Ventilator-associated pneumonia: A Literature Review

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Abstract

Ventilator-associated pneumonia or known as VAP is known to be the most prevalent and lethal nosocomial infection in critical care occurred after 48 hours of endotracheal intubation. Mostly patients may have already been extubated by the time VAP started. It can be treated by antibiotics according to the early or late onset of the infection. Head of bed elevation, dental care with chlorhexidine, stress ulcer prophylaxis, deep venous thrombosis prophylaxis, daily sedation evaluation, and spontaneous breathing trials are all included in the five-part Institute of Healthcare Improvement (IHI) VAP bundle, and are thought to be able to prevent VAP. This study aims to review past literature and studies regarding ventilator associated pneumonia.

Keywords: ventilation associated pneumonia; literature review

1. Introduction

Ventilator-associated pneumonia or known as VAP is known to be the most prevalent and lethal nosocomial infection in critical care occurred after 48 hours of endotracheal intubation. Mostly patients may have already been extubated by the time VAP started. It's affecting one-third of total patients with need of mechanical ventilation without infectious admission. It is defined by the presence of a new or ongoing infiltration, infection symptoms (fever, rising count of the white blood cell), sputum content changes, and the identification of a causative agent. Half of the total number of the hospital-acquired pneumonia caused by VAP. VAP is thought to occur in 9–27% of all mechanically ventilated patients, with early hospitalization being the time period with the highest risk [1].

2. Epidemiology

From all of the patients with invasive mechanical ventilation more than 2 days duration, 5-40% acquired VAP. The results varied for different countries, ICU and VAP diagnosis criteria being used. Numbers of infected cases seems to be lower in US compared to European countries. Whereas lower income countries showed significantly higher incidence of VAP, compared to US hospitals and high-income countries (18.5 vs 9.0 per 1000 ventilator-days) [2] [3] [4] [5].

Variety of VAP incidents in each part of the world correlated with differences of VAP definitions applied in each area also diagnostic limitations and sampling methods of the parasite. It is calculated that VAP has the highest occurrence between day 5-9 of mechanical ventilation [6].

Different population being studied are showing different incidence rates. Cancer patients have relatively high rate of VAP as high as 24.5 per 1000 ventilator-days [7]. VAP also widely occurred in trauma patients based in one of the studies (17.8% from total of 511 patients) [8]. The incidence rate is thought to be varied according

to the different function of immune following the damage caused by acute trauma, aspiration from brain injury and lung contusion [5]. High prevalence is accumulated due to lots of micro aspiration and bacterial colonization (defective mucociliary clearance), a prolonged duration of invasive mechanical ventilation (muscular weakness), altered local and general host defense mechanisms, and the increased incidence seen in chronic obstructive pulmonary disease (COPD) patients may all contribute to this increased incidence. Acute respiratory distress syndrome (ARDS) cause a higher risk of VAP [9].

According to studies, age is not correlated with risk of pneumonia in ventilated patients. According to a analysis of a European cohort research, patients with the age ranges from 45 until 64 had 13.7 VAPs per 1000 ventilation days, patients between the ages of 65 and 74 had 16.6, and patients beyond the age of 75 had 13.0 VAPs per 1000 ventilation days. With the method of logistic regression analysis, there's no evidence of greater incidence in older patient population [10]. However, male gender is thought to be a risk factor for VAP [11]. Still, underlying. Medical conditions of the patients, comorbidities and severity of disease especially are the biggest risk factor for VAP.

3. Pathogenesis

The development of the disease is half influenced by the intricate connection between the endotracheal tube, risk factors, invasive bacteria aggressiveness, and the immunity of the host itself. The most significant risk factor is unquestionably the presence of an endotracheal tube, that cause the body's natural defense system compromising with the (the glottis and larynx's cough reflex) micro aspiration around the tube's cuff [12] [13]. Infectious bacteria then enter the lower respiratory tract directly with the processes as: (1) micro aspiration, which can happen during intubation; (2) biofilm formation inside the endotracheal tube that filled with bacteria (usually Gram-negative bacteria and fungal species); (3) secretions pooling and trickling around the cuff area and (4) disturbance of mucociliary clearance of secretions with gravity dependence of mucus [1].

