatal bacterial infectious pneumonia

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Abstract: Objective: The goal of this study was to analyze the clinical efficacy and safety of meropenem for the treatment of severe neonatal bacterial infectious pneumonia. Methods: A total of 110 cases of neonates with bacterial infectious pneumonia that were admitted to Qilu Children's Hospital of Shandong University from December 2014 to December 2017 were gathered and divided into an experimental group (n=55) and a control group (n=55) according to the parity of their admission order. The control group was treated with imipenem, while the experimental group was treated with meropenem, and then the two groups were compared in efficacy, adverse reactions, and inflammatory indexes. Results: There was no statistical difference in nutritional status and inflammatory indexes between the two groups before treatment (all P>0.05). Compared with the control group, the experimental group showed better efficacy, lower incidence of adverse reactions as well as lower indexes of procalcitonin, white blood cell, c-reactive protein, and neutrophils after treatment, and the differences were statistically significant (all P<0.05). Conclusion: Meropenem can effectively improve the condition of neonates with bacterial infectious pneumonia, and it has fewer adverse reactions, which is safer and more reliable.

Keywords: Meropenem, severe neonatal bacterial infectious pneumonia, clinical efficacy, safety

Introduction

Severe neonatal bacterial infectious pneumonia is an extremely common neonatal disease. Due to weak immune function, neonates may easily suffer from severe bacterial pneumonia if they are not treated in a timely manner or appropriate method once they are infected, which increases mortality. In addition, due to poor excretion function of kidney and liver, the safety index is relatively low during drug use among neonates and various toxic side effects are prone to occur. Therefore, it is an issue with high clinical attention to select an effective and safe drug for severe neonatal bacterial infectious pneumonia. The high incidence of this disease is an important cause of neonatal death [1]. Moreover, due to incomplete development of liver and kidney function, the metabolic rate of drugs in the liver is slow, so it is easy to cause other toxic side effects for high drug concentration. Imipenem is a commonly used drug for clinical treatment of severe bacterial infectious pneumonia, but it can easily lead to elevated alanine aminotransferase, nausea, vomiting, and rash, so patients with allergic constitution should use it cautiously [2]. Antibiotics selection for clinical treatment is particularly important. Based on the above study, in order to analyze the clinical efficacy and safety of meropenem in the treatment of neonatal bacterial infectious pneumonia, 110 cases of neonates with bacterial infectious pneumonia admitted to Qilu Children's Hospital of Shandong University from December 2014 to December 2017 were gathered and reported as follows.

Materials and methods

Baseline data

Study objects: A total of 110 cases of neonates with bacterial infectious pneumonia admitted to Qilu Children's Hospital of Shandong University from December 2014 to December 2017 were gathered and divided into an experi-

Table 1. Comparison of general information between the two groups ($\bar{x}$ ±sd)

	Experiment group (n=55)	Control group (n=55)	χ^2/t	P
Gender (n, %)				
Female	23 (41.82)	25 (45.45)	0.1478	0.7006
Male	32 (58.18)	30 (54.55)		
Average days of age (d)	13.51±5.92	13.19±6.28	0.2749	0.7839
Average body mass (kg)	3.23±0.64	3.17±0.56	0.5232	0.6019
Plasma albumin (mg/dL)	25.69±8.26	25.65±8.32	0.0253	0.9799
Hemoglobin (mg/dL)	98.26±9.25	98.35±9.16	0.0512	0.9592
Pre-plasma albumin (pg/dL)	112.02±11.02	111.98±12.01	0.0181	0.9855

mental group (n=55) and a control group (n=55) according to the parity of their admission order. In the experimental group, the ratio of female to male was 23:32; the minimum age was 2 days; the maximum age was 25 days; the average age was (13.51±5.92) days; the body mass was (2.2-4.1) kg and the average body mass was (3.23±0.64) kg. In the control group, the ratio of female to male was 25:30; the minimum age was 3 days; the maximum age was 23 days; the average age was (13.19±6.28) days; the body mass was (2.4-3.8) kg and the average body mass was (3.17±0.56) kg.

Inclusion criteria: 1) All neonates met the diagnostic criteria for severe neonatal bacterial infectious pneumonia in the Pediatrics (the 3rd version) [3]. Namely, the leukocyte level was above $2.0*10^9$/L; serum antibody detection and fluorescent antibody detection showed that IgM and IgG significantly increased and cord blood IgM was above 200-300 mg/L; X-ray examination showed changes of interstitial pneumonia; and blood examination showed c-reactive protein (CRP) level increased significantly. 2) All study objects were full-term neonates.

Exclusion criteria: 1) neonates with other congenital diseases; 2) neonates with unsound liver and kidney functions; 3) neonates whose family members did not support this study; 4) neonates born after multiple pregnancy; 5) premature neonates; 6) neonates whose mothers had maternal complications such as gestational diabetes mellitus and hypertension; 7) neonates without complete clinical data.

This study was approved by the Ethics Committee of Qilu Children's Hospital of Shandong University, and family members signed the informed consent.

