

Original Article

Analysis of prognostic factors and drug resistance of central venous catheter-related bloodstream infection caused by multidrug-resistant *Acinetobacter baumannii*

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Received November 25, 2015; Accepted February 13, 2016; Epub April 15, 2016; Published April 30, 2016

Abstract: To analyze and discuss the prognostic factors and drug resistance multidrug-resistant *Acinetobacter baumannii*. In central venous catheter-related bloodstream infection, 165 patients with central venous catheter (CVC) were included in this study. Univariate and multivariate logistic regression analysis were used to analyze the factors that may affect the prognosis for 15 patients with a poor prognosis. Multidrug-resistant *Acinetobacter baumannii* was found in 15 patients out of 165 patients (9.09%). *Acinetobacter baumannii* showed 100% resistance to piperacillin, piperacillin/tazobactam, and aztreonam. It also showed resistance to cefoperazone/sulbactam and ceftazidime. The reasons included poor health condition (86.67%), prolonged use of carbapenems (93.33%), low nutritional requirements for growth of *Acinetobacter baumannii* (100.00%), strong resistance to disinfectants and long-term survival in the hospital environment (93.33%). The factors that may affect the prognosis include Acute Physiology and Chronic Health Evaluation (APACHE) II score (OR=2.023), central venous catheter indwelling time (OR=1.347), total parenteral nutrition (OR=1.026), and acceptance of carbapenem antibiotics 14 days before bacteria culture (OR=2.561). The reasons accounting for drug resistance of multidrug-resistant *Acinetobacter baumannii* in central venous catheter-related bloodstream infection include patients' poor health condition, prolonged use of carbapenems, low nutritional requirements for growth of *Acinetobacter baumannii*, and strong resistance to disinfectants and long-term survival in the hospital environment. The factors that may affect the prognosis include Acute Physiology and Chronic Health Evaluation (APACHE) II score, total parenteral nutrition, central venous catheter indwelling time, and acceptance of carbapenem antibiotics 14 days before bacteria culture.

Keywords: Multidrug-resistance, *Acinetobacter baumannii*, central venous catheter-related bloodstream infection, causes of antibiotic resistance, prognosis

Introduction

Central venous catheter (CVC) has been widely used for rehydration and administration, blood transfusion, total parenteral nutrition, and hemodynamics for patients in intensive care unit. Although the use of CVC brings convenience for clinical treatment, it may also cause adverse complications including catheter exit site infection, catheter pathogen colonization, catheter-related bloodstream infections, which could seriously impact the prognosis of patients. It has been shown that central venous catheter-related bloodstream infections (CRBSI) is the most common and dangerous complications [1, 2]. Previous study showed that the incidence of CRBSI in US was 5.3/1000. CRBSI

extends the length of stay, increases burden of hospitalization, affects rehabilitation prognosis. *Acinetobacter baumannii* (*A. baumannii*) is one of the common pathogenic bacteria. *A. baumannii* colonizes mainly in patient's skin, respiratory tract, gastrointestinal and genitourinary tract. It also colonizes in soil, water and hospital environments. It is one of the most common non fermenting gram-negative bacteria, which belong to opportunistic pathogens. With strong adhesion capability, it can adhere to skin surface, rapidly colonize, survive, and therefore it becomes an important pathogen of hospital-acquired infections. Studies showed that the drug resistance of *A. baumannii* increased gradually and multi-drug resistant *A. baumannii* has been found and causes a lot of

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drugs have little or no effect which, to some extent, increases the difficulty of treatment and seriously affects outcomes. The therapeutic effects against multi-drug resistant *A. baumannii* are unstable and easily to be influenced by other factors, resulting in a poor prognosis. In this study, we analyze and discuss the prognostic factors and drug resistance of *A. baumannii* in CRBSI.

