

Research and analysis of 74 bloodstream infection cases of *Acinetobacter baumannii* and drug resistance

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Abstract. – OBJECTIVE: We aimed at investigating the clinical and bacteriological features and drug resistance of bloodstream infection of *Acinetobacter baumannii*, so as to provide new evidence for treatment of bloodstream infection of *Acinetobacter baumannii*.

PATIENTS AND METHODS: Statistical analysis was carried out for the clinical and bacteriological features and drug sensitivity of 74 bloodstream infection cases of *Acinetobacter baumannii* who were admitted to this hospital between July 2016 and June 2017.

RESULTS: Among 74 patients, about 72.0% of them were admitted to the ICU and Respiratory Department; the average age of these patients was 63 years old. Among 74 patients, 62 patients stayed in the hospital for over 2 weeks (83.8%), and 35 for over 1 month (47.3%); 72.0% of patients experienced intrusive operation, in which 28.0% of patients dead. The experiment of drug sensitivity showed that tigecycline had the highest sensitivity (100%), sequentially followed by amikacin (over 90.0%) and other anti-bacterial drugs (less than 40.0%). Pan-drug resistance was identified in 42 patients, accounting for 56.8%. Comparison between the pan-drug resistant and non-pan-drug resistant patients showed that in the first two weeks before the positive blood culture, there were statistically significant differences in administration of carbapenem antibiotics and intrusive operation ($p < 0.05$). Among the patients, the lowest resistance to carbapenem antibiotics was 8.16%, while the rate of resistance to other 12 antibiotics was more than 40.00%. Multiple-resistant strain mainly originated from the ICU and the burn center.

CONCLUSIONS: In patients with bloodstream infection of *Acinetobacter baumannii*, the pan-drug resistant strains account for a vast majority with a high mortality rate. Age, intrusive operation and length of stay in hospital longer than 2 weeks are the common susceptible factors, while the administration of carbapenem antibiotics and intrusive operations might be the high-risk factors leading to pan-drug resistant cases.

Key Words:

Acinetobacter baumannii, Bloodstream infection, Antibiotics, Multiple-resistant strain.

Introduction

Acinetobacter baumannii, a kind of Gram-negative bacilli with no glucose-fermentation ability, negative response to oxidases and no motility, can be widely found in nature, and also on the surface of ward wall, anesthetic and ventilation machines, as well as the skin, respiratory tract and urinary tract of healthy people, and has been considered as the major pathogens leading to hospital infection. With the aging of population as well as increases in intrusive operations and administration of broad-spectrum antibacterials, people have noted that the incidence rate of bloodstream infection of *Acinetobacter baumannii* and detection rate of drug-resistant bacteria are also increasing year by year^{1,2}, leading to an elevation in the mortality rate and medical expense of patients³⁻⁵. To investigate the drug resistance and clinical features of *Acinetobacter baumannii* in our hospital, we analyzed the clinical distribution and drug resistance of *Acinetobacter baumannii* isolated from patients who were admitted to this hospital between July 2016 and June 2017.

Patients and Methods

Patients

Origin of bacteria: from the clinical samples collected from July 2016 to June 2017 in our hospital, a total of 74 patients were identified with infection of *Acinetobacter baumannii*, among which there were 48 males and 26 females. The

Table I. Distribution of *Acinetobacter baumannii* in different inpatient areas between July 2016 and June 2017.

Inpatient area	Number of strain	Detection rate (%)
Department of Hematopathology	5	6.8
ICU	39	52.7
Respiration Department	14	18.9
Digestion Department	2	2.6
Burns Department	7	9.6
Pediatric Department	2	2.6
Surgery Department	5	6.8
Total	74	100.0

age of patients ranged from 0 to 94 years old with an average of 63 years old, and there were 62 patients with a length of stay in the hospital longer than 2 weeks, and 35 longer than 1 month. Among all the patients, 14 patients were diagnosed with cancer. This study was approved by the Local Medical Research Committee. The research was conducted in accordance with the Declaration of Helsinki and the United National Institutes of Health.

Bacteria for Quality Control

Escherichia coli ATCC25922 and *Pseudomonas aeruginosa* ATCC27853 were purchased from National Center for Clinical Laboratories (Beijing, China).

Major Instruments and Reagents

HN-303 electric thermostat incubator (manufactured by Nantong Hunan Scientific Instrument Factory, Changsha, China); ATB-expression automatic bacteria analyzer and drug sensitivity analyzer (BioMérieux Corporate, Marcy-l'Étoile, France). Gram stain for bacteria (Maccura, Sichuan, China); oxidase, ATB culture medium, API NaCl 0.85% culture medium, ID32E bacteria test paper, JAMES reagent (BioMérieux Corporate, Marcy-l'Étoile, France).

