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Retrospective Study

Cefoperazone sodium/sulbactam sodium vs piperacillin sodium/tazobactam sodium for treatment of respiratory tract infection in elderly patients

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Abstract**BACKGROUND**

Respiratory tract infections in the elderly are difficult to cure and can easily recur, thereby posing a great threat to patient prognosis and quality of life.

AIM

To investigate the therapeutic effects of different antibiotics in elderly patients with respiratory tract infection.

METHODS

Seventy-four elderly patients with respiratory tract infection were randomly allocated to a study ($n = 37$; treated with cefoperazone sodium/sulbactam sodium) or control ($n = 37$; treated with piperacillin sodium/tazobactam sodium on the basis of routine symptomatic support) group. Both groups were treated for 7 d. Time to symptom relief (leukocyte recovery; body temperature recovery; cough and sputum disappearance; and rale disappearance time), treatment effect, and laboratory indexes [procalcitonin (PCT), C-reactive protein (CRP), white blood cell count (WBC), and neutrophil percentage (NE)] before and 7 d after treatment and the incidence of adverse reactions were assessed.

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RESULTS

In the study group, the time to WBC normalization (6.79 ± 2.09 d), time to body temperature normalization (4.15 ± 1.08 d), time to disappearance of cough and sputum (6.19 ± 1.56 d), and time to disappearance of rales (6.68 ± 1.43 d) were shorter than those of the control group (8.89 ± 2.32 d, 5.81 ± 1.33 d, 8.77 ± 2.11 d, and 8.69 ± 2.12 d, respectively; $P = 0.000$). Total effective rate was higher in the study group (94.59% *vs* 75.68%, $P = 0.022$). Serum PCT (12.89 ± 3.96 µg/L), CRP (19.62 ± 6.44 mg/L), WBC ($20.61 \pm 6.38 \times 10^9/L$), and NE ($86.14 \pm 7.21\%$) levels of the study group before treatment were similar to those of the control group (14.05 ± 4.11 µg/L, 18.79 ± 5.96 mg/L, $21.21 \pm 5.59 \times 10^9/L$, and $84.39 \pm 6.95\%$, respectively) with no significant differences ($P = 0.220, 0.567, 0.668, \text{ and } 0.291$, respectively). After 7 d of treatment, serum PCT, CRP, WBC, and NE levels in the two groups were lower than those before treatment. Serum PCT (2.01 ± 0.56 µg/L), CRP (3.11 ± 1.02 mg/L), WBC ($5.10 \pm 1.83 \times 10^9/L$), and NE ($56.35 \pm 7.17\%$) levels were lower in the study group than in the control group (3.29 ± 0.64 µg/L, 5.67 ± 1.23 mg/L, $8.13 \pm 3.01 \times 10^9/L$, and $64.22 \pm 8.08\%$, respectively; $P = 0.000$). There was no significant difference in the incidence of adverse reactions between the groups (7.50% *vs* 12.50%, $P = 0.708$).

CONCLUSION

Piperacillin sodium/tazobactam sodium is superior to cefoperazone sodium/sulbactam sodium in the treatment of elderly patients with respiratory tract infection with a similar safety profile.

Key Words: Cefoperazone sodium; Sulbactam sodium; Piperacillin sodium; Tazobactam sodium; Respiratory tract infection; Elderly

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Core Tip: Antibiotics are the main treatment for respiratory tract infection in elderly patients. Piperacillin sodium/tazobactam sodium belongs to the β-lactam antibiotics class, with a wide antibacterial spectrum, and plays an important role in the treatment of diseases. In this study, the authors wanted to determine the therapeutic value and safety of different antibiotics.

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INTRODUCTION

As a class of clinical multiple diseases, respiratory tract infections include lower respiratory tract infections and upper respiratory tract infections. Infection can occur in any age group, and most patients can achieve good recovery after active and standardized intervention. However, the respiratory mucosa of the elderly population has poor clearance. Additionally, immunity and resistance are poor in this population, and respiratory tract infections can easily occur due to external pathogen invasion and infection[1-3]. At the same time, respiratory tract infections in elderly patients are difficult to cure and can easily reoccur, thereby posing a great threat to patient prognosis and quality of life. As a consequence, it is very important to take effective measures to treat these patients as soon as possible[4,5].

