CHAPTER 7

Ventilator-associated pneumonia

The committee for The Japanese Respiratory Society guidelines in management of respiratory infections

The Japanese Respiratory Society

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DEFINITION

Ventilator-associated pneumonia (VAP) is defined as pneumonia in patients who have undergone tracheostomy and endotracheal intubation and developed pneumonia-related symptoms at least 48 h after the initiation of assisted respiration on a ventilator. Patients must not have contracted the pneumonia prior to endotracheal intubation and the start of mechanical ventilation.

AETIOLOGY OF VAP

Colonisation by causative microorganisms in the oral cavity has been emphasised as one of the important aetiological factors in VAP. Subglottic secretions drain through the outer layer of endotracheal tubes, enter tubes, and form a bio-film on the inside surface of the tube. As a result, pathogenic bacteria presumably are disseminated to the periphery of the respiratory tract by the ventilator. Pathogenic bacteria may also be disseminated in the respiratory tract by regurgitation of gastric contents (Fig. 1).

EPIDEMIOLOGY

The incidence of pneumonia is extremely high in the ICU. The incidence of VAP remains as high as 9–24%, 48 h or more after the start of respiratory management with a ventilator, thus showing no improvement in the incidence of VAP.1 The incidence of VAP rises to 1%/day in the ICU on non-surgical wards for adults.2 Epidemiologically, the use of a ventilator and the virulence of causative bacteria link VAP to the host and the duration of respiratory management. Risk factors include long-term respiratory management with a ventilator, re-intubation, administration of antibacterial agents before the onset of pneumonia, primary disease (burns, trauma, central nervous system diseases, respiratory diseases, and heart diseases), obvious aspiration and the use of muscle relaxants. Other risk factors for VAP include low cuff pressure in the endotracheal tube, transfer from the ICU, and a supine position. Moreover, the incidence of VAP increases up to day 5 after the start of respiratory management with a ventilator. Thereafter, the incidence of VAP has been reported to drop in critically ill patients.

DIAGNOSIS3

Confirmed diagnosis

Ventilator-associated pneumonia is diagnosed when all of the following criteria are fulfilled. Clinically the patient has (i) fever, leukocytosis, decreased PaO\textsubscript{2}; (ii) develops abnormal infiltration on chest X-rays that spreads; and (iii) has purulent respiratory secretions. Ventilator-associated pneumonia is confirmed if bacteriological examinations reveal at least one of the following findings: (i) the presence of bacteria demonstrated by direct aspiration from pulmonary lesions, and (ii) $10^3$ CFU/g tissue in histological examinations and quantitative bacterial culture tests of tissue (10°CFU/g) obtained by open lung biopsy (Fig. 2).

Probable VAP

Ventilator-associated pneumonia is suspected (i.e. probable VAP) if at least one of the following criteria are fulfilled in addition to the clinical signs listed above: (i) quantitative bacterial culture tests reveal CFU $>10^{4-5}$/mL (BAL by bronchoscopy) or CFU $>10^3$/mL (PSB); (ii) blood cultures are positive for bacterial species isolated from the lower respira-
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- Routes of bacterial invasion via the oral cavity and intestinal tract
- Retention of secretion on the top of the glottis
- Inflow from the surrounding tissues where an intubation tube was inserted
- Dissemination of discharge via airflow

**Figure 1** Aetiological mechanism of ventilator-associated pneumonia (schematic representation).

- Cough
  - Inhibitory factors: sedatives, opioid sedatives, and muscle relaxants.
- Mucosal ciliary clearance

**Figure 2** Diagnosis and treatment of ventilator-associated pneumonia

**Clinical definition of VAP**
- Fever, increased WBC count, decreased PaO₂
- Abnormal shadow on a chest X-ray
- Purulent airway secretions

**VAP suspected**
- Quantitative bacterial culture of BAL or PSB specimens (10⁴ cfu/ml or 10³ cfu/ml, respectively)
- Positive blood culture matching the results of culture of a lower respiratory tract specimen.
- Positive pleural fluid culture matching the results of culture of lower respiratory tract specimen.

**Definite diagnosis of VAP**
- Demonstration of the presence of bacteria in a specimen aspirated directly from a pulmonary abscess.
- Histological proof and a quantitative bacterial culture count of 10³ cfu/g tissue obtained from an open-lung biopsy specimen.

