REPORT

Prevalence of hospital acquired *Burkholderia cepacia* infection and its antimicrobial susceptibility in a Chinese hospital

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Abstract: This study aimed to investigate antimicrobial susceptibility of hospital acquired *Burkholderia cepacia* infection in Shanxi (China) during August 2009 and December 2012. To characterize an emerging nocosomial infection. The medical records of 112 patients that were tested positive for *B. cepacia* were retrospectively analyzed. The K-B disk diffusion method was used to determine the drug susceptibility of the isolated strains. A hundred and fifty strains of *B. cepacia* were isolated from 112 patients. The sensitivity rates of *B. cepacia* to meropenem, imipenem, cotrimoxazole, minocycline and ceftazidime were 65.7%, 14.3%, 76.0%, 68.1% and 74.1%, respectively. All patients suffered from more than two underlying diseases, 89 (79.5%) from another bacterial infection and 92 (82.1%) with indwelling catheter. All patients were given antibiotics, including 62 patients that received carbapenem antibiotics. The average duration of hospitalization before detection of *B. cepacia* was 31±24 days, after which 65 patients (58.0%) improved, 22 (19.0%) died, 8 (7.1%) quit the therapy, and 17 (15.2%) were discharged after full recovery. The prevalence of hospital acquired *B. cepacia* infection and drug-resistance in the hospital is reported and risk factor exploration requires further study.

Keywords: *Burkholderia cepacia*; nosocomial infection; antibiotic resistance; China.

INTRODUCTION

Widespread and indiscriminate use of certain antibiotics has enabled multi drug-resistant non-fermenting gram-negative bacilli (NFGNB) to emerge as a concerning healthcare-associated pathogen (Chawla *et al.*, 2013, Clinical and Laboratory Standards Institute, 2013). Many previous studies have focused on the identification of *Pseudomonas spp*. and *Acinetobacter spp*. because of their high isolation rates (Chusri *et al.*, 2014, Li *et al.*, 2014). Other NFGNB, such as *Burkholderia cepacia*, may also cause disease in immunocompromised patients (Choh *et al.*, 2013, Horsley and Jones, 2012) or in intensive care unit (ICU) settings. Previous studies have shown that the identification rate of *B. cepacia* is increasing constantly, and it is highly resistant to existing antimicrobial agents (Chiarini *et al.*, 2006). This report presents a descriptive report of the *B. cepacia* infections recorded at Shanxi Medical University Second Hospital, China, during August 2009 and December 2013.

MATERIALS AND METHODS

Subjects and strain collection

This cross-sectional, descriptive study involved the retrospective analysis of the microbiological reports of *B. cepacia*-positive cultures isolated and identified from 112 patients hospitalized between August 1st, 2009 and December 31st, 2013 at Shanxi Medical University Second Hospital. Data from consecutive patients hospitalized within the internal medicine, general surgery, intensive care and neurosurgery units were included. The study was approved by the Medical Ethics Committee of the Shanxi Medical University Second Hospital, Taiyuan, China. All patients provided written informed consent.

Culture and identification of Burkholderia cepacia

The collected samples were inoculated on a blood agar and eosin methylene blue agar disk in a SW-II-A/B_3 biological safety cabinet and incubated for 24 hours at 37ºC in a Heraeus BB5060 CO_2 incubator. Bacterial strains were identified using the bio Merieux VITEK-60 microbe automatic identification system. *Escherichia coli* (ATCC 25922) and *Pseudomonas aeruginosa* (ATCC 27853) were used as quality control standards.

Antimicrobial susceptibility tests

Antimicrobial susceptibility tests were performed by the K-B broth micro dilution method according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI 2013) (Clinical and Laboratory Standards Institute, 2013). Susceptibility to cotrimoxazole (SMZ), minocycline (MNO), ceftazidime (CAZ), meropenem (MEM) and imipenem (IPM) was assessed.

