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Antimicrobial resistance pattern in ventilator–associated pneumonia in an intensive care unit of Babol, northern Iran

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ABSTRACT

Objective: To investigate antibiotic resistance pattern of ventilator-associated pneumonia (VAP) generating microorganisms, and quantitative culture and determining antibiotic sensitivity. **Methods:** This cross sectional study was performed on 50 patients suffering from VAP in intensive care unit of Ayatollah Rouhani Hospital, Babol, Iran during 2014–2015. VAP was probable for them based on clinical signs and the criteria of Clinical Pulmonary Infection Score standards. Lower respiratory samples were given under bronchoalveolar lavage and quantitative culture was done on them. Afterwards by microdilution method, minimal inhibitory concentration based on respective microorganisms, considering clinical pulmonary infection score were determined. **Results:** From 50 investigated samples in this study, the most common microorganisms were *Acinetobacter baumannii (A. baumannii)* (70%) then *Pseudomonas aeruginosa* (12%), *Staphylococcus aureus* (8%) and *Klebsiella pneumonia* (3%). In our study *A. baumannii* showed approximate 100% resistance to all antibiotics, in a way that *A. baumannii* resistance to imipenem and meropenem and piperacillin/tazobactam each was 97.1%. The most resistance of *Pseudomonas aeruginosa* was 66.7% to each cefepime and ceftazidime and clavulanate/ticarcillin. *Staphylococcus aureus* showed 75% resistance to nafcillin, cloxacillin and resistance in case of vancomycin was not seen. **Conclusion:** In current study, *A. baumannii* had the most prevalence among VAP and this species is resistant to most of antibiotics. Using ceftazidime, cefepime and clavulanate/ticarcillin, in treatment of the patients suffering VAP is not reasonable.

1. Introduction

Ventilator-associated pneumonia (VAP) is one of the most common infectious complications and the leading cause of death in intensive care units (ICUs)[1,2]. VAP based on time event is divided into two types: early VAP that occurs within 4 d and late VAP which happens after the 5th day of hospitalization[3]. Risk factors of VAP include oropharyngeal colonization, trauma, surgery, imunosuppression, old age, urgent intubation, prolonged admission in ICU, sedative drugs steroids usage and previous hospitalization. Prevalent etiological agents in generating VAP in several studies

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consist of *Staphylococcus aureus (S. aureus)*, *Pseudomonas. aeruginosa (P. aeruginosa)*, *Acinetobacter baumannii (A. baumannii)* [4,5]. Generally, etiological agents of VAP are different based on hospital or geographical position and their antibiotic resistance rates is also different among various areas[6]. The results of the different studies show that resistance rates of bacteria are increasing[7]. Increasing resistance to antibiotics raises the mortality rate, admission duration and expenses, in patients who suffer VAP in ICU. The mortality rate in VAP was reported 20%– 76% in different studies[8,9].

In various studies of *P. aeruginosa* and *A. baumannii* in VAP the mortality of was 65% and 87% and for MRSA to was 84%[10].

In some study, using antibiotics of choice for treating VAP based on antibiotic resistance pattern in the same hospitals could decrease usage of inappropriate antibiotics and increase treatment success[11]. Considering that a study based on Bronchoscopy sampling method and bronchoalveolar lavage (BAL) and quantitative culture performance and investigating microorganisms resistance with microdilution method and determining minimal inhibitory concentration (MIC) of antibiotic, has not been carried out so far in ICU of Ayatollah Rouhani Hospital of Babol (northern Iran), this study was done with the purpose of determining microorganisms involved in creating pneumonia from ventilation and their antibiotic resistance evaluation noticing method above.

2. Materials and methods

This cross sectional study was conducted on 50 patients suffering ventilator associated pneumonia in ICU of Ayatollah Rouhani Hospital of Babol during the 2014–2015.