Antibiotics are the main treatment for respiratory tract infection in the elderly. Cefoperazone sodium/sulbactam sodium is more commonly used, and can relieve the clinical symptoms to some extent, but the overall effect is not optimal[6,7]. In addition, piperacillin sodium/tazobactam sodium is also commonly used in respiratory tract infections. Piperacillin sodium/tazobactam sodium belongs to the β-lactam antibiotics class, with a wide antibacterial spectrum, and plays an important role in the treatment

of diseases[8].

This study selected 74 elderly patients with respiratory tract infection at our hospital to determine the therapeutic value and safety of different antibiotics.

MATERIALS AND METHODS

General information

A total of 74 elderly patients with respiratory tract infection treated at our hospital from January 2019 to October 2020 were randomly allocated into either a study group ($n = 37$) or a control group ($n = 37$). In the study group, there were 19 males and 18 females, aged from 61 to 79 years, with an average age of (70.04 ± 6.78) years, and the disease types included lung abscess ($n = 6$), bronchiectasis with infection ($n = 6$), bacterial pneumonia ($n = 11$), and chronic bronchitis ($n = 14$). In the control group, there were 22 males and 15 females, aged from 60 to 82 years, with an average age of (71.12 ± 7.03) years, and the disease types included pulmonary abscess ($n = 4$), bronchiectasis with infection ($n = 7$), bacterial pneumonia ($n = 13$), and chronic bronchitis ($n = 13$). The clinical data such as sex, age, and type of disease were comparable between the two groups ($P > 0.05$).

Selection criteria

Inclusion criteria: The inclusion criteria were: (1) Patients who were confirmed with respiratory tract infection by laboratory examinations such as radiography and blood routine examination; (2) Age ≥ 60 years old; (3) Having been briefed regarding the details of this study and having signed a consent form; and (4) Not taking related treatment before being included in the study.

Exclusion criteria: The exclusion criteria were: (1) Patients with organic diseases such as kidney and liver disease; (2) Allergic constitution; (3) Allergic history to known drugs; (4) Patients who showed poor compliance and were unable to cooperate with the investigators; and (5) Patients with other systemic infectious diseases.

Methods

After admission, the two groups of patients were treated with routine symptomatic support, including relieving asthma, resolving phlegm, and relieving cough symptoms. Different medication schemes were adopted on this basis. The control group was treated with cefoperazone sodium/sulbactam sodium [Zhijun (Shenzhen) Pharmaceutical Co., Ltd., Chinese medicine standard H20040401] *via* an intravenous drip of 3 g/once/12 h. The study group was treated with piperacillin sodium/tazobactam sodium (Hainan General Kangli Pharmaceutical Co., Ltd., H20103063) *via* an intravenous drip of 3.375 g piperacillin sodium/tazobactam sodium + sodium chloride injection 250 mL once/6 h. Both groups were treated for 7 d.

Observation indexes

The main indexes were as follows: (1) The time to symptom relief of the two groups was calculated, including the time to recovery of white blood cells, body temperature, cough and sputum, and rales; (2) After 7 d of treatment, the therapeutic effects of the two groups were assessed. The treatment was deemed markedly effective if the blood routine examination was normal and the clinical symptoms disappeared completely, and the X-ray examination showed that the absorption of pulmonary lesions was more than 90%. The treatment was deemed effective if the clinical symptoms partially disappeared, and the X-ray examination showed that the absorption of pulmonary lesions was 50%-89%. The treatment was deemed invalid if it was not up to the above standard. The total effective rate was calculated as (markedly effective + effective) / total number of cases $\times 100\%$ [9]; (3) The levels of laboratory indexes [procalcitonin (PCT), C-reactive protein (CRP), leukocyte count (WBC), and neutrophil percentage (NE)] were counted both before and 7 d after treatment; and (4) The incidence of adverse reactions in the two groups was calculated.

