Emerging Antibiotic Resistance in Psedomonas and Acinetobacter Strains Isolated from ICU Patients: Comparison of Years 1999, 2006 and 2009

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Abstract

Objectives: Pseudomonas and Acinetobacter spp. which are usually resistant to many antibiotics, are the most important infectious pathogens in intensive care units (ICUs). The aim of this study was to determine the antibiotic resistance patterns of these agents and to follow variation in resistance among the years of 1999, 2006 and 2009.

Methods: The resistance rates of various antibiotics for 21, 38 and 54 acinetobacter and 26, 44 and 66 pseudomonas bacteria which were isolated from blood cultures of ICU patients in years 1999, 2006 and 2009 respectively were compared with Fischer’s qui square test statistically.

Results: The most effective antibiotics were amikacin (88%), cephaperazone-sulbactam (85%), piperacillin-tazobactam (85%), ceftazidim (75%) and imipenem (75%) for Pseudomonas spp. and imipenem (76%), cephaperazone-sulbactam (71%), ciprofloxacin (52%) and amikacin (48%) for Acinetobacter spp. in 1999. Decreasing sensivities to amikacin (76%), cephaperazone-sulbactam (53%), piperacillin-tazobactam (71%), ceftazidim (53%) and imipenem (64%) for Pseudomonas spp. and decreasing sensivities to imipenem (28%), cephaperazone-sulbactam (37%), ciprofloxacin (13%) and amikacin (17%), piperacillin for Acinetobacter spp in 2009 were significant (p<0.05).

Conclusions: These results suggested that significant resistance development for imipenem, cephaperazone-sulbactam and ciprofloxacin occurred against acinetobacter strains and for cephaperazone-sulbactam, amikacin and ceftazidime against pseudomonas strains. Increased resistance in our ICU is significant in Acinetobacter spp. The usage of some antibiotics have been limited and multidrug-resistant or pan-resistant strains have been monitored by infection control committee of our hospital. Protective measures like good hand hygiene, strict contact isolation and control strategies for rational antibiotic usage may be effective factors for infection control caused by these pathogens in ICUs.

Introduction

Antibiotic-resistant bacteria are an emerging problem in intensive care units (ICUs). Infections caused by multidrug-resistant organisms may result in prolonged hospitalization, increased mortality rates and costs. Pseudomonas aeruginosa is a certain nosocomial pathogen with notable virulence factors and the ability to exhibit antibiotic resistance. Acinetobacter species have been associated with numerous outbreaks of infection, especially in ICUs (1). Multidrug resistant P.aeruginosa and Acinetobacter species shows an increased risk of infection in patients in ICUs and clonal dissemination of multidrug-resistant strains occurs commonly (1). In addition, Fagon et al (2) reported that pneumonia with Acinetobacter spp. or P.aeruginosa was related with increased mortality rates (40%). Similarly, Blot et al (3) reported a crude hospital mortality rate of 42% for patients with A.baumannii bacteraemia. The use of broad spectrum antibiotics may lead the colonization with these pathogens and consequently to serious infections. The most important determinants for reduction of incidence of infections caused by Pseudomonas and Acinetobacter species in ICUs are rational antibiotic management, investigation of environmental sources of infection and strict contact isolation procedures. Optimizing empirical therapy requires knowledge of antimicrobial resistance patterns.

The aim of this study was to determine the antibiotic resistance patterns of Pseudomonas and Acinetobacter species and to follow variation in resistance among the years of 1999, 2006 and 2009.

Methods

Settings

Our hospital, is a 550-bed tertiary hospital. The adult internal and surgical ICU was founded with six beds in 1999 and 16 beds were added in 2007. There is an
infection control committee and with two infection control nurses. The infection control nurses inform and liaise with the ward staff for isolation procedures and infection control measures based on microbiological results. Universal precautions are practiced by all health care workers. Infection control problems are also discussed in clinical meetings.

