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Original Article

Application value of new β-lactam antibiotics in complicated intra-abdominal infections

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Abstract: Objective: To explore the application value of new β-lactam antibiotics in complicated intra-abdominal infections (cIAI). Methods: From January 2018 to December 2019, 80 patients with cIAI after abdominal tumor treatment in the ICU department of our hospital were selected as the research subjects. 80 patients were randomly sorted into experimental group and control group, with 40 each group. The experimental group was given a new β-lactam antibiotic Tienam (Imipenem/Cilastatin sodium); the control group was given a conventional cephalosporin antibiotic injection. The clinical treatment efficacy, adverse reactions, complete bacterial clearance rate, simplified acute physiology score (SAPS3) and sequential organ failure score (SOFA) were compared. Results: The overall treatment efficacy rate was 67.50% of the control group while the experimental group showed significantly higher overall clinical efficacy rate of 90.00% (χ^2 = 6.050, P = 0.014). In comparison of the incidence (37.50%) of adverse reactions during the treatment of the control group, the experimental group showed significantly lower incidence (17.50%) of adverse reactions during the treatment (χ^2 = 4.013, P = 0.045). In comparison to the control group, the experimental group showed lower SAPS3 and SOFA scores when they left the ICU, and the difference was viewed as statistically significant (t = 2.097, P = 0.039; t = 2.457, P = 0.016). Conclusion: New β-lactam antibiotics have high application value in complicated abdominal infections.

Keywords: New β-lactam, antibiotics, complicated intra-abdominal infections

Introduction

Complicated intra-abdominal infection (cIAI) means that the infection is not limited to abdominal organs, but has spread to the surroundings, causing localized or diffuse peritonitis [1, 2]. Without timely treatment and effective control, it can cause complications such as septic shock and sepsis, and cause harm to patients' life and health [3]. Antibiotics are commonly used in clinical treatment of pathogenic bacterial infections. However, due to the excessive use of antibiotics, the production of inactivated enzymes (such as narrow-spectrum, broad-spectrum, sporesinase, etc.) of many antibacterial drugs, as well as the change of the target of antibacterial drugs and the decrease in drug permeability, have caused bacterial resistance to many antibiotics [4-7]. Therefore, medicinal chemists have developed new antibiotics, the most successful of which is the new β-lactam antibiotics, which have strong antibacterial activity, broad antibacterial spectrum, low toxicity, good efficacy, wide indications, and it has many varieties, that are widely used in clinic. However, there are few reports on the application of new β-lactam antibiotics in cIAI. Therefore, this article explores the application value of new β-lactam antibiotics in cIAI and provides a basis for the selection of clinical cIAI antibacterial drugs.

Materials and methods

General information

The patients with cIAI in the General surgery/ICU department of our hospital from January 2018 to December 2019 were enrolled as the research subjects. Inclusion criteria: (1) Complete clinical data, age ≥18 years old; (2) All patients undergoing abdominal inflammatory

disease; (3) Postoperative diagnosis conforms to cIAI diagnostic criteria [1], bacteriological culture results are positive; (4) Patients and their families were informed about the content of this study and provided a written informed consent prior to participation. Exclusion criteria: (1) People with hepatic and renal dysfunction; (2) People with mental illness; (3) People allergic to new-type β-lactam antibiotics; (4) Previous abdominal infections and the use of imipenem/cilastatin, supra, Ticolanin and other antibacterial drug history. A total of 80 patients met the inclusion and exclusion criteria, and these 80 patients were randomly sorted into an experimental group and a control group, with 40 in each group. This study has received approval from the ethics committee of our hospital.

Therapeutic methods

The experimental group was given a new compound β-lactam antibiotic imipenem and cilastatin sodium as a combination agent "tienam" (Manufacturer: Merck Sharp & Dohme Corp. National Pharmaceutical Standard: J20180060), the maintenance dose was 500 mg/every 8 h, via intravenous drip, and the course of treatment was 14 days. The control group was given conventional cephalosporin antimicrobial injections. The injection dose was determined according to the patient's condition and the course of treatment was 14 days.

