J Med Bacteriol. *Vol. 4, No. 3, 4 (2015): pp.56-60* *jmb.tums.ac.ir*

Prevalence of Carbapenem Resistance in *Acinetobacter baumannii* Isolates from Burn and Non-Burn Patients in Tehran

*Zahra Ghareboghy Sarmad, Fereshteh Eftekhar **

Department of Microbiology, Faculty of Biological Sciences, Shahid Beheshti University, Tehran, Iran.

ARTICLE INFO

Article type:
Short Communication

Article history:
Received: 18 June 2015
Revised: 27 June 2015
Accepted: 10 July 2015

Keywords:
Acinetobacter baumannii, Antibiotic resistance, Imipenem, Meropenem, Carbapenem

ABSTRACT

***Background*:** *Acinetobacter baumannii* has become one of the most important causes of nosocomial infections in recent years. The organism seems to be resistant to most classes of antibiotics. Carbapenems are considered the most effective drugs for treatment of these infections. However, increasing emergence of carbapenem resistant *A. baumannii* has become a major healthcare problem.

***Methods*:** The present study was conducted to compare the antibiotic susceptibility of 61 isolates of *A. baumannii* (31 from patients with burn infections and 30 from non-burn patients) to 12 antibiotics including imipenem and meropenem by disc diffusion.

***Results*:** Both groups of the isolates showed high levels of resistance to all classes of antibiotics except for aminoglycosides. Imipenem resistance was observed in 96.7% of the non-burn isolates and 100% among the burn strains.

***Conclusion*:** On the other hand, resistance to meropenem was significantly higher in non-burn isolates (83.3%) compared to the burn strains (6.4%).

- ***Please cite this paper as:*** Ghareboghy Sarmad Z, Eftekhar F. Prevalence of Carbapenem Resistance in *Acinetobacter baumannii* Isolates of Burn and Non-Burn Patients in Tehran. *J Med Bacteriol*. 2015; 4 (3, 4): pp. 56-60.

*Corresponding Author: Fereshteh Eftekhar, Department of Microbiology, Faculty of Biological Sciences, Shahid Beheshti University, Tehran, Iran.

Tel: +98-21-29903208, *Email*: f-eftekhar@sbu.ac.ir

Introduction

Emergence and spread of multidrug resistant (MDR) *A. baumannii* in nosocomial infections has become a serious concern for clinicians. The organism commonly targets the most vulnerable hospitalized patients; those who are critically ill, particularly in intensive care units (ICU) and burn wards (1). Infections include bacteremia, ventilator-associated pneumonia, meningitis, urinary tract, wounds and burn infections (1-3). *A. baumannii* has a broad range of resistance mechanisms to all existing antibiotic classes including active drug efflux, modification of drug target sites and most importantly, enzymatic inactivation of the antimicrobial agents (2). Carbapenems, especially imipenem are often the drugs of choice for treatment of *A. baumannii* infections. However, high levels of resistance have emerged causing failure in treatment (4). The organism is capable of producing a number of β-lactamases including extended-spectrum β-lactamases (ESBLs), AmpC β-lactamases and carbapenemases (5). The most common mechanism responsible for carbapenem resistance in *A. baumannii* is production of carbapenemases (2, 6, 7). Among the carbapenem hydrolyzing enzymes identified in *A. baumannii*, metallo β-lactamases (MBLs) and class D β-lactamases (oxacillinases) confer high levels of resistance to carbapenems. MBLs mediate resistance to all β-lactams except for aztreonam and are mostly associated with class 1 integrons (1, 8). Class D β-lactamases have been reported to have a greater affinity for imipenem than meropenem in (9). The present study was undertaken to compare the antibiotic resistance profiles, specifically carbapenem resistance between burn and non burn *A. baumannii* clinical isolates.