Laboratory procedures
The resistance rates of various antibiotics for 21, 38 and 54 acinetobacter and 26, 44 and 66 pseudomonas bacteria which were isolated from blood cultures of ICU patients in years 1999, 2006 and 2009 respectively were compared with Fischer’s qui square test statistically.

Blood cultures processed by automated BacT/Alert 3D® system (Bio Merieux, France) and only one sample was studied from each patient. Positive signaled samples in BacT/Alert® were cultured to chocolate agar and after 18-24 hours of incubation at 37°C, suspected colonies for *Pseudomonas* and *Acinetobacter* species identified with conventional biochemical procedures. The antimicrobial susceptibilities of ampicillin-sulbactam (SAM), gentamicin (GN), amikacin (AK), ceftriaxone (CRO), ciprofloxacin (CIP), cefoperazone-sulbactam (CFP), meropenem (MEM), piperacillin-tazobactam (TZP), cefepime (FEP) and ceftazidime (CAZ) were investigated by Kirby Bauer disc diffusion method on Mueller Hinton agar plates according to Clinical Laboratory Standard Institution (CLSI) recommendations (4).

Results
A total of 136 *Pseudomonas* spp. And 113 *Acinetobacter* spp. strains were evaluated for susceptibility to different antibiotics i.e. SAM, GN, AK, CRO, CIP, CFP, MEM, TZP, FEP and CAZ. Out of 136 pseudomonas strains, 26 were isolated in 1999, 44 were in 2006 and 66 were in 2009. Of all acinetobacter strains, 21 were isolated in 1999, 38 were in 2006 and 54 were in 2009. The most effective antibiotics were AK (88%), CFP (85%), TZP (85%), CAZ (75%) and MEM (75%) for *Pseudomonas* spp. Out of 136 *Pseudomonas* spp. in 2009 were significant (*p<0.05*). For *Acinetobacter* strains, there were significant decreasing sensivities to MEM (28%), CFP (37%), CIP (13%) and AK (17%), in 2009 too (*p<0.05*) (Figure 1 and 2).

**Figure 1.** Resistance patterns of *Pseudomonas* spp. by years 1999, 2006 and 2009.

**Figure 2.** Resistance patterns of *Acinetobacter* spp. by years 1999, 2006 and 2009.

Discussion

*Pseudomonas* and *Acinetobacter* species have emerged as the major causes of nosocomial infections, particularly in ICUs. Despite advances in sanitation and hygiene facilities and the introduction of new antimicrobial agents for management of nosocomial infections, Acinetobacter and pseudomonas infections still remains as a major factor related with hospital mortality and threats in critically ill patients.