After the treatment, an abdominal drainage tube, T-tube drainage, and abdominal puncture were used for different cases, and the procedures were strictly followed to ensure that there was no contamination of specimens with foreign bacteria. Through bacteriological testing, it can be determined whether the specimen pathogen is completely cleared, or not cleared, or replaced.

Observation indicators

(1) Observe the clinical efficacy of the two groups at the end of treatment, and the evaluation criteria refer to the "Guidelines for the Clinical Trial of Antimicrobial Drugs". Cure: the patient's clinical symptoms and signs completely disappeared, and the imaging and microbiological indicators returned to normal. The signs and symptoms have basically disappeared, and the imaging and microbiological indicators have partially improved. Ineffective: the patient's clinical symptoms, signs, and imaging and microbiological indicators have not changed significantly or showed an increasing trend. (2) Observe the PCT level of the two groups after treatment. (3) Observe the bacteriological test results of the two groups after treatment to identify whether they are completely cleared, or not cleared, or replaced. (4) Observe the adverse reactions related to drugs during the treatment of the two groups, such as diarrhea, nausea, vomiting, rash, and double fungal infection. (5) Observe SAPS3 and sSOFA before and after entering the General surgery/ICU in the two groups.

Statistical methods

SPSS 18.0 (Bizinsight [Beijing] Information Technology Co., Ltd.) was adopted for statistical analysis. The quantitative data was described by mean ± standard deviation, using t test. The t-test uses t-distribution theory to infer the probability of the difference, so as to compare whether the two averages are significantly different. The count data is described by the rate (%), using chi-square test. The chi-square test is usually used in the statistical inference of categorical data, including the chi-square test for comparing two rates or two constituent ratios, multiple rates or chi-square test of multiple composition ratio comparison. $P < 0.05$ indicates a significant difference. GraphPad Prism 8 was used to illustrate the data.

Results

General data

The age of the experimental group was (41.78 ± 7.24) years old, of which 29 cases were male and 11 cases were female. The age of the control group was (42.15 ± 7.53) years old, of which 27 cases were male and 13 cases were female. No statistical difference existed between the two groups in terms of gender, age, and type of primary tumor ($P > 0.05$, as shown in **Table 1**).

Pathological data of patients

A total of 98 pathogenic bacteria were isolated from 80 patients, including 52 Gram-negative bacteria, 42 positive bacteria, and 4 fungi. The most common Gram-negative bacteria were

Table 1. Comparison of general data of two groups of patients [n (%), ± s]

General information	Experimental group (n = 40)	Control group (n = 40)	t/χ^2	*P*
Age (year)	41.78±7.24	42.15±7.53	0.224	0.823
Gender			0.238	0.626
Male	29 (72.50)	27 (67.50)		
Female	11 (27.50)	13 (32.50)		
Primary tumor type			0.807	0.848
Gastric cancer	21 (52.50)	19 (47.50)		
Pancreatic duodenal carcinoma	12 (30.00)	13 (32.50)		
Colorectal cancer	5 (12.50)	7 (17.50)		
Biliary tract neoplasms	2 (5.00)	1 (2.50)		

Table 2. Etiological data of patients

Pathogen	Number of bacterial strains (n = 98)	%
Gram-negative bacteria	52	53.06
Pseudomonas aeruginosa	18	18.37
E.coli	11	11.22
Enterobacter cloacae	8	8.16
Klebsiella pneumoniae	7	7.14
Morganella	3	3.06
Klebsiella oxytoca	2	2.04
Acinetobacter baumannii	2	2.04
Stenotrophomonas maltophilia	1	1.02
Gram-positive bacteria	42	42.86
Enterococcus faecalis	14	14.29
Enterococcus faecium	10	10.2
Staphylococcus epidermidis	5	5.1
Staphylococcus aureus	4	4.08
Staphylococcus haemolyticus	4	4.08
Enterococcus avium	3	3.06
Enterococcus raffinose	2	2.04
Fungus	4	4.08
Candida albicans	3	3.06
Candida glabrata	1	1.02

Pseudomonas aeruginosa, followed by Enterobacteriaceae; the most common positive bacteria are enterococci, followed by staphylococci (**Table 2**).

