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Research Article

Identification of Bacterial Pathogens in Blood Specimens and Antibiotic Resistance Profiles of *Acinetobacter* Species in a University Hospital, Konya

Abstract

Acinetobacter species are important nosocomial pathogens because they can develop resistance to antibiotics and survive for a long time in the hospital environment. This study aimed to investigate the changes in antibiotic resistance profiles of *Acinetobacter* spp. strains isolated from blood specimens of hospitalized patients in our hospital.

Between 01.01.2014 – 31.12.2015, 19244 blood samples from hospitalized patients with suspected bacteremia in different departments of the Meram Medical Faculty were incubated by automated blood culture system BacT / Alert 3D (BioMerieux, France).

Of the 19244 blood specimens collected from different wards of the hospital, 3347 samples (17,3%) showed bacterial growth after incubation. Identification and antimicrobial susceptibilities of clinical isolates were determined by conventional methods and an automated system (VITEK 2 Compact, Biomerieux, France) according to Clinical and Laboratory Standards Institute (CLSI).

Distribution of strains isolated from blood culture were identified as Coagulase Negative Staphylococcus (n=1755, 52%), Enterococcus spp. (n=267, 8%), Klebsiella spp. (n=182, 5%), E.coli (n=182, 5%), Candida spp. (n=153, 5%), Pseudomonas spp. (n=91, 3%), Staphylococcus aureus (n=72, 2%) and other bacteria. The identified isolates as *Acinetobacter baumannii* (n=152, 5%) and *Acinetobacter* spp. (n=2, 0,1%) from blood specimens which were collected from intensive care units (n=111, 72.2%) and other clinics (n=43, 27.8%) of our hospital, all specimens in the study were consisted of hospitalized patients.

In this study, the results of in vitro antibiotic susceptibility test of *Acinetobacter* strains isolated from blood culture will be evaluated. Susceptibility to ceftazidime was 8%, amikacin 25%, imipenem 5%, meropenem 6%, tigesiklin 94%, colistin 98%, gentamicin 34%, cefepime 5%, ceftazidim 8%, piperacillin-tazobactam 5%, ampicillin-sulbactam 7%, ciprofloxacin 5%, levofloxacin 4%. Results of antibiotic susceptibility tests for *Acinetobacter* species initiated that the most effective antibiotics were colistin and tigecycline with the resistance ratio 2%, 6%, respectively. Compared with other antibiotics, lower rates of resistance to amikacin and gentamicin were observed.

The in-vitro antimicrobial susceptibility test results of this study reveal that *Acinetobacter* species strains demonstrated high resistance ratio against all beta-lactam drugs including carbapenems and quinolones.

In conclusion, the presents of this study determine that colistin has the best activity against *Acinetobacter* species strains. Moreover, amikacin and gentamicin may be good choices for the empirical treatment because of lower resistance ratio than other antibiotics.

Introduction

Acinetobacter spp. is aerobic, nonfermentative, nonmotile, Gram negative, rod shape bacteria (cocobacillus), usually found in soil and water samples [1,2]. It is possible that *Acinetobacter*

species can colonize on the skin of healthy people. However, it will frequently not result infection [3-6]. It is occasionally isolated from skin of hospitalized patients, secretion, even through hands of medical staffs and on surface of medical equipments [1,2]. These common soil organisms can cause

severe infections in especially immunocompromised patient. Recently, it has emerged as an important nosocomial pathogen [7].

Recent surgery, catheterization, mechanical ventilation, total parenteral nutrition, trauma and use of broad spectrum antibiotics were the principal risk factors identified [8-10]. A great deal of studies have supplied the novel investigation that *Acinetobacter baumannii* is the essential genomic species associated with outbreaks of nosocomial infection. *Acinetobacter spp.* are responsible for severe hospital-acquired infections including bacteremia, urinary tract infection, meningitis. However, their superior role is as agents of nosocomial pneumonia, particularly ventilator-associated pneumonia among patients admitted to the intensive care unit [10,11]. Mortality and morbidity in patients with *Acinetobacter baumannii* infection vary according to the severity of the underlying disease [12,13].

Acinetobacter baumannii, which can develop resistance to antibiotics and disinfectants, can survive for long periods in the hospital environment and can cause epidemics through hospital personnel or by spreading between medical equipment and patients. Carbapenems have been widely used in the treatment of multiple drug resistant *Acinetobacter* infections. This treatment has been reported to cause resistance to many antibiotics, including carbapenems [14]. Colistin is an antimicrobial with bactericidal effectiveness against *Acinetobacter* species. However, resistance to polymyxins has been reported [15]. Tigecycline also has been found to be an effective antibiotic against MDR *Acinetobacter* species [16].