Material and method

Sixty one isolates of *A. baumannii* were employed of which 31 were from burned patients collected from Shahid Motahari Burn Hospital and 30 from non-burn infections obtained from Imam Hussein Hospital from October 2011 to April 2012. The burn isolates were mostly from wounds (n=25) followed by blood (n=4) and urine (n=2). The majority of the non burn isolates were collected from the intensive care unit (n=19) and were mostly from sputum (n=17) followed by wound specimens (n=4), catheters (n=3), blood (n=3), cerebral spinal fluid (n=2) and trachea (n=1). The identity of the isolates was confirmed by the conventional biochemical methods including catalase and oxidase tests, sugar fermentation and H2S production on triple sugar iron agar (TSI), oxidation/fermentation of glucose (O/F test), growth on MacConkey agar and growth at 37 and 42 °C. The isolates were stored at -20 °C in brain heart infusion broth (Oxoid, UK) containing 10% dimethyl sulfoxide (v/v). Antibiotic susceptibility of the isolates to 12 antibiotics was determined using the disc diffusion method according to the CLSI guidelines (10). The antibiotics discs (MAST, UK) were: aztreonam (ATM, 30 µg), amikacin (AN, 30 µg), gentamicin (GM, 10 µg), tobramycin (TN, 10 µg), cefepime (CPM, 30 µg), cefotaxime (CTX, 30 µg), ceftazidime (CAZ, 30 µg), ciprofloxacin (CIP, 5 µg), imipenem (IMP, 10 µg), meropenem (MEM, 10 µg), piperacillin (PRL, 100 µg) and piperacillin-tazobactam (PTZ, 110 µg). Multidrug resistance (MDR) was defined as resistance to 3 or more classes of antibiotics. Comparison of the antibiotic resistance profiles between burn and non burn groups and among ICU and non ICU patients were made using the two-tailed Mann-Whitney test in SPSS software version 20.

Result

Biochemical test results confirmed the identity of all isolates as *Acinetobacter baumannii*. Disc diffusion results (Figure 1) revealed that majority of the isolates in both burn and non-burn groups were 100% resistant -lactam antibiotics including ceftazidime, piperacillin, piperacillin-

tazobactam, cefepime, cefotaxime as well as ciprofloxacin. The non-burn isolates were 96.7% resistant to imipenem (with only one intermediately resistant strain), 86.7% to amikacin (no intermediate resistance), 83.3% to meropenem (three intermediately resistant), 53.3% to tobramycin (two intermediately resistant), and 43.3% to gentamicin (two intermediately resistant). The burn isolates showed 100% resistance to imipenem followed by 90.3% resistance to azetronam (two intermediately resistant), 71% to amikacin (eight intermediately resistant, 25.8%), 58% to gentamicin (one intermediately resistant), 6.4% to meropenem (fourteen intermediately resistant, 45.2%) and 3.2% to tobramycin (no intermediate resistance). Aminoglycosides were the most effective drugs against the *A. baumannii* isolates in both groups with tobramycin as the most active member of the class followed by gentamicin and amikacin, respectively. Resistance to meropenem, tobramycin and amikacin was significantly higher in non-burn isolates compared to the burn strains ($p<0.05$). In addition, 93.6% of the burn isolates were susceptible to tobramycin compared to the 40% found in non-burn isolates. An important observation was that even though high levels of imipenem resistance was observed in both groups (96.7% in non-burn and 100% in burn isolates), almost half of the burn isolates (48.4%) were susceptible to meropenem compared to the non-burn isolates (6.7%). The number of non-burn isolates with intermediate resistance to all tested antibiotics was low and within the range of 0-3 isolates (0-10%).

However, among the burn group, 25.8% and 45.2% of the isolates showed intermediate resistance to amikacin and meropenem, respectively. All intermediately resistant burn isolates to meropenem showed inhibition zones of 15 mm which is just 1 mm below the zone indicated for susceptibility.

