Ventilator-Associated Pneumonia

Subjects: Pediatrics

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Ventilator-associated pneumonia (VAP) is defined as pneumonia not present or incubating at the time of admission and occurring after more than 48 hours of mechanical ventilation (MV). This is the second-most common healthcare-associated infection (HAI) in neonatal intensive care units (NICUs). VAP is associated with increased morbidity and mortality, an increased length of stay in the NICU and hospital costs.

Keywords: ventilator-associated pneumonia (VAP) ; mechanical ventilation (MV) ; neonatal intensive care units (NICUs) ; diagnosis

1. Introduction

The survival rates of preterm neonates have increased in the past decades due to the advances in intensive care treatment. This achievement is the result of the use of antenatal steroids, exogenous surfactant supplementation, improved nutrition, and mechanical ventilation (MV). Unfortunately, mechanical ventilation is associated with a substantial risk of ventilator-associated pneumonia (VAP) [1][2]. This type of nosocomial infection (NI) can be caused by aspirations of secretions, colonization of the respiratory tract, and the contamination of devices and medications used for the treatment of the hospitalized neonate [3].

Neonates, and more specifically premature babies and those born with a low (<2500 g) or very low birth weight (<1500 g) (LBW and VLBW) are more vulnerable to VAP due to an impaired or immature immune system and the necessity for the use of a combination of invasive devices during their hospital stay. The incidence of VAP in NICUs can vary significantly in different regions from 1 to 63 episodes per 1000 ventilation days which can reflect differences in diagnostic procedures, definitions used, and the burden of disease [4][5][6]. Different strategies have been discussed for the prevention of VAP such as hand hygiene, stress ulcer prophylaxis, head of bed elevation, early extubation, and suction practices [7] but still there is no consensus on which are the most suitable and cost-effective strategies.

One of the setbacks when it comes to VAP and comparing data from different studies is the lack of unified criteria and a gold standard for a VAP diagnosis. There are different definitions but there is still no consensus on this matter.

According to the Centers for Disease Control and Prevention (CDC) and National Nosocomial Infections Surveillance (NNIS), VAP is defined as a pneumonia that develops at least 48 h after initiation of mechanical ventilation [8]. To diagnose VAP, the patient needs to exhibit a combination of radiological, clinical, and microbiological findings. One of the drawbacks of the CDC/NNIS definition for VAP for infants younger than 1 year is that there are no specific criteria for newborns and premature infants. Despite this, most of the studies of VAP in NICUs use the CDC/NNIS criteria [9].

There are several other possible definitions for VAP provided by other researchers and study groups. The “Neo-KISS” module of the German National Nosocomial Infection Surveillance System (Krankenhaus Infektions Surveillance System [KISS]) provides a VAP definition for infants with very low birth weight [10]. A Dutch study group established their own definition for VAP in neonates, which are more inclusive than the CDC definitions [11]. The criteria for diagnosis of Neo-KISS module and the Dutch study group are presented in **Table 1**.

Table 1. Definitions for ventilator-associated pneumonia.

Neo-KISS Module [10]	Van der Zwett et al. [11]
Radiological findings • New or progressive infiltrate • Consolidation • Pleural or interlobar effusion **AND** **Deterioration of gas exchange, drop in saturation** **AND FOUR of the following criteria** • New/increased bradycardia (<80/min) **or** • New increased tachycardia (>200/min) • New/increased tachypnea (>60 min) **or** • New/increased apnea (>20/s) • Purulent tracheal secretions • Increased respiratory secretions • Isolation of a microorganism from tracheal secretion • New/increased dyspnea (retractions, nostril flaring) • Temperature instability/fever/hypothermia • CRP > 2.0 mg/dL • I/T ratio > 0.2	**Clinical findings** **One of the following:** • Purulent sputum • Changes in sputum characteristics • Deterioration of ventilation conditions **Radiological findings** **New emergence or progression of the following** • Infiltration • Consolidation • Pleural adhesion • Pleural effusion **Microbiological findings *** • Isolation of a pathogenic microorganism or detection of a bacteria/viral antigen in tracheal aspirate, bronchial secretion, or sputum

* If no microorganisms have been isolated in order to diagnose pneumonia, administrations of antimicrobial therapy for at least seven days prescribed by a physician should be present.

