

RISK FACTORS RELATED TO PNEUMONIA ASSOCIATED WITH MECHANICAL VENTILATION

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Abstract: **Goal:** Ventilator-associated pneumonia (VAP) is a type of hospital-acquired pneumonia (HAP) that occurs 48 to 72 hours after endotracheal intubation and institution of invasive mechanical ventilation and is considered one of the most fearful adverse effects of intensive care. Thus, the study aims to identify risk factors related to this pathology in the literature. **Methods:** This is a literature review whose search took place in the databases Scielo, PubMed, ``*Jornal Brasileiro de Pneumologia*`` (JBP), ``*Revista Brasileira de Clínica Médica*``, ``*Revista Baiana de Enfermagem*``, ``*Universidade Federal de Pernambuco*``, ``*Revista Cathedral*``, ``*Agência Nacional de Vigilância Sanitária*`` (Anvisa), scientific journal Faema, Up to date and the Brazilian Society of Anesthesiology, to gather and synthesize publications and subsequently critically evaluate the risk factors for pneumonia associated with mechanical ventilation. The inclusion criteria were articles published between 2006 and 2023, in Portuguese, English and Spanish and that addressed the proposed subject. Duplicate articles that were not available in full and that did not address the proposed topic were excluded. This way, 13 materials were selected to prepare the work. **Results:** The main risk factors associated with the development of VAP are previous respiratory diseases, trauma, age, previous and inadequate use of antibiotics, exposure to mechanical ventilators, prolonged use of MV, lack of patient oral hygiene, lack of hand hygiene of the professional and incorrect positioning in the bed. **Conclusion:** The risk factors identified need to be disseminated to all professionals in order to be capable of direct actions with a short-term impact on the prevention and effective control of pneumonia associated with mechanical ventilation.

Keywords: Pneumonia associated with mechanical ventilation; risk factors; hospital

pneumonia; mechanical ventilation;

prevention and clinical intervention strategies.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a type of hospital-acquired pneumonia (HAP) that develops in patients intubated on mechanical ventilation for more than 48 hours. VAP also includes PAH that occurs within 48 hours of extubation (12). Most patients with VAP present with a gradual or sudden onset of symptoms such as dyspnea and signs such as fever, tachypnea, increased or purulent secretions, hemoptysis, snoring, rales, reduced respiratory sounds and bronchospasm, more than 48 hours after intubation (12).

Unfortunately, mortality rates in patients with VAP are considerably high. The onset of VAP may occur several days after the institution of mechanical ventilation. The SOFA score is useful for predicting fatal outcomes. Factors associated with mortality can help guide therapeutic decisions and determine the prognosis, therefore, there is a need to discuss these topics (2).

The factors that contribute to the development of VAP can be categorized as modifiable and non-modifiable. Among the non-modifiable ones are age, male sex, the patient's severity when admitted to the ICU and comorbidities (3). Non-modifiable factors are associated with the ICU environment and the misuse of antibiotics (5). Therefore, we must seek to reduce the number of multi-resistant bacteria, making appropriate use of antibiotics targeted for each type of infection.

From this perspective, given the relevance of the topic in the context of healthcare-associated infections (HAIs) and their epidemiological importance, this study proposes the risk factors associated with the development of VAP. Therefore, the objective was to understand in the literature what are the risk factors related to pneumonia associated with mechanical ventilation to guide effective

METHODOLOGY

This is an integrative literature review article carried out from February to March 2024. The aim of the work is to analyze the risk factors related to pneumonia associated with mechanical ventilation and has the following descriptors: "hospital pneumonia", "factors risk" and "mechanical ventilation".

The study was carried out through research in databases such as: Scielo, PubMed, ``*Jornal Brasileiro de Pneumologia*`` (JBP), ``*Revista Brasileira de Clínica Médica*`, ``*Revista Baiana*`` of ``Universidade Federal de Enfermagem de Pernambuco``, ``*Revista Cathedral*``, National Health Surveillance Agency (Anvisa), scientific journal Faema, Up to date and the Brazilian Society of Anesthesiology.

Articles and bibliographic reviews in English, Spanish and Portuguese were included, available in full, published from 2006 to 2023 and that addressed the proposed subject. Duplicate articles that were not available in full and that did not address the proposed topic were excluded. This way, 13 materials were selected to prepare the work.

The selected articles were evaluated in a comparative way, associating the relationship between pneumonia and mechanical ventilation in hospitalized patients and risk factors related to the condition. The results were presented in descriptive form at the end of the work.