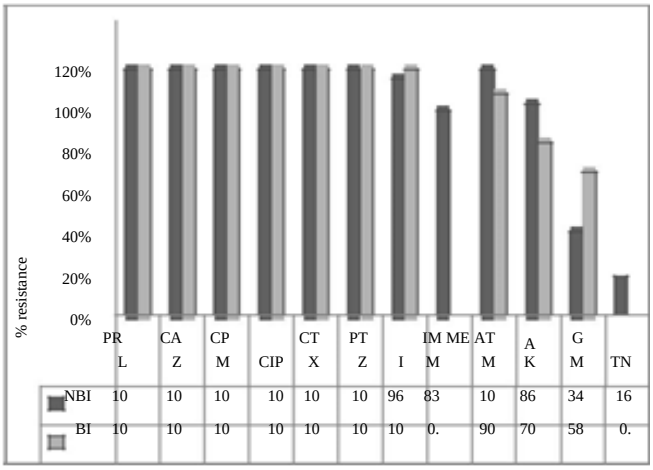

Figure 1. Comparison of antibiotics resistanc profiles between burns isolates (BI) and non-bur isolates (NBI) of Acinetobacter baumannii.PRL Piperacillin; CAZ, ceftazidime; CPM, cefepime CIP, ciprofloxacin; CTX, cefotaxime; PTZ piperacillin-tazobactam; IMI, imipenem; MEM meropenem; ATM, azetronam; AK, amikacin; GM gentamicin; TN, tobramycin.

Discussion

In the recent decades, *A. baumannii* infections have become one of the main causes of high mortality rates in hospitalized patients, especially in intensive care units and burn wards (11). Azimi et al. reported a 12% mortality rate in Motahari Burn Hospital in 2011, where at least 1 positive *Acinetobacter* culture was recovered from all patients (12). *A. baumannii* targets the most vulnerable hospitalized patients, mostly in intensive care or burn units and has an uncanny ability to survive for prolonged periods throughout a hospital environment, thus potentiating its ability for nosocomial spread (11-13). We found that all our *A. baumannii* isolates were resistant to all β -lactam antibiotics tested except for aztreonam. This could be explained by the fact that *Acinetobacter* can produce an array of β-lactamases such as ESBLs and AmpC β-lactamases. Carbapenem resistance in *A. baumannii* is mediated by MBLs and class D β-lactamases. It has been proposed that some

class D β -lactamases have a greater affinity for imipenem compared to meropenem (9). In fact, meropenem has been shown to have a greater potency than imipenem against *A. baumannii* and P. aeruginosa (14, 15). Carbapenem-associated outer membrane protein (CarO) channels were shown to bind imipenem (but not meropenem) depending on their primary structures (16). In contrast, Lesho et al. demonstrated that meropenem was inferior in activity to imipenem (17). In the present study, imipenem resistance was high in both groups of the isolates.

On the other hand, 48.4% of the burn isolates were susceptible to meropenem compared to 6.4% of the non-burn isolates. Unlike the non-burn isolates where negligible intermediate resistance was observed, 45.2% of the burn isolates showed intermediate resistance to meropenem which could raise the alarm for the extensive use of this antibiotic. The prevalence of imipenem and meropenem resistance is similar in most of the studies in Iran. However, Mostofi et al. found that among the clinical isolates of *A. baumannii* collected from 3 hospitals in Tehran, resistance to imipenem was 76% compared to 35% to meropenem (18).

Conclusion

These conflicting results may be due to different carbapenem therapies and show that susceptibility to one carbapenem is not an indication of sensitivity to the other, especially against non-fermentative Gram-negative pathogens. In addition, the organisms found in different clinical settings (ICU vs. Burn wards) could be clonally different.

Acknowledgments

This research was financially supported through a special grant by the Shahid Beheshti University Research Council.

Conflict of interest

None declared conflicts of interest.

Financial disclosure

The authors declare that there is no conflict of interests to publish this article.

