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VENTILATOR ASSOCIATED PNEUMONIA IN ICU PATIENTS: RISK FACTORS AND TREATMENT

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Abstract:

Introduction: Ventilator-associated pneumonia is defined as pneumonia in that developed within 48 to 72 hours following the application of endotracheal intubation. More than 50% of hospital-acquired pneumonia cases are classified into ventilator-associated pneumonias. Patients usually show systemic signs of infection like hyperthermia, and changes in white blood cells counts. They also show alterations in the characteristics of sputum. The causative agent is usually detected in blood stream. Methodology: We conducted this review using a comprehensive search of MEDLINE, PubMed, and EMBASE, January 1985, through February 2017. The following search terms were used: ventilator associated pneumonia, intensive care unit complication, risk factors for ventilator associated, treatment of ventilator associated pneumonia Aim: In this review, we aim to study the prevalence, risk factor, and causative organisms for ventilator associated pneumonia. We will also study the treatment of such pneumonia in the intensive care unit. Conclusion: Ventilator-associated pneumonia is a major complication that occurs to patients on mechanical ventilation and mainly in the intensive care unit. No gold standard is available yet for diagnosing ventilator-associated pneumonia. Recent studies have suggested the use of samples from the lower respiratory tract. The best measurement in ventilator-associated pneumonia is prevention, with avoiding known risk factors. In patients with suspected ventilator-associated pneumonia, early ampere antibiotic treatment is essential, with later transfer to narrow-spectrum antibiotics according to culture findings.

Keywords: *ventilator- associated pneumonia, intensive care unit, hospital acquired pneumonia*

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INTRODUCTION:

The definition of ventilator-associated pneumonia is made in patients who developed pneumonia within 48 to 72 hours following the application of endotracheal intubation. Ventilator-associated pneumonia usually shows progressive enlarging infiltrates with an increasing number. Patients usually show systemic signs of infection like hyperthermia, and changes in white blood cells counts. They also show alterations in the characteristics of sputum. The causative agent is usually detected in blood stream. More than 50% lf hospital-acquired pneumonia cases can actually be classified into ventilator-associated pneumonias **[1]**. Moreover, up to 27% of patients with mechanical ventilation can develop ventilator-associated pneumonia. Risk of developing ventilator-associated pneumonia is highest early in hospitalization. In addition, ventilator-associated pneumonia is considered to be the most common cause of systemic infection in patients with mechanical ventilation, and the second most common cause of systemic infection in patients admitted to the intensive care unit. Previous reports have estimated that about half the antibiotics used for patients in the intensive care unit are in fact to treat ventilator-associated pneumonia. Ventilator-associated pneumonia can be classified into early onset (occurring within less than four days of intubation and is usually caused by organisms sensitive to normal antibiotics), and late onset (occurring after four days of ventilation and is usually caused by organisms resistant to multiple drugs). Therefore, ventilator-associated pneumonia is considered a major complication in patients with mechanical ventilation and is associated with significant comorbidities and high costs **[2]**.

Risk factors

Several risk factors have been linked with the occurrence of ventilator-associated pneumonia. These factors can be categorized into: host factors and intervention factors.

Host factors

Post-surgical and burns patients

Previous reports have estimated that up to 33% of post-operative patients can have infiltrates in lungs. Moreover, Garibaldi et al, have found that up to 17% post-operative patients can have pneumonia. The risk of developing ventilator-associated pneumonia following surgery increases significantly in long surgeries, and in smokers. Burns also increase the risk of developing ventilator-associated pneumonia significantly, especially when there is also inhalational injury or intoxication **[3]**.

Acute respiratory distress syndrome (ARDS)

Following lung injury or acute respiratory distress syndrome, the incidence of ventilator-associated pneumonia increases significantly. It is possible that this occurs in these patients due to long duration of being mechanically ventilated, rather than being caused by the lung injury itself. In a study on the effect of acute respiratory distress syndrome on ventilator-associated pneumonia, Chastre et al, reported that patients with acute respiratory distress syndrome have 55% risk of developing ventilator-associated pneumonia, which is about double the risk in patients who do not have acute respiratory distress syndrome **[4]**. This increase in risk was attributed to the long duration of being under mechanical ventilation. Another study on the diagnosis of ventilator-associated pneumonia in patients with acute respiratory distress syndeoms concluded that a diagnosis of ventilator-associated pneumonia was able to be confirmed by positive cultures in about 60% of cases. Organisms that were most commonly found in these cases included S*taphylococci* and gram-negative bacilli. Moreover, patients with acute respiratory distress syndrome had a significantly higher risk of developing ventilator-associated pneumonia caused by *Methicillin-resistant Staphylococcus aureus* (MRSA) **[5]**.

Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease is a known risk factor for ventilator-associated pneumonia. Some researchers suggest that this is due to the old age of patients, the presence of bacterial colonies in lower respiratory tract, the inhibited cilia (most likely due to smoking), the absence of effective coughing (most likely due to obstruction), and the weak immune system in patients with chronic obstructive pulmonary disease (most likely due to the use of corticosteroids). In patients with chronic obstructive pulmonary disease, ventilator-associated pneumonia is usually caused by *Methicillin-resistant Staphylococcus aureus, H. influenza, Aspergillus, or Pseudomonas* species **[6]**.