Material and methods

Object selection

165 patients with CVC from January 2013 to January 2015 were included in this study. All catheters were introduced by using Sheldinger technique. All patients were diagnosed as multi-drug resistant *A. baumannii* caused-CRBSI according to the diagnostic criteria, intravascular catheter-related infection prevention and treatment guidelines, which was issued by Chinese Medical Association. In all patients, multi-drug resistant *A. baumannii* was detected 48 h after CVC introduction, catheter tip culture (5 cm) was positive, and quantitative catheter cultures showed more than 15 CFU. Other sources of infection can be excluded except the intravascular catheters. Clinical symptoms include fever, chills, low blood pressure, elevated white blood cell count, and elevated C-reactive protein. Patients with autoimmune diseases and cancer, or patients showed fever, chills, low blood pressure, elevated white blood cell count, and elevated C-reactive protein before introduction of CVC were excluded in this study.

General information

Among the 165 patients, there are 82 males and 83 females with an average age of (67.34±9.04).

Methods

Ten ml of peripheral venous blood and 10 ml of central venous blood were drawn and cultured. The tips of CVC (5 cm) were cultured in 5% sheep blood agar plate according to semi-quantitative roll plate method described by Maki et al. Blood and tips were cultured for 24-72 h at 37°C. Bacteria were biochemically analyzed, multi-drug resistant *A. baumannii* was isolated and the causes of drug resistance were ana-

lyzed. After a follow-up survey, 15 out of 165 patients had CRBSI caused by multi-drug resistant *A. baumannii*.

The effects of age, number of catheters, total parenteral nutrition, APACHE II score, central venous catheter indwelling time, and acceptance of carbapenem antibiotics 14 days before bacteria culture on prognosis were analyzed.

In a six-month follow-up survey of those 15 patients with CRBSI caused by multi-drug resistant *A. baumannii*, we found that all the 15 patients had poor prognosis (poor prognosis criteria: there are different degrees of underlying disease relapse, rehospitalization, and even death etc.). Therefore, the factors that may affect prognosis were analyzed first using univariate analysis and multivariate logistic regression analysis.

Outcome measures

The drugs used to analysis the drug resistance include piperacillin, piperacillin/tazobactam, aztreonam, imipenem/cilastatin, gentamicin, amikacin, ciprofloxacin, levofloxacin, meropenem, cefepime, cefoperazone/sulbactam, ceftazidime. Results were classified to sensitive and resistant. Causes of drug resistance analyzed in this study includes poor health condition (with one or more chronic diseases, lowered resistance to infection, or lowered functional fitness), prolonged use of carbapenems (more than 2 weeks), low nutritional requirements for growth of *A. baumannii*, strong resistance to disinfectants, and long-term survival in the hospital environment.

The factors that may affect prognosis analyzed in this study includes age (56-70, 71-85), number of catheters (≤ 2 , > 2), total parenteral nutrition, APACHE II score (≥ 20), central venous catheter indwelling time (≥ 14 d), and acceptance of carbapenem antibiotics 14 days before bacteria culture (≥ 7 d). Univariate analysis was used first and followed by multivariate logistic regression analysis.

Statistical analysis

SPSS16.0 was used for the statistical analysis. A Chi-square test was used to analyze count data. The significance of univariate analysis

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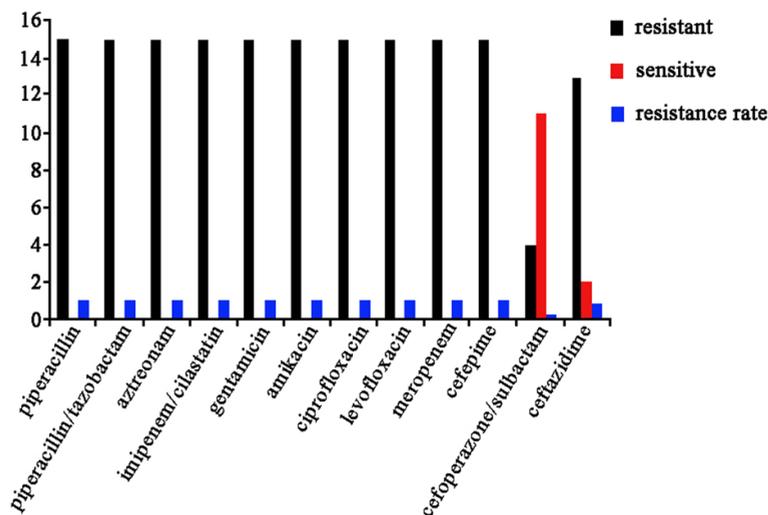


Figure 1. Drug resistance analysis of multi-drug resistant *A. baumannii*.

