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Clinical importance and cost of bacteremia caused by nosocomial multi drug resistant acinetobacter baumannii

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SUMMARY

Background: A. baumannii is an important nosocomial pathogen associated with high mortality, morbidity and medical cost.
Aim: The aim of this study was to investigate risk factors for MDR *A. baumannii* bacteremia and also evaluate cost of hospitalization of these patients.
Methods: Study was conducted in Ankara Atatürk Training and Research Hospital. Patients who were hospitalized in ICU and diagnosed for nosocomial blood stream infection (BSI) between January 2007 and December 2010 were checked retrospectively. Patients with nosocomial BSI caused by multidrug resistant *A. baumannii* were compared with the patients who had BSI caused by other Gram-negative microorganisms in terms of risk factors, mortality and medical costs.
Findings: In multivariate analysis previous use of carbapenem, quinolone and metronidazole, and SAPS II score were found as independent risk factors. In case group; immunosupression, SAPS II score, and hospital stay until infection were independently associated with mortality in multivariate analysis.
Conclusion: Our results suggest that the occurrence of MDR *A.baumannii* bacteremia was related with the usage of the wide spectrum antibiotics, and mortality rates were increased in patients that high SAPS II scores, long term hospitalization. Infection control procedures and limited antibiotic usage are very important for prevent nosocomial infections.

1. Introduction

Hospital acquired infections are leading causes of morbidity and mortality due to increasing rate of antibiotic resistance. Especially, patients followed in the intensive care units (ICU) are under high risk of infections caused by resistant microorganisms.[1]

Rapid development and global spread of *A. baumannii* as a major cause of nosocomial infections is really remarkable. This organism tends to develop resistance against many antimicrobials from different groups.[2,3] In the 21st century, *A. baumannii* is frequently observed as a nosocomial infection which causes high mortality, morbidity and hospitalization cost.[4,5] Crude mortality rate and attributable mortality of the infection were reported to be 52% and 10-35%, respectively.[6]

The aim of this study was to explore the risk factors in patients with multi-drug resistant (MDR) *A. baumannii* bacteremia and perform a cost analysis of this clinical problem.

2. Material and Methods

This retrospective cohort study has included the patients who had nosocomial blood stream infections (BSI) caused by MDR *A. baumannii* and hospitalized in General Intensive Care (GICU) and Neurology-Neurosurgery Intensive Care (NNICU) Units of Ankara Atatürk Training and Research Hospital between 01 January 2007 – 31 December 2010.

2.1. Patients

Forty-one patients with diagnosis of nosocomial BSI and MDR *A. baumannii* detected in the blood culture were enrolled as the patient group. Forty-five patients who were hospitalised in the

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same ward in the same period with the patient group and had positive blood cultures for Gram-negative microorganisms other than *A. baumannii* were accepted as control group. Patient characteristics were retrospectively scanned and recorded to study forms.

2.2. Definitions

When a patient had at least one of the clinical findings of fever (38.0 °C), chills or hypotension at least 48 hours after hospitalization, *A. baumannii* was isolated in at least one of the blood cultures obtained from a peripheral vein or central catheter and no *A. baumannii* was isolated in any other culture related with other sources of infection, then diagnosis of bacteremia was accepted. Catheter related BSI was considered as primary BSI. *A. baumannii* isolation in blood culture secondary to any other source of infection was considered as secondary BSI.

Multi-drug resistance was defined as the resistance of *A. baumannii* isolates in ≥ 3 antimicrobial category to ≥ 1 agent from antimicrobial groups aminoglycosides, anti-pseudomonal penicillins + beta lactamase inhibitors, extended spectrum cephalosporins, folate pathway inhibitors, penicillins and inhibitors and polymyxin group antimicrobials.

Septic shock was defined as the sepsis state in which persistant hypotension despite fluid replacement (average arterial pressure ≤ 70 mmHg), organ dysfunction and perfusion abnormalities are observed.

Immunosuppression was defined as presence of corticosteroid treatment equivalent to at least 10 mg/day prednisolone for fifteen days, human immunodeficiency virus (HIV) seropositivity, solid organ transplantation, bone marrow transplantation, history of radiotherapy or chemotherapy for an underlying malignancy in last 6 months and presence of acquired immune deficiencies (hypogammaglobulinemia, combined immunodeficiency syndrome).

Previous antimicrobial usage was defined as systemic antimicrobial treatment for at least 72 hours in 30 days before isolation of Gram-negative microorganism in blood culture.