Because of the widespread resistance of these bacteria to major antibiotic groups, clinicians have difficulties in treating infections. Therefore, careful monitoring of antimicrobial resistance profiles against *Acinetobacter spp.* is important in determining empirical treatment and antibiotic usage policies.

In this study, our primary objective was to determine the frequency of *Acinetobacter* strains isolated from patients in our hospital and to evaluate the resistance status to antibiotics retrospectively.

Materials and Methods

Bacterial strains

This retrospective study was conducted at the Meram Medical Faculty, University Hospital in Konya, Turkey. We reviewed the medical records of patients admitted to the several clinics of Meram Medical Faculty between January 2014 and December 2015. The culture results of the 19244 blood samples sent to patients suspected of having bacteremia in various clinics of our hospital were evaluated and the results of in vitro antibiotic susceptibility testing of *Acinetobacter* strains isolated from blood culture were retrospectively analyzed in our study.

Culture and Identification

Blood specimens were cultured using BacT / Alert 3D (

BioMerieux, France). Gram stain were carried out on positive bottles and followed by inoculation on to blood agar and Eosin Methylene Blue (EMB) agar. Cultured microorganisms were described by conventional methods and automated systems (VITEK 2 Compact, BioMerieux, France).

Antimicrobial Susceptibility Testing

Antibiotic susceptibility testing was conducted by VITEK®2 (BioMerieux, France) according to Clinical Laboratory Standards Institute (CLSI) Criteria (17) for *Acinetobacter* strains. When tigecycline resistant isolates were observed disc diffusion method was used and the results were supported by gradient test (E-test) (AB Biodisk, Sweden). Sensitivity tests of colistin resistant isolates were repeated with E-test. If the disk diffusion and E-test results are compatible with the automated system, the test result is reported.

Results

Bacterial growth was observed in 3347 of 19244 blood samples sent from various clinics of our hospital after incubation. Samples that were shorter than 3 days from the same patient were not included in the study.

Acinetobacter baumannii was isolated in 152 samples out of 3347 blood specimens (5% prevalence) from the entire hospital. The distributions of other bacterial strains isolated from blood culture are as follows: *Coagulase Negative Staphylococcus* (n=1755, 52 %), *Enterococcus spp.* (n=267, 8 %), *Klebsiella spp.* (n=182, 5%), *E.coli* (n=182, 5 %), *Candida spp.* (n=153, 5 %), *Pseudomonas spp.* (n=91, 3 %), *Acinetobacter spp.* (n=2, 0,1 %) and *Staphylococcus aureus* (n=72, 2 %). The distributions of bacterial strains isolated from blood culture are shown in Table 1.

All patients with *Acinetobacter* species isolated from blood culture were hospitalized and the majority of them were intensive care units patients (n=111, 72,2 %). Antibiotics with the lowest resistance to *Acinetobacter* strains were colistin (2 %) and tigecycline (6 %). A comparatively lower resistance was found when amikacin and gentamicin were compared with other antibiotics. Antibiotic resistance ratios of *Acinetobacter* species are given in Table 2.

Table 1: Numerical and percent distribution of bacteria isolated from blood culture (n=3347).

Name of isolates	Number of isolates	% of isolates
Coagulase Negative Staphylococcus	1755	52
<i>Enterococcus spp.</i>	267	8
<i>Klebsiella spp.</i>	182	5
<i>E.coli</i>	182	5
<i>Candida spp.</i>	153	5
<i>Acinetobacter baumannii</i>	152	5
<i>Pseudomonas spp.</i>	91	3
<i>Staphylococcus aureus</i>	72	2
<i>Acinetobacter spp.</i>	2	0,1
Other bacteria	491	15

Table 2: Antibiotic resistance ratios of *Acinetobacter* species (n=154).

Antimicrobial agent	Number of susceptible strains	Number of resistant strains	Percent Resistance (%)
Imipenem	8	146	95
Meropenem	10	144	94
Tigecyclin	145	9	6
Colistin	151	3	2
Amikacin	38	116	75
Gentamicin	53	101	66
Cefepime	8	146	95
Ceftazidime	12	142	92
Piperacillin/tazobactam	8	146	95
Ampicillin/ sulbactam	11	143	93
Ciprofloxacin	8	146	95
Levofloxacin	22	132	96

Discussion

Acinetobacter species have become widespread in the past two decades and are among the major hospital pathogens. *Acinetobacter baumannii* has been found to have the ability to survive on abiotic surfaces in hospital environments and colonize in medical devices and on the skin of patients [10]. *Acinetobacter* species rarely cause community-acquired infections. However, they are often isolated from nosocomial infections and develop resistance to antibiotics [18].