Table 1. Analysis of causes of drug resistance

Poor health condition	Prolonged use of carbapenems	Low nutritional requirements	Strong resistance to disinfectants	Long-term survival in the hospital environment
13	14	15	14	14
86.67%	93.33%	100.00%	93.33%	93.33%

and multivariate logistic regression analysis was set to $P < 0.05$.

Results

Drug resistance analysis of multi-drug resistant A. baumannii

Fifteen out of 165 patients were found multi-drug resistant *A. baumannii* positive (9.09%). Results showed that the multi-drug resistant *A. baumannii* were 100% resistance against piperacillin, piperacillin/tazobactam, aztreonam, imipenem/cilastatin, gentamicin, amikacin, ciprofloxacin, levofloxacin, meropenem, and cefepime; 26.67% resistance against cefoperazone/sulbactam; and 86.67% resistance against ceftazidime (**Figure 1**).

Analysis of causes of drug resistance

Study showed that the health condition of 13 out of 15 (86.67%) patients with CRBSI caused by multi-drug resistant *A. baumannii* was very poor. Fourteen out of 15 patients (93.33%) had prolonged use of carbapenems. All 15 *A. bau-*

mannii showed low nutritional requirements for growth (100.00%). Fourteen out of 15 *A. baumannii* (93.33%) showed strong resistance to disinfectants and could survive for a long time under hospital environment (**Table 1**).

Univariate analysis of factors affecting prognosis

Results showed that age and number of catheters did not have a significant effect on prognosis. However, total parenteral nutrition, APACHE II score (≥ 20), CVC indwelling time (≥ 14 d), and acceptance of carbapenem antibiotics 14 days before bacteria culture (≥ 7 d) did have significant effects on prognosis (**Table 2**).

Multivariate logistic regression analysis of factors affecting prognosis

A six-month follow-up survey on those 15 multi-drug resistant *A. baumannii* positive patients showed that all 15 patients had poor health condition, 8 out of 15 had disease relapse, 4 out of 15 rehospitalized, and 3 patients died.

Multivariate logistic regression analysis showed that the factors affecting prognosis were (in descending order): APACHE II score (OR=2.023), CVC indwelling time (OR=1.347), total parenteral nutrition (OR=1.026), and acceptance of carbapenem antibiotics 14 days before bacteria culture (OR=2.561) (**Table 3**).

Discussion

In this study, 15 multi-drug resistant *A. baumannii* were isolated out of 165 cases. Those 15 *A. baumannii* had high drug resistance rate. They showed 100% resistance against piperacillin, piperacillin/tazobactam, aztreonam, imipenem/cilastatin, gentamicin, amikacin, ciprofloxacin, levofloxacin, meropenem, and cefepime. The reasons for drug resistance was attributed to poor health condition, prolonged use of carbapenems, low nutritional require-

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Table 2. Univariate analysis of factors affecting prognosis

Factor	Case	Case of infection	χ^2	P
Age	56-70	39	0.80	>0.05
	71-85	124		
Number of catheters	≤2	92	0.80	>0.05
	>2	73		
Total parenteral nutrition	Yes	55	8.25	<0.05
	No	110		
CVC indwelling time	≥14 d	29	14.05	<0.05
	<14 d	136		
APACHE II score	≥20	60	18.04	<0.05
	<20	105		
Acceptance of carbapenem antibiotics 14 days before bacteria culture	≥7 d	39	22.58	<0.05
	<7 d	126		

Table 3. Multivariate logistic regression analysis of factors affecting prognosis

Factor	β	SD	Wald χ^2	P	OR	95% CI
CVC indwelling time	0.798	0.862	0.984	0.035	1.347	0.258~0.926
Acceptance of carbapenem antibiotics 14 days before bacteria culture	1.642	1.324	2.956	0.017	2.561	1.573~3.235
Total parenteral nutrition	0.373	0.459	0.647	0.061	1.026	0.847~1.478
APACHE II score	1.392	0.958	1.426	0.030	2.023	1.493~2.583

ments for growth of *A. baumannii*, strong resistance to disinfectants, and long-term survival under hospital environment.