2.3. Microbiological Analysis

Blood cultures were incubated in BACTEC 9050 system and were identified by BD BBL Crystal identification system. Antimicrobial susceptibility profiles were determined by Kirby Bauer Disc Diffusion Method in accordance with Clinical and Laboratory Standarts Institute (CLSI) recommendations.[7] Due to increase in resistance against antimicrobials like cephoperazone sulbactam and netilmisin, colistin susceptibility test also has been added to the profile since, 2010 thus colistin susceptibility was also evaluated in 7 isolates which were isolated in 2010.

2.4. Cost Analysis

Total hospitalization cost was determined by using the central hospital information system and recorded both case and control group patients. Unit cost of antimicrobial agents that were used during bacteremia episode was acquired from hospital purchase department and cost of antimicrobial therapy and hospitalization were calculated in American Dollars(US$).

2.5. Statistical Method

SPSS 15.0 for Windows was used for statistical analysis of the data. The table of numbers was presented for categoric variables while definitive statistics (mean, standart deviation, median, minimum, maximum) were presented for numerical variables. In order to make paired categorical comparisons, Chi square test was used for independent groups with normal distribution while Fisher's exact test was used for independent groups with no normal distribution. For numerical comparions, t test was used in independent groups with normal distribution while Mann Whitney U test was used in independent groups without normal distribution. Regression analysis of infection and mortality related risk factors was performed by using Forward-Stepwise method. Kaplan Meier test was also used for survival analysis and Backward-stepwise, forward stepwise methods and cox regression analysis were used to determine the risk factors affecting survival rate. A p value less than 0.05 was accepted to be statistically significant.

3. Results

In this study, case group was comprised of 41 patients (23 female, 18 male), of which the mean age was 58.3 ± 21.9 years while the control group had 45 patients (16 female, 29 male) whose mean age was 60.6 ± 20.5 years.

When the case group was evaluated, the percentages of patients in case and control groups with concomitant MDR *A. baumannii* infection other than BSI were 78% and 34%, respectively.

Univariate analysis revealed that the presence of an arterial catheter, high SAPS II score, low serum albumin level, antibiotic treatment with carbapenem, quinolone, metronidazole, glycopeptides and aminoglycosides prior to BSI were the risk factors for MDR *A. baumannii* BSI (Table 1, Table 2).

In multivariate analysis, it was detected that antibiotic treatment with carbapenem (odds ratio (OR) 11.96; 95% confidence interval(CI) 3.31- 43.3; $p < 0.001$), quinolone (OR 6.71; 95% CI 1.31 – 34.40; $p = 0.02$), metronidazole (OR 1.06; 95% CI 2.59 – 391.22; $p = 0.007$) prior to diagnosis of MDR Acinetobacter BSI and SAPS II score (OR 1.06; CI 1.01 – 1.11; $p = 0.1$) were the independent risk factors for MDR *A. baumannii* infection (Table 3).

Crude mortality rate in the case group was 53.7% while 14-day and 28-day mortality rates were 52.4% and 30%, respectively. Mortality attributed to *A. baumannii* BSI was detected as 24.4%. Mean age of patients who died, immunosuppression rates and SAPS II scores were statistically high in univariate analysis ($p < 0.001$, $p = 0.02$, $p = 0.001$, respectively) (Table 4). In multivariate analysis, immunosuppression (OR 4.67; CI 1.19 – 18.36; $p = 0.02$), SAPS II score (OR 0.1.10; CI 1.09 – 1.16; $p < 0.001$), hospitalization stay until BSI (OR 0.95; CI 0.92 – 0.98; $p = 0.001$) were determined as independent risk factors (Table 4).

The mean hospitalization costs of patients in case and control groups were calculated as US$35277 ± US$31758 and US$26333 ± US$20398, respectively and no significant difference was detected between them ($p = 0.282$). Mean costs of antibiotics were calculated for alive patient from each group and were US$1052 ± US$613 and US$836 ± US$567 for case and control groups, respectively. There was no significant difference between the two groups with respect to the cost of antibiotics ($p = 0.249$).

4. Discussion

Nosocomial A. *baumannii* infections are frequently observed especially in intensive care units. Besides being resistant to many antimicrobial agents, this microorganism also has the potential to develop resistance against many antimicrobials during treatment via new mechanisms. In many studies, it was shown that incidence of nosocomial infections caused by MDR *A. baumannii* is increasing worldwide.[8–11]

This study assessed the risk factors for the development of MDR *A. baumannii* BSI, mortality related factors, and cost of this clinical picture. Risk factors for MDR *A. baumannii* implicate variables