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Original Article

Risk factors for healthcare-associated infection caused by carbapenem-resistant *Pseudomonas aeruginosa*

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Abstract *Background/purpose:* The incidence of carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) related healthcare-associated infection (HAI) has increased in recent year worldwide. This study is to investigate the risk factors associated with CRPA infections in a university hospital setting in Taiwan to provide more information for clinician and infection control system.
Methods: A retrospective cross-sectional study was conducted from January 1st, 2009 to June 30th, 2014. Patients with *P. aeruginosa* related HAI were included and divided into the CRPA case group and carbapenem-susceptible *Pseudomonas aeruginosa* (CSPA) control group. The medical records were reviewed to identify risk factors for CRPA HAI and mortality. Patients with prior use of any anti-pseudomonal carbapenems were included in subgroup analysis.
Results: 395 cases of *P. aeruginosa* infection were enrolled from total of 3263 HAI events; 63 were CRPA and 332 were CSPA. The prevalence of CRPA was 15.9% (63/395). Significant risk factors related to CRPA infection were longer time at risk, prior use of anti-pseudomonal carbapenems, and prior use of aminoglycoside ($p < 0.05$, 0.01, and 0.05). Furthermore, anti-pseudomonal carbapenem monotherapy did not significantly increase risk for CRPA infection.
Conclusion: The worldwide CRPA prevalence has been on the raise and Taiwan has been also keeping up with the trend. Antimicrobials usage should be monitored carefully, especially with

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carbapenems and aminoglycoside. Clinicians should be award of and understand about the risk of CRPA infection, which increases by 1% with each hospitalization day.

Introduction

Antimicrobials resistance has been an ever growing concern globally.[1] Many broad-spectrum antibiotics such as Carbapenems have been widely used and followed by the raise of drug resistance in many microorganisms, one of whom is *Pseudomonas aeruginosa*.[2]

Pseudomonas aeruginosa, as one of the major pathogens of healthcare-associated infections (HAI), is associated with substantial higher mortality and morbidity rates compared to other pathogens.[1,3] Infections caused by *P. aeruginosa* have always been challenging to healthcare providers due to their intrinsic resistance against a wide variety of antimicrobials.[2,4] The 2nd-quarter report of Taiwan Nosocomial Infection Surveillance System (TNIS) from the Center for Disease control (CDC) in Taiwan indicated that 7.5%—9.2% of HAI have been caused by *P. aeruginosa* in 2014.

Carbapenems, a class of broad-spectrum β-lactam antibiotics, are often the last resort against treating nosocomial infections when all else has failed. As a result, resistance to this class of antimicrobials may limit clinical therapeutic choice. According to the annual report of TNIS, carbapenem-resistant *P. aeruginosa* (CRPA) was responsible for approximately 15.5% (medical centers) to 18.8% (regional hospitals) of healthcare-associated *P. aeruginosa* infections during the first half of 2014.

From 2009 to the first half of 2014, in intensive care units (ICU) setting of regional hospitals and medical centers in Taiwan, the overall prevalence of CRPA was between 14% and 20%. Furthermore, if we analyze only the ICUs of Taipei, the prevalence was reported to be even higher, between 15% to 23%. It was no exception for Taipei Medical University hospital (TMUH), a teaching hospital in Taipei. Our rates of CRPA in ICU patients have been on the raise since 2013; the prevalence rate was 10%, and reached 25% for the first half of 2014 and 33.3% during the second half of 2014. As a result, the infection control office of TMUH have been motivated to deal with this healthcare-related epidemic.

This study not only aims to identify the possible risk factors for acquiring healthcare-associated CRPA infection in a university hospital. Moreover, it was conducted with the intention of identifying possible risk factors regarding antibiotics resistance in the effort to guide clinicians in the future to infection control.

Methods

Study population and study design

Taipei Medical university hospital (TMUH) is a private, tertiary care, an 800-bed general teaching hospital in Taiwan. The hospital contains an emergency department with medical and surgical intensive care units.

This retrospective cross-sectional study was conducted at TMUH with a time frame set from January 1st, 2009 to June 30th, 2014. Patients were diagnosed as having *P. aeruginosa* related HAI 48 h after admission. The definition of HAI is consistent with the definition and criteria for specific types of infections from CDC.[5]

Patients with *P. aeruginosa* related HAI were included in this study and divided into the CRPA case group and CSPA control group. Patients with incomplete medical record were excluded. The primary outcome was to analyze possible risk factors for CRPA infection and the secondary outcome was to compare the 30-day all-cause mortality rate in two groups analyzed by logistic regression. Patients with prior use of any anti-pseudomonal carbapenems were then selected for subgroup analysis (Fig. 1).

Bacterial isolates and antimicrobial susceptibility testing

Phoenix Automated Microbiology System (Becton Dickinson, Sparks, MD, USA) was used to determine the antimicrobial susceptibility of *P. aeruginosa* isolates. Antimicrobials susceptibility to anti-pseudomonal agents such as imipenem, meropenem, amikacin, ceftazidime, cefepime, ciprofloxacin, gentamycin, levofloxacin, piperacillin, piperacillin/tazobactam, were also determined by the MIC results in the department of laboratory in TMUH according to the criteria of the Clinical and Laboratory Standards Institute (CLSI) guidelines.[6,7]

In our study, CRPA defined as MIC of imipenem and/or meropenem $\geq$8 μg/mL and remained *P. aeruginosa* isolates as CSPA.

Data collection

We reviewed patients' charts for data collection, including patients' age, gender, underlying disease, infection site, ward type, room number, hospitalization days, the time at risk, mortality, the prior exposure of invasive procedure during time at risk, prior use of antimicrobials, and the antimicrobials susceptibility test of the culture. The definition of the time at risk is the number of hospitalization days before positive culture of *P. aeruginosa*.

Invasive procedures such as central catheter (including central venous catheter, permanent catheter, port-A catheter, double lumen catheter, peripherally inserted central catheter and arterial catheter), urinary catheter, chest tube, mechanic ventilation, and extra-corporeal membrane oxygenation (ECMO) were recorded routinely and marked down as prior exposure of invasive procedures as followed during time at risk.

Prior use of antimicrobials was defined as any antimicrobials use within 90 days before the positive *P. aeruginosa*

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