Risk Factors and Mortality for Ventilator-Associated Pneumonia Due to Endemic Multidrug-Resistant/Impenem-Resistant Pseudomonas Aeruginosa at a Medical-Surgical Intensive Care Unit in a Major Brazilian Teaching Hospital

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Abstract

The aim of this study was to evaluate the risk factors and mortality of ventilator-associated pneumonia (VAPs) due to endemic multidrug-resistant P. aeruginosa (MR-PA) in a medical-surgical intensive care unit. A retrospective case-control study was carried out at a 15-bed medical-surgical in a Brazilian university-affiliated hospital. All patients who had VAPs caused by PA were included in the study. Univariate and multivariate analyses were used to determine risk factors for PA-VAP. This organism was recovered from 38 patients and seventy eight controls (72) during the study. In multivariate analysis, previous colonization, tracheostomy and prior > three classes of antibiotics use were the only independent risk factors for PA-VAP. The hospital mortality rate of 62.10% (P<0.05) was higher in those patients with MR-PA VAP versus susceptible isolates (18.80%). Patients with tracheostomy previous colonization and >3 different classes of antibiotics ran a elevated risk of VAP and UTI-mortality was associated with MR PA.

Introduction

Pseudomonas aeruginosa is the most common pathogen among critically ill patients, and strains that have become multidrug-resistant are increasingly isolated in both epidemic and endemic colonizations and infections in the intensive care unit [1-4] Resistance can result in treatment failure, increased morbidity and mortality, especially in critically ill patients, prolonged hospitalization and higher healthcare costs [5, 6]

As an high endemic incidence rate of respiratory infection due to Pseudomonas aeruginosa (RIPA) has been observed at our Intensive care Unit (ICU) after 47 cases outbreak was reported a few years ago [7] in our unit we conducted this study to assess the risk factors and mortality associated with endemic acquisition of IR RIPA Ventilation Associated Pneumonia (VAPs) in critically ill patients.

Materials and Methods

A retrospective case-control study was carried out at a 15 bed medical-surgical ICU at Clinics Hospital, a 550-bed university-affiliated hospital in Uberlândia, MG, Brazil, January 2009 to January 1010. All demographic and clinical data were prospectively collected, by medical records analysis. All VAP patients due to P. aeruginosa were included in the study. Univariate and multivariate analyses were used to determine risk factors for PA-VAP. This organism was recovered from 38 patients and seventy eight controls (72) during the study. In multivariate analysis, previous colonization, tracheostomy and prior > three classes of antibiotics use were the only independent risk factors for PA-VAP. The hospital mortality rate of 62.10% (P<0.05) was higher in those patients with MR-PA VAP versus susceptible isolates (18.80%). Patients with tracheostomy previous colonization and >3 different classes of antibiotics ran a elevated risk of VAP and UTI-mortality was associated with MR PA.

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eligible, and only the first VAP episode was considered in risk factors analysis. In this study 38 patients who had VAP due to P. aeruginosa were included (cases) as well as 72 control patients without VAP, hospitalized in the same unit and matched to case patients (ratio 1:1.9). No informed consent was required by Ethic Committee because of the retrospective design of the study.

Definitions

VAP was defined as nosocomial/unit pneumonia in patients on mechanical ventilator support for ≥48 hs during the unit stay, and the diagnostic criteria for pneumonia were clinical, radiographic, and leukocytosis >11.0 x 10⁹ cells/mL and end tracheal aspirate count >10⁶ bacteria/mL. Patient could not be entered into the study more than once. Colonization was defined according to previously published criteria (<10⁶ bacteria/mL) [8]. Mortality was defined as death within 30 days of the diagnosis of pneumonia due to P. aeruginosa.

Microbiologic Methods

Isolates were identified as P. aeruginosa and other lung pathogens by classic tests [9] and resistant by disk diffusion method using the techniques of the Clinical and Laboratory Standards Institute [10].

Statiscal Analysis

Proportions were compared by the X² test or Fisher’s exact test, as appropriate, whereas continuous variables were compared using independent samples t-test. To determine independent risk factors, a multivariate logistic regression model was used. All variables with P<0.05 on univariate analysis were included in the multivariate model and P<0.05 was considered statistically significant.