Poor health condition and prolonged use of carbapenems are two of the major reasons for drug resistance of *A. baumannii*. Poor health condition provided the conditions for drug resistance and its enhancement. It sometimes is hard to determine the type of pathogenic microorganisms because of the complexity of the disease and non-specific symptoms of hospital-acquired infections. In order to avoid misdiagnosis, doctors often use antimicrobial de-escalation strategies and take a conservative treatment with antibiotics. Because of the popularity, carbapenems are among the preferred choices in the conservative treatment [3]. However, extensive use of empiric antimicrobial agents increases the selective pressure of antibiotics to some extent and increases the chances of the emergence of multidrug-resistant strains. Studies showed that optimization the use of carbapenem antibiotics plays an important role in the prevention of CRBSI caused by multi-drug resistant *A. baumannii* [4].

Low nutritional requirements for growth, strong resistance to disinfectants, and long-term survival under hospital environment are some of the important features of multi-drug resistant *A. baumannii*. Low nutritional requirements for growth and strong resistance to disinfectants demonstrate that *A. baumannii* has a strong ability to survive. Long-term survival under hospital environment provides a good foundation for the enhancement of its drug resistance. Poor health condition, long-term use of carbapenem antimicrobial, and increased selective pressure of antibiotics prompt the enhancement of drug resistance of *A. baumannii* [5, 6].

Total parenteral nutrition and prolonged CVC indwelling time (≥14 d) increase the probability of infection. It has been showed that the longer the CVC indwelling time, the more pathogens on catheter tips. This is because daily cleaning and skin disinfection is very important after administration of CVC, the bacteria on the skin surface will invade into the catheter through the puncture site when disinfection was not done properly, which increases the incidence of CRBSI caused by multi-drug resistant *A. bau-*

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mannii [7]. The main ingredients of total parenteral nutrition are sugar and lipids, which afford conditions that are very conducive to bacterial growth. The intravenous nutrition solute is relatively thick, so it is inevitable that some solute and solution will attach to the catheter surface, narrow the lumen diameter, thus affect the patency of the catheter and provide favorable conditions for microbial proliferation [8]. In addition, due to lack of food and energy during fasting, the gastrointestinal mucosa cells are in the shrinking state, which likely to cause intestinal bacterial translocation and increase the probability of CRBSI caused by multi-drug resistant *A. baumannii* [9].

APACHEII score collected 24 hours before culture of peripheral blood and catheter specimen are important indicators used to assess the severity of symptoms and can reflect the patients' clinical and physical condition to a certain extent. The higher the APACHEII the score, the worse the clinical and physical condition of the patient. The patients in this study were old. With the increase of age, body resistance weakened, the capability of resistance to bacteria reduced, whereas the dependence on CVC became stronger which increases the indwelling time of CVC and leads to the colonization and infection of multi-drug resistant *A. baumannii* [10-13]. Fei et al. recommended that actively carry out clinical screening to get early diagnosis and timely intervention to enhance the outcomes [14-16].

Acceptance of carbapenem antibiotics for more than 7 days before bacteria culture is also a risk factor of CRBSI caused by multi-drug resistant *A. baumannii*. Liu et al. found that long time acceptance of carbapenem antibiotics significantly promoted drug resistance of *A. baumannii* and thereby increased the probability of CRBSI caused by multi-drug resistant *A. baumannii*. It also has been shown that CVC indwelling time correlated with and the occurrence of CRBSI [16-20].

Taken together, reduction of the amount and time of usage of carbapenem antibiotic usage, shortening the time of total parenteral nutrition and restore of enteral nutrition as soon as possible, disinfection and cleaning of patient's skin, and avoidance of prolonged CVC indwelling could reduce the incidence of CRBSI caused by multi-drug resistant *A. baumannii* and improve clinical outcome.

Disclosure of conflict of interest

None.

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