The virulent strains will take over the area that used to be filled with normal flora alongside with the accumulation of the pathogenic material in nearby anatomic regions such the stomach, sinuses, nasopharynx, and oropharynx [13] [14] [15]. The ventilator's positive pressure is also continually pushing this bacterium-rich material forward. Non-invasive positive pressure ventilation is tested to be correlated with the decreasing of the VAP rates, however reintubation after extubation raises VAP rates [12]. The severity of VAP and occurrence of VAP are based on the underlying condition, prior surgery and exposure of the antibiotics counted as the host variables linked to VAP. [2]

4. Diagnosis

VAP could be difficult to diagnose quickly as a result from limitation of diagnostic tools, and varieties of diagnosis with patients in ICU needing oxygen, experiencing leukocytosis and secretions. Diagnosis could be identified with aspiration either seen or suspected, and also decreasing respiratory ability with fever and productive cough following behind, showing typical clinical manifestations of pneumonia. The IDSA/ATS is recommending using clinical manifestation criteria to diagnose VAP, despite the fact that scoring systems like the Clinical Pulmonary Infection Score are used to guide the management of community-acquired pneumonia [16] [17]. According to the guideline, VAP diagnosis can be made through the meetings of clinical manifestations such as infiltration of the lung shown by chest imaging, that wasn't there before the ventilation, deterioration of the breathing, fever and productive cough. With no new infiltrate in chest imaging to be found,

the likelihood of VAP is mostly zero, and could be differed to other diagnoses such as pulmonary embolism [16] [17].

4.1. Noninvasive tests [18]

Noninvasive test could be conducted after HAP or VAP is suspected due to infiltrate in chest imaging resulting to the breathing deterioration. The test is needed to isolate the pathogen and finding the perfect antibiotics, to attack the causative organism effectively. Blood cultures are strongly suggested for individuals with HAP or VA [1]. From total of VAP cases, 15% of them are bacteremia and up to 25% shown indicative bacteria of a secondary, non-pulmonary infection source.

Blood cultured is dependable and trusted to identify the causative agent causing HAP or VAP. If the result shown to be negative, the physician to be alert of other causative infections unrelated with the respiratory tract. Bacteria from the genus of Candida and Enterococcus species are not known to cause pneumonia, cause identifying them in the bloodstream may alert the physician to another potential location of infection, such as a catheter-related bloodstream infection.

Patients who acquired HAP and non-intubated patients with VAP, should rely on sputum culture instead. This method could be performed with patients who are able to excrete adequate amount of sputum sample, and have few to no squamous epithelial cells on Gram stain. To reduce the cost and harm to the patient, semiquantitative sputum samples obtained by noninvasive methods such as endotracheal aspiration is preferred rather the invasive ways for the patients in example bronchoscopy and blind bronchial sampling (mini-bronchoalveolar lavage). This method can be used for patients with limitation producing enough sputum sample. The result of test may change due to antibiotics usage prior to the sputum collecting process, causing lab result came out unimpressive, and the therapy to come to a halt.

In order to identify the bacteria that cause HAP and VAP and to guide antibiotic stewardship initiatives, polymerase chain reaction (PCR) testing has become increasingly popular. During a study using population of 10% prevalence of MRSA, the result showed a PCR-based test with S. aureus nasal swab with significant negative value for colonization of the S. aureus with methicillin-resistant [14]. This test showed higher sensitivity for HAP compared to VAP (85% vs 40% with the specificity 92% vs 94%) Antibiotic resistant founding has been formed by using the nasal swab examination, and showed correct prediction of which species in Staphylococcus may cause pneumonia in the patient. Anti-MRSA therapy is safe to administer when the results come out as negative.

Procalcitonin lab test is used in patients with either HAP or VAP to differentiate between the causative agents whether it is caused by viral or bacterial agents, and may showed possible cases of coinfection. Rising number of procalcitonin is usually shown in people with pneumonia, but numbers are considerably higher in typical bacteria compared to the atypical one, or with the virus as the causative agents, will also show a relatively higher number. Procalcitonin is marker that can be found in blood, and the production itself is enhanced with cytokines, connected to the infections caused by bacteria, inhibited by the interferon's correlation with the viral infections. If the procalcitonin amount isn't increased by minimum of 23% of the common bacterial infection, the test could be told as not optimum. Study was conducted to compare treatment initiated with procalcitonin lab result and clinical judgement with the use of systematic review and meta-analysis with randomized controlled trials in ICU patient's method, but showed no difference in the mortality numbers.