2. Clinical Findings

For the diagnosis of ventilator-associated pneumonia, the most common clinical criteria that are used are fever, worsening gas exchange, new onset or increasing bradycardia (<80/min) or tachycardia (>200/min), new onset or increasing tachypnea (<60/min) or apnea (>20 s), new onset or increasing dyspnea (retractions, nasal flaring, grunting), and purulent secretions. Unfortunately, those criteria are non-specific. Apisarnthanarak et al. [12] reported that hypothermia (79%) and new-onset tachypnea (63%) were the most common clinical symptoms in extremely preterm neonates. In their study, Khattab et al. [13] conducted a comparison between newborns with and without ventilator-associated pneumonia (VAP). They found that 80% of the neonates with VAP exhibited chest auscultation abnormalities and mucopurulent endotracheal tube discharge.

3. Radiological Findings

The most common radiologic criteria used to diagnose VAP in neonates are the presence of new or progressive infiltrate, adhesions or fluid in lobar fissures/pleura, or cavitations, pneumatocele, or air bronchograms on chest X-ray. In comparison to infiltrates, the presence of air bronchograms shows a higher sensitivity (58–83%) [14]. In complicated instances, including infants with underlying cardiac or pulmonary disease, sequential chest X-rays (days 0, 2, 3, and 7) aid in the confirmation of VAP. VAP is known to exhibit a wide range of non-specific radiographic abnormalities that can mimic other lung conditions, such as respiratory distress syndrome (RDS) brought on by a surfactant deficiency which can further complicate an accurate diagnosis [15].

4. Microbiological Findings

Currently, there are two techniques—invasive (bronchoscopic) and minimally invasive (tracheal aspirate)—to obtain a sample for microbiologic examination. Bronchoalveolar lavage (BAL) is the most reliable method for sampling in the neonate population and is highly specific but difficult to employ in all cases and requires experienced specialists due to the small diameter of the endotracheal tube (ETT) [16]. On the other hand, the minimally invasive method for collection of specimens through tracheal aspirates (TA) is easy to use but there is a risk of over-diagnosing VAP, which can lead to the overuse of antibiotics [17]. Baltimore [9] acknowledged the challenges associated with diagnosing ventilator-associated pneumonia (VAP) in the neonatal intensive care unit (NICU) population, namely regarding the interpretation of endotracheal tube (ETT) cultures. The colonization of the endotracheal tube by both Gram-positive and Gram-negative organisms usually happens after 48 h of intubation and MV. This is also the time when the diagnosis of VAP is initially evaluated [18][19]. Hence, distinguishing between colonization and infection is challenging, and the reliability of tracheal aspirate cultures is uncertain.

In order to find out how different professional opinions and criteria can affect the identification of VAP cases, Cordero et al. [20] undertook a study. Using the CDC classification and a positive tracheal aspirate, 37 newborns hospitalized in the NICU were diagnosed with VAP by designated infection control practitioners (ICPs). Of the 37 patients recognized by the ICPs as VAP cases, seven were diagnosed with VAP by the NICU's neonatologists. Additionally, radiologists were also asked to examine the X-rays of the 37 patients and in 8 of the 11 patients with equivocal signs of infection, they stated that there were radiographic changes suggestive of VAP. These authors came to the conclusion that a single positive tracheal aspirate does not differentiate between airway colonization and VAP, and radiography findings without conclusive clinical and laboratory evidence may be erroneous.

The signs and symptoms that most of the available definitions for VAP use are subjective and this can lead to variabilities in the reported cases between researchers [21][22]. This might be the possible explanation why the CDC introduced the so-called ventilator-associated episode (VAE) definitions to better capture the wide range of complications that might occur during mechanical ventilation [23]. VAEs are brought on by persistent rises in ventilator settings following a period of stable or declining ventilator settings. Pediatric VAE (PedVAE) is defined as an increase in the daily minimum mean airway pressure of 4 cmH_2O that is sustained for 2 calendar days after 2 days of stable or decreasing daily minimum mean airway pressure, or an increase in the FiO_2 of 25 points that is sustained for 2 days after 2 days of stable or decreasing daily minimum FiO_2s in children and neonates [24]. This type of definition and classification is not routinely implemented by NICUs but can help in the future to better differentiate the different complications that might occur in this fragile population during mechanical ventilation.

Despite improvements in other NICU care practices that have considerably increased the survival of extremely low birth weight (ELBW) (<1000 g) infants, the diagnosis and management of VAP in the NICU setting have not evolved over the past few decades. Therefore, there is an urgent need to enhance the diagnostics of VAP in this population of patients through research that emphasizes establishing more sensitive and accurate diagnostic techniques and biomarkers [25].

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