In this study with daily visit of hospitalized patients in Ayatollah Rouhani ICU, considering clinical criteria based on Clinical Pulmonary Infection Score (CPIS), patients who at least acquired six points based on CPIS and from the clinical signs, diagnosis of pnenumonia was possible for them, were under sampling method BAL and bronchoscopy[12]. The samples were cultured in blood agar and MacConkey agar, and culture media after 24–48 h incubation at (35±2) ℃ were evaluated. Samples were cultured under quantitative method and if growth of more than 10^4 CFU/mL bacteria were detected presumped as VAP etiological agents, in next step for determining sensitivity of microorganisms, Broth microdilution method was used. Ninety six part microplate which was applied in this method, has 12 columns that hole of the 11^{th} column as negative control and the 12^{th} column as positive control were used. In hole of the first group and the first hole of negative control, 200 mL of brain heart infusion (BHI) culture area of broth were poured and then in the rest of holes, 100 mL of BIH broth area were added. In the next step, antibiotic were added to the entire first column hole and the first hole of negative column and then based on standard method, suitable dilution of antibiotic in holes were prepared and after that diluted bacteria suspension to 0.1 and 5 mL of bacteria was added to holes except the negative control hole. Eventually, the final volume of all holes was 100 mL. The negative control was without bacteria and positive control was without antibiotic. Then micro plate were incubated in the temperature of 37 ℃ for 24 h. After 24 h micro plate were investigated under the light of the lamp and the last hole which turbidity wasn't seen in it, was considered as MIC and by comparison with the table CLSI 20/3, resistance, semi-sensitivity or sensitivity of the bacteria relative to antibiotic was reported[13]. In this study, the investigated antibiotics for gram-positive bacteria included nafcillin, cloxacillin, co-trimoxazole, cefazolin, vancomycin and the investigated antibiotics for gram-negative bacteria included ciprofloxacin, ceftazidime, piperacillin/tazobactam, gentamycin, amikacin, cefepime, clavulanate/ticarcillin, meropenem and imipenem.

All of the applied antibiotics in this recent study were produced and made by German company Merk and information yield from. All data were analyzed by SPSS software 16.

3. Results

Of the 50 patients who suffer VAP in our study, 33 (66%) are male and 17 (34%) were female. The mean age of the patients was 67.43 year old. Among the patients 52% previously admitted in hospital and 60% had a history of antibiotic use in past 3 months (Table 1).the most common cause of admission of patients was neurologic disease (36%) and then respiratory disease. 12% of patients admitted with sepsis. And16%of patients was on stroid therapy. Demographic data of the patients are shown in Table 1. The most common microorganisms in our study were *A. baumannii* (70%), *P. aeruginosa* (12%), *S. aureus* (8%) and *Klebsiella pneumonia* (*K. pneumonia*) (6%). Meanwhile, from these 50 investigated samples, two samples (4%) did not grow in culture media.

3.1. Evaluation of antibiotics resistance based on microdilution method in Acinetobacterbaumannii

Five antibiotics did not have any effect on 35 samples of *A. baumannii* in our study including that ciprofloxacin, ceftazidime, amikacin, clavulanate/ticarcillin and cefepime. Meropenem, imipenem and piperacillin/tazobactam had 97.1% resistance respectively, and gentamycine had 94.3% resistance (Table 1).

Table 1

Resistance pattern of antibiotics in *A. baumannii* [*n*, (%)].

Antibiotics	Sensitive	Intermediate	Resistant
Ciprofloxacin	0(0.0)	0(0.0)	35(100.0)
Ceftazidime	0(0.0)	0(0.0)	35(100.0)
Piperacillin/tazobactam	1(2.9)	0(0.0)	34(97.1)
MeroPenem	1(2.9)	0(0.0)	34(97.1)
ImiPenem	1(2.9)	0(0.0)	34(97.1)
Amikacin	1(2.9)	0(0.0)	35(100.0)
Gentamycin	2(5.7)	0(0.0)	33(94.3)
Cefepime	0(0.0)	0(0.0)	35(100.0)
Clavunalate/Ticarcillin	0(0.0)	0(0.0)	35(100.0)

3.2. Evaluation of antibiotic resistance based on micro dilution method in P. aeruginosa

In our study, the most resistance was related to ceftazidime, clavulanate/ticarcillin, cefepime, (each with 66.7% resistance) and the least resistance was related to imipenem (16.7%) and gentamycin (16.7%) (Table 2).

Table 2

Resistance pattern of antibiotics in *P. aeruginosa* [*n*, (%)].

Antibiotics	Sensitive	Intermediate	Resistant
Ciprofloxacin	3(50.0)	1(16.7)	2(33.3)
Ceftazidime	1(16.7)	1(16.7)	4(66.7)
Piperacillin/tazobactam	4(66.7)	0(0.0)	2(33.3)
MeroPenem	4(66.7)	0(0.0)	2(33.3)
ImiPenem	4(66.7)	1(16.7)	1(16.7)
Amikacin	4(66.7)	0(0.0)	2(33.3)
Gentamycin	5(83.3)	0(0.0)	1(16.7)
Cefepime	2(33.3)	0(0.0)	4(66.7)
Clavunalate/Ticarcillin	2(33.3)	0(0.0)	4(66.7)

3.3. Evaluation of antibiotic resistance based on microdilution method in K. pneumonia

Among the three samples of *K. pneumonia* in our study, the most resistance was related to ceftazidime, cefepime and clavulanate/ticarcillin eaach with 100% of resistance. Gentamycin, meropenem, imipenem, piperacillin/tazobactam and ciprofloxacin each with 33.3% had the least resistance (Table 3).

