

Ventilator-associated Pneumonia: A Narrative Review

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ABSTRACT

The difficulty of early diagnosis, the proper anti-microbial chosen, and the relatively high morbidity and mortality; make us collect the related subjects to deal with the most critical complication (ventilator-associated pneumonia) showing the major points needed for every intensivist. Ventilator-associated pneumonia is considered the most common respiratory complication (infection) in intensive care unit patients. Ventilator-associated pneumonia can be defined as a hospital-acquired infection of the lung parenchyma that occurs after 2 days of mechanical ventilation. Its incidence is about 9-25% in intubated patients for more than 2 days. We could classify ventilator-associated pneumonia as early and late; the first one happened within four days of receiving mechanical ventilation, otherwise, the late onset occurred after day four. Some patients with hospital stays before intensive care unit admission and intubation are considered to have late ventilator-associated pneumonia regardless of the period of mechanical ventilation because those patients might have had pathogens previously (nosocomial). Severe ill patients, prolonged mechanical ventilation, and failed extubation trials (recurrent intubation) lead to the development of ventilator-associated pneumonia rapidly and aggressively. Furthermore, ventilator-associated pneumonia is attributed to prolonged hospitality as well as high morbidity and mortality. We aimed in this narrative review to discuss ventilator-associated pneumonia regarding the etiology, causative agents, risk factors, strategies for early diagnosis, accurate treatment, and optimal prevention protocols.

Keywords: Ventilator-associated pneumonia Pneumonia; Intubation; Mechanical ventilation; Antibiotics.

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INTRODUCTION

Although cardinal strategies and techniques for the management of patients on mechanical ventilation and frequent optimal procedures to disinfect the ventilators and other associated equipment, ventilator-associated pneumonia is still the most common respiratory complication with relatively high morbidity and mortality [1]. The mortality rate of ventilator-associated pneumonia is about 25-50% and sometimes reaches 75% in some cases when the infection is caused by highly violent microbes, in contrast to the more frequent organs liable for infections like skin and urinary tract, their mortality rate is low (1-4%) [2].

New studies reveal that early diagnostic procedures and accurate antibiotic treatment improve outcomes [3]. Just to keep in mind, ventilator-associated pneumonia develops tenfold more in patients with mechanical ventilation than in non-ventilated ones [4]. Post-mortem autopsy (on people after prolonged mechanical ventilation) reveals three pulmonary pathologies: tracheobronchitis, bronchopneumonia, and bronchiolitis (tiny airway inflammation without pneumonia involvement) [5]. We aimed to highlight various aspects of ventilator-associated pneumonia, including its epidemiology, predisposing factors, causative agents, diagnostic tools, treatment, and prevention.

EPIDEMIOLOGY

The reported incidence of ventilator-associated pneumonia ranges from 5% to 40% of subjects receiving invasive mechanical ventilation for more than 48 hours, this wide difference

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depends on the country, type of the intensive care unit, and diagnostic criteria of ventilator-associated pneumonia [6, 7].

Poor decontamination and sterilisation of respiratory care equipment are thought to be the sources of the effective pathogens of ventilator-associated pneumonia; aerobic gram-negative bacillus, which has been implicated as a significant cause of morbidity and mortality in intensive care unit hospitalised patients, as well as the frequency of mechanical ventilation [8]. Despite applying infection control measures, ventilator-associated pneumonia remains the most common intensive care unit-acquired infection. The risk of developing this type of pneumonia is related to the patient's factors and the duration and severity of exposure to this type of bacteria [9]. A recent multicenter Canadian study assessed more than one thousand mechanically ventilated patients and found the following anticipated factors: burns, multi-organ trauma, multi-system diseases (central nervous, respiratory, and cardiac), aspiration, mechanically ventilated for more than 24 hours, and use of muscle relaxant drugs [10]. The important findings from this study include; increasing the daily severity of ventilator-associated pneumonia till day five of mechanical ventilation and positive systemic effects of the proper antibiotics. Other findings in multiple studies are low pressure of the endotracheal tube cuff, the patient having previously been hospitalized in more than one ward, supine position, and poor oral hygiene [11].

