Aerosolized Antibiotics for Treating Ventilator-associated Pneumonia

Essay

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Contents

List of Abbreviations

A. baumannii	:	Acinetobacter baumannii
ARDS	:	Acute respiratory distress syndrome
ASA	:	American Society of Anesthesiologists
BAL	:	Bronco alveolar lavage
CDC	:	Centers for Disease Control
CMS	:	Colistimethate sodium
COPD	:	Chronic obstructive pulmonary disease
CPIS	:	Clinical pulmonary infection score
CRP	:	C-reactive protein
DVT	:	Deep venous thrombosis
EF	:	Elastin fiber
ETT	:	Endotracheal tube
FDA	:	Food and Drug Administration
H.influenzae	:	Haemophilus influenzae
HAP	:	Hospital acquired pneumonia
HMEs	:	Heat-and-moisture exchangers
HSV	:	Herpes simplex virus
ICP	:	Infection control practitioner
ICU	:	Intensive care unit
IHI	:	Institute of healthcare improvement
ISIBTS	:	Isotonic saline instillation before tracheal suctioning
MDR	:	Multiple drug resistance
MIC	:	Minimum inhibitory concentration
MRSA	:	Methicillin-resistant Staphylococcus aureus
MS	:	Mucus shaver
MSSA	:	Methicillin-sensitive Staphylococcus aureus

List of Abbreviations (Cont.)

NIV	:	Noninvasive mechanical ventilation
NP	:	Nosocomial pneumonia
NSQIP	:	National Surgical Quality Improvement Program
P. aeruginosa	:	Pseuodomonase aeruginosa
Pc	:	Intracuff pressure
PCT	:	Pro-calcitonin
PEEP	:	Positive end expiratory pressure
PSB	:	Protected specimen brushing
PSS	:	Patient Safety in Surgery
RF	:	Respiratory failure
S. aureus	:	Staphylococcus aureus
S. pneumonia	:	Streptococcus pneumoniae
SDD	:	Selective decontamination of the digestive tract
sTREM	:	Soluble triggering receptor expressed on myeloid cells
USA	:	United State of America
VAP	:	Ventilator associated pneumonia

List of Tables

List of Figures

Introduction

Pneumonia can be generally defined as inflammation of the lung parenchyma, in which consolidation of the affected part and a filling of the alveolar air spaces with exudates, inflammatory cells and fibrin is characteristic **(Baltimore, 2003).**

The placement of an endotracheal tube increases the risk of developing ventilator-associated pneumonia (VAP) by 6-20 fold compared to critically ill patients who are not intubated **(Niederman et al., 2005).**

Development of ventilator-associated pneumonia (VAP) is undoubtedly associated with significant morbidity and mortality rates that range from 5.8% to 27% **(Valles et al., 2007).**

Traditionally administered intravenous antibiotics do not reach a bactericidal concentration in the tissue of lungs: intravenously administered antibiotics are primarily detected in respiratory segments of lungs, but not in sputum **(Hoiby, 2011) (Moroz et al., 2007).** Also complicating this therapy is a significantly increased rate of antimicrobial resistance in recent years giving further limiting treatment options (**Nicasio et al., 2008).**

Aerosol antibiotics administration offers the theoretical advantages of achieving high drug concentrations at the infection site and low systemic absorption **(Dhand, 2007),** it have been shown to be useful adjuncts to systemic antibiotic therapy for reducing morbidity and mortality due to VAP **(Luyt et al., 2009).**

In addition, aerosolized antibiotics typically have minimal systemic absorption, which can decrease the risk of adverse drug events such as nephrotoxicity with aminoglycosides and colistimethate compared with intravenous therapy (**Wood et al., 2007).**

Recent studies have indicated that aerosolized aminoglycosides and colistin may be safe and effective for the treatment of VAP caused by *P. aeruginosa* or *A. baumannii* (**Mohr et al., 2007), (Michalopoulos et al., 2008).**

Aim of the work

The Aim of this work is to discuss the management of ventilator-associated pneumonia and the role of aerosolized antibiotics as adjunctive to systemic antibiotics in the treatment of patients with VAP.

Ventilator Associated Pneumonia (VAP)

Definitions

Nosocomial pneumonia or hospital acquired pneumonia is defined as an infection of the lung parenchyma that was neither present nor incubating at the time of hospital admission **(Fishman, 2008).**

Mechanical ventilation is an essential feature of modern intensive care unit (ICU) care. Unfortunately, mechanical ventilation is associated with a substantial risk of ventilator-associated pneumonia (VAP). VAP is the most common nosocomial infection in the ICU **(Bouadmaa et al., 2012)**.

