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CHAPTER 41

Ventilator-associated Pneumonia

Vinayak Patki, Santosh Soans

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INTRODUCTION

Ventilator-associated pneumonia (VAP) is the most frequent life-threatening nosocomial infection in intensive care units (ICU). The diagnosis is difficult because radiological and clinical signs are inaccurate and could be associated with various respiratory diseases. The concept of infection-related ventilator-associated complication has been proposed as a surrogate of VAP to be used as a benchmark indicator of quality of care. Indeed, bundles of prevention measures are effective in decreasing the VAP rate **(Figs. 1 and 2)**. In case of VAP suspicion, respiratory secretions must be collected for bacteriological secretions before any new antimicrobials. Quantitative distal bacteriological examinations may be preferable for a more reliable diagnosis and, therefore, a more appropriate use antimicrobials. To improve the prognosis, the treatment should be adequate as soon as possible, but should avoid unnecessary broad-spectrum antimicrobials to limit antibiotic selection pressure. For empiric treatments, the selection of antimicrobials should consider the local prevalence of microorganisms along with their associated susceptibility profiles. Critically ill patients require high dosages of antimicrobials and more specifically continuous or prolonged infusions for beta-lactams. After patient stabilization, antimicrobials should be maintained for 7–8 days. The evaluation of VAP treatment based on 28-day mortality is being challenged by regulatory agencies, which are working on alternative surrogate endpoints and on trial design optimization.

ETIOLOGY OF VENTILATOR-ASSOCIATED PNEUMONIA

Early Onset

- Occurs in first four days of hospitalization
- More likely to be caused by *Moraxella catarrhalis, H. influenzae*, or *S. pneumoniae.*

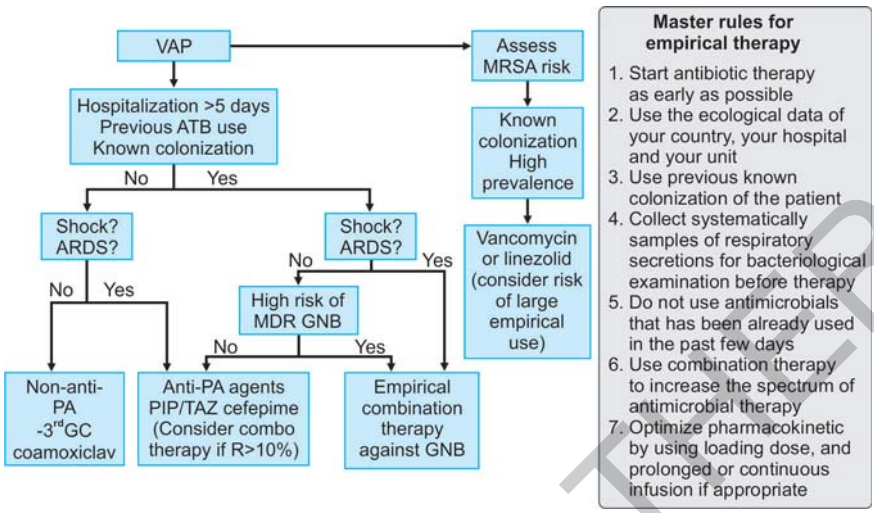

Fig. 1: Proposed strategy for empirical therapy.
3rd GC: third-generation cephalosporin; ARDS: acute respiratory distress syndrome; ATB: antibiotics; GNB: Gram-negative bacteria; MDR: multidrug-resistant; MRSA: methicillin-resistant *Staphylococcus aureus*; PA: *Pseudomonas aeruginosa*; PIP/TAZ: piperacillin-tazobactam; R: Resistant; VAP: ventilator-associated pneumonia.
Source: Timsit JF, Esaied W1, Neuville M, et al. Update on ventilator-associated pneumonia. F1000Res. 2017;6:2061.

Late Onset

- Occurs five or more days into hospitalization
- Often caused by gram-negative bacilli, or *S. aureus* (including MRSA), yeasts, fungi
- *Legionellae* and *Pneumocystis carnii.*

CHALLENGES IN VENTILATOR-ASSOCIATED PNEUMONIA PREVENTION

- Pre-existing conditions (non-modifiable risk factors):
  - Head trauma
  - Coma
  - Nutritional deficiencies
  - Immunocompromised
  - Multiorgan system failure
  - Acidosis
  - Comorbidities
  - History of smoking or pulmonary disease.

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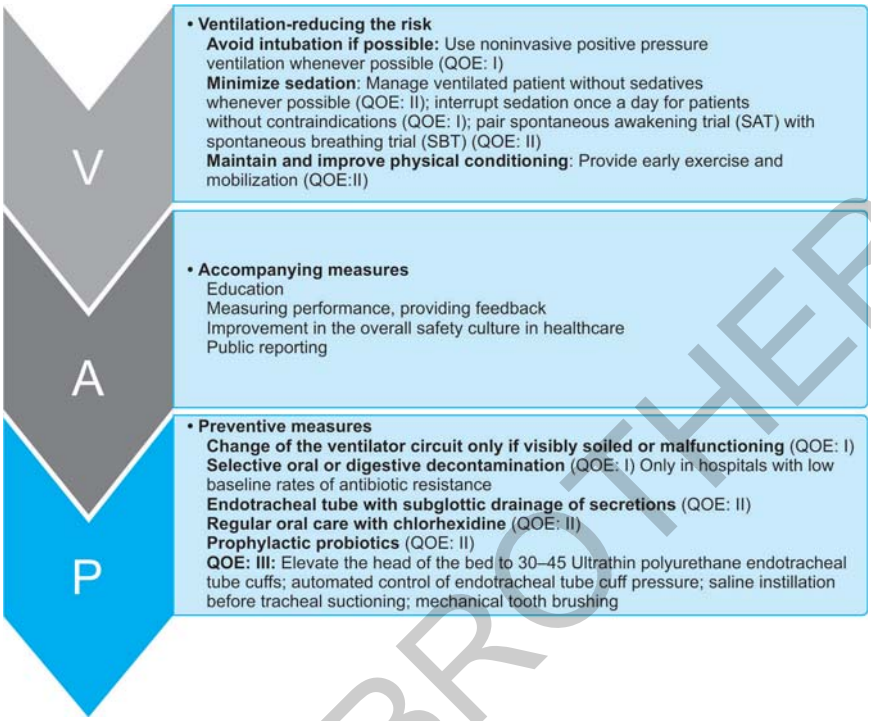

Fig. 2: Preventive measures of ventilator-associated pneumonia.
(QOE: quality of evidence)

Source: Schwebel C, Clec'h C, Magne S, et al. Safety of intrahospital transport in ventilated critically ill patients: a multicenter cohort study. Crit Care Med. 2013;41:1919-28.
Klompas M, Branson R, Eichenwald EC, et al. Strategies to prevent ventilator associated pneumonia in acute care hospitals: 2014 update. Infect Control Hosp Epidemiol. 2014; 35(Suppl 2):S133-54.

- Modifiable risk factors:
  - *Prevent aspiration of secretions*
    - Maintain elevation of head of bed (HOB) 30–45°
    - Avoid gastric over-distention
    - Avoid unplanned extubation and re-intubation
    - Use cuffed endotracheal tube with inline or subglottic suctioning
    - Encourage early mobilization of patients with physical/occupational therapy
  - *Reduce duration of ventilation*
    - Conduct "sedation vacations"
    - Assess readiness to wean from vent daily
    - Conduct spontaneous breathing trials

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- *Reduce colonization of airway and digestive tract*
  - Use noninvasive ventilation methods when possible [e.g., continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP)]
  - Use orotracheal over nasotracheal intubation
  - Nasotracheal tube may cause sinusitis, which increases VAP risk
  - Use cuffed endotracheal tube (ETT) with inline or subglottic suctioning
  - Minimizes secretions above cuff; prevents contamination of lower airway
  - Avoid acid suppressive therapy for patients not at high risk for stress ulcer or stress gastritis
  - Increases colonization of the digestive tract
- *Reduce colonization of airway and digestive tract-continued*
  - Use cuffed ETT with inline or subglottic suctioning minimizes secretions above cuff; prevents contamination of lower airway
  - Avoid acid suppressive therapy for patients not at high risk for stress ulcer or stress gastritis increases colonization of the digestive tract
- *Prevent exposure to contaminated equipment*
  - Use sterile water to rinse reusable respiratory equipment
  - Remove condensate from ventilatory circuits
  - Change ventilatory circuit only when malfunctioning or visibly soiled
  - Store and disinfect respiratory equipment effectively.