RISK FACTORS

First of all, the presence of the endotracheal tube is considered the greatest risk factor for ventilator-associated pneumonia because it interferes with the normal physiological protective mechanism of the upper airways to inhibit the cough reflex; allowing the pharyngeal secretions to aggregate, causing macro and even micro-aspiration [12]. The significant alteration in host-defense mechanism plus colonization of the bacteria pooled over the cuff of the tracheal and increased their adhesion to the upper respiratory mucous membrane. Re-intubation after failed trials of extubation also increases the risk of ventilator-associated pneumonia [13]. Colonization of aerobic Gram-negative bacteria after sickness, improper antibiotic intake. The secretions containing pathogens gain access through the endotracheal tube to the respiratory tract [14]. Mechanical ventilation pushes the microbes distally and sprays them throughout the airway. Immunosuppression and smoking are associated with severe sickness and contribute to developing ventilator-associated pneumonia [15]. Surgical patients post-operatively (especially thoracic and upper abdominal) were also at risk for ventilator-associated pneumonia [16]. Table 1 summarises the risk factors for ventilator-associated pneumonia.

CAUSATIVE AGENTS

According to the intensive care unit stayed patients, the microorganisms causing ventilator-associated pneumonia will be different. Many documents and studies reveal that anaerobic gram-negative bacteria cause more than 60% of ventilator-associated pneumonia [17]. Some investigations have reported that gram-positive bacteria have played a role in this pathology in 20% of patients, especially *S. aureus* [18]. The major anaerobic gram-negative bacteria are *P. aeruginosa*, *Acinetobacter* spp., *Proteus* spp., *Escherichia coli*, *Klebsiella* spp., and *H. influenza* [19]. In some cases, patients with underlying diseases are liable for infection with specific organisms;

Table 1. Independent various risk factors of ventilator-associated pneumonia.

1	Age above ≥ 60 years
2	Respiratory distress syndrome and chronic obstructive pulmonary disease
3	Burn and trauma
4	Aspiration
5	Severe illness and/or organ failure
6	Prior antibiotic or no antibiotic
7	Supine, endotracheal tube, and/or nasogastric tube
8	Muscle relaxant agents, continuous sedation
9	Previous respiratory tract colonization
10	Diabetes mellitus, steroids, immunosuppressed patients

Table 2. Independent various risk factors of ventilator-associated pneumonia.

Patient's illness	Causative micro-organisms
Stable general condition	<i>P. aeruginosa</i> , <i>Acinetobacter</i> spp., <i>Proteus</i> spp., <i>Escherichia coli</i> , <i>Klebsiella</i> spp. and <i>H. influenzae</i>
Chronic obstructive pulmonary disease	<i>H. influenza</i> , <i>Moraxella catarrhalis</i> and <i>S. pneumoniae</i>
Cystic fibrosis	<i>P. aeruginosa</i> and <i>S. aureus</i>
Trauma	<i>S. aureus</i>
Post-surgery	<i>H. influenzae</i> or pneumococci
Neurosurgery and aspiration	<i>Acinetobacter baumannii</i>

chronic obstructive pulmonary disease patients are more exposed to infection with *H. influenza*, *Moraxella catarrhalis*, and *S. pneumoniae*. Patients with cystic fibrosis are more liable to be infected with *P. aeruginosa* and *S. aureus* [20]. Traumatic patients are infected commonly with *S. aureus*. Surgical intensive care unit patients are mostly infected with *H. influenzae* or pneumococci [20, 21]. Neurosurgery, head trauma, and massive aspiration cause ventilator-associated pneumonia due to *Acinetobacter baumannii*. Anaerobes contribute only to 21% of ventilator-associated pneumonia patients [20].

DIAGNOSIS

Without a precise definition, intensivists agree that accurate diagnosis remains a challenge because it lacks sensitivity and specificity, leading to both over or under-diagnosis of the condition [22]. But in the presence of respiratory failure accompanied by critical illness, which usually indicates "pneumonia" added to that, the role of mechanical ventilation will refer the diagnosis to "ventilator-associated pneumonia" [23]. The diagnosis should be suspected when there is a new persistent infiltration on the chest radiograph (Figure 1) plus two or more of the following:

1. Purulent tracheal secretion.
2. Leukocytosis >12000 white blood cells/L or leukopenia <4000 white blood cells /L.
3. Pyrexia > 38.5 C.

The laboratory blood tests and radiology (X-ray) will be weak indicators of broncho-alveolar lavage [24].



Figure 1. A 43-years-old gentleman construction worker. He had a history of falling from height and admitted to the intensive care unit because of flail chest. Chest X-ray shows acute respiratory distress syndrome of moderate severity with right lower pneumonia.

Invasively obtained samples are examined quantitatively to differentiate them from the low concentration of oropharyngeal secretion. Just one French study showed a reduction in morbidity and mortality when the intensivists used an invasive diagnostic procedure, while several other studies found no difference [25].