The incidence of VAP ranging from 9% to 40%, and is associated with prolonged hospitalization, increased health care costs, and a 15-45% attributable mortality **(Safdar et al., 2005).**

VAP is defined as subtype of nosocomial pneumonia developing in mechanically ventilated patients within 48hrs or more after intubation, with an endotracheal tube or tracheostomy tube with no clinical evidence suggesting the presence or probable development of pneumonia at the time of initial intubation. Based on differences in causes, VAP has been divided into early (≤96hrs of admission) and late onset (>96hrs of admission) **(Fishman, 2008).**

Incidence

In a systematic review of 38 prospective cohort and nonrandomized studies including approximately 48000

mechanically ventilated patients, the incidence of ventilator-associated pneumonia varied from 10 to 20% with twice the mortality of similar patients without VAP. The crude mortality for VAP has ranged from 13 to 70%, but most investigators have reported rates in the range of 20 to 40% **(Fishman, 2008).**

In the United States of America, VAP has recently been proposed as a quality-of-care indicator for hospitals because it is generally believed that VAP increases both morbidity and mortality of ICU patients **(Klompas and Platt, 2007).**

This belief is predominantly based on the results of observational studies, using a (matched) cohort design. However, a systematic approach to combine quantitatively the results of all available studies evaluated the association between the development of VAP and mortality does not exist **(Melsen et al., 2009).**

Pathogenesis of VAP

Understanding the pathogenesis of VAP is essential to devising strategies for prevention of these infections. Advances in the understanding of pathogenesis have led to the development of specific measures that can greatly reduce the risk of VAP **(Tablan et al., 2004).**

▫*Defense Mechanisms for Prevention of Respiratory Infection in the Normal Host*

The major defense mechanisms in the normal host include anatomic airway barriers, cough reflexes, mucus, and mucociliary clearance. The ciliated mucosa of the upper respiratory tract has a major role in removing particulate

matter and microbes that have gained access to the bronchial tree. Composition of airway secretions, an effective mucociliary reflex, and an effective cough below the terminal bronchioles, the cellular and humoral immune systems are essential components of host defense. Alveolar macrophages and leukocytes remove particulate matter as well as potential pathogens, elaborate cytokines that activate the systemic cellular immune response, and act as antigen-presenting cells to the humoral arm of immunity. Immunoglobulin and Complement inactivate and opsonize bacteria and bacterial products within the respiratory tract facilitate phagocytosis **(Strieter et al., 2003).**

▫*In the mechanically ventilated patient:*

A number of factors conspire to compromise host defenses: critical illness, comorbidities, and malnutrition impair the immune system, and, most importantly, endotracheal intubation thwarts the cough reflex, compromises mucociliary clearance, injures the tracheal epithelial surface, and provides a direct conduit for rapid access of bacteria from above into the lower respiratory tract **(Safdar et al., 2005).**

It would probably be more accurate pathogenetically to rename VAP as "Endotracheal-intubation-related pneumonia." Invasive devices and procedures and antimicrobial therapy create a favorable milieu for antimicrobial-resistant nosocomial pathogens to colonize the aerodigestive tract **(Safdar and Maki, 2004).** This combination of impaired host defenses and continuous exposure of the lower respiratory tract to large numbers of potential pathogens through the endotracheal tube (ETT)

puts the mechanically ventilated patient at great jeopardy of developing VAP **(Safdar et al., 2005).**

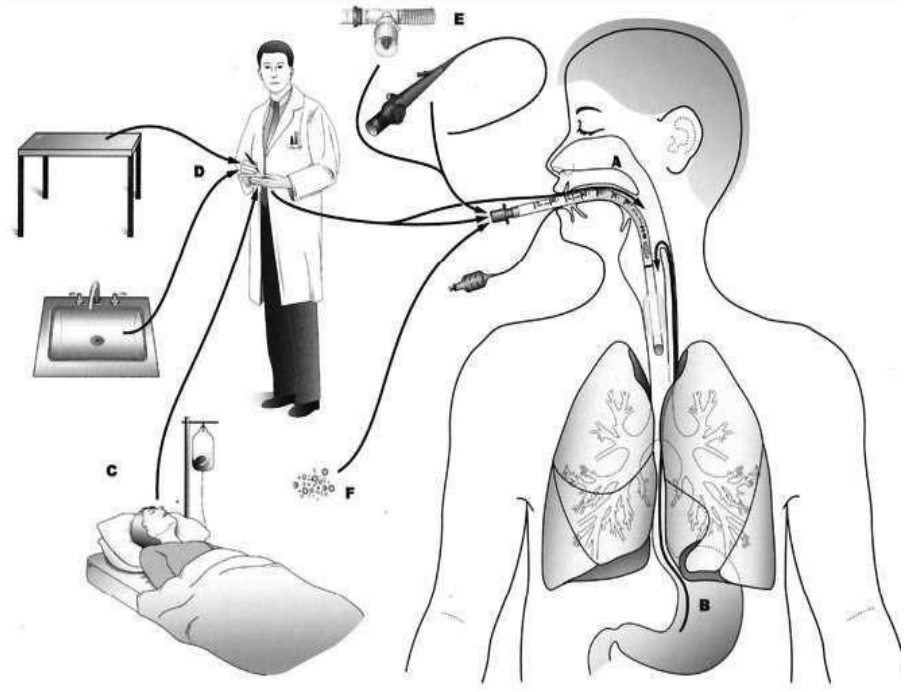

Fig.(1): Routes of colonization/infection in mechanically ventilated patients. Colonization of the aerodigestive tract may occur endogenously (A and B) or exogenously (C through F). Exogenous colonization may result in primary colonization of the oropharynx or may be the result of direct inoculation into the lower respiratory tract during manipulations of respiratory equipment (D), during using of respiratory devices (E), or from contaminated aerosols (F) **(Safdar et al., 2005).**

Oropharyngeal Colonization

The normal flora of the oropharynx in the non intubated patient without critical illness is composed predominantly of viridians streptococci, Haemophilus