Comparison of clinical efficacy between the experimental and control groups

In comparison to total effective rate (67.50%) of the control group, the experimental group showed a significantly higher total effective rate (90.00%). The difference was viewed as statistically significant (χ^2 = 6.050, P = 0.014, **Table 3**).

Comparison of bacteriological test results after treatment between the two groups

The number of cases where the bacteria were completely cleared in the experimental group was significantly higher than in the control group, and the difference was statistically significant (χ^2 = 7.912, P = 0.005, **Figure 1**).

Comparison of the morbidity of unwanted reactions during the treatment of the experimental and control groups

In comparison to the (37.50%) unwanted reactions during the treatment of the control group, the experimental group showed significantly lower percentage (17.50%) of unwanted reactions during the treatment. The difference was viewed as statistically significant (χ^2 = 4.013, P = 0.045, **Table 4**).

Comparison of SAPS3 and SOFA scores before and after entering the ward

The SAPS3 and SOFA scores of the two groups before entering the ward were not statistically significant (P > 0.05). In comparison to the control group, the experimental group showed lower SAPS3 and SOFA scores when leaving the ward, and the difference was viewed as statistically significant (t = 2.097, P = 0.039; t = 2.457, P = 0.016, **Table 5**).

Comparison of the average PCT level between the experimental group and the control group

The average PCT level value of the experimental group before treatment was (30.52±4.57)

Table 3. Comparison of clinical efficacy of the two groups [n (%)]

Groups	Cure	Effective	Ineffective	Total effective rate
Experimental group n = 40	27 (67.50)	9 (22.50)	4 (10.00)	36 (90.00)
Control group n = 40	22 (55.00)	5 (12.50)	13 (32.50)	27 (67.50)
χ^2				6.050
P				0.014

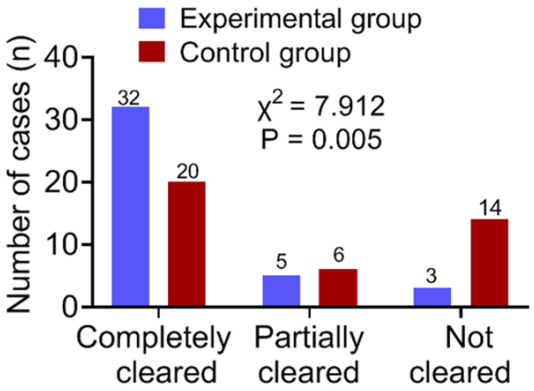

Figure 1. Comparison of bacteriological test results after treatment between the two groups.

ng/mL, and the average PCT level value after treatment was (1.12±0.34) ng/mL. The average PCT level value of the control group before treatment was (31.67±4.25) ng/mL, and the average PCT level value after treatment was (13.20±3.11) ng/m L. There was a significant difference in the average PCT level between the two groups after treatment (t = 35.801, P < 0.0001, **Table 5**).

Discussion

cIAI occurs after abdominal inflammatory disease. Most of the cases are postoperative gastrointestinal defects or anastomotic leakage. The structure of the abdominal cavity is broken, and a large amount of organ contents flow out, causing infection [8]. Because there are a large number of normal strains or conditionally pathogenic bacteria in the human intestine, once these bacteria enter an originally sterile environment, it may cause infection. With analysis of the patient's etiology in this study we found that once the gram-negative bacteria or gram-positive bacteria were isolated, there were some normal flora in the human intestine, and opportunistic pathogens [9], once these flora shifted after reaching the peritoneal membrane, it may immediately enter the bloodstream, causing localized or diffuse peritonitis [10]. Severe case patients can also have systemic multiple organ failure, which is life-threatening [11]. Therefore, exploring effective antimicrobial therapy has an important impact on the prognosis of the disease.