TREATMENT

Always remember that the treatment of ventilator-associated pneumonia is with anti-microbial drugs that cover all the pathogens isolated from the pulmonary secretions [16]. Patients with suspected ventilator-associated pneumonia should receive optimal empirical antibiotics prior to bronchoalveolar lavage; an invasive diagnostic procedure should be performed to isolate and culture the microorganisms from the secretions [26, 27]. Intensivists found that suitable antibiotics given in the first eight days were associated with less severe early-onset ventilator-associated pneumonia [26–29]. Intensivists found that suitable antibiotics given in the first eight days were associated with less severe early-onset ventilator-associated pneumonia [28, 29]. The primary antibiotic is chosen based on the associated factors, which include the severity of the disease, the patient's physical and physiological factors, the length of hospitality, and previous antibiotic intake [30]. Despite the fact that there is no typical regimen that has been established, the chosen antibiotic should be highly active against aerobic gram-negative bacteria [31]. The guidelines of the British Society for Antimicrobial Chemotherapy mention that; Co-amoxiclav or Cefuroxime for early-onset ventilator-associated pneumonia without antibiotics received before and the patients have no other risk factors [32]. For those who have risk factors or have received antibiotics earlier, third-generation Cephalosporin, Fluoroquinolone, or Piperacillin-Tazobactam will be useful [33]. Ceftazidime, Ciprofloxacin, Meropenem, and Piperacillin-Tazobactam are useful for late-onset ventilator-associated pneumonia because it is commonly related to the drug-resistant micro-organisms, especially *P. aeruginosa* [21, 33]. When Methicillin-resistant *S. aureus*

(MRSA) is suspected, Vancomycin or Linezolid should be used [34]. Empirical broad-spectrum monotherapy has better results than a combination of drugs because it reduces the cost effect and exposure to the antibiotic [35]. Anti-microbials could be safely discontinued after eight days if there are positive clinical findings (improvement in SPO₂ level, the white blood cell count returns to normal range, reduction in C-reactive protein level, and the temperature begins to be in the normal range) [36].

PREVENTION OF THE VENTILATOR-ASSOCIATED PNEUMONIA

Five main strategies we could use to decrease the chance of ventilator-associated pneumonia incidence are: antiseptic care of the oral cavity, a nursery of the patient with a semi-sitting position, prevent aspiration, fight the colonization of pathogenic bacteria, and reduce the time of mechanical ventilation [3, 37].

PROGNOSIS

Even though there is a high rate (up to 50%) of death due to ventilator-associated pneumonia, there is certainly controversy concerning the level at which this disease contributes to death in intensive care unit cases. Anyhow, ventilator-associated pneumonia prolongs the period of mechanical ventilation and hospitalization [3].

Various previous investigations estimate the mortality rate due to ventilator-associated pneumonia. These include cohort investigations with conflicting findings [38, 39]. The drawbacks of these studies include the retrospective nature of the studies and heterogenous patient enrollment [40]. Owing to there being no fixed timing (during the first 10 days of hospitalization) for the acquisition of ventilator-associated pneumonia, there is an effect of the severity of the patient's disease on the mortality (more severe cases have a high death rate and short hospital stay) [41]. The mortality rate in adult respiratory distress syndrome (41.8%) with ventilator-associated pneumonia was higher than without ventilator-associated pneumonia (30.7%). However, when considering the confounding factors, ventilator-associated pneumonia was not related to the death rate [42]. Similar findings were reported in patients with cancer or traumatic brain injury associated with ventilator-associated pneumonia [43, 44]. Randomized-controlled trials are the solution to preventing any confounding factors that might affect the mortality rate of ventilator-associated pneumonia in patients with certain severe diseases. In one such study, the mortality rate was found to be 9% [45].

CONCLUSION

Prevention is better than aggressive treatment for any patient admitted to the intensive care unit. This can be carried out by an optimal and full decontamination and sterilization of the intensive care unit equipment, breathing circuit, and patient's bed. When the admission comes from the ward in which the patient stayed for more than two days, ventilator-associated pneumonia should be suspected, and the patient should be kept under close observation, the respiratory system should be examined, and blood sent for laboratory tests to identify inflammatory markers, as well as X-ray examination, should be available to detect any finding in the lung. Bronchoalveolar lavage has the decision to choose the proper antibiotics.

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Consent for Publication

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Availability of Data and Material

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Authors' Contributions

Alkayssi HA was responsible for writing the whole manuscript. Alkayssi HA read and approved the final manuscript draft.

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