Unfortunately, many of infectious disease physicians have recently been confronted with multidrug-resistant *P.aeruginosa* and *Acinetobacter* isolates which are resistant to all beta-lactams and quinolones. In fact, inadequate empirical treatment has been related with mortality exceeding 30% (5) and delays in initiation of appropriate antimicrobial agent contribute prolonged hospitalization and persistence of infection (6). The prediction and selection of appropriate antimicrobials require active surveillance of emerging resistance trends. Obritsch et al (7) reported that significant increase in resistance rates of pseudomonas strains obtained from ICU patients from 1993 to 2002 for ciprofloxacin, imipenem, tobramycin and aztreonam. They also found that multidrug-resistance rates had increased from 4% in 1993 to 14% in 2002. Similarly, multi-drug resistant acinetobacter strains have been detected in recent years in our ICU. These multi-drug resistant acinetobacter strains could disseminate after contamination of the hospital environment and by nosocomial transmission especially by the hands of hospital staff among critically ill patients in our ICU. The infection control nurses of our hospital inform and liaise with the ward staff for isolation procedures and infection control measures when multi-drug resistant acineobacter strains isolated in the ICU. These problems are also discussed in clinical meetings. However, dissemination of these pathogens in the ICU could not be prevented despite regular training of personnel, due to inadequate number of staff, frequent staff changes and ward staff with low compliance to the preventive measures for infections in our hospital.
Dual resistance rates for beta-lactams and quinolones were the highest among all antibiotics in this study (7). It is noticeable in our study that the sensitivity to quinolones and aminoglycosides also decreased remarkably beside the sensitivity to carbapenem and beta-lactam antibiotics decreased in particularly acinetobacter strains. In a review that analyzed the risk factors associated with development of multi-drug resistant \textit{A. baumannii} and \textit{P. aeruginosa}, deficiencies in the implementation of infection control guidelines and the use of broad-spectrum antibiotics were determined to be the most important risk factors (8). It has been found that use of carbapenems and third-generation cephalosporins appear to be associated with the development of an MDR phenotype by \textit{A. baumannii}, while carbapenems and fluoroquinolones are implicated in MDR \textit{P. aeruginosa}. As though, the antibiotic treatment is regulated by the infectious disease physicians and use of redundant antibiotics is avoided carefully in our ICU, nevertheless, the decrease in the antibiotic sensitivities of the acinetobacter and pseudomonas strains isolated in our ICU couldn’t have been prevented until 2009. Beside the use of redundant antibiotics, it has also been demonstrated that the factors associated with patients such as hospitalization at ICU and bad general conditions have been suggested to be the facilitating factors for the resistant acinetobacter infections (9). In the recent years, hospital infections and ICU outbreaks such as primarily VIP due to multi-drug resistant \textit{A. baumannii} have been reported (10-2). In fact, increased resistance in our ICU is significant in Acinetobacter spp. between years of 1999 and 2009. In compliance with our results, there are many reports from Turkey and other countries mentioned about increased antimicrobial resistance in Acinetobacter spp. \textit{A. baumannii} has been one of the most frequently detected pathogens and the approximately half of the strains were found resistant to carbapenem in a multi-center study that has been conducted in Turkey and that investigated the infectious factors at ICU (13). In the MYSTIC Study that investigated the antimicrobial sensitivities of the nosocomial Gram negative pathogens, the sensitivities of \textit{P. aeruginosa} strains to ceftazidime, cefepime and tobramycin were found 48%, 41% and 35% respectively, whereas 67% of the \textit{A. baumannii} strains were found multi-drug resistant and those sensitivities of \textit{A. baumannii} strains to carbapenem, tobramycin, cefepime, ciprofloxacin and ceftazidime were detected to be 53%, 44%, 37%, 29% and 22%, respectively (14). The resistance change rates of the ICU-sourced \textit{P. aeruginosa} and \textit{A. baumannii} strains between the years 2003 to 2006 was analyzed in another study conducted in Turkey and a significant decrease has been found in the sensitivity of the pseudomonas strains to carbapenem, beta-lactam and quinolone. The sensitivity of the \textit{A. baumannii} isolates to carbapenem, beta-lactam antibiotics, quinolones and aminoglycosides significantly decreased in the year 2006 (15). In a multi-center study performed by participation of 13 different ICUs that investigated device-associated hospital-acquired infection rates, the resistance rates of the \textit{P. aeruginosa} strains to ciprofloxacin and ceftazidime, imipenem, piperacillin/tazobactam were found 51%, 38% and 30%, respectively, whereas the resistance rate of \textit{A. baumannii} to piperacillin/tazobactam was detected to 87% (16). Also, The 2009 Report of the International Nosocomial Infection Control Consortium (INICC) has reported according to the surveillance results with the participation of 173 ICUs in Latin America, Europe, Asia and Africa that device-associated infection rates were remarkably higher than the US ICU infection rates, rate of imipenem resistant acinetobacter was 46,3% and rate of quinolone-resistant pseudomonas was 50% (17). In another study that analyzed the episodes of the ICU-sourced 96 nosocomial bacteraemia developed by \textit{A. baumannii}, use of central venous catheter and ventilator, previous colonization with \textit{A. baumannii}, respiratory-cardiovascular deficiency were determined to be a risk factor for \textit{A. baumannii} bacteraemia in univariate analysis. In the multivariate analyses of the same study; previous colonization and cardiovascular deficiency were demonstrated to be independent risk factors. The cumulative survival curves of \textit{A. baumannii} bacteraemia showed no difference when compared with control group, hospitalization duration and cost were found significant (18).

