

Antimicrobial Susceptibility of *Acinetobacter baumannii* complex Isolated From Different Clinical Samples In A Tertiary Care Hospital

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Abstract

Introduction: Increasing resistance to antimicrobial agents used in the treatment of infections based on *Acinetobacter baumannii* complex strains has become an important health issue.

Aim: The aim in this study is to determine the antimicrobial resistance ratios in *A. baumannii* complex strains isolated from the patients staying at our hospital.

Methodology: Antibiotics resistance ratio of 163 *A. baumannii* complex strains isolated from the samples sent to our laboratory from different clinics between January 2012 and June 2015 were evaluated retrospectively in our study. Identification and antibiograms of *A. baumannii* complex isolates were determined by automatized system VITEK2 (bioMérieux, France).

Result: For *A. baumannii* complex isolates, a resistance was determined in amikacin (35.2%), cefepime (93.7%), ceftazidime (96.8%), ciprofloxacin (97.3%), colistin (5.5%), gentamicin (77.2%), imipenem (89.1%), levofloxacin (95.2%), meropenem (90.3%), tigecycline (41.3%), netilmicin (19.5%), cefoperazone-sulbactam (79%) and trimethoprim sulfamethoxazole (68.9%) ratio.

Conclusion: As a result, as antibiotics resistance can change in different areas, the susceptibility ratios of this kind of resistant bacteria should be known in situation requiring empirical treatment especially. The antibiotics with highest effect on *A. baumannii* complex isolates isolated in our study are colistin, netilmicin and amikacin in order. On the other hand, the high resistance ratios to carbapenems and other antibiotics also draw attention.

Keywords: *Acinetobacter baumannii* complex; Antibiotic; MIC

Introduction

An *Acinetobacter* bacterium has become the most commonly isolated factor in hospital infections, especially those in intensive care unit, in recent years [1,2]. *Acinetobacter baumannii* complex is mostly isolated from clinical samples among *Acinetobacter* types [3]. Ventilator-associated pneumonia, urinary tract infections, septicemia and scar infections can be named among the severe nosocomial infection epidemics caused by *A. baumannii* complex [4,5]. Today, the increasing resistance to the antimicrobial agents used in the treatment of infections caused by *A. baumannii* complex isolates has become an important health problem as in the whole world [1,6]. As the antibiotic resistance rates change between hospitals, knowing the resistance of bacteria which is a problem in all hospitals is important in determining the antibiotic protocol appropriate for the treatment [7,8]. The aim of this study is to determine the antimicrobial resistance ratios in *A. baumannii* complex isolates isolated from the patients staying in our hospital and contributing to the studies made on this subject.

Materials and Methods

Antibiotics resistance ratios of 163 *A. baumannii* complex isolates isolated from the samples sent from different clinics to Sabuncuoglu Serefeddin Education and Research Hospital Medical Microbiology Laboratory between January 2012 and June 2015 were reviewed retrospectively. The hospital has 465 patients' beds capacity and catchment population of this region is three hundred thousand. This hospital consists of one main building. The samples were sent for culturing and inoculated to sheep blood agar and Eosin Methylene Blue Agar (EMB). At the end of 18-24 hour incubation at 37 °C, isolated microorganisms were identified and antibiograms were determined by automatized system VITEK2 (bioMérieux, France).

Amikacin, netilmicin, colistin, gentamicin, trimethoprim-sulfamethoxazole, cefoperazone-sulbactam, meropenem, imipenem, levofloxacin, ciprofloxacin, cefepime and ceftazidime (Mast Diagnostics, Merseyside, UK) resistance rates of *A. baumannii* complex isolates were explored retrospectively and the results were interpreted according to CLSI 2013 standards. No tigecycline interpretative criteria universally accepted for *Acinetobacter* spp, therefore the Food and Drug Administration approved breakpoints for members of the family *Enterobacteriaceae* have been used. *Pseudomonas aeruginosa* ATCC 27853 has been used as control strain in laboratory.

Results

Among 163 *A. baumannii* complex isolates, 86 (52.7%) were originated from respiratory tract, 45 (27.6%) from blood, 20 (12.3%) from surgical scars and 12 (7.4%) from urinary samples. Samples from which the strains were isolated from are shown in Table 1.

Sample	n (%)
Respiration samples*	86(52.7)
Blood	45(27.6)
Scar sediment	20(12.3)
Urine	12(7.4)
Total	163

n: Total samples number, *Mucus, deep tracheal aspirate, bronchoalveolar lavage

Table 1: Distribution of *A. baumannii* complex strains in clinical samples

The samples which *A. baumannii* strains were isolated from were mostly from the samples sent from Intensive Care Units (139 patients 85.2%). The clinical distribution of the samples from which *Acinetobacter* strains were isolated is shown in Table 2.