Statistical analysis

The data were analyzed with SPSS version 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). The measurement data are described as the mean \pm SD and comparisons between treatment groups were made using Student's *t*-tests. The counting data are described as frequency and constituent ratio (%) and were tested by the χ^2 test. A non-parametric test was used to

compare the measurement data that were not normally distributed. $P < 0.05$ indicated that the difference was statistically significant.

RESULTS

Time to symptom relief of the two groups

The times to recovery of leukocytes, body temperature, cough and sputum, and rales in the study group were 6.79 ± 2.09 d, 4.15 ± 1.08 d, 6.19 ± 1.56 d, and 6.68 ± 1.43 d, respectively, which were significantly shorter than those in the control group (8.89 ± 2.32 d, 5.81 ± 1.33 d, 8.77 ± 2.11 d, and 8.69 ± 2.12 d, respectively) ($P = 0.000$ for all) (Table 1).

Therapeutic effects of the two groups

The total effective rate of the study group (94.59%) was significantly higher than that of the control group (75.68%; $P = 0.022$) (Table 2).

Serum levels of laboratory indexes in the two groups before and 7 d after treatment

There was no significant difference in serum levels of PCT, CRP, WBC, or NE between the study group (12.89 ± 3.96 $\mu\text{g/L}$, 19.62 ± 6.44 mg/L, $20.61 \pm 6.38 \times 10^9/\text{L}$, and $86.14 \pm 7.21\%$, respectively) and the control group (14.05 ± 4.11 $\mu\text{g/L}$, 18.79 ± 5.96 mg/L, $21.21 \pm 5.59 \times 10^9/\text{L}$, and $84.39 \pm 6.95\%$, respectively) before treatment ($P = 0.220$, 0.567 , 0.668 , and 0.291 , respectively). After 7 d of treatment, the levels of serum PCT, CRP, WBC, and NE in both groups were lower than those before treatment. The serum levels of PCT, CRP, WBC, and NE in the study group (2.01 ± 0.56 $\mu\text{g/L}$, 3.11 ± 1.02 mg/L, $5.10 \pm 1.83 \times 10^9/\text{L}$, and $56.35 \pm 7.17\%$, respectively) were lower than those in the control group (3.29 ± 0.64 $\mu\text{g/L}$, 5.67 ± 1.23 mg/L, $8.13 \pm 3.01 \times 10^9/\text{L}$, and $64.22 \pm 8.08\%$, respectively) ($P = 0.000$ for all) (Table 3).

Incidence of adverse reactions in the two groups

There was no significant difference in the incidence of adverse reactions between the study group (7.50%) and the control group (12.50%; $P = 0.708$) (Table 4).

DISCUSSION

Respiratory tract infection is a common type of disease in respiratory departments. The incidence of respiratory infection continues to increase in recent years. It is affected by many factors such as environmental pollution, smoking, and the aging of the population. At present, it has become especially a serious threat to the quality of life and the physical and mental health of the elderly population[10,11]. As a consequence, there is an urgent need to find a safe and effective antibiotic regimen for the treatment of respiratory tract infection in the elderly.

