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Ventilator-associated pneumonia: the influence of bacterial resistance, prescription errors, and de-escalation of antimicrobial therapy on mortality rates

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ABSTRACT

Ventilator-associated pneumonia is the most prevalent nosocomial infection in intensive care units and is associated with high mortality rates (14–70%).

Aim: This study evaluated factors influencing mortality of patients with Ventilator-associated pneumonia (VAP), including bacterial resistance, prescription errors, and de-escalation of antibiotic therapy.

Methods: This retrospective study included 120 cases of Ventilator-associated pneumonia admitted to the adult adult intensive care unit of the Federal University of Uberlândia. The chi-square test was used to compare qualitative variables. Student's *t*-test was used for quantitative variables and multiple logistic regression analysis to identify independent predictors of mortality.

Findings: De-escalation of antibiotic therapy and resistant bacteria did not influence mortality. Mortality was 4 times and 3 times higher, respectively, in patients who received an inappropriate antibiotic loading dose and in patients whose antibiotic dose was not adjusted for renal function. Multiple logistic regression analysis revealed the incorrect adjustment for renal function was the only independent factor associated with increased mortality.

Conclusion: Prescription errors influenced mortality of patients with Ventilator-associated pneumonia, underscoring the challenge of proper Ventilator-associated pneumonia treatment, which requires continuous reevaluation to ensure that clinical response to therapy meets expectations.

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Introduction

Although there have been advances in preventing ventilator-associated pneumonia (VAP), it remains the most prevalent nosocomial infection in intensive care units (ICU).[1] VAP impairs patient recovery by increasing length of hospitalization, duration of mechanical ventilation, and hospitalization costs.[2] Moreover, VAP is associated with high mortality rates (14–70%), which are higher in infections due to resistant bacteria, inappropriate antimicrobial therapy use, and incorrect antimicrobial prescription or de-escalation therapy.[3,4]

VAP is often caused by resistant bacteria, which may limit therapeutic options and compromise patient outcomes in clinical practice.[5]

As VAP is associated with significant morbidity and mortality, the choice of initial empiric treatment should take into account the risk of infections caused by resistant organisms. In addition, proper prescription of antimicrobial therapy should also consider the type, dosage, and duration of drug administration. Despite the availability of guidelines for VAP diagnosis and treatment, therapy still varies significantly between institutions and the occurrence of incorrect therapy prescription is quite high, ranging from 10% to 73%.[6,7]

The aim of this study was to evaluate factors influencing the mortality of patients diagnosed with VAP, including bacterial resistance, prescription errors, and de-escalation of antimicrobial therapy.

Methods

This retrospective study reviewed medical records of patients admitted to the adult ICU of the Federal University of Uberlândia (Adult ICU/UFU), between January 1st and July 31st, 2013. The patients included in the study were 18 years or older who were diagnosed with VAP. Diagnosis was based on criteria established by the *American Thoracic Society and the Infectious Diseases Society of America*,[8] including: mechanical ventilation for at least 48 h and appearance of new or progressive pulmonary infiltrate on chest radiographs associated with at least two clinical signs and/or laboratory changes suggesting an ongoing infection, including fever (>38 °C) or hypothermia (<35 °C); leukocytosis (>10,000/mm^3) or leukopenia (<4000/mm^3); purulent tracheal secretions; and oxygenation changes.

Out of the total of 467 medical records of patients admitted to the Adult ICU/UFU during the study period analyzed, there were 132 cases of VAP in 120 patients, since 12 patients had two episodes of infection. In patients who had more than one episode of VAP diagnosed during the study period, we included only the first identified case of VAP. The study was approved by the Ethics Committee of the Federal University of Uberlândia (protocol number 775.657) and registered as a clinical trials service of the U.S. National Institutes of Health (protocol number 30121978).

Medical records were abstracted to obtain information on patient age, gender, primary diagnosis at admission, comorbidities, prognostic indexes (Acute Physiology and Chronic Health Disease Classification System II [APACHE II] and Simplified Acute Physiology Score III [SAPS III]); causative bacteria identified and sensitivity profiles, the characteristics of antimicrobial prescriptions, and outcome (discharge or death).

Based on data in the medical records, specifics about prescription and administration of antimicrobial therapy were obtained, including whether treatment was administered after having obtained the results of sensitivity profiling using quantitative culture, as well as de-escalation (interruption of antimicrobial treatment or replacement by an antimicrobial with limited-spectrum coverage); escalation (addition of a new antimicrobial or replacement by a broad-spectrum antimicrobial); or maintenance (maintenance of antimicrobial initially prescribed or replacement by an antimicrobial with the same coverage profile).[8]

Errors in antimicrobial prescription were classified as follows: inappropriate choice (different choice from literature recommendations); errors in loading or maintenance dose (prescription of a higher or lower dose compared to the indicated dose); errors in the interval between doses (higher or lower interval between doses compared to the indicated interval); delay in starting antimicrobial therapy (more than one hour between prescription and administration of the first antimicrobial dose); inappropriate adjustment for body weight (no dose correction based on patient weight); inappropriate adjustment for renal function; errors in treatment duration (prescription for shorter or longer duration than the indicated period). To analyze treatment adequacy based on the literature, we used guideline recommendations for management and health care of adults with nosocomial pneumonia associated with mechanical ventilation from the *American Thoracic Society and the Infectious Diseases Society of America*.[8] *The Sanford Guide to Antimicrobial Therapy*[8] were used as standards for decisions about starting time; dose and indicated dosage; and adjustments, when necessary, for weight and renal function.[9] Error in starting of antibiotic therapy was defined by the *Surviving Sepsis Campaign*[10] as more than one hour between prescription of the first antibiotic dose by the attending physician and administration to the patient.

Multidrug-resistant bacteria were defined as bacteria resistant to three or more classes of antimicrobials. Gram-positive bacteria were assessed for oxacillin resistance.[9] According to local characteristics the resistance profile of the Adult ICU/UFU has been defined as follows: *Staphylococcus aureus* and *Staphylococcus epidermidis* sensitive or not to oxacillin (MRSA), *Pseudomonas aeruginosa and Acinetobacter baumannii* resistant to carbapenems (imipenem and meropenem), enterobacteriaceae (*Escherichia coli*, *Enterobacter spp*, *Klebsiella pneumoniae spp*, *Serratia spp*) for the production of beta-lactamase extended spectrum (ESBL) and *Stenotrophomonas maltophilia* resistant to trimethoprim/sulfamethoxazole.

Statistical analysis

Chi-square test was used to compare qualitative variables. Student's *t* test was used to compare means between groups of normally distributed quantitative variables.

Multiple logistic regression analysis was used to evaluate mortality independent predictors in the ICU. SPSS Statistics for