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Antibiotic Strategies for Prevention of Nosocomial Pulmonary Infections in Mechanically

Ventilated Patients

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Ventilator associated pneumonia (VAP) still remains a leading cause of morbidity and mortality from hospital-acquired infections. Antibiotic strategies for VAP prevention include antibiotic rotation and antibiotic mixing, preventive topical antibiotics in the respiratory tract, selective digestive decontamination (SDD) and preventive systemic antibiotic therapy. However, these strategies have limited utility in the critical care setting. It is, therefore, imperative to select the subgroup of patients that could benefit from antibiotic prevention. Rational antibiotic use is the most useful pharmacological strategy for prevention of nosocomial pneumonia in the ICU.

Introduction

Ventilator-associated pneumonia (VAP) is the specific type of nosocomial pneumonia (NP) that occurs after the first 48 hours of initiating mechanical ventilation (American Thoracic Society 1996). NP still remains a leading cause of death from hospital-acquired infections. Crude mortality rates range from 24% to 76% depending on the population and clinical setting studied (Fagon et al. 1989; Kollef 1993; Torres et al. 1990).

A variety of measures has been described for the prevention of NP (Dodek et al. 2004; Tablan et al. 2004; Torres & Carlet 2001). The non-antibiotic strategies for preventing NP have been reviewed before (Ferrer et al. 2005). The antibiotic strategies are the main topic of this review (see table 1).

Antibiotic Rotation and Antibiotic Mixing

Previous antibiotic treatment is a risk factor for the presence of potentially drug-resistant bacteria, requiring a much more potent antimicrobial regimen than would normally be employed (Trouillet et al. 1998). It is therefore important to be rational in our choice and use of antibiotics, restricting excessive and inappropriate use. When antibiotics are needed, an adequate and inexpensive measure could be to change the antibiotic class used in the ICU according to an annual schedule, to avoid the development of local resistance. Data from a study, investigating this issue for suspected gramnegative bacterial infections in patients undergoing cardiac surgery, suggested that scheduled changes can reduce the incidence of VAP attributed to antibiotic-resistant gram-negative bacteria (Kollef et al. 1997). However, when more than one antibiotic is employed, mathematical modeling indicates that sequential use of different antibiotics is always inferior to treatment strategies in which, at any given time, equal fractions of the population receive different antibiotics – a type of antibiotic use called mixing (Bergstrom et al. 2004). A recent comparison showed that a strategy of monthly rotation of antibiotics performed better than a strategy of mixing in preventing the acquisition of resistant P. Aeruginosa (Martinez et al. 2006).

Preventive Topical Antibiotics in the Respiratory Tract

Although early studies found that the application of prophylactic topical polymixin B or aminoglycosides to the lower respiratory tract reduced the incidence of nosocomial pneumonia in intubated patients, there was no overall reduction in mortality. Indeed, the microorganisms causing pneumonia were often resistant, and in many cases the pneumonia proved fatal (Feeley et al. 1975). Consequently, this method of prevention is not recommended today.

Selective Digestive Decontamination (SDD)

Bacterial oropharingeal and gastric colonisation is an important aetiopathogenic mechanism to develop VAP. The systematic use of topical antibiotics (usually polymyxin, tobramycin and amphotericin B) in the oropharynx and stomach, together with intravenous administration of cefotaxime, has been shown to reduce the incidence of nosocomial pneumonia(Abele-Horn et al. 1997; Cockerill et al. 1992; Vandenbroucke-Grauls & Vandenbroucke 1991), although not all studies have confirmed this finding (Ferrer et al. 1994; Hammond et al. 1992; Wiener et al. 1995).

The effect of SDD is difficult to assess, because the trials were performed in different types of patients, with different antibiotic agents and with non-specific clinical criteria for diagnosis of pneumonia. However, in a recent meta-analysis of 15 years of clinical research in antibiotic prophylaxis, D'Amico et al. concluded that a combination of systemic and topical antibiotics can reduce respiratory tract infections and overall mortality in critically ill patients. In this meta-analysis, the reduction in mortality was observed only when topical and systemic antibiotics were administered. The authors also concluded that the use of topical antibiotics alone would not have been justified by the available data. (D'Amico et al. 1998)

When using SDD, a microbiologic control is necessary to detect the overgrowth of resistant organisms during the prophylaxis. The long-term risk for emergence of antibiotic- resistant bacteria when topical antibiotics are administered in the digestive tract or the trachea is unclear and is potentially harmful. This method of prevention is not universally accepted for prevention of nosocomial pneumonia, although it may be useful in selected populations, such as trauma patients, immunosupressed patients (i.e. transplant patients) or in some specific risk surgical patients (i.e. esophageal cancer patients) with a high incidence of nosocomial pneumonia.

Preventive Systemic Antibiotic Therapy

Four decades ago, systemic antibiotics were used as a method of prophylaxis for nosocomial pneumonia. However, the results were discouraging (Pertersdorf et al. 1957): incidence and mortality did not differ between treated patients and the placebo group. In addition, the microorganisms involved in lung infection in the treated group were more resistant to the antibiotic resources available at that time. For these reasons, the use of systemic antibiotics as a method of VAP prevention was discontinued.

In an Italian multicentre study in 23 ICUs in 1989, Mandelli et al. analysed the utility of intravenously administrated antibiotics in the prevention of early-onset pneumonia in mechanically ventilated patients (Mandelli et al. 1989). The authors administered antibiotics during the first 24 hours of mechanical ventilation, and divided the patients into three groups: a control group, a group treated with cefoxitin, and a group treated with penicillin. The incidence of early-onset pneumonia was 6.1% in the groups with antibiotic prophylaxis, and 7.2% in the control group.

However, the administration of cefuroxime (two 1,500-mg doses, 12 hours apart after intubation) to patients with structural coma after head injury or stroke represents an effective prophylactic strategy (Sirvent et al. 1997). The incidence of microbiologically confirmed pneumonia could be reduced from 50% in the control group to 24% in the group of patients who received cefuroxime. No difference was found with regard to morbidity in the two study groups, but the authors reported a decrease in total hospital stay when patients with pneumonia were compared to those without.

Our personal view is that the administration of short–term, high doses of antibiotics is a useful preventive measure for early-onset aspiration pneumonia. We cannot extrapolate these results to late-onset pneumonia. Further investigations are necessary to determine the safety and the utility of this strategy in this type of patient.

Conclusion

Antibiotics have a limited utility for prevention of nosocomial pneumonia in the ICU. Rational antibiotic use seems the most useful pharmacological strategy for this goal.

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