**Therapy targeting the causative organism**

**Empirical Therapy** (in Figure 1 Chapter 5)

**Therapy targeting the causative organism**
• Inhibitory factors: inhalation of highly concentrated oxygen, decreased moisture for inhalation, and endotracheal intubation itself.  
Trachea  
• Tracheal injuries stimulate wound healing and bacterial colonization.  
Alveoli  
• The maximum bactericidal effect is achieved at a ratio of 10 bacteria/one neutrophil.

**TREATMENT**

**Morbidity and Mortality**

Morbidity and mortality largely depend on the treatment of VAP, namely, whether adequate antibiotics (to which the causative bacteria are sensitive) have been administered. When mortality rates were compared in pneumonia patients with and without VAP whose pneumonia severity ratings were comparable, the mortality rate was 23.7% in the patients with VAP, and 17.9% in the patients without VAP, clearly demonstrating that the outcome of the patients with VAP was poorer. Duration of stay of patients who developed VAP in the ICU was prolonged, whether they survived or died.⁵

**Bacteriological Examinations**

A wide variety of bacteria are responsible for VAP, and the prevalence of causative bacteria may vary considerably with the institution or ICU. Gram-negative rod bacteria have frequently been isolated (by invasive procedures) from patients diagnosed with VAP, and several types of causative bacteria are often present in the pulmonary lesions. On the other hand, the role of anaerobes in VAP has been over-emphasised in the past, and recent scrutiny⁶ of this issue has shown that anaerobes are rarely isolated from patients with VAP even from tissue samples collected at autopsy.⁵ Some investigators have reported finding that inhalation of *Legionella* from contaminated water in the heated-wire humidifiers of a ventilator can occur and care should be exercised in this regard.

**Selection of antibacterial agents**

As a rule, it is most important to administer adequate antibacterial agents to which the causative bacteria are sensitive. When assessing the results of cultures the following criteria must be fulfilled to provide evidence that the respiratory secretions in smear specimens definitively originated in the lower respiratory tract: neutrophil count ≥ 25/LPF (low power field) and squamous epithelial cells £ 10/LPF (low power field) (Fig. 3a,b).

If VAP is suspected, it is desirable to administer antibacterial agents to which the predicted causative bacteria are sensitive as soon as possible.⁹ If patients have been treated with a wide range of antibacterial agents prior to the onset of VAP and after long-term use of a ventilator, always consider the possibility that resistant bacteria are causative bacteria. *Pseudomonas aeruginosa*, *Acinetobacter* species, and *Stenotrophomonas maltophilia* are the most important causative bacteria. There is also the possibility of MRSA infection if patients have been on a ventilator for more than five days, have been hospitalised for more than five days, or are treated with adrenocortical hormone preparations. Also, if patients have organic pulmonary diseases or are being treated with immunosuppressive agents, MRSA may be one of the causative bacteria. Antibacterial agents with anti-MRSA activity should be administered to such patients in addition to conventional antibiotics.

In any event, it is desirable to use two different types of antibacterial agents with different modes of action if there is a high risk that the causative bacteria of VAP are resistant. Resistant bacteria are more fre-
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frequently isolated from patients admitted to the ICU than from patients on other wards, and the prevalence of resistant bacteria may vary considerably from institution to institution. Taking all of the above into consideration, it is extremely important to identify current trends in the prevalence of pathogenic bacteria. To minimise the occurrence of resistant bacteria, it may be necessary to switch to antibiotics with a narrow sensitivity range, based on the results of bacterial culture tests. If the possibility of infection is ruled out, antibacterial therapy must be terminated.

PREVENTION OF VAP

Preventive measures without using drugs

1. Washing hands, gloves and gowns
   There is no strategy better than prevention. It is most important for health care workers and the hospital staff to recognise the importance of washing hands and gloves in the prevention of VAP. It is also important to establish a prevention programme and enforce it. Washing hands is one of the most effective means of preventing VAP but it is unnecessary to wear gloves and gowns during routine patient care.

2. Patients’ posture
   Due to the high risk of aspiration in the supine position, it is desirable to maintain patients in the semi-Fowler position. It is also important to avoid self-extubation and re-intubation.

3. Gastric contents
   Since pulmonary aspiration of gastric contents has been documented as one of the factors contributing to the development of VAP, it is advisable to avoid abdominal fullness. It is also advisable to avoid the use of narcotics and anticholinergic agents. In patients receiving enteral feeding, it is desirable to maintain the tip of the nasogastric tube distal to the ligament of Treitz’s. When Ferrer and associates investigated the effect of nasogastric tube size on gastroesophageal reflux and microaspiration in intubated patients,10 they found no significant difference in the incidence of VAP according to nasogastric tube size.