Cefoperazone sodium/sulbactam sodium is a common compound preparation for the clinical treatment of respiratory tract infection. Cefoperazone belongs to the third generation cephalosporins, but it lacks good stability in the presence of β -lactamase. In addition, combined with sulbactam sodium, it can produce significant synergistic antibacterial activity against negative bacteria[12,13]. Piperacillin sodium/tazobactam sodium is also commonly used in respiratory tract infection, and it is also a compound preparation. Piperacillin sodium is a penicillin antibiotic, which can inhibit the synthesis of pathogenic bacterial cell wall, so as to achieve bactericidal and bacteriostatic purposes. Tazobactam sodium is a β -lactamase inhibitor, which has a good inhibitory effect on clinically important β -lactam and type I enzymes mediated by some chromosomes. Moreover, the inhibition intensity and breadth of tazobactam sodium are significantly better than those of sulbactam sodium. As a consequence, the combination of piperacillin sodium and tazobactam sodium can effectively broaden the antibacterial spectrum, regulate the sensitivity of drug-resistant bacteria, and improve the antibacterial effect[14,15]. The results of Bao *et al*[16] show that the total effective rate of piperacillin sodium/tazobactam sodium can reach 97.50%, and the time for the drug to take effect, the time to symptom improvement, and the time for physical signs to disappear are relatively short after elderly patients with respiratory tract infection are treated with piperacillin/tazobactam. Torres *et al*[17] confirmed that the clinical efficacy (93.33%) and bacterial clearance rate (93.33%) of piperacillin tazobactam in elderly patients with respiratory tract infection were significantly higher

Table 1 Comparison of time to symptom relief between the two groups (mean \pm SD, d)

Group	<i>n</i>	Time to recovery of white blood cells	Time to recovery of body temperature	Time to disappearance of cough and expectoration	Time to disappearance of rales
Study	37	6.79 \pm 2.09	4.15 \pm 1.08	6.19 \pm 1.56	6.68 \pm 1.43
Control	37	8.89 \pm 2.32	5.81 \pm 1.33	8.77 \pm 2.11	8.69 \pm 2.12
<i>t</i>		4.091	5.894	5.981	4.781
<i>P</i> value		< 0.001	< 0.001	< 0.001	< 0.001

Table 2 Comparison of therapeutic effects between the two groups, *n* (%)

Group	<i>n</i>	Remarkably effective	Effective	Invalid	Total effectiveness
Study	37	23 (62.16)	12 (32.43)	2 (5.41)	35 (94.59)
Control	37	17 (45.95)	11 (29.73)	9 (24.32)	28 (75.68)
χ^2					5.232
<i>P</i> value					0.022

Table 3 Comparison of laboratory indexes between the two groups before and 7 d after treatment (mean \pm SD)

Group	<i>n</i>	PCT (ug/L)	CRP (mg/L)	WBC ($\times 10^9/L$)	NE (%)
Before treatment					
Study	37	12.89 \pm 3.96	19.62 \pm 6.44	20.61 \pm 6.38	86.14 \pm 7.21
Control	37	14.05 \pm 4.11	18.79 \pm 5.96	21.21 \pm 5.59	84.39 \pm 6.95
<i>t</i>		1.236	0.575	0.430	1.063
<i>P</i> value		0.220	0.567	0.668	0.291
After 7 d of treatment					
Study	37	2.01 \pm 0.56	3.11 \pm 1.02	5.10 \pm 1.83	56.35 \pm 7.17
Control	37	3.29 \pm 0.64	5.67 \pm 1.23	8.13 \pm 3.01	64.22 \pm 8.08
<i>t</i>		9.155	9.745	5.232	4.432
<i>P</i> value		< 0.001	< 0.001	< 0.001	< 0.001

PCT: Procalcitonin; CRP: C-reactive protein; WBC: White blood cell count; NE: Neutrophil percentage.

Table 4 Comparison of the incidence of adverse reactions between the two groups, *n* (%)

Group	<i>n</i>	Pain at injection site	Skin itch	Vomiting and nausea	Gastrointestinal reaction	Total incidence rate
Study	37	1 (2.50)	0 (0.00)	2 (5.00)	0 (0.00)	3 (7.50)
Control	37	1 (2.50)	2 (5.00)	1 (2.50)	1 (2.50)	5 (12.50)
χ^2						0.140
<i>P</i> value						0.708

than those (70.00% and 83.33%, respectively) of ceftazidime. Piperacillin sodium/tazobactam sodium and cefoperazone sodium/sulbactam sodium were used to treat elderly patients with respiratory tract infection at our hospital. The time to symptom relief in the study group was significantly shorter than that in the control group. The total effective rate of 94.59% in the study group was significantly higher than that of 75.68% in the control group. Besides, there was no significant difference in adverse reactions between the two groups. The results showed that compared with cefoperazone sodium/sulbactam sodium, piperacillin sodium/tazobactam sodium