References

1. Peleg A, Seifert H, Paterson D. *Acinetobacter baumannii*: Emergence of a Successful Pathogen. *Clin Microbiol Rev* 2008; **21**: 538-82.
2. Manchanda V, Sanchaita S, Singh N. Multidrug Resistant *Acinetobacter*. *J Glob Infect Dis* 2010; **2**: 291-304.
3. Maragakis L, Perl T. *Acinetobacter baumannii*: Epidemiology, Antimicrobial Resistance and Treatment Options. *Clin Infect Dis* 2008; **46**: 1254-63.
4. Poirel L, Nordmann P. Carbapenem resistance in *Acinetobacter baumannii*: mechanisms and epidemiology. *Clin Microbiol Infect* 2006; **12**: 826-36.
5. Lu P, Doumith M, Livermore D, et al. Diversity of carbapenem resistance mechanisms in *Acinetobacter baumannii* from a Taiwan Hospital: spread of plasmid-borne OXA-72 carbapenemase. *J Antimicrob Chemother* 2009; **63**: 641-47.
6. Zarrilli R, Giannouli M, Tomasone F, et al. Carbapenem resistance in *Acinetobacter baumannii*: the molecular epidemic features of an emerging problem in health care facilities. *J Infect Dev Ctries* 2009; **3**: 335-41.
7. Yang H, Lee H, Suh J, et al. Outbreaks of imipenem resistant *Acinetobacter baumannii* producing OXA-23 β-Lactamase in a tertiary care hospital in Korea. *Yonsei Med J* 2009; **50**: 764-70.
8. He´ritier C, Poirel L, Fournier P, et al. Characterization of the naturally occurring oxacillinase of *Acinetobacter baumannii*. *Antimicrob Agents Chemother* 2005; **49**: 4174-79.

9. Walther-Rasmussen J, Høiby N. OXA-type carbapenemases. *J Antimicrob Chemother* 2006; **57**: 373-83.
10. Clinical and laboratory standards institute (CLSI). Performance standards for antimicrobial testing supplement. Twenty-First Informational Supplement. 2011; **31**: 62-3.
11. Albrecht MA, Griffith ME, Murray CK, et al. Impact of *Acinetobacter* infection on the mortality of burn patients. *Am College Surg* 2006; **203**: 546-50.
12. Azimi L, Motevallian A, Ebrahimzadeh A, et al. Nosocomial infections in burned patients in Motahari Hospital, Tehran, Iran. *Dermatol Res Pract* 2011; 1-4.
13. Sunenshine RH, Wright MO, Maragakis LL, et al. Multidrug-resistant *Acinetobacter* infection mortality rate and length of hospitalization. *Emerg Infect Dis* 2007; **13**: 97-103.
14. Jones RN, Sader HS, Fritsche TR, et al. Carbapenem susceptibility discords among *Acinetobacter* isolates. *Clin Infect Dis* 2006; **42**: 158.
15. Rhomberg PR, Jones RN. Antimicrobial spectrum of activity for meropenem and nine broad-spectrum antimicrobials: report from the MYSTIC Program in North America (2002). *Diagn Microbiol Infect Dis* 2003; **47**(1): 365-72.
16. Ferreira M, Coadou G, Molle V, et al. Structure–function relationships of Caro, the carbapenem resistance associated outer membrane protein of *Acinetobacter baumannii*. *J Antimicrob Chemother* 2011; **66**: 2053-56.
17. Lesho E, Wortmann G, Moran K, et al. Fatal *Acinetobacter baumannii* infection with discordant carbapenem susceptibility. *Clin Infect Dis* 2005; **41**(5): 758-59.
18. Mostofi S, Mirnejad R, Masjedian F. Multi-drug resistance in Acinetobacter baumannii strains isolated from clinical specimens from three hospitals in Tehran-Iran. *Afr J Microbiol Res* 2011; **5**(21): 3579-82.