Intervention factors

Duration of mechanical ventilation

To make a diagnosis of ventilator-associated pneumonia, pneumonia should happen after at least two days of intubation of the patient. This helps determine the cause and not mistake it with any community-acquired infection that started to show clinical manifestations late. Significant risk factors

that determine the risk of developing ventilator-associated pneumonia is the duration of mechanical ventilation. Moreover, ventilator-associated pneumonia due to infection with *Methicillin-resistant Staphylococcus aureus, or Pseudomonas* is significantly associated with longer ventilation duration. In addition, reports estimate that up to 60% of late-onset ventilator-associated pneumonia are caused by *Methicillin-resistant Staphylococcus aureus, or Pseudomonas* **[7]**.

Prone position

The position of the patient while being ventilated can play an important role in developing ventilator-associated pneumonia, and lungs trauma. For example, supine position during mechanical ventilation aids the development of compression atelectasis of the dorsal lung, and barotrauma of the ventral lung. On the other hand, prone position aids the entry of more air into the dorsal lung. Finally, lateral position will achieve less rates of pulmonary trauma, and will decrease the risk of infection by preventing aspiration **[8]**.

Re-intubation

Another risk factor for developing ventilator-associated pneumonia is repeated re-intubation. This is thought to be to gastric aspiration, or the presence of subglottic dysfunction and alter mental status in these patients who require repeated re-intubation **[9]**.

Paralytic agents or sedation

Sedative agents and paralytic drugs have been found to be associated with an increased risk of pneumonia risk. Usually in therapeutic procedures, paralytic drugs are used to facilitate the procedure. For example, midazolam is usually used while performing bronchoscopy to induce bronchial muscles relaxation. However, this effect on bronchial muscles can be prolonged leading to high risk of aspiration. In addition, sedative agents can also cause aspiration and lead to the development of pneumonia. Both sedation for a long-duration, and cardiopulmonary resuscitation have been independently linked with early onset ventilator-associated pneumonia **[10]**.

H2 blockers

It has been found that patients who receive H2 blockers along with other drugs to prevent stress ulcer, have a higher risk of developing ventilator-associated pneumonia. Moreover, several studies have established a direct association between bacterial colonization and alkaline PH in the stomach. In addition, several clinical trials have been conducted, with all evidence supporting the association between the use of H2 blockers and the increase in ventilator-associated pneumonia risk **[11]**.

Treatment

Recently, guidelines to empirically treat ventilator-associated pneumonia have been published by the ATS. In these guidelines, the ATS categorizes patients into two groups: patients who have a high risk of developing antibiotics-resistant ventilator-associated pneumonia, and patients who do not have this risk. There are many risk factors that put a patient at high risk of developing antibiotics-resistant ventilator-associated pneumonia, these include: a prior therapy with antibiotics (especially within the last three months), hospital stay longer than five days (regardless of being in the normal ward or the intensive care unit), the high prevalence of antibiotics resistance in the area or in the same hospital, and the presence of other co-morbidities that put the patient in an immunosuppression state. It is essential for physicians to be able to distinguish between ventilator-associated pneumonia, and nosocomial infections, which also present with antibiotics resistance **[1]**.

In patients who lack risk factors for an antibiotics-resistant ventilator-associated pneumonia, physicians are recommended to initiate empiric antibiotics therapy that covers *Haemophilus influenza*, methicillin-sensitive *Staphylococcus aureus*, antibiotic-sensitive gram-negative enteric organisms, and *Streptococcus pneumonia*. Such therapies may include quinolones (including moxifloxacin, levofloxacin, or ciprofloxacin), ertapenem, ceftriaxone, and/or ampicillin/sulbactam **[12]**.

On the other hand, in patients who show risk factors for an antibiotics-resistant ventilator-associated pneumonia, physicians are recommended to consider the previously mentioned organisms, and add to them *Serratia, Klebsiella, Stenotrophomonas maltophilia, Pseudomonas aeruginosa, Burkholderia cepacia, Enterobacter,* methicillin-resistant *S. aureus*, and *Acinetobacte.* In such cases, empiric antibiotics treatment is widened and could include aminoglycoside (like amikacin, gentamicin, or tobramycin) plus linezolid or vancomycin or an antipseudomonal fluoroquinolone (like ciprofloxacin or levofloxacin), given in addition to an antipseudomonal cephalosporin, an antipseudomonal carbepenem, or a β-lactam/β-lactamase inhibitor **[13]**. There is still some debates about the use of combination therapy versus monotherapy in patients with ventilator-associated pneumonia. Combination therapy has a main goal: prevent the occurrence of drug resistance. Other goals of combination therapy

include to improve clinical outcomes, and give enough coverage against bacteria. However, a recent meta-analysis has concluded that combination failure was found to be associated with higher rates of clinical failure that monotherapy. Moreover, combination therapy led to the development of significant adverse events, like nephrotoxicity when using an aminoglycoside. In general, most physicians still prefer to use combination therapy because of high mortality rates associated with ventilator-associated pneumonia **[14]**.

Later, when cultures and antibiotics-sensitivity tests are ready, clinicians should consider the turn from the empiric wide-spectrum treatment to narrow-spectrum treatment that only covers the causing organisms. This is essential as it significantly reduces the rates of resistance development **[12]**.

CONCLUSION:

Ventilator-associated pneumonia is a common and significant complication that occurs to patients on mechanical ventilation and mainly in the intensive care unit. No gold standard is available yet for diagnosing ventilator-associated pneumonia. Recent studies have suggested the use of samples from the lower respiratory tract. The best measurement in ventilator-associated pneumonia is prevention, with avoiding known risk factors. In patients with suspected ventilator-associated pneumonia, early ampere antibiotic treatment is essential, with later transfer to narrow-spectrum antibiotics according to culture findings.

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