Journal of Microbiology, Immunology and Infection (2014) **47**, 311—317

Available online at www.sciencedirect.com

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ORIGINAL ARTICLE

Risk factors for imipenem-nonsusceptible *Acinetobacter nosocomialis* bloodstream infection

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Received 18 July 2012; received in revised form 5 January 2013; accepted 15 February 2013
Available online 1 May 2013

KEYWORDS
Acinetobacter nosocomialis;
Bacteremia;
Imipenem resistance;
Risk factors

Background: The emergence of imipenem-nonsusceptible (INS) *Acinetobacter baumannii* complex has had a great impact on healthcare systems worldwide. Understanding the risk factors related to INS infection is useful for infection control. The risk factors for INS *A. baumannii* have been well documented; however, the risk factors related to INS *Acinetobacter nosocomialis* infection lack documentation. The purpose of this study was to identify the risk factors associated with INS *A. nosocomialis* bacteremia.
Methods: This retrospective 9-year study included 329 adults with *A. nosocomialis* bacteremia in a tertiary medical center in Taiwan. *Acinetobacter nosocomialis* was identified using a multiplex polymerase chain reaction method and sequence analysis of a 16S—23S intergenic spacer.
Results: Among 329 patients with *A. nosocomialis* bacteremia, 67 had INS isolates (20.4%). Patients with INS isolates tended to have a more severe form of the diseases [with ICU admission and a higher APACHE (Acute Physiology and Chronic Health Evaluation) II score], specific underlying diseases (associated with chronic lung diseases and end-stage renal diseases, but less commonly alcoholism and chemotherapy), multiple invasive procedures, pneumonia as a

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http://dx.doi.org/10.1016/j.jmii.2013.02.002

primary focus of infection, and prior antimicrobial use (sulbactam, antipseudomonal penicillins, aminoglycosides, and carbapenems). Multivariable analysis showed that ICU admission, chronic lung diseases, arterial line catheterization, total parenteral nutrition, and prior use of carbapenems were independent risk factors; prior use of carbapenems was found to be the most influential (odds ratio 6.36, 95% confidence interval 2.00—20.21; $p = 0.002$).
Conclusion: To our knowledge, this is the first study describing the risk factors associated with INS *A. nosocomialis* bacteremia. Regulated antibiotic control policy, especially for carbapenem, and infection control measures targeting patients hospitalized in ICU, with chronic lung diseases and multiple invasive procedures, may be helpful in reducing INS *A. nosocomialis* infection.

Introduction

Nosocomial infections have become a serious problem worldwide in recent years. One of the nosocomial pathogens is *Acinetobacter baumannii* complex (ABC), which frequently causes outbreaks of infection with high mortality in hospitalized patients.[1] With the widespread use of broad-spectrum antibiotics and the increasing number of immunocompromised patients, we are now facing the emergence of drug-resistant ABC worldwide.[2] Currently, most ABCs are highly resistant to many of the commonly used antibiotics because of both intrinsic and acquired mechanisms.[3,4] In Europe, the rate of resistance to carbapenems has been reported to be 27%,[5] whereas the SENTRY Surveillance Program found that it was 42.3% in the Asia-Pacific Rim nations.[6] In Taiwan, according to the annual report of the Taiwan Nosocomial Infections Surveillance System, the resistance rate to imipenem had increased to 66.8% in 2010.[7] Studies show that antibiotic resistance significantly prolongs the duration of intensive care unit (ICU) stays and hospitalization,[8,9] leading to increased hospitalization costs. In addition, patients with resistant ABC infection have a higher mortality rate than those infected with bacterial strains susceptible to antibiotics.[8,10,11]

The effective control of drug-resistant ABC outbreaks is, therefore, an important issue requiring knowledge of the infected population so that the dynamics of the spread of endemic and epidemic strains can be investigated and appropriate control measures can be introduced in a timely manner.[12] Numerous clinical studies on the risk factors for imipenem-nonsusceptible (INS) ABC infections, including bacteremia, have been published.[13,14] However, ABC comprises not only *A. baumannii*, but also *Acinetobacter nosocomialis* and *Acinetobacter pittii*, which can only be differentiated by molecular methods.[15,16] Information concerning the risk factors for INS *A. nosocomialis* infection is absent. Therefore, the purpose of this study was to identify the risk factors associated with INS *A. nosocomialis* bacteremia.

Materials and methods

Study population

This retrospective study was conducted between 2000 and 2008 in Taipei Veterans General Hospital, a 2900-bed tertiary care medical center in Taiwan. All adults with *A. nosocomialis* bacteremia and concurrent symptoms and signs of sepsis were included. Patients who were less than 18 years of age or whose medical records were not complete were excluded. The medical records were reviewed and recorded on a standard form. Demographic data, disease severity represented by the Acute Physiology and Chronic Health Evaluation (APACHE) II score, comorbidities, invasive procedures, antimicrobial agents administered within 1 month prior to the onset of bacteremia, and infection foci were recorded for analysis.

Definitions

Chronic lung diseases included chronic obstructive pulmonary diseases, tuberculosis, and asthma. Chronic kidney disease was defined as a glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2, whereas end-stage renal disease was defined as a GFR < 15 mL/min/1.73 m^2 or receipt of permanent renal replacement therapy for more than 3 months. Neutropenia was defined as an absolute neutrophil count <500 cells/mm^3. Immunosuppressant therapy included treatment for neoplastic diseases and organ transplantation, as well as the use of corticosteroids (equivalent to more than 10 mg of prednisolone daily for 5 days) within 4 weeks of the onset of bacteremia. Long-term intravenous access included Hickman catheters, port-A-catheters, and other permanent catheters. The origin of the bacteremia was defined as previously suggested.[17] This study was approved by the institutional review board of Taipei Veterans General Hospital.

Genomic species identification and antimicrobial susceptibility testing

ABC was phenotypically identified by the 32 GN system (bioMérieux, Marcy l'Etoile, France). The bacteria were stored at $-70^{\circ}C$ in trypticase cystine agar (Difco Laboratories, Le Pont de Claix, France) supplemented with 15% glycerol before use. A multiplex polymerase chain reaction[15] was used to identify *A. baumannii*. The non-*baumannii Acinetobacter* species were identified by amplification and sequence analysis of the 16S—23S rRNA intergenic spacer using universal primers.[16] The susceptibility and non-susceptibility of imipenem and other antimicrobial agents were determined by agar dilution methods. The interpretation was performed according to the guidelines of the Clinical and Laboratory Standards Institute.[18] For imipenem, a minimum inhibitory concentration (MIC) ≤ 4 mg/L was considered to reflect susceptibility, whereas an MIC > 4 mg/L was considered to show a nonsusceptible organism.