REVIEW OF LITERATURE

Scientific advances in the area of medical assistance have guaranteed increased survival in the acute event of chronic diseases (2). In the case of respiratory complaints, mechanical ventilation (MV) is one of the therapeutic options available in Intensive Care Units (ICU) essential to guarantee oxygen supply

to patients with significant respiratory failure, using tracheostomy or endotracheal intubation. (1). The tube inserted into the patient sometimes becomes one of the sources of contamination by multi-resistant microorganisms, capable of transforming airway colonization into serious infections and sepsis (1) (2). Ventilator-Associated Pneumonia (VAP) is one of the main infections associated with MV in patients hospitalized in ICUs (31%), second only to urinary tract infection (34.5%) (2). On average, 10% of patients who use MV end up with PAVM, and in this case, the mortality rate ranges between 20 and 50% (2).

The main risk factors for infections in the ICU environment due to the use of MV are: immunological changes caused by comorbidities, when present; the recent illness that left the patient in a serious condition; use of invasive medical instruments for a long period of time; prolonged stay in environments colonized by virulent and multi-resistant germs (2). The multiplication of these multidrug-resistant agents occurs due to the inflammatory response of the lung parenchyma, compromised immunity and, in MV, the absence of the cough and swallowing reflex (1).

Regarding the pathophysiology of VAP, the mechanism of its development is essentially related to the presence of an ETT or tracheostomy, both of which interfere with the normal anatomy and physiology of the respiratory tract, specifically the mechanisms involved in clearing secretions (coughing and mucociliary action). Furthermore, intubated patients have a reduced level of consciousness that impairs the voluntary clearance of secretions, which can then accumulate in the oropharynx. This leads to macroaspiration and microaspiration of contaminated secretions from the oropharynx that are rich in harmful pathogens. Normal oral flora can

begin to proliferate and is able to pass along the tracheal tube, forming an antibiotic-resistant biofilm that eventually reaches the lower airways. Critically ill patients exhibit an impaired ability to mount an immune response to these pathogens, leading to the development of pneumonia. The presence of additional predisposing factors, such as pulmonary edema in these patients, can also accelerate the process (13).

In a study carried out in the ICU of a hospital in Buenos Aires, Argentina, with 24 beds, using parameters for Prolonged Mechanical Ventilation (PMV) such as MV for 21 days or more for at least 6 hours/day; and PAMV with clinical and radiological criteria: one of two major criteria ($TC > 38^{\circ}C$ and leukocytes greater than 12,000 cells/mm³ or less than 4,000 cells/mm³) and at least one of three minor criteria (purulent sputum, decreased peripheral oxygenation and Rx -chest with the presence of new or persistent infiltrates), from the National Association for Medical Direction of Respiratory Care and Hospital Infections Surveillance Program of Argentina, respectively; revealed the clinical characteristics of patients who developed the most recurrent VAP: male gender and age over 70 years (50%) (2). Furthermore, advanced age, SOFA Score, use of vasoactive drugs such as norepinephrine and dopamine, and COPD were associated with higher mortality (1) (2). Blood culture revealed that VAP were caused exclusively by gram-negative bacilli, the majority being by *Pseudomonas aeruginosa* (2).

Even so, the use of invasive ventilatory support has been a major advance in the treatment of respiratory failure over the last 50 years. However, MV can have consequences for the population, including: hemodynamic instability (especially if the patient is hypovolemic), respiratory tract infections and injuries caused by mechanical ventilation.

These can lead to greater morbidity, as they cause systemic effects that lead to increased hospitalization costs and higher mortality (3). In this scenario, ventilator-associated pneumonia (VAP) emerges as one of the most worrying adverse effects in the intensive care environment (3).

VAP is characterized as a lung infection that manifests itself 48 to 72 hours after endotracheal intubation and the start of invasive mechanical ventilation (3). It can be more precisely classified into early onset (within the first 96 hours of MV) and late onset (more than 96 hours after the onset of MV), which is most commonly attributed to multidrug-resistant pathogens (13). VAP appears when new or progressive pulmonary infiltrates are identified on chest x-rays, accompanied by clinical symptoms. Physical signs and laboratory changes include fever, leukocytosis or leukopenia and the presence of purulent tracheal secretions. Furthermore, the presence of more than a clinical criterion associated with radiological criteria to increase sensitivity and specificity (3).

The factors that contribute to the development of VAP can be categorized as modifiable and non-modifiable. Among the non-modifiable ones are age (>70 years), male gender, the patient's severity when admitted to the ICU and comorbidities (3). The factors that can be changed are associated with the environment (microbiota) of the ICU and the improper use of antibiotics, which are selective for a certain microbiota, leading to VAP caused by multi-resistant bacteria. This microbial resistance is an important factor in the high mortality of critically ill patients on mechanical ventilation in the ICU (10).