5. Management of VAP

Antibiotics are chosen based with the duration of the mechanical ventilation done in the patients. Patients with early onset of VAP (4 days) are treated with antibiotics in the limited spectrum category whereas patients with late onset VAP (more than 4 days) are known to require broad spectrum antibiotics [2]. To fulfil the goal

of effective initial empiric therapy, updated antibiogram of locals based on regional bacteriological forms and susceptibilities are known to be important for institution and ICU [2]. Antibiotic therapy is a crucial factor in the management of VAP. Every delayed of the initial empiric antibiotic therapy, will causing bigger chance of resistance formation [19]. Bigger rates of mortality risk is associated with the delay of antibiotic treatment [2].

Both early and late onset of the VAP are using cephalosporin antibiotics. Second or third generation is being used in the early onset such as ceftriaxone with the dose of 2 g per day and 2 g of cefotaxime per 8 hours, while for the late onset cefepime of 1-2 g for every 8 hours and ceftazidime within the dose of 2 g per 8 hours is being used. Early onset VAP cephalosporin could be traded with fluoroquinolones such as levofloxacin 750 mg daily and moxifloxacin 400 mg per day, or the choice of aminopenicilin and beta-lactamase inhibitor (ampicillin sulbactam 3 g per 7 hours) or ertapenem daily as much as 1 gram.

For Late onset, carbepenem could be used with the example of imipenem cilastin within the 500 mg dosage for every 6 hours or a gram for every 8 hours and meropenem 1 g per 8 hours). Beta-lactamase inhibitor also used for another lineage of therapy such as piperacilin tazobactam 4.5 g per 6 hours alongside with aminoglycoside (amikacin 20 mg/kg/day; gentamicin 7mg/kg/day; tobramycin 7 mg/kg/day), or another in line, antipseudomonas fluoroquinolone (ciprofloxacin 400 mg every 8 hours; levofloxacin 750 mg daily) plus coverage for MRSA (vancomycin 15 mg/kg every 12 hours) or linezolid 600 mg every 12 hours

Therapy using combination of antibiotics is preferred compared to monotherapy with the high rate of resistance of P. aeruginosa. Carbapenems are thought to be the most effective antimicrobial agents for Acinetobacter and Enterobacteriaceae with ESBLs. Other therapy mentioned to be effective are colistin, polymyxin B and ampicillin sulbactam [20] [21]. Even though MDR organism usually related with late-onset VAP, recent studies showed different result which is frequent connection to early onset VAP [21] [22]. Antibiotics with inhalation methods are not recommended due to uncertain effect compared to systemic antibiotics [2]. Treatment for early VAP lasts for 8 days usually but it is normal to be longer for late-onset VAP and MDR organism cases [1].

Treatment with no result of clinical improvement will be needing reevaluation of the causative agents and thought to be right to look for other options of causes adding the signs and symptoms. IDSA/ATS guidelines prioritize the need of reevaluation of the patients in 48-72 hours after the initial antibiotic treatment, to decide the therapy being continued or stopped, or if other diagnose should be obtained regarding the difficulties associating in VAP diagnoses finding especially for the early-onset. Swoboda et al., mentioned half of the patients without pneumonia findings, are prescribed for the prophylaxis antibiotic to prevent VAP in two surgical ICUs [23].

6. Prevention

According to the Institute of Healthcare Improvement (IHI) in the VAP section, there are ways to prevent VAP, such as elevating the head of the bed, maximizing dental care with the use of chlorohexidine, prophylaxis therapy for stress ulcer, deep venous thrombosis, evaluation of daily sedation and trials of the spontaneous breathing [24].

Each intervention contribution to the efficiency and significance data quality is questionable, but it showed factors mentioned above lower the risk of VAP. A lot of trials regarding VAP have showed failure to show clinical and financial success [25]. VAP rates showed significant decrease with IHI methodology-based prevention bundled. It also contributes to MRSA occurrence and usage of antibiotics being minimalized. [26]. But nor the length of mechanical ventilation usage and ICU admission were reduced [26].

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