Clinic	n	(%)
General Intensive Care	84	51.5
Neurology Intensive Care	55	33.7
Surgery clinics	14	8.6
Other Clinics	10	6.2
TOTAL	163	100

#: Resistance percentage, n: Total strains number

Table 2: Distribution of *A. baumannii* complex strains in clinics

The most effective antibiotics were colistin and netilmicin when the strains were evaluated. Their antibiotic resistance ratios were determined as 5.5% and 19.5% in order. Amikacin with a ratio of 35.2% and tigecycline with a resistance ratio of 41.3% followed. Resistance rates to other antibiotics changed between 68.9% and 96.8%. Antibiotic resistance of isolated strains is shown in Table 3.

When we compare year over year, there are some differences of antibiotic resistance especially during the 2012 and 2013. Resistance to cefoperazone-sulbactam, gentamicin, and carbapenems were very high in 2013. Resistance to amikacin, and netilmicin were very high in 2015. Resistance to trimethoprim-sulfamethoxazole was very high in 2012. Ceftazidim, resistance to ciprofloxacin, levofloxacin and cefepime became full resistance after 2012. Resistance to colistin changed from 6.2% to 9% from 2012 to 2015 (Table 3).

ANTIBIOTICS	2012		2013		2014		2015		TOTAL	
	N/n	(%)	N/n	(%)	N/n	(%)	N/n	(%)	N/n	(%)
Imipenem	39/47	82.9	51/53	96.2	32/35	91.4	17/21	80.9	139/156	89.1
Meropenem	39/45	86.6	51/53	96.2	33/36	91.6	18/22	81.8	141/156	90.3
Gentamicin	34/45	75.5	46/54	85.1	25/36	69.4	17/23	73.9	122/158	77.2
Netilmicin	1/28	3.5	14/51	27.4	4/30	13.3	6/19	31.5	25/128	19.5
Amikacin	12/40	30	20/52	38.4	12/38	31.5	10/23	43.4	54/153	35.2
Cefoperazone-sulbactam	27/44	61.3	48/53	90.5	29/33	87.8	17/23	73.9	121/153	79
SXT	37/46	80.4	29/54	53.7	29/37	78.3	14/21	66.6	109/158	68.9
Ceftazidim	39/44	88.6	53/53	100	37/37	100	23/23	100	152/157	96.8
Cefepime	29/36	80.5	49/50	98	24/24	100	19/19	100	121/129	93.7
Ciprofloxacin	38/41	92.6	53/53	100	33/34	97	22/22	100	146/150	97.3
Levofloxacin	22/25	88	51/52	98	27/29	93.1	19/19	100	119/125	95.2
Tigecycline	4/15	26.6	24/54	44.4	13/32	40.6	9/20	45	50/121	41.3
Colistin	2/32	6.2	3/52	5.7	1/37	2.7	2/22	9	8/143	5.5

N: Resistant strains number, n: Total strains number, SXT: Trimethoprim-sulfamethoxazole

Table 3: Antibiotics resistance of *A. baumannii* complex isolates

Discussion

Acinetobacter strains which are among the most important nosocomial pathogens survive for a long time by colonization in different environments, on the surfaces of mechanical devices used in hospitals, patients and hospital staff [9]. Hospital infections are mostly observed in intensive care units. *Acinetobacter* infections are also most common in intensive care units [1]. Ozdem *et al.* [10] isolated 58.9%, Balci *et al.* [11] 63% and Dogan *et al.* [12] 66.2% of *A. baumannii* complex isolates from the patients in intensive care units. Again in this study, *A. baumannii* complex isolates were isolated mostly from the intensive care unit patients (85.2% from General Intensive Care and Neurology Intensive Care).

There is a difference in the distribution of samples in which *Acinetobacter* strains were commonly isolated from. Although *A. baumannii* complex infections are observed in all body parts, they are mostly observed in the respiratory system and scar infections [3,13]. *A. baumannii* complex isolates were 43% in respiratory system, 24% in scars by Balci *et al.* [11], 30% in mucus, 29% in scar by Aral *et al.* [14], 48% in tracheal aspirate samples by Atasoy *et al.* [15]. Similar to other studies, *A. baumannii* complex was isolated mostly from respiratory tract samples (52.7%).