Increased antibiotic resistance has been detected in *Acinetobacter baumannii* strains in our country, both in regional and multicentre studies [23]. According to the results of Turkey surveillance study conducted in 2000 by Eraksoy et al. [19], "Meropenem Yearly Susceptibility Test Information Collection (MYSTIC)", it was observed that carbapenems were the antibiotics with the highest activity in *Acinetobacter* strains. Resistance rates of more than 90 % have been reported in many studies today for carbapenems, previously the most important treatment option in resistant *Acinetobacter* strains [20,21]. It is evident that in our country, resistance to *Acinetobacter* infections has increased rapidly in the short term due to possible misuse of antibiotic usage policies.

In this study, imipenem and meropenem resistance were detected at similar rates and carbapenem resistance was observed at 94 %. In a study conducted by Doğan et al. [22], in our hospital, carbapenem resistance was reported as 91% in *Acinetobacter* strains isolated between 2011 and 2013. In our hospital, imipenem resistance in *Acinetobacter* strains determined by Özdemir et al. as a nosocomial agent was observed as 70 % [24]. These resistance rates for carbapenem are lower than those in our study. Although carbapenem studies have reported lower rates for resistance, increasing rates of carbapenem resistance appear to be a serious problem. According to this information, increasing resistance to carbapenems in *Acinetobacter* species is noteworthy.

Resistance ratios was found to be 32-71 % for amikacin and 35-93 % for gentamicin in various studies [25-30]. In similar

studies conducted in our region, Özdemir et al. [24], detected amikacin (76%) and gentamicin resistance (82%) at higher rates; In the study of Kurtoğlu et al. [31], resistance to amikacin and gentamicin were 52 %; 86 %, respectively. Resistance rates for amikacin (67.5%) and gentamicin (68.6%) are relatively low in study conducted by Dogan et al. [22]. In this study, gentamicin resistance was 66% and amikacin resistance was 75%.

In this study, ciprofloxacin resistance was 95 % and levofloxacin resistance was 96%. Özdemir and colleagues [24], reported ciprofloxacin resistance to 86% while Kurtoğlu et al. [31], reported 91 % ciprofloxacin resistance for 2010 in our region. Dogan et al. [22], found resistance in 91.7% of ciprofloxacin and 90.9 % of levofloxacin in all of the years 2011-2013. The high resistance rates in different trials in Turkey indicate that ciprofloxacin resistance is increasing and that quinolones are no longer a good choice for *Acinetobacter* infections [31].

The result of this study is consistent with the other studies conducted in our country. In this study was indicated that increasing resistance to many antibiotics, including carbapenems, was detected over time. Determining in vitro antibiotic susceptibility is becoming increasingly important for hospitals to predict specific empirical treatment strategies.

According to this study, considering the resistance rates to other antibiotics, it may be useful to observe the aminoglycoside group antibiotics before the last option in the empirical treatment approach.

Colistin is an important antimicrobial, especially in the treatment of carbapenem resistant *A.baumannii* infections [32]. The possibility of resistance is lower than that of carbapenem. However, resistance to this agent may develop over the years. In the study of Özdemir et al. [24], and in the study conducted by Öksüz et al. [33]. in 2012, no resistance to colistin was detected. Kurtoğlu et al. [31], reported 5% resistance to colistin; Dogan and his colleagues [22], reported 1.4% resistance to colistin. In this study, colistin resistance was found to be 2%.

Tigecycline, a new option in the treatment of *Acinetobacter* infections, has entered clinical use in Turkey in 2008 and is a broad spectrum antibiotic with tetracycline similarities [34]. Altunok et al. [35], reported a tigecycline resistance rate as high as 37.7%, while Özdemir et al. [36], found tigecycline resistance as 5.5%. The studies in our region, Kurtoğlu et al. [31], reported tigecycline resistance in 2009 - 2010; 12% and 21% respectively; Özdemir et al. [21], reported that the resistance rate of tigecycline in our hospital was 1%. Dogan et al. [22], also reported tigecycline resistance ratio as 6.9 %. We found tigecycline resistance to be 6 % in our study. Although tigecycline resistance is low compared to similar studies, it can be said that this resistance tends to increase over the years compared to the study of Özdemir et al. [24].

As a result, the present study showed a predominance of various *A. baumannii* species and high prevalence of carbapenem resistance and quinolone resistance among blood culture isolates of *Acinetobacter* species in our hospital.

In conclusion, the findings of this study demonstrate that colistin has the best effectiveness against *A. baumannii* whereas ampicillin and gentamicin may be choices for the empirical treatment of *A. baumannii* infections. In addition, continuous monitoring of in vitro susceptibility profiles to prevent inappropriate antibiotic use and determination of rational treatment protocols is essential for effective infection control.

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