Methods

All study subjects gave sputum for culture, blood for culture, blood for routine examination, and had a CRP test before taking the drugs. The control group was treated with imipenem (Hisun Pfizer Pharmaceutical Co., Ltd., 1 g per dosage) 10-20 mg/kg dissolved in 250 mL 0.9% sodium chloride solution, which was administered once daily through intravenous drip for a treatment course of 7 days.

The experimental group was treated with meropenem (Shenzhen Haibin Pharmaceutical Co., Ltd., 0.25 g per dosage) 10-20 mg/kg dissolved in 100 mL 0.9% sodium chloride solution, which was administered once every eight hours through intravenous drip for a treatment course of 7 days.

Observation indexes

Efficacy: Recovery referred to the situation where all indexes in laboratory tests returned to normal and all clinical symptoms disappeared. Marked effect referred to the situation where only one index in laboratory tests had not returned to normal or only one clinical symptom did not disappear. Effect referred to the situation where all indexes in laboratory tests and all clinical symptoms showed improvement. No effect referred to the situation where all indexes in laboratory tests and all clinical symptoms showed no significant change after 72 hours of treatment, and there was even a deterioration trend. The total effective rate=Number of cases of (recovery+marked effect+effect)/total number of cases*100% [4, 5].

Adverse reaction: The incidence of secondary fungal infection, elevated transaminase activity, rash, and vomiting was statistically calculated.

Inflammatory index: 5 mL of fasting venous blood was drawn from all study objects before and after treatment for centrifugation to detect white blood cell (WBC) count, neutrophils (N),

Table 2. Comparison of efficacy between the two groups (n, %)

	Recovery	Marked effect	Effect	No effect	Total effective rate
Experiment group (n=55)	18 (32.73)	25 (45.45)	10 (18.18)	2 (3.64)	53 (96.36)
Control group (n=55)	10 (18.18)	18 (32.73)	14 (25.45)	13 (23.64)	42 (76.36)
χ^2					9.3404
P					0.0022

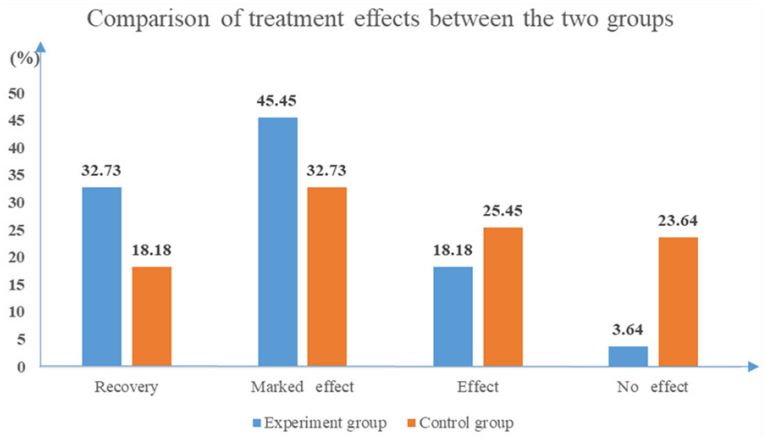

Figure 1. Comparison of efficacy between the two groups (%).

procalcitonin (PCT) and CRP through an automatic biochemical analyzer (Shenzhen iCubio Biomedical Technology Co., Ltd., model: iChem-520). The levels of the above indexes were positively correlated with the severity of infection in patients [6, 7].

Recurrence rate: The recurrence rates of the two groups through 3 months of follow-up were statistically calculated.

Statistical method

Study data in this paper was statistically analyzed with SPSS23.0 software. The measurement data (inflammation index) is represented in mean±standard deviation ($\bar{x}$±sd) as shown using a t-test. The enumeration data (adverse reaction, efficacy and recurrence rate) is expressed as a percentage, and was processed with χ^2 test. P<0.05 is considered statistically significant.

Results

Comparison of general information between the two groups

In comparison of general information such as gender, days of age, body mass, nutritional indexes between the two groups, the statistical results were all P>0.05, which showed no significant difference as shown in **Table 1**.

Comparison of efficacy between the two groups

The total effective rate in the experiment group was significantly higher than that in the control group, which showed statistical difference (P<0.05) as shown in **Table 2** and **Figure 1**.

Comparison of incidence of adverse reactions between the two groups

The incidence of adverse reactions in the experiment group was significantly lower than that in the control group (3.64% and 20.00%, respectively), which showed statistical difference (P<0.05) as shown in **Table 3**.

Comparison of inflammatory indexes between the two groups

There was no statistical difference between the two groups of indexes of PCT, WBC, CRP and N before treatment (all P>0.05). After treatment, those indexes in the experimental group were significantly lower than those in the control group, and the difference was statistically significant (all P<0.05) as shown in **Table 4**.

Comparison of recurrence rate between the two groups

The recurrence rate in the experimental group was significantly lower than that in the control group (3.64% and 20.00%, respectively), which was statistically significant (P<0.05) as shown in **Table 5**.