had significant therapeutic advantages in elderly patients with respiratory tract infection. Piperacillin sodium/tazobactam sodium could shorten the time to symptom relief and improve the therapeutic effect for the disease. The similar adverse reaction incidence between the two treatments suggests that piperacillin sodium/tazobactam sodium is just as safe as cefoperazone sodium/sulbactam sodium. The main reason is that piperacillin sodium can inhibit the synthesis of bacterial cell wall, so as to achieve the antibacterial purpose, and can effectively treat the infection caused by *Pseudomonas aeruginosa* and Gram-negative bacilli. Tazobactam sodium can inhibit β -lactamases and type I enzymes mediated by some chromosomes. Besides, their combination can complement each other and improve the antibacterial effect[18,19]. Meanwhile, the study of Hitt *et al*[20] showed that piperacillin sodium and tazobactam sodium could improve the drug resistance of bacteria. The concentrations of piperacillin sodium and tazobactam sodium in plasma could rapidly increase to the peak levels after intravenous drip, and are not affected by the administration time or dose. Moreover, the pharmacokinetic characteristics of piperacillin sodium and tazobactam sodium are similar; hence, they could act in synergy.

PCT, CRP, WBC, and NE are all commonly used laboratory indexes for clinical evaluation of infectious diseases. Their serum levels are low under normal physiological conditions; however, in case of infections, their levels significantly increase, with a significant positive correlation between their increase and the degree of infection. In addition, their expression levels can be gradually decreased after patients receive corresponding standard treatment. Therefore, they can be used to evaluate the diagnosis, curative effect of treatment, and prognosis of infectious diseases[21]. The results of this study showed that after 7 d of treatment, the serum levels of PCT, CRP, WBC, and NE in the two groups were both lower than the levels before treatment. However, the above indexes in the study group were significantly lower than those in the control group ($P < 0.05$). The serum factors therefore further confirm that piperacillin sodium/tazobactam sodium has high application value in elderly patients with respiratory tract infection. It can reduce the level of serum inflammatory factors and reduce the degree of inflammatory reaction *in vivo*, and may be of great significance as a treatment to ensure optimal treatment effect for respiratory tract infection in the elderly and to promote good outcomes.

This study had some limitations. This is a single-center sample study; therefore, whether the results of the study are broadly valid still needs to be further examined by expanding the sample selection range and increasing the sample size in future investigations.

CONCLUSION

In general, piperacillin sodium/tazobactam sodium is better than cefoperazone sodium/sulbactam sodium in the treatment of respiratory tract infection in elderly patients. It can effectively relieve clinical symptoms; down-regulate the contents of serum PCT, CRP, and other factors, and reduce the degree of inflammatory reaction; and has a comparable degree of safety.

ARTICLE HIGHLIGHTS

Research background

Respiratory tract infections in elderly patients are difficult to cure and can easily reoccur, thereby posing a great threat to patient prognosis and quality of life. It is very important to take effective measures to treat these patients as soon as possible.

Research motivation

Elderly patients who have severe pulmonary infections require antibiotic treatment.

Research objectives

This study aimed to determine the therapeutic value and safety of different antibiotics in elderly patients with respiratory tract infection.

Research methods

Seventy-four elderly patients with respiratory tract infection were randomly allocated

to a study ($n = 37$; treated with cefoperazone sodium/sulbactam sodium) or control ($n = 37$; treated with piperacillin sodium/tazobactam sodium on the basis of routine symptomatic support) group.

Research results

Total effective rate was higher in the study group. There was no significant difference in the incidence of adverse reactions between the groups.

Research conclusions

Piperacillin sodium/tazobactam sodium is better than cefoperazone sodium/sulbactam sodium in the treatment of respiratory tract infections in elderly patients, and they can reduce the degree of inflammatory reaction, and have a comparable degree of safety.

Research perspectives

Rationality and safety of antibiotic application.

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