Results

In the total, 220 patients remained hospitalized for a period ≥48 hours, using a Mechanical ventilation, 100 (45.5%) developed late-onset VAP, 38 (38.0%) by Pseudomonas aeruginosa and the remaining by other microorganisms. Additionally, 48 patients were excluded from the research because they had a diagnosis of community pneumonia. Although pneumonia was the main infection caused by Pseudomonas aeruginosa other cases as urinary tract infection (8.52%), bloodstream (6.38%) and surgical wound infections (4.25%) by this bacterium were also detected. About half (42.0%) cases of VAP by Pseudomonas aeruginosa were by multiresistant samples, especially the carbapenemsresistant ones (Figure 1).

Figure 1: Frequency P. Aeruginosa Isolates with Susceptibility and Resistance to Antimicrobial Agents in the Etiology of VAP's Adult HC-UFU, Period of September/2008 to August/2009

Risk factors related to the development of these pneumonias showed statistical significance on univariate analysis: mechanical ventilation ≥07 days, tracheostomy, use of ≥3 antimicrobials drugs, use of carbapenems, malignancy, diabetes mellitus and previous colonization of the oropharyngeal mucosa by this microorganism (Table 1). These characteristics were subjected to multiple logistic regression analysis, verifying that, tracheostomy, use of ≥3 antimicrobials and prior oropharyngeal colonization persisted as independent factors for the development of VAP (Table 2). Hospital mortality after 30 days of P. aeruginosa VAP diagnosis, which was 46.10% in case group. This result showed significance when compared to 25.0% of
mortality in control group (P≤0.05).

The mortality rate among cases due to multidrug-resistant-PA was significantly higher (62.5%) than by susceptible ones (18.8%) (P≤0.05). VAP development by multidrug resistant P. aeruginosa was the main prognostic factor for death as opposed to age and co morbidities (Table 3).

Discussion

Multidrug-resistant P. aeruginosa is a leading cause of nosocomial infections in many Brazilian ICUs, with this organism ranking first as a cause of nosocomial pneumonia [11] as seen in our Unit (38.0%). High carbapenem resistance rates have been reported among these isolates, resulting from the dissemination of an epidemic clone designated clone SP and also related to the emergence of resistant strains under antimicrobial selective pressure [12]. Carbapenem resistance rates ranged from 40% to 59% in most Brazilian studies, our data was 42.0%, with SPM-1 metallo–β-lactamase were detected in almost half of these isolates. IMP and VIM have been eventually detected, but SPM-1 is by far the most prevalent Brazilian metallo–β-lactamase [13, 14] SPM-1 was originally described in São Paulo, and its gene was detected in plasmids and not carried out by integrons, allowing a more effective horizontal dissemination [12].

The emergence of ESBLs has necessitated the increased use of carbapenems, but this drug of last resort may be contributing to the emergence of multidrug resistant non-fermentors as P. aeruginosa and A. baumannii [15, 16].