4. Endotracheal intubation
   The incidence of nosocomial maxillary sinusitis is quite high among patients who undergo nasogastric intubation, and thus it is advisable to avoid nasogastric intubation for 48 h or more from the standpoint of preventing VAP. As a rule, endotracheal intubation must be performed via the oral route.

5. Management of the ventilator circuit
   Instead of increasing the incidence of VAP, its incidence tended to decline when circuit exchange time was prolonged. Kollef and associates reported absolutely no difference in the incidence of VAP with or without a 7-day circuit change.11 However, this issue is still controversial, and there is no consensus concerning the optimisation of ventilator circuit exchange.

6. Effectiveness of suction of subglottic secretions
   The incidence of VAP has been reported to rise significantly when subglottic secretions are not aspirated, indicating that this procedure is very effective in preventing VAP. However, it is still uncertain whether continuous aspiration is necessary. The incidence of VAP dropped from 29% to 13% when subglottic secretions were aspirated continuously and dropped from 32.5% to 18.5% when subglottic secretions were aspirated intermittently.

7. Use of a catheter for suction
   Two types of catheters are currently available for aspiration of respiratory secretions, closed-system type catheters and open-system type disposable catheters. However, no significant difference has been observed in the incidence of VAP according to the type of catheter used. The use of closed-system type catheters has been recommended from the standpoint of medical cost and respiratory management.

8. Heated-wire humidifiers and artificial noses
   The use of so-called ‘artificial noses’ has become very popular in recent years and the incidence of VAP has been reported to decline as a result of their use.12 ‘Artificial noses’ have been reported to be safe up to one week, despite the fact that some technical problems remain to be solved, such as obstruction.

9. Changing patient posture
   Prevention of nosocomial pneumonia in intubated patients by postural change has been investigated, and special beds have been adopted for this purpose. Nevertheless, there is no convincing evidence of the effectiveness of changing patients’ posture. Moreover, respiratory therapy is still problematic, because, for example, there is a report of respiratory therapy inducing hypoxemia. Thus, the effectiveness of respiratory physical therapy is still unknown.

Preventive measures with the use of drugs

1. Acute gastric mucosal lesions
   Antacids and H₂ blockers have been administered to intubated patients to prevent so-called ‘stress ulcer’, but there is no consensus concerning the effect of changes in the pH of gastric contents on prevention of VAP. At this stage of the investigations, acidification of enteral nutrients needs to be avoided. A multicentre prospective study of VAP in acute respiratory distress syndrome (ARDS) patients revealed a higher incidence of VAP among patients treated with sucralfate.13

2. Antibacterial agents
   Administering antibacterial agents systemically prior to the onset of VAP is problematic, because resistant bacteria may emerge. Colonisation by *Pseudomonas aeruginosa* and MRSA in the lower respiratory tract, in particular, has been very closely linked to the onset of VAP. Avoidance of unnecessary administration of antibacterial agents is most important to prevent the emergence and spread of antimicrobial-resistant microorganisms in hospitals, which is the number one strategy for preventing VAP.

3. Combination therapy
   Combination therapy has been reported to be effective in preventing the emergence and spread of drug-resistant microorganisms, but there is no evidence to prove it. Combination therapy should be restricted to patients infected with several
different types of pathogenic bacteria or suspected of having contracted drug-resistant microorganisms in hospitals.

4 Prophylactic administration of antibiotics
Topical administration of antibacterial agents by inhalation therapy has not been proven to be effective in preventing VAP and inhalation therapy is also problematic because of the emergence and spread of drug-resistant microorganisms. Similarly, when the clinical effect of selective digestive tract decontamination (SDD) was scrutinised, several problems were found to be associated with its use. These included the emergence and spread of drug-resistant microorganisms as well as adverse events, and these issues remain to be solved. In spite of these problems, SDD has been reported to be effective in the prevention of VAP in trauma patients.

5 Rinsing the oral cavity
Chlorhexidine is particularly effective in the prevention and control of dental plaque and other oral diseases, and it is also effective in preventing VAP. Chlorhexidine is effective in preventing VAP in postoperative patients who have undergone cardiovascular surgery, and it is definitely a promising agent. However, there is the problem of colonisation by chlorhexidine-resistant bacteria and the risk of promoting other types of infectious diseases. Therefore, care should be exercised in regard to administration of chlorhexidine.

6 Immunoglobulin preparations
Prophylactic intravenous administration of standard immunoglobulin preparations has been reported to significantly lower the incidence of hospital-acquired pneumonia. However, their prophylactic intravenous administration must be restricted because of the high cost and the adverse events attributed to them.

REFERENCES