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Sensitivity of Acinetobacter baumannii and Pseudomonas aeruginosa Microorganisms to Colistin Antibiotic by MIC (E-test) in Patients Admitted to the Intensive Care Unit of Firoozgar Hospital

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ABSTRACT

Background: Nosocomial infections are associated with increased morbidity, mortality, and medical burdens. Pseudomonas aeruginosa and Acinetobacter baumannii are not-fermentative gram-negative bacteria that considered as the most important nosocomial infection. In the current study, we have aimed to evaluate the sensitivity of Acinetobacter baumannii and Pseudomonas aeruginosa microorganisms to the colistin antibiotic.

Methods: In this descriptive cross-sectional study, patients admitted to the ICU ward of Firoozgar Hospital from July 2018 to March 2019 were evaluated, and 169 Patients infected with Acinetobacter baumannii, and Pseudomonas aeruginosa were included. Acinetobacter baumannii and Pseudomonas aeruginosa were isolated, and antibiotic sensitivity was determined by the disk diffusion method according to Clinical & Laboratory Standards Institute (CLSI) criteria. E test was also used to determine MIC-50 and MIC-90 of colistin.

Results: Acinetobacter baumannii was around 8 times more frequent than Pseudomonas aeruginosa. Colistin resistance was detected in only 4(2.4%). The mean age of patients infected by Acinetobacter baumannii was significantly higher than those infected with Pseudomonas aeruginosa. Moreover, the mean time of the hospitalization period did not show any significant differences in the different groups.

Conclusion: Our findings indicated that the majority of isolated Pseudomonas aeruginosa and Acinetobacter baumannii were sensitive to Colistin. Therefore, it could be effectively used for patients with a confirmed diagnosis of Pseudomonas aeruginosa and Acinetobacter baumannii.

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Introduction

Nosocomial infections are associated with increased morbidity, mortality, and medical burdens. These infections occur 5 to 7 times more among patients admitted to the Intensive Care Unit (ICU) than those admitted to other units. Antibiotic resistance in Gram-negative bacilli

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is the cause of nosocomial infections, especially in the ICU (1). The increased prevalence of Multidrug-Resistant (MDR) infections with Gram-negative bacteria is being considered as a severe threat to global health (2).

Pseudomonas aeruginosa and Acinetobacter baumannii are not-fermentative gram-negative bacteria that can cause various infections in burn patients, cystic fibrosis, neutropenia, and immunocompromised patients through their various virulence-factors (3, 4). Recently, it has been reported that P. aeruginosa and A. baumannii are accounted for 37.3% and 18.49% of nosocomial infection in Iran, respectively. These bacteria are inherently resistant to a wide range of antibiotics and, more importantly, they could acquire antibiotic resistance through unusual mechanisms (5). The bacteria well adapted to the hospital units, which turn them into the most important nosocomial pathogens. Despite the bacteria differences in clinical and epidemiological characteristics, both of them could cause severe respiratory tract infections, although they are capable of colonization anywhere of the body. Infections caused by these bacteria are associated with high mortality and morbidity, especially when it caused by drug-resistant strains of the Pseudomonas aeruginosa (6). The most significant drug resistance mechanisms in these bacteria are the production of beta-lactamase, efflux of antibiotics by drug pumps, and changes in membrane permeability (7).

Increased drug resistance in gram-negative bacteria, especially Pseudomonas aeruginosa and Acinetobacter baumannii, encountered the health organization to critical concern. Limited treatment options have forced specialists of infectious diseases to reassess the clinical applications of colistin, a polymyxin antibiotic discovered more than 50 years ago. It is a multi-component antibiotic polypeptide first developed from colistin A and B. In 1960, for clinical use and rapidly replaced newly discovered less-toxic antibiotics by using it in the 1970s (8). There are two commercially available forms of colistin: colistin sulfate for oral and topical use and colistimethate for parenteral use. Both of them could be administered by inhalation (9).

Monitoring the regional distribution of MDR bacteria strains would provide valuable information for implementing an appropriate strategy to prevent the spread of them. Therefore, in the current study, we have aimed to evaluate the sensitivity of Acinetobacter baumannii and Pseudomonas aeruginosa microorganisms to the colistin antibiotic in Patients Admitted to the Intensive Care Unit of Firoozgar Hospital, educational tertiary care hospital in Tehran, Iran.

Methods

In this cross-sectional study, patients admitted to the ICU ward of Firoozgar Hospital were evaluated. Patients infected with Acinetobacter baumannii and Pseudomonas aeruginosa were included. Patients who declined to participate, and those with the compromised immune system were excluded from the study. The patients' demographic information (age, gender) and clinical history (antibiotic consumption history, chief complaint, type of bacteria) were extracted from the files. Finally, 169 patients were studied by the census method. The study was confirmed by the ethical committee of Iran University of Medical Sciences (IR.IUMS.FMD.REC1397.234). All participants have signed informed consent.

Patients hospitalized in the intensive care unit of Firoozgar Hospital due to multi-drug resistant microorganisms were evaluated for antibiotic resistance. Acinetobacter baumannii and Pseudomonas aeruginosa were isolated from blood, urine, sputum and etc. Bacterial isolation and identification were performed according to standard laboratory methods.

Isolated bacteria were cultured in the Mueller-Hinton agar medium. MIC Test Strip was added to the culture plate and incubated in 35 degrees Celsius for 24 hours. The antibiotic sensitivity was determined by the disk diffusion method according to Clinical & Laboratory Standards Institute (CLSI) criteria. E test was also used to determine MIC-50 and MIC-90 of colistin against Acinetobacter baumannii and Pseudomonas aeruginosa. In this regard, Escherichia coli strains were considered as control. Specimens that respond to Less than or equal to 1 µg / ml of colistin considered sensitive and those that need more than or equal to 1 µg / ml defined as resistant.

Data were analyzed and reported only for patients who completed the trial. Statistical analysis of data was performed using SPSS version 22 software (SPSS Inc., Chicago, IL, USA). The normal distribution of all studied parameters was checked with the Kolmogorov-Smirnov test. Student t-test was used for variables that were distributed in a normal way, besides the Mann-Whitney test was performed for variables that have not a normal distribution. The two-tailed p-values < 0.05 were considered significant.

Results

During the study time, 169 patients were included. The mean age of patients was 62.9 years. The majority of them were male (57.4%). The mean hospitalization time in the patients was 32.8, in the range of 2-180 days. Three patients had antibiotic consumption history in 30 last days of admission. The most common chief complaints were Intracranial Hemorrhage, sepsis, and wound infection. Specimen origin in more than 50% of patients was sputum. Acinetobacter baumannii was around 8 times more frequent than Pseudomonas aeruginosa. Colistin resistance was detected in only 4 (2.4%) patients (Table1).

Table 1. Descriptive analysis.

Characteristics	Mean± SD (range) - Frequency(%)
Age	62.9±18.24 (5-95)
Gender(male)	97 (57.4%)
Hospitalization(days)	32.8±25.1 (2-180)
Antibiotic consumption history	3 (1.8%)
Chief complaint	
Intracranial hemorrhage	42 (25.0%)
wound infection, sepsis, and abscess	42 (25.0%)
Cancer	23 (13.7%)
Tuberculosis and pneumonia	22 (13.1%)
Gastrointestinal bleeding, pancreatitis, cholecystitis, cirrhosis and ascites	12 (7.1%)
Fracture, trauma and osteomyelitis	9 (5.4%)
Seizures, delirium, dementia and ALS	8 (4.8%)
Other	10 (6%)
Specimen origin	
Sputum	88 (52.1%)
Trachea	31 (18.3%)
Urine	16 (9.5%)
Blood Culture	10 (5.9%)
Wound Discharge	8 (4.7%)
*Other**	16 (9.5%)
Type of Bacteria	
Acinetobacter baumannii	150 (88.8%)
Pseudomonas aeruginosa	19 (11.2%)
Colistin Resistance	4 (2.4%)

*bronchoalveolar lavage, Ascites, Abscess, Pleura, Spine.

The patients were divided into two groups based on the type of microorganism infection. Using T-test, the mean age of patients infected by Acinetobacter baumannii was significantly higher than those infected with Pseudomonas aeruginosa (P=0.003). The male to female ratio was significantly different in the groups. Moreover, the mean time of the hospitalization days in both groups did not show any significant differences in the Mann Whitney U test (P=0.68). The specimen origins have shown statistically significant differences between the groups (P=0.01). While the rate of Colistin resistant was similar in both groups (P=0.382) (Table2).

Table2. Comparison of patients infected with different microorganisms.

Characteristics	*Acinetobacter baumannii*	*Pseudomonas aeruginosa*	p value
Age	64.38±17.6	51.36±18.9	0.003
Gender(male)	85(56.7%)	12(63.2%)	0.632
Hospitalization	33.14±25.3	30.6±24.42	0.68
Antibiotic onsumption history	3(2%)	0(0)	1
Chief complaint			0.417
Intracranial hemorrhage	40(26.8%)	2(10.5%)	
wound infection, sepsis, and abscess	37(24.8%)	5(26.3%)	
Cancer	18(12.1%)	2(10.5%)	
Tuberculosis and pneumonia	20(13.4%)	2(10.5%)	
Gastrointestinal bleeding, pancreatitis, cholecystitis, cirrhosis and ascites	10(6.7%)	2(10.5%)	
Fracture, trauma and osteomyelitis	7(4.7%)	2(10.5%	
Seizures, delirium, dementia and ALS	7(4.7%)	1(5.3%)	
Other	10(6.7%)	0	
Specimen origin			0.01
Sputum	82(54.7%)	6(31.6%)	
Trachea	29(19.3%)	2(10.5%)	
Urine	10(6.7%)	6(31.6%)	
Blood Culture	9(6%)	1(5.3%)	
Wound Discharge	6(4%)	2(10.5%)	
*Other**	14(9.3%)	2(10.5%)	
Colistin Resistance	3(2%)	1(5.3%)	0.382

*bronchoalveolar lavage, Ascites, Abscess, Pleura, Spine.