Discussion

Severe neonatal bacterial infection is a common clinical disease. It is mainly caused by bacterial invasion in the blood circulation system of patients in the neonatal period, and growth and

Table 3. Comparison of incidence of adverse reactions between the two groups (n, %)

	Secondary fungal infection	Elevated activity of transaminase	Rush	Vomiting	Incidence
Experiment group (n=55)	0	1 (1.82)	0	1 (1.82)	2 (3.64)
Control group (n=55)	2 (3.64)	3 (5.45)	3 (5.45)	3 (5.45)	11 (20.00)
χ^2					7.0658
P					0.0078

Table 4. Comparison of inflammatory indexes between the two groups ($\bar{x}\pm sd$)

	Experiment group (n=55)	Control group (n=55)	t	P
PCT (ng/mL)				
Before treatment	6.69±2.14	6.66±2.22	0.0721	0.9426
After treatment	2.29±0.15	5.42±0.37	58.1408	<0.001
WBC (*10^9/L)				
Before treatment	28.62±3.28	28.59±3.33	0.0475	0.9621
After treatment	18.02±2.06	24.69±2.86	14.0342	<0.001
CRP (ng/mL)				
Before treatment	12.63±2.69	12.59±2.71	0.0776	0.9382
After treatment	7.47±1.05	10.27±1.15	13.5087	<0.001
N (*10^9/L)				
Before treatment	15.26±2.12	15.22±2.31	0.0946	0.9248
After treatment	8.26±1.03	11.06±1.17	13.3215	<0.001

Note: PCT, procalcitonin; WBC, white blood cell; CRP, c-reactive protein; N, neutrophils.

Table 5. Comparison of recurrence rate between the two groups

	Case of recurrence (n)	Recurrence rate (%)
Experiment group (n=55)	2	3.64
Control group (n=55)	11	20.00
χ^2		7.0658
P		0.0079

reproduction of bacteria in the blood circulation system, which can easily lead to systemic infection. Severe neonatal bacterial infectious pneumonia is the most typical form, which has a relatively high incidence in neonatal diseases and is also an important cause of disability or death in neonates [8, 9]. Imipenem has been clinically applied in the treatment of various infectious diseases, but patients allergic to lidocaine should be forbidden from using it. In addition, Imipenem can easily cause patients to experience various allergic reactions and gastrointestinal reactions, which significantly reduces the tolerance in neonatal treatment, so its clinical safety is poor [10, 11]. Moreover, because of unsound development of organ function, poor excretion function of kidney and liver of neonates, and low safety index of clinical medication, improperly controlled drugconcentrationcaneasilycause a variety of toxic side effects, threatening the lives of patients [12, 13].

Carbapenems meropenem c an easily penetrate most gram-negative and gram-positive bacteria, and inhibit the composition of cell walls after reaching the effect target, thus killing bacteria. Its anti-inflammatory effect is markedly beneficial [14, 15]. The results of this study showed that the levels of PCT, WBC, CRP, and N in the experimental group were significantly lower than those in the control group, which showed statistical difference and confirmed the anti-inflammatory effects of meropenem. After entering a human body, meropenem is mainly distributed in extracellular fluid, and mostly filtered through glomerulus. Compared with imipenem, meropenem has relatively lower nephrotoxicity, and can provide relatively high bacterial clearance rate. It can penetrate a cell walls and has a good inhibitory effect on cell wall synthesis, with remarkable antibacterial effect and high stability [16-18]. The results of this study showed that efficacy in the experimental group was significantly better than that in the control group, and the recurrence rate in the experimental group was significantly lower than that in the control group, the differences were statistically significant. It confirmed the effectiveness of meropenem in the treatment

of severe neonatal bacterial infectious pneumonia.

In addition, the affinity between meropenem and Gamma-aminobutyric acid (GABA) receptor is relatively weak, which can effectively avoid adverse reactions in the central nervous system. The distribution volume of meropenem in premature infants is higher than that in adults, and the clearance rate of meropenem in which is lower than that in adults [19-21]. With continuous growth of the neonates, the clearance rate of meropenem will continue to increase. Compared with imipenem and other drugs, meropenem has a weaker affinity with GABA receptors in cerebral nerve cells. Therefore, there are few central nervous system reactions such as convulsion and irritability in the neonates, and the tolerance is relatively high [22-24]. The results of this study show that the incidence of adverse reactions in the experimental group is significantly lower than that in the control group, which showed statistical difference and confirmed the safety of meropenem in the treatment of severe neonatal bacterial infectious pneumonia. With a wider scope of application, meropenem effectively makes up for the deficiencies of imipenem, which is worthy to be the first choice of treatment for severe bacterial pneumonia in neonates and has high reference value for clinical treatment of bacterial infectious diseases.

However, this study has several limitations, because the sample size is not large, the specific dosage and treatment course of meropenem in the treatment of severe bacterial pneumonia remain to be studied. Therefore, the next step is to further expand the sample size and analyze the optimal use phase, suitable dosage, and duration of treatment of meropenem, so as to provide guidance for clinical treatment of severe bacterial pneumonia.

In summary, in the treatment of neonates with severe bacterial infectious pneumonia, meropenem can effectively lighten the clinical symptoms of the neonates and the side effects of drugs and will cause relatively low recurrence rate, so it has relatively high safety and is worthy of further investigation.

Disclosure of conflict of interest

None.

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