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Current Controversies in Ventilator-Associated Pneumonia

Part 1: Epidemiology and Pathophisiology

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Ventilator-associated pneumonia (VAP) is a common complication in mechanically ventilated patients and is associated with a considerable increase in morbidity and costs. Despite many years of research and important advances in our understanding of the pathogenesis of VAP, many issues surrounding the diagnosis and management of VAP remain unresolved. Indeed, even the terminology provides a point for debate with some experts preferring the term “endotracheal-tube-associated pneumonia” or even “artificial-airways-associated pneumonia”, particularly with the increased use of non-invasive ventilation.

The ongoing controversies surrounding VAP were the focus of a summit meeting just prior to the ESICM congress last October in Berlin, which gathered six European experts (Dr. Jean-Yves Fagon, France; Dr. Salvatore Maggiore, Italy; Dr. Jordi Rello, Spain; Dr. Antonio Torres, Spain; Dr. Jean-Louis Vincent, Belgium; and Dr. Tobias Welte, Germany) in this field to present an overview of the key aspects currently under debate. In this article, we will focus on ongoing controversies in the areas of epidemiology and pathophysiology discussed during that meeting, and in the next issue of ICU Management, we will concentrate on the diagnosis and management of VAP.

Agreement and Controversy in the Epidemiology of VAP

General Agreement

One aspect for which there seems to be universal agreement is that VAP is a frequent complication in mechanically ventilated patients. A recent systematic review, which included 89 studies that assessed the incidence of VAP, reported that 10- 20% of patients receiving mechanical ventilation for more than 48 hours will develop VAP (Safdar et al. 2005). Meta-analyses group results from various study types, studies of different sizes, different populations, and even using different definitions, and their conclusions are therefore limited by the nature of the studies included. Nevertheless, the 10-20% incidence seems to be fairly representative of the figures quoted in individual, high quality, prospective studies. There is also general agreement that VAP is associated with increased durations of ICU and hospital stay, with increased resource use, and increased costs, which have been calculated to be in excess of $10,000 per patient (Safdar et al. 2005).

Risk factors for VAP have been fairly widely reported and are so numerous that it is almost not worth while listing them; generally, the sicker the patient the more likely he or she is to develop VAP. Importantly, the incidence rate of VAP seems to increase with increasing duration of mechanical ventilation, reaching a peak daily risk of developing VAP of 3.3% on day 5, and then decreasing to a risk of just 1.3% by day 15 (Cook et al. 1998). More controversially, the use of antibiotics prior to intubation has been associated with a reduced risk of developing VAP, depending on the underlying microorganism.

Ongoing Controversy

In terms of epidemiology, perhaps the topic that generates most controversy is the so-called “attributable mortality”. Attributable mortality refers to the mortality that occurs directly as a result of the development of VAP. Multiple studies have assessed this issue over the last twenty years or so and provided widely differing results, with some studies reporting no increase in mortality rates and, therefore, no attributable mortality, while others suggest an increase in mortality of more than 40%! One of the problems with assessing mortality in intensive care unit (ICU) patients as a whole and in VAP patients in particular, is that multiple factors can influence outcomes in this group of seriously ill patients, including the presence of comorbid diseases, the specific infecting organism, the time of onset of disease, the severity of the host response, and whether or not the patient has received appropriate and timely antibiotic therapy. In studies assessing the impact of VAP on mortality, it is difficult to control for all the possible exogenous and endogenous factors that may influence outcomes, making interpretation of attributable mortality rates challenging.

Agreement and Controversy in the Pathophysiology of VAP

General Agreement

The classical, generally accepted factors involved in the pathophysiology of VAP are presented in Figure

1. Colonisation of the oropharyngeal cavity with abnormal hospital-acquired pathogens is considered one of the most important factors in the development of VAP. Sinus colonisation, body position, and dental plaque may also play a role. The role of gastric colonisation and aspiration is more controversial. Importantly, the endotracheal tube can influence the development of VAP by several mechanisms, including a direct impact of the cuff on the local mucosa, an enhanced capacity of tracheobronchial cells to bind Gram-negative organisms, the creation of additional binding sites for bacteria due to exposure of the basement membrane of the bronchial tree, the creation of a biofilm in the endotracheal tube serving as a reservoir for bacteria, and the presence of pooled subglottic secretions that accumulate between the cuff of the endotracheal tube and the tracheal wall leading to increased aspiration.

Focussing on the last two factors, several studies have demonstrated reduced VAP rates in patients who undergo continuous subglottic suctioning of secretions. Similarly, low cuff pressures may be associated with increased rates of VAP as this facilitates leakage of colonised subglottic secretions around the tube (Rello et al. 1996), and continuous cuff pressure monitoring may be better than manual monitoring as it provides more stable cuff pressures.

Biofilms are aggregates of microorganisms and form in endotracheal tubes over 24-72 hours, and perhaps even sooner. The bacteria in biofilms can be inoculated into the distal lower airways by aspiration or by positive pressure ventilation and can be projected up to 45 cm. This phenomenon occurs in all tube types and is most manifest at the tip of the tube. Biofilm formation is a dynamic phenomenon with several phases including attachment, growth, and detachment. Antimicrobial penetration and leukocyte function are impaired within biofilms. Several prospective studies have demonstrated that microorganisms causing VAP coincide with those cultured from biofilms (Adair et al. 1999; Feldman et al. 1999).

Ongoing Controversy

Although the formation of biofilms is widely acknowledged, a definite causal link between biofilm formation and development of VAP has still not been clearly demonstrated. Indeed, some would argue that if biofilm formation is important, why does the risk of VAP not continue to increase with time? One reason for this apparent discrepancy is that biofilm formation is just one of the many factors influencing the development of VAP.

However, if biofilms are important, should we be replacing endotracheal tubes at regular intervals? This would be practically difficult as reintubation in itself is associated with risks. Another approach may be to perform a tracheostomy; the shorter tube length and better oral hygiene reduce the problem of biofilm formation in such patients. A recent retrospective study suggested that early tracheostomy was indeed associated with a reduced incidence of VAP (Nseir et al. 2007), but other studies have suggested increased rates of VAP in patients with tracheostomy (Ibrahim et al. 2001).

Summary

Despite considerable research in the field of VAP, many areas remain controversial. In Part I of this report, we have focused on some of the ongoing controversies in the epidemiology and pathophysiology of VAP. In Part II, we will concentrate on controversies in diagnosis and antimicrobial management. Whatever the field, controversy generally suggests a lack of adequate available evidence in support of one or other argument, and results of ongoing studies should help resolve some of the current debates.

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