Clinical treatment of cIAI patients mainly includes surgical and interventional guidance of drainage of effusion, or control of infection, supplemented by broad-spectrum antibacterial anti-infective therapy [12-15]. Reasonable empirical antimicrobial therapy can increase the success rate of clinical treatment and reduce the length of hospital stay; on the contrary, inappropriate treatment can lead to treatment failure, prolong the length of hospital stay, and increase the risk of death. Imipenem/Cilastatin, as a new β-lactam broad-spectrum antibacterial drug, is the first drug that received approval from the US FDA for the treatment of cIAI. Current guidelines recommend that for cIAI, antimicrobial drugs be used for seven to fourteen days, depending on the patient's clinical response. Studies have shown that the failure of imipenem/cilastatin treatment may be related to the duration of medication [16]. To this end, this article takes conservative treatment, the duration of medication is 14 days. The drug has good antibacterial activity against various pathogens isolated from cIAI patients, especially drug-resistant pathogens, and has a low toxicity. In this study, patients with cIAI were treated with imipenem/cilastatin. The results showed that their efficacy was significantly better than conventional cephalosporin antibacterial injections, and the complete bacterial clearance rate after treatment was higher than conventional cephalosporin antibacterial injection, with adverse reactions during medication being lower than conventional cephalosporin antimicrobial injections. The effectiveness of the new β-lactam imipenem/cilastatin antibacterial drug in cIAI treatment was confirmed. It also shows that injection of conventional cephalosporin antibacterial drugs has difficulty to inhibit the mixed infection of multiple bacteria.

Table 4. Comparison of the incidence of adverse reactions during the treatment of the two groups [n (%)]

Group	Diarrhea	Disgusting	Vomiting	Skin rash	Fungal infection	Total incidence
Experimental group (n = 40)	2 (5.00)	1 (2.50)	1 (2.50)	1 (2.50)	2 (5.00)	7 (17.50)
Control group (n = 40)	4 (10.00)	1 (2.50)	2 (5.00)	3 (7.50)	5 (12.50)	15 (37.50)
χ^2						4.013
P						0.045

Table 5. Comparison of SAPS3 and SOFA scores before and after entering the ward (±s)

Group	SAPS3 (score)		SOFA (score)		PCT (ng/mL)	
	Before entering ward	When leaving the ward	Before entering ward	When leaving the ward	Before entering ward	When leaving the ward
Experimental group (n = 40)	56.58±11.35	36.04±6.22	7.34±1.98	4.18±0.76	30.52±4.57	1.12±0.34
Control group (n = 40)	57.18±11.12	38.95±6.19	7.41±2.06	4.62±0.84	31.67±4.25	13.20±3.11
t	0.239	2.097	0.155	2.457	1.165	35.801
P	0.812	0.039	0.877	0.016	0.247	< 0.0001

Studies have shown that high SAPS3 and SOFA scores are risk factors for poor prognosis in patients with cIAI [17]. In this study, treatment of cIAI patients with imipenem/cilastatin found that the SAPS3 and SOFA scores of patients when they left the ward were lower than those of received conventional cephalosporin antimicrobial injections. It is suggested that the new β-lactam imipenem/cilastatin antibacterial drug has the potential to improve the prognosis of patients with cIAI. This may be related to the overall administration of imipenem/cilastatin to adjust the immune imbalance in patients [18], because immune imbalance is conducive to the return of the disease.

In summary, the application of new β-lactam imipenem/cilastatin antibacterial drugs in cIAI can improve the clinical efficacy of patients, and the adverse drug reactions are low, and the clearance rate of pathogens is high. However, owing to the limited sample size in this research, the result is likely to be biased, and a larger sample size is still needed to further corroborate our results.

Disclosure of conflict of interest:

None.

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