Methods

Once the clinical manifestations, such as fever, shivering and septic shock appeared, 10 mL sample of whole blood were collected for culture. Culture, isolation, identification and drug sensitivity test of bacteria were conducted in strict accordance with The National Clinical Test Regulation of Operation⁶, and ATB-expression instruction. Identification was also carried out using VITEK-2 compact automatic microbiological analyzer.

Observation of Indicators

We analyzed the ward, age, length of stay in hospital and intrusive operations within 2 weeks before positive blood cultures, such as central venous indwelling catheter, trachea cannula/tracheotomy, use of peritoneal cavity drainage tube or ureter. We also analyzed the administration of antibiotics of patients who were confirmed with infection of *Acinetobacter baumannii*. The results of drug sensitivity test also underwent statistical analysis.

Statistical Analysis

Statistical Product and Service Solutions (SPSS) 11.0 software (SPSS Inc., Chicago, IL, USA) was applied for data processing, and the *p*-value was calculated with the Fisher's exact probability test. *p*<0.05 suggested that the difference had statistical significance.

Results

Baseline Data of Patients

Among the 74 samples collected from patients infected by *Acinetobacter baumannii*, the sputum samples accounted for 87.8% (65/74), followed by the secretion samples from the trauma (7/74) and the urine samples (2/74). The detection rates of *Acinetobacter baumannii* in all inpatient areas were shown in Table I, and the detection in different age groups was shown in Table II.

Ratio of Intrusive Operations and Administration of Antibiotics (%)

Within 2 weeks before the positive blood cultures in 74 patients infected by *Acinetobacter baumannii*, the distribution of intrusive operations and administration of antibiotics is shown in Table III.

Table II. Distribution of *Acinetobacter baumannii* in different ages among 74 patients.

Age (years)	Number of strain	Ratio (%)
0-9	3	4
20-39	4	5.4
40-49	5	6.8
50-59	7	9.6
60-69	13	17.5
70-79	19	26.6
80-94	23	30.1
Total	74	100

Table III. Ratio of intrusive operation and administration of antibiotics.

Item	N	Ratio
Intrusive operations	106	100
Indwelling central venous catheters	33	31.1
Abdominal/thoracic surgery	26	24.5
Trachea cannula/tracheotomy	23	21.7
Indwelling abdominal drainage tube	15	14.1
Indwelling urethral catheter	9	8.6
Administration of antibiotics	121	100
Carbapenems	47	38.8
Penicillin	30	24.8
Cephalosporin	27	22.3
Quinolones	17	14.1

High-Risk Factors

According to the results of drug sensitivity test, patients were divided into the pan-drug resistant group and the non-drug resistant group, and we also performed the statistical analysis of the factors, like administration of antibiotics, intrusive operations and length of stay in the hospital within 2 weeks before the positive blood cultures in the two groups. Results showed that the differences in the administration of carbapenems and intrusive operations had statistical significance ($p < 0.05$; Table IV).

Sensitivity of Drugs

After the culture of whole blood, we found that in a total of 74 samples infected by *Acinetobacter baumannii*, pan-drug resistance was identified in 41 samples (55.4%); drug resistance to the first- and second-generation cephalosporins was found in 68 samples (91.9%). *Acinetobacter baumannii* was

more sensitive to tigecycline and amikacin with sensitive rates over 90.0%; but the sensitive rates to other antibiotics were lower than 40.0% (Table V).

Drug resistant rate

The resistance of *Acinetobacter baumannii* to 14 antibiotics is shown in Table VI.

Prognosis

Among the 74 patients with bloodstream infection of *Acinetobacter baumannii*, 24 patients experienced the septic shock (32.4%), and 21 were dead (28.4%), in which there were 18 with septic shock.

Discussion

Acinetobacter baumannii, as the major opportunistic pathogen acquired in hospital, is widely distributed in the environment of hospital⁷. It is often found in the clinical cultures of sputum samples. Although the bloodstream infection caused by *Acinetobacter baumannii* is rare, the mortality of it is very high⁸. In addition, hospital-acquired *Acinetobacter baumannii* usually showed drug resistance to multiple antibiotics, which increases the difficulties in clinical treatment^{9,10}. From the results in Table I and II, we found that *Acinetobacter baumannii* mainly originated from the sputum samples in this hospital, and is the major pathogen accounting for infection in the respiratory tract. Elder patients dominated among the patients of infection with *Acinetobacter baumannii*. As shown in Table II, we found that patients aging between 80 and 94 years were the most, fol-

Table IV. Ratio of the high-risk factors in the pan-drug resistant group and non-drug resistant group (%).