Discussion

In the current study, 169 infected patients were studied. Out of them, 165 patients had shown a colistin-sensitive antibiogram. The rate of colistin-resistant was not statistically significant differences in both infections. In general, in both Acinetobacter and Pseudomonas groups, the overwhelming majority of individuals were sensitive to colistin, indicating that resistance to colistin antibiotics in Acinetobacter and Pseudomonas bacteria is still low.

In 2006, Sadeghifard et al., utilized the standard disk diffusion method on 66 isolates of Acinetobacter baumannii in order to assay the antibiotic susceptibility of the isolates. They demonstrated that all the strains were sensitive to Colistin, however resistant to a multitude of antibiotics,

including Cefoprazone, Ceftizoxime, Ceftazidime, Ticarcillinl Clavulanic acid, Cephotaxime, Aztreonam, Meropenem, Cefixime, Ceftriaxone, Carbenicillin, Cephotaxime, Ticarcillin, third-generation cephalosporins and broad- spectrum penicillins (10). We achieved similar results compared to them, though Sadeghifard et al., used the standard disk diffusion method to evaluate the sensitivity of Acinetobacter baumannii to colistin.

Furthermore, in 2013, De Francesco et al., evaluated the collected data of 167 Acinetobacter baumannii isolates and 2797 Pseudomonas aeruginosa isolates from 2007 to 2010. Among Amikacin, Colistin, Ceftazidime, Ciprofloxacin, Imipenem, and Piperacillin/tazobactam, the first two antibiotics were the most effective agents against Acinetobacter baumannii strains. Also, Colistin was effective upon all Pseudomonas aeruginosa isolates, and afterward, Amikacin and Piperacillin/tazobactam were the most effective ones with 86% and 75% activity against Pseudomonas aeruginosa isolates, respectively (11). Our results showed great similarity to the study of De Francesco et al. although they used the standard disk diffusion method.

Boustanshenas et al., used 83 PCR-approved Acinetobacter baumannii isolates to investigate the three distinct methods including E-test, disk diffusion and micro broth dilution in the detection of colistin-resistant Acinetobacter baumannii strains. The Micro broth dilution as a gold standard, E-test and disc diffusion methods exhibited that 43%, 23% and 44% of the isolates were resistant to colistin, respectively (12). The results of their study proposed that our utilized E-test method has inefficacy to correctly determines the colistin-susceptible isolates.

The average age of our patients is approximately 62 years old, which might indicate that middle-aged and older people are more likely to be affected by bacteria such as Pseudomonas and Acinetobacter, that may be as a result of their compromised immune system as well as the presence of comorbidities. The mean hospitalization time was 32.1 days in the range of 2 to 180 days. It could show the heterogeneity of our studied samples, which covers a wide range of samples. The mean age of patients infected by Acinetobacter baumannii was significantly higher than those infected with Pseudomonas aeruginosa. It has been shown in some similar studies that Acinetobacter baumannii mostly infects older people; for example, Huang et al., in a comprehensive multi-centric study, indicated that aging is a major risk factor for Acinetobacter baumannii infection because in their study 163 out of 193 patients with multidrug-resistant Acinetobacter baumannii had aged over than 60 (13). Moreover, Sengstock et al., in another study, have shown that 839 out of 1441 (58%) patients with Acinetobacter baumannii have aged more than 60 years (14). All are indicating that older age is associated with increased mortality in patients infected with Acinetobacter baumannii, which is in line with our findings. Therefore, preventive actions are vital in elderly patients to decrease the Acinetobacter baumannii infection rate.

The specimen origins have shown statistically significant differences between the groups. Although the majority of specimens were collected from respiratory secretions, more than 31% of Pseudomonas aeruginosa were isolated from the urine. It may be caused by the sampling bias because of the low number of Pseudomonas aeruginosa infected cases than those infected with Acinetobacter baumannii. Nevertheless, more studies are needed to confirm the findings. Compared with the study of De Francesco et al., although it can be said that the Acinetobacter frequency was similar to ours, Pseudomonas infected cases were higher than our study (11). The relatively low sample size was the main limitation of our study. Further multi-centric studies are recommended.

Our findings indicated that the majority of isolated Pseudomonas aeruginosa and Acinetobacter baumannii were sensitive to Colistin. Therefore, it could be effectively used for patients with a confirmed diagnosis of pseudomonas aeruginosa and Acinetobacter baumannii.

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