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Table 1: Susceptibility of *B. cepacia* to antibiotics

Antibiotic	Sensitivity		
	Sensitive (n, %)	Intermediate (n, %)	Resistant (n, %)
Meropenem	65 (65.7)	6 (6.1)	28 (28.3)
Ceftazidime	83 (74.1)	8 (7.1)	21 (18.8)
Cotrimoxazole	76 (76.0)	5 (5.0)	19 (19.0)
Minocycline	64 (68.1)	13 (13.8)	17 (18.1)
Imipenem	1 (14.3)	1 (14.3)	5 (71.4)

STATISTICAL ANALYSIS

Normally distributed data were presented as mean ± SD and categorical data were presented as percentages. Data were analyzed using SPSS 18.0 (SPSS, Chicago, IL, USA).

RESULTS

Baseline characteristics of B. cepacia infected patients

There were 75 male (67.0%) and 37 female (33.0%). The mean age of the patients was 57.8±32.2 years. The average duration of hospitalization was 31±24 days and the patients had been in hospital for 18.8±13.0 days before samples tested positive for *B. cepacia* and 10.3±9.9 days (range, 1-44 days) after tracheotomy and/or tracheal intubation. Seventeen patients (15.2%) fully recovered, 65 (58.0%) improved, 8 (7.1%) gave up treatment and 22 (19.6%) patients died at the hospital.

A total of 150 *B. cepacia*-positive samples were obtained from these 112 patients, including 48(32.0%) from patients admitted to the ICU, 25(16.7%) from patients treated in the hematology department, 18(12.0%) from the respiratory department and the remaining were from various departments.

Use of antibacterial agents before B. cepacia diagnosis

Sixty-one patients (54.5%) had received carbapenems, 70 (62.5%) had received third generation cephalosporins, three (2.7%) had received fourth generation cephalosporins, 47 (42.0%) had received antifungals (fluconazole, voriconazole, itraconazole, or caspofungin), 33 (29.5%) had received teicoplanin, linezolid, or vancomycin, 31 (27.7%) had received enzyme inhibitor complex agents, 28 (25.0%) had received fluoroquinolone drugs.

Antimicrobial sensitivity of B. cepacia

Among the 150 strains of *B. cepacia*, 28.3% strains were resistant to MEM, 18.8% were resistant to CAZ, 19.0% were resistant to SXT, 18.1% were resistant to MNO and 71.4% were resistant to IEM (table 1).

DISCUSSION

These observations suggest that the elderly and men were prone to infection compared with younger patients and women, consistent with previous findings (Li *et al.*, 2013, Lu *et al.*, 2010). Of the 150 *B. cepacia* harboring specimens analyzed, most were acquired from patients within the ICU, hematology, respiratory medicine, and neurology departments. Patients in the ICU are particularly susceptible to nosocomial infections as a result of frequent medical interventions (Wang *et al.*, 2013, You *et al.*, 2013). In order to reduce the incidence of nosocomial infection, the indications of the antibiotics should be monitored when antimicrobial agents are used, and the ward environment hygiene should be kept clean.

The majority of samples tested positive for *B. cepacia* were collected from sputum and bronchoalveolar lavage fluid specimens. The respiratory tract is a common site of *B. cepacia* colonization. *B. cepacia* may spread by contaminated medical equipment, particularly ventilator pipes, fittings, and wet flasks (Sun *et al.*, 2009).

B. cepacia is multi-drug resistant due to innate and acquired resistance mechanisms (Podnecky *et al.*, 2015, Rhodes and Schweizer, 2016). The permeability of its outer membrane is poor, and thus antimicrobial agents are very slow to reach in the bacteria. *B. cepacia* is naturally resistant to polymyxin, gentamicin and amikacin amino glycosides (Wang *et al.*, 2012). Clinical application of cephalosporins and imipenem may induce *B. cepacia* to produce β-lactamase. *B. cepacia* also has the outer membrane lipoprotein pumping system (MexA-MexB-OprM), which confers resistance to quinolones and chloramphenicol. The antibacterial to which most of the isolated strains of *B. cepacia* remained sensitive was cotrimoxazole, which suggests that this antibiotic may be applied following detection of *B. cepacia*. *B. cepacia* is relatively insensitive to imipenem (Wang, Li *et al*., 2012).

The conclusions of this study are limited by the relatively small sample size and single site. Further larger multi-site surveys will be required to characterize the prevalence of and risk factors for *B. cepacia* infection spread.

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