There is a correlation between rates of carbapenem

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>CASE N = 38 (%)</th>
<th>CONTROL N = 72 (%)</th>
<th>P</th>
<th>OR 95% CI</th>
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<tbody>
<tr>
<td><strong>DEMOGRAPHICS</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Male gender</td>
<td>30 (79)</td>
<td>41 (56.9)</td>
<td>0.55</td>
<td>2.74</td>
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<tr>
<td>age ≥ 60 years</td>
<td>10 (26.3)</td>
<td>22 (30.5)</td>
<td>0.59</td>
<td>0.70</td>
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<td><strong>INVASIVE PROCEDURES</strong></td>
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<td></td>
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</tr>
<tr>
<td>MV1 ≥ ≥7DAYS</td>
<td>36 (94.7)</td>
<td>30 (41.6)</td>
<td>0.001*</td>
<td>25.20</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>26 (68.5)</td>
<td>8 (11.1)</td>
<td>0.001*</td>
<td>17.33</td>
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<td>Central venous catheter</td>
<td>34 (89.7)</td>
<td>62 (86.1)</td>
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<td>1.37</td>
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<td>Nasogastric tube</td>
<td>37 (97.3)</td>
<td>69 (95.8)</td>
<td>0.68</td>
<td>1.61</td>
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<tr>
<td>Clinic</td>
<td>15 (39.5)</td>
<td>36 (50)</td>
<td>0.39</td>
<td>0.65</td>
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<tr>
<td>Surgical</td>
<td>04 (10.5)</td>
<td>7 (9.72)</td>
<td>0.84</td>
<td>1.09</td>
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<td>Trauma</td>
<td>19 (50)</td>
<td>29 (40.2)</td>
<td>0.43</td>
<td>1.48</td>
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<td><strong>ANTIMICROBIAL THERAPY</strong></td>
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<tr>
<td>≥ 3 antimicrobial</td>
<td>28 (81.5)</td>
<td>16 (22.2)</td>
<td>0.001*</td>
<td>9.80</td>
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<tr>
<td>Use of carbapenems</td>
<td>23 (60.5)</td>
<td>15 (20.8)</td>
<td>0.0001*</td>
<td>5.82</td>
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<td><strong>COMORBIDITIES</strong></td>
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<td>Diabetes</td>
<td>07 (18.42)</td>
<td>02 (2.7)</td>
<td>0.01*</td>
<td>7.90</td>
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<tr>
<td>Cardiopathies</td>
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<td>06 (8.33)</td>
<td>0.77</td>
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<td>Neoplasia</td>
<td>08 (21.05)</td>
<td>04 (5.55)</td>
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<td>4.38</td>
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<tr>
<td>Oropharyngeal colonization</td>
<td>28 (73.6)</td>
<td>35 (48.6)</td>
<td>0.02*</td>
<td>2.96</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>16 (46.1)</td>
<td>18 (25)</td>
<td>0.07</td>
<td>2.34</td>
</tr>
</tbody>
</table>

Table 1: Univariate Analysis of Risk Factors for VAP P. Aeruginosa in Hospitalized Patients in the Adult ICU of HC-UFU, from September/2008 to August/2009
consumption and the prevalence of carbapenem-resistant Pseudomonas aeruginosa [17, 18].

Consumption of imipenem is much higher in our Unit than in both US and Europe ones [18]. The first patient with a hospital infection by Imipenem resistant Pseudomonas aeruginosa was diagnosed in a woman with wound infection transferred from another hospital in the city and result in a major outbreak with 66 cases and 65% hospital mortality [7]. Low level of infection control practices, mainly low adherence to hand washing and isolation [19], result in a shift of an epidemic toward an endemic situation with spreading to the non-critical areas of the hospital [20].

Despite previous epidemiologic studies that have documented the risks associated with P. aeruginosa infection in ICU patients [21], there are few reports on the risk factors for endemic infections in the intensive care unit caused by multidrug-resistant P. aeruginosa [21]. Risk factors associated with P. aeruginosa VAP included many variables (Table 01) as duration of mechanical ventilation, neoplasia, and carbapenem use, but after multivariate analysis only tracheostomy (OR 13.16, CI 3.44–50.34, P 0.0002) >3 classes of antibiotic use (OR 15.71, CI 2.92–84.58, P 0.0013) and prior colonization with P. aeruginosa (OR 0.16, CI 0.04-0.78, P 0.0228) were independent variables associated with pneumonia (Table 3).

VAPs caused by MR Pseudomonas aeruginosa are difficult to treat and increase morbidity and mortality in critically ill patients [21]. About two-third of our isolates were multidrug resistant recovered from patients who where ventilated longer (tracheostomy) and who receive more classes of antibiotics, with more chance to have received inappropriate antibiotics [18], with a higher mortality rate related to MR isolates of 65.5% in these critically ill patients compared with 18.8% when caused by susceptible strains (P<0.05).

The study has many limitations as this is a retrospective study conducted with patients/isolates collected from a single Unit and the heterogeneity of the predisposing factors and disease severity of the patients, choice of antibiotics might have precluded us from identifying all the relevant factors.

In this current study a high incidence of multi-resistant P. aeruginosa was seen in patients submitted to tracheostomy use and who received more and ineffective antibiotics treatment are more susceptible to mortality. Thus, the emergence and propagation of antibiotic resistance in P. aeruginosa as consequence of both inappropriate antibiotic treatments besides antibiotic pressure where infection control measures are suboptimal become easy in our ICU.

**References**


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