It was observed that the isolation of multi resistant strains and gradually increasing antibiotic resistance cause a decrease in empirical treatment options of clinicians on patients hospitalized with *A. baumannii* complex infection suspicion [16,17]. *A. baumannii* complex which causes infections with high mortality and is more resistant to many antibiotics [18]. Wide use of high spectrum antibiotics such as ureidopenicillins, fluoroquinolones and third generation cephalosporins resulted in *Acinetobacter* types being more resistant to antibiotics [19]. In different studies in Turkey, it was observed that quinolones and cephalosporin resistance rates were over 90% [12,20]. In our study the resistance rates were detected as 97.3% in ciprofloxacin, 95.2% in levofloxacin, 96.8% in ceftazidime and 93.7% in cefepime and the results were similar to the results of other recent studies in our country. This result might be construed to mean that neither third-generation cephalosporins nor quinolones appear suitable for *A. baumannii* complex infections.

Aminoglycosides are the antibiotics commonly used in *A. baumannii* complex infections. The resistance rates determined were Ozdemir *et al.*[21] gentamicin 82%, amikacin 76%, netilmicin 25%, Kurtoglu *et al.*[22] gentamicin 86%, amikacin 52%, İraz *et al.*[20] gentamicin 54%, amikacin 69%, netilmicin 15%. In our study, the resistance rates determined were gentamicin in 77.2%, amikacin in 35.2% and netilmicin in 19.5%. The most effective aminoglycoside derivative of netilmicin to *A. baumannii* complex types is antibiotic. Resistance to gentamicin, and was very high in 2013 but resistance to amikacin, and netilmicin were very high in 2015. This is because increasing prevalence of gentamicin resistance physicians used to prefer amikacin and netilmicin more after 2013.

Tigecycline is a tetracycline group glycylcyclin. It inhibits the protein synthesis in ribosome level. It was effective in bacterium including multi medicine resistant *Acinetobacter* and *Pseudomonas* strains [23]. Different results were observed in many tigecycline studies. In a study made by Alpat *et al.* [24] in 2010, no tigecycline resistance was determined and in the studies made in 2011, Ozdemir *et al.*[10] determined tigecycline resistance as 5.5% and Kurtoglu *et al.*[22] as 16%. Tigecycline resistance was found 41% in our study. Because of high resistance of *A. baumannii* complex to other antibiotics physician began to use tigecycline from 2013. So tigecycline resistance demonstrated a tendency to increase over years.

With gradually increasing resistance rates against this antibiotic group, carbapenem is the primary antibiotic group which should be preferred in infections caused by *Acinetobacter* [25,26]. In 2005 Gazi *et al.* [27] detected meropenem resistance rate as 36.3% and imipenem resistance rate as 40.5% and in a study by Bacakoglu *et al.*[28] in 2009, imipenem resistance rate was 78%, meropenem resistance rate was 55% and in 2013 Gozutok *et al.* determined resistance rates in their study as 91% imipenem and meropenem. In this study, imipenem resistance was found 89.1% and meropenem resistance 90.3%. Resistance to carbapenems were very high in 2013. We think that the gradually increasing carbapenem resistance is due to its common use in empirical treatment.

Colistins are the most common polymyxin derivatives used in clinical practice. These antibiotics are effective against many gram-negative bacterium including *Acinetobacter* types *Paeruginosa*, *Klebsiella* and *Enterobacter* [30]. While Ozdemir *et al.* [21] and Gozutok *et al.* [29] determined no resistance to colistin, İraz *et al.* [20] determined a resistance rate of 1% and Dogan *et al.* [12] a resistance of 1.4%. The colistin resistance was found 5.5% in our study. As colistin was used more commonly but we can emphasize that resistance ratios would increase in time.

These results of resistance to antibiotic show us that we have to be careful when using antibiotics. We have documented that during the 2011-2013 study period the use of a large number of broad spectrum antibiotics used, the infection caused by *Acinetobacter baumannii* complex has become more serious with resistant to carbapenems. Also we demonstrated that these isolates were not genotypic similarity [31]. One of the limitation of this study is that we did not presented the clinical and demographic data of patients. But other information may help physician to use true antibiotic therapy and take care about the patients isolation.

As a results a high resistance ratio develops against imipenem, levofloxacin, meropenem and gentamicin which are the antibiotics commonly used until recent years for *A. baumannii* complex, with a resistance ratio increasing constantly in the whole world. The resistance to colistin which had a rare resistance in previous years was 5.5%. This demonstrated that a higher ratio of resistance might develop against colistin in the future. As antibiotic resistance increases, hardships will be experienced in *A. baumannii* complex treatment unless the necessary precautions are taken and new antibiotics are discovered. In order to prevent the spreading

of resistant *Acinetobacter* strains, infection control measures should be taken, clinicians and laboratory workers should cooperate during antibiotic use and hospital hygienic rules should be observed.

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