Item		Pan-drug (n=41)		Non-drug (n=33)		<i>p</i> -value
		Case (n)	Ratio	Case (n)	Ratio	
Carbapenems	Yes	35	85.4	12	36.4	<0.05
	No	6	14.6	21	63.4	
Cephalosporin	Yes	15	36.6	21	63.4	>0.05
	No	26	63.4	12	36.4	
Penicillin	Yes	21	51.2	9	27.3	>0.05
	No	20	48.8	24	72.7	
Quinolones	Yes	12	29.3	6	18.2	>0.05
	No	29	70.7	27	81.8	
Intrusive operations	Yes	35	85.4	15	45.5	<0.05
	No	6	14.6	18	54.5	
Length of stay in hospital > 2 weeks	Yes	38	92.7	21	63.4	>0.05
	No	3	7.3	12	36.6	

Table V. Sensitive rates of 74 samples infected by *Acinetobacter baumannii* to the common antibiotics

Antibiotics	Number of strains	Sensitive rates [%]
Tigecycline#	26	100
Amikacin	71	95.9
Levofloxacin	26	35.1
Cefepime	26	35.1
Gentamicin	26	35.1
Piperacillin/Sulbactam	24	32.4
Imipenem	24	32.4
Ciprofloxacin	21	28.4
Ampicillin/Sulbactam	18	24.3

Note: # only 26 samples in 74 ABA cases underwent the drug sensitivity test of tigecycline.

lowed by those with age between 70 and 79 years. The proportion of elder patients with age above 60 years accounted for 74.3%. The *Acinetobacter baumannii* mainly originated from the ICU and Respiratory Department. Many other factors, such as age, intrusive operation, and staying in the hospital longer than 2 weeks, might be the susceptible factors leading to bloodstream infection of *Acinetobacter baumannii*. Plus, some characteristics of *Acinetobacter baumannii* might also be correlated to bloodstream infection, such as a relatively low pathogenicity, less requirement in growth, and easiness formation of bacterial colonization¹¹. The mortality of bloodstream infection of *Acinetobacter baumannii* remains as high as 28.4%. From the aspect of bacteriology, pan-drug resistant strains accounted for a large proportion (55.4%), and this rate keeps increasing year by year¹². High-risk factors inducing the pan-drug resistance within two weeks may include the administration of carbapenems antibiotics and intrusive operations^{13,14}. The test of drug sensitivity of bacteria revealed that 26 strains of *Acinetobacter baumannii* exhibited sensitivity to tigecycline (100%), while the sensitivity to amikacin was also higher than 90.0%, and that to other antibiotics was less than 40.0%. Moreover, rational use of antibiotics remains to be a problem that requires in-depth study because the available antibiotics that can be used for clinical treatment are decreasing. Currently, the antibiotics for *Acinetobacter baumannii* mainly include carbapenems, polymyxin, sulbactam, piperacillin/tazobactam, tigecycline, and aminoglycosides. However, the combined administration is preferred in the treatment of many cases since the drug resistance is rapidly induced in *Acinetobacter baumannii*,

and the ratio of strains with drug resistance keeps increasing¹⁵. In addition to the combined administration of those conventional drugs, it was reported that combined medication of rifampicin and vancomycin also gains some efficacy¹⁶⁻¹⁸, but the effective combination remains uncertain. Among 74 patients, significant efficacy was only found in 3 patients among those who received the tigecycline treatment. Tigecycline, a kind of tetracycline antibiotics that are newly marketed, is expected to be applied in the treatment of infection by drug-resistant bacteria with the ability to antagonize the bacterial efflux pump as a protein synthesis inhibitor, but the overall effect on bloodstream infection requires further studies. Infection is very common and a big threaten for all the patients^{19,20}.

Conclusions

To reduce the incidence of hospital infection of *Acinetobacter baumannii* and prevent infection of the strains with high resistance, staffs managing the hospital and patients should try their best to perform in accordance with the following guidelines: a) improve the hospitalization by regular detection and bacterial culture to avoid the cross infection between medical staffs and patients, or among patients; b) replace intrusive operations with other available options as much as possible, and if necessary, the physicians or nurses should

Table VI. Results of *in vitro* drug sensitivity test of *Acinetobacter baumannii* and the drug resistant rate.

Drug	Number of strains	Drug resistant rate (%)
Ticarcillin	42	56.8
Ticarcillin/clavulanic acid	39	52.7
Piperacillin	47	63.5
Piperacillin/tazobactam	33	44.6
Ampicillin/sulbactam	36	48.6
Ceftazidime	33	44.6
Cefepime	35	47.3
Imipenem	6	8.1
Meropenem	6	8.1
Ciprofloxacin	36	48.6
Gentamicin	39	52.7
Tobramycin	41	55.4
Amikacin	33	44.6
Trimethoprim/sulfamethoxazole	41	55.4

Note: # only 26 samples in 74 ABA cases underwent the drug sensitivity test of tigecycline.

strictly conform to the regime of disinfection in intrusive operation to protect the patients from the exogenous infection; c) prophylactic examines should be taken as early as possible on patients who are susceptible to infection through improving their immunity, in attempt to avoid the endogenous infection caused by the variation of parasite position of some bacteria; d) for patients with infection, rational administration of antibiotics should be taken according to the clinical condition to delay the generation of drug-resistant strains, and control the spread and prevalence of these strains.

Conflict of Interest

The Authors declare that they have no conflict of interest.

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