Therefore, to try to reduce the number of multiresistant bacteria, appropriate use of antibiotics targeted for each type of infection must be made. In this sense, in relation to the microbiota, studies demonstrate that aerobic

gram-negative bacilli, including *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* and some species of the *Acinetobacter* genus, represent approximately 60% of cases. However, the main causes of VAP are *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Enterobacteriaceae*, varying depending on the patient, persistence and antimicrobial therapy in the unit (8). Therefore, to try to reduce VAP due to multidrug-resistant germs, it is essential to understand the most common germs in the unit, which facilitates the logical and targeted prescription of antimicrobials (3), which must be done as soon as VAP is suspected (4). It is worth mentioning that before starting broad-spectrum antibiotics, respiratory samples from the patient must be sent to microbiology. This can be performed either by non-bronchoscopic sampling (tracheobronchial aspiration or mini bronchoalveolar lavage) or via bronchoscopic sampling (bronchoalveolar lavage or protected bronchial brushing) (13).

According to (4), there are some specific risk factors that predispose to the development of VAP, such as previous use of antimicrobials; antacids; H₂ receptor blockers; immunosuppressive drugs; need for reintubation; supine position; use of a nasogastric cannula; presence of tracheostomy; level of consciousness; immunological conditions; shock; progression of chronic obstructive pulmonary disease (COPD); antibiotic treatment as prophylaxis; lifestyle (alcoholism, smoking and malnutrition); environmental and occupational factors (air pollution); chronic and debilitating diseases (diabetes, neoplasms, chronic obstructive pulmonary disease); immunodeficiencies; splenectomy; and transport within the hospital. VAP occurs due to aspiration of secretions from the oropharynx, condensate formed in the respirator circuit, or gastric

contents colonized by pathogenic bacteria.

According to the National Health Surveillance Agency (Anvisa) (9), in patients under mechanical ventilation, colonization of the oropharynx by gram-negative microorganisms generally occurs in the first 48 to 72 hours after the patient is admitted to the ICU. In agreement with this, studies presented in the article: "***Pneumonia associated with mechanical ventilation in Intensive Care Units: factors that influence its development and means of prevention***" (8), It has been shown that the chances of pneumonia increase by approximately 3% per day in the first five days of mechanical ventilation. After this period, it increases by approximately 2% for each subsequent day.

In view of this, taking into consideration, that the majority of patients admitted to the ICU are on MV, and the incidence of pneumonia is 7 to 21 times higher than in those who do not require MV (10), and pneumonia related to VM has high mortality and morbidity, knowledge of its risk factors and the study of its prevention measures is essential. Therefore, it is extremely important to educate health professionals, reduce the length of time the patient is kept on MV, take measures to aspirate orotracheal secretions, maintain a decubitus position at 30 to 45 degrees to reduce regurgitation and aspiration of secretions. Care must also be taken to keep the endotracheal intubation cuff pressure between 20 and 30 cmH₂O to avoid bronchial aspiration of secretions from the oropharynx into the lower airways; hand hygiene to prevent the microbial transmission route; daily check of sedation level, routine aspiration of subglottic secretion (9). Decontamination of the digestive tract was studied as a method of reducing the incidence of VAP by decreasing colonization of the upper respiratory tract. The methods used include antiseptics such as chlorhexidine in the oropharynx and non-

absorbable antibiotics, which can be applied to the oropharynx (selective decontamination of the oropharynx [DSO]) or administered enterally (selective decontamination of the digestive tract [DSTD]). However, DSTD never became standard practice, largely due to concerns about long-term microbial ecology within the ICU and the selection of drug-resistant organisms. OSD using chlorhexidine mouthwashes has indeed become a routine practice, although it has more recently been restricted to VAP prevention kits for patients who have undergone cardiac surgery (13).

FINAL CONSIDERATIONS

Mortality rates in patients with VAP are considerably high.

As VAP can occur several days after the institution of mechanical ventilation, the SOFA score is used to predict fatal outcomes, together with factors associated with mortality to guide therapeutic decisions and determine the prognosis. The factors that contribute to the development of VAP can be categorized as modifiable and non-modifiable. Non-modifiable factors include the ICU environment and misuse of antibiotics. Therefore, we must seek to reduce the number of multi-resistant bacteria, making appropriate use of antibiotics targeted for each type of infection.

Taking into consideration, that the majority of patients admitted to the ICU are on MV, and the incidence of pneumonia is 7 to 21 times higher than in those who do not require MV, knowledge of their risk factors and the study of their Prevention measures are essential. It is concluded that it is extremely important to address risk factors and knowledge of appropriate treatment among health professionals, in order to reduce the prevalence and morbidity and mortality of the condition.

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