In conclusion, resistance development for commonly used antibiotics against acinetobacter and pseudomonas strains in the ICU has been increased between years of 1999 and 2009. Increased resistance in our ICU is significant in Acinetobacter spp. Regular surveillance of ICU infections and adopting basic infection control practices that have been shown to prevent healthcare associated infections are very important steps towards the reduction of these infections (16). Improving hand hygiene practices of healthcare workers, strict contact isolation procedures and aseptic care of vascular catheters are important measures to prevent pseudomonas and acinetobacter colonisation and may provide decrease in the incidence of related bacteraemia. In addition, there is a need to emphasize on the rational use of antimicrobials and strictly adhere to the concept of “reserve drugs” to minimize the misuse of available antimicrobials. Therefore,
restricted antibiotic policies, antibiotic cycling and shorter antibiotic usage may be effective in reducing antibiotic resistance.

References

Illustrations

Illustration 1

Table 1: Antimicrobial resistance rates of 136 Pseudomonas spp. isolates

<table>
<thead>
<tr>
<th>Years</th>
<th>CN</th>
<th>AK</th>
<th>CAZ</th>
<th>CIP</th>
<th>CFP</th>
<th>MEM</th>
<th>TZP</th>
<th>FEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1999 (n:26)</td>
<td>53</td>
<td>11,5</td>
<td>25</td>
<td>46,1</td>
<td>15,3</td>
<td>25</td>
<td>15,3</td>
<td>34,6</td>
</tr>
<tr>
<td>2006 (n:44)</td>
<td>61,3</td>
<td>31,8</td>
<td>34</td>
<td>36,3</td>
<td>18,1</td>
<td>20,4</td>
<td>22,7</td>
<td>29,5</td>
</tr>
<tr>
<td>2009 (n:66)</td>
<td>59,1</td>
<td>24,2</td>
<td>46,9</td>
<td>53</td>
<td>46,9</td>
<td>36,4</td>
<td>28,8</td>
<td>45,5</td>
</tr>
</tbody>
</table>

Table 2: Resistance rates of 113 Acinetobacter spp. Isolates

<table>
<thead>
<tr>
<th>Years</th>
<th>SAM</th>
<th>CN</th>
<th>AK</th>
<th>CRO</th>
<th>CIP</th>
<th>CFP</th>
<th>MEM</th>
<th>TZP</th>
<th>FEP</th>
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</thead>
<tbody>
<tr>
<td>1999 (n:21)</td>
<td>66,6</td>
<td>80,9</td>
<td>52,3</td>
<td>71,4</td>
<td>47,6</td>
<td>28,5</td>
<td>23,8</td>
<td>66,6</td>
<td>-</td>
</tr>
<tr>
<td>2006 (n:38)</td>
<td>52,6</td>
<td>76,3</td>
<td>55,2</td>
<td>92,1</td>
<td>78,4</td>
<td>23,6</td>
<td>21</td>
<td>68,4</td>
<td>42,1</td>
</tr>
<tr>
<td>2009 (n:54)</td>
<td>61</td>
<td>90,7</td>
<td>83,3</td>
<td>94,4</td>
<td>87</td>
<td>63</td>
<td>72,2</td>
<td>90,7</td>
<td>79,6</td>
</tr>
</tbody>
</table>

Illustration 3

Pseudomonas spp.

Figure 1. Resistance patterns of Pseudomonas spp. by years 1999, 2006 and 2009.
Figure 2. Resistance patterns of Acinetobacter spp. by years 1999, 2006 and 2009.
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