Table 3

Resistance pattern of antibiotics in *K. pneumonia*[*n*, (%)].

Antibiotics	Sensitive	Intermediate	Resistant
Ciprofloxacin	1(33.3)	1(33.3)	1(33.3)
Ceftazidime	0(0.0)	0(0.0)	3(100.0)
Piperacillin/tazobactam	1(33.3)	1(33.3)	1(33.3)
MeroPenem	2(66.7)	0(0.0)	1(33.3)
ImiPenem	2(66.7)	0(0.0)	1(33.3)
Amikacin	2(66.7)	0(0.0)	1(33.3)
Gentamycin	2(66.7)	0(0.0)	1(33.3)
Cefepime	0(0.0)	0(0.0)	3(100.0)
Clavunalate/Ticarcillin	0(0.0)	0(0.0)	3(100.0)

3.4. Evaluation of antibiotic resistance based on microdilution method in S. aureus

Among the four samples of *S. aureus* in our study, resistance to cloxacillin and nafcillin was 75%. 25% of cases were sensitive to co-trimoxazole and no complete resistance to vancomycin was reported (Table 4).

Table 4

Resistance pattern of antibiotics in *S. aureus* [*n*, (%)].

Antibiotics	Sensitive	Intermediate	Resistant
Co-trimoxazole	1(25)	1(25)	1(25)
Cefazolin	0(0)	3(75)	1(25)
Cloxacillin	1(25)	0(0)	3(75)
Nafcillin	1(25)	0(0)	1(25)
Vancomycin	3(75)	1(25)	0(0)

4. Discussion

Considering the extension of antibiotic resistance, early diagnosis of VAP and identification of the type of microorganisms and antibiotics resistance pattern, can modify the method of antibiotic prescription and as result decrease medication resistance. In our study the most common microorganisms of causing VAP were *A. baumannii*, *P. aeruginosa* and *S. aureus* that these results are similar to other studies[14-16].

The resistance rate of *A. baumannii* to carbapenemes like imipenem and meropenem in our study was 97.1% and in study done with Balkhy *et al.*, in Saudi Arabia was 64.1% and in study of Salehifar *et al.*, in Imam khomeili hospital of sari (Iran) was 100%[15,16]. In current study, the resistance rate of *P. aeruginosa* to carbapenem as meropenem was 33.3% and to imipenem 16.7%, while the resistance rate to carbapenem was reported 14.7% in study of Jamaati *et al*, that was accomplished in Masih Daneshvari hospital of Tehran and it was reported 32.8% by Balkhy *et al.*, in Saudi Arabia[16].

The resistance rate of *S. aureus* in our study to nafcillin and cloxacillin was 75% and it was reported 80%, 41.1%, 65.4% and 66.7% bysome studies[16-18]. One of the features of this study in comparison with many other studies, like the study was carried outby Aziz Japoni *et al.*, in shiraz in 2008–2009 and Balkhy *et al.*, study that was done in Saudi Arabia in 2004 to 2009 was related to sampling method that in our study bronchoscopy method and BAL were applied which were often more precise than ETA method[16,19]. Also, in our study one of the characteristics was using CPIS and performing quantitative culture in order to positive consideration of BAL sample with colon of more than 10^4 cfu/mL[10,20]. The value of quantitative culture was much more than qualitative culture for diagnosing and deciding to start the treatment of VAP.

The prevalence of *A. baumannii* in our study was 70% and it was reported by some studies 35.1%, 29% and 18% which shows that high prevalence of *A. baumannii* as a producing organism of VAP at our hospital relative to the other studies and can be a serious warning in outbreaks of hospital acquired infections caused by *A. baumannii*[15, 17].

The clear role of *A. baumannii* types among gram-negative microorganisms in hospital acquired infections like bacteremia, urinary tract infection, soft tissue infections and especially VAP and also high ability of these microorganisms in generating

antibiotic resistance with various mechanisms, now a days is a major problem[21,22]. Various studies about antibiotic resistance of *A. baumannii* was carried out which often they have reported high resistance of this microorganism[23,24].

In many countries, in case of severe infections of *A. baumannii*. Use of carbapenems as a treatment choice is a rule but resistance toward them is also increasing[25-27].

The most common microorganisms involved in were *A. baumannii*, *P. aeruginosa* and *S. aureus* that among them *A. baumannii* was much more one and antibiotic resistance on all of the investigated antibiotics was about 100%. Noticing the results, high resistance of gram negative organisms to ceftazidime, cefepime and clavulanate/ticarcillin makes their use in empirical treatment of the VAP patients not appropriate.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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