Table 1: Suggested empiric treatment options for clinically suspected ventilator-associated pneumonia in units where empiric methicillin-resistant *Staphylococcus aureus* (MRSA) coverage and double antipseudomonal/gram-negative coverage are appropriate.

A. Gram-positive antibiotics with MRSA activity	***B. Gram-negative antibiotics with antipseudomonal activity: β-lactam–based agents***	***C. Gram-negative antibiotics with antipseudomonal activity: non β-lactam–based agents***
Glycopeptides[a] Vancomycin 15 mg/kg IVq 8–12 h (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	*Antipseudomonal penicillins*[b] Piperacillin-tazobactam 4.5 g IVq 6 h[b]	*Fluoroquinolones* Ciprofloxacin 400 mg IVq 8 h Levofloxacin 750 mg IVq 24 h
OR	OR	OR

Contd…

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Contd…

A. Gram-positive antibiotics with MRSA activity	*B. Gram-negative antibiotics with antipseudomonal activity: β-lactam–based agents*	*C. Gram-negative antibiotics with anti-pseudomonal activity: non β-lactam–based agents*
Oxazolidinones Linezolid 600 mg IVq 12 h	*Cephalosporins*[b] Cefepime 2 g IVq 8 h Ceftazidime 2 g IVq 8 h	*Aminoglycosides*[a,c] Amikacin 15–20 mg/kg IVq 24 h Gentamicin 5–7 mg/kg IVq 24 h Tobramycin 5–7 mg/kg IVq 24 h
	OR	OR
	Carbapenems[b] Imipenem 500 mg IVq 6 h[d] Meropenem 1 g IVq 8 h	
	OR	
	Monobactams[f] Aztreonam 2 g IVq 8 h	*Polymyxins*[a,e] Colistin 5 mg/kg IV×1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IVq 12 h (maintenance dose) Polymyxin B 2.5–3.0 mg/kg/d divided in 2 daily IV dose

(CrCl: creatinine clearance; IV: intravenous)

Choose one gram-positive option from column A, one gram-negative option from column B, and one gram-negative option from column C. Note that the initial doses suggested in this table may need to be modified for patients with hepatic or renal dysfunction.

[a]Drug levels and adjustment of doses and/or intervals required.

[b]Extended infusions may be appropriate. Please see section XIII on pharmacokinetic/pharmacodynamic optimization of antibiotic therapy.

[c]On meta-analysis, aminoglycoside regimens were associated with lower clinical response rates with no differences in mortality.

[d]The dose may need to be lowered in patients weighing less than 70 kg to prevent seizures.

[e]Polymyxins should be reserved for settings where there is a high prevalence of multidrug resistance and local expertise in using this medication. Dosing is based on colistin-base activity (CBA); for example, one million IU of colistin is equivalent to about 30 mg of CBA, which corresponds to about 80 mg of the prodrug colistimethate. Polymyxin B (1 mg = 10,000 units).

[f]In the absence of other options, it is acceptable to use aztreonam as an adjunctive agent with another β-lactam–based agent because it has different targets within the bacterial cell wall.

Source: Kalil AC, Metersky ML, Klompas M, et al. Management of Adults With Hospital-acquired a Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016;63:e61-111.

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IAP Textbook of
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IAP Textbook of Pediatric ICU Protocols tends to be too exhaustive to read, understand and use it in PICU for day-to-day affairs. Protocol-based books are of great value not only for residents, postgraduate fellows but also for PICU consultants also to deliver evidenced-based updated management in readily available format. This not only improves quality of care in PICU but also brings uniformity in the treatment. With above-mentioned goals in the mind, under the action plan of IAP, third edition of this book was conceived to be edited by national experts in this vast field of pediatric critical care. Contributors have been many consultant pediatric intensivists and academicians from all over India. Few international pediatric intensivists have also contributed. Evidence-based and practical-oriented updated protocols have been used in easy-to-read format with flowcharts and diagrams as much as possible.

It is hoped that this edition would be available in all emergency room and pediatric intensive care units as well as medical colleges, and would be used to improve the outcome of critically ill children.

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