Review

Clinical review: Non-antibiotic strategies for preventing ventilator-associated pneumonia

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Abstract

Prevention of nosocomial pneumonia (NP) is the most important step towards reducing hospitalisation costs. The non-antibiotic prevention strategies include measures related to the correct care of the artificial airway, strategies related directly to the maintenance of the mechanical ventilator and the equipment, strategies focused in the gastrointestinal tract, and strategies related to the position of the intubated patients. While simple methods should be part of routine practice, the use of more invasive and expensive preventive measures should be used only in patients who are at high risk of NP. The appropriate use of these techniques can reduce the incidence of NP in intensive care unit patients.

Keywords airway, mechanical ventilation, pneumonia, prevention

Ventilator-associated pneumonia (VAP) is the specific type of nosocomial pneumonia (NP) that occurs after the first 48 hours of initiating mechanical ventilation, and can be further differentiated into early VAP (<5 days after tracheal intubation) and late-onset VAP (>5 days after tracheal intubation) [1]. NP still remains the leading cause of death from hospital-acquired infections. Crude mortality rates range from 24% to 76% depending on the population and clinical setting studied [2–5].

The average additional cost for NP was estimated to be as high as US$1255 per patient in 1982 [6]. A similar study in 1985 reported an average extra cost of US$2863 per patient and case of NP [7]. In trauma patients, this figure may eventually reach US$40,000 per patient [8]. It is almost impossible to directly evaluate extra costs associated with NP; however, the excess morbidity as a direct consequence of pneumonia may also be a good measurement.

Initial reports found that NP extended the intensive care unit (ICU) stay threefold [9], whereas Jimenez *et al*. estimated the excess morbidity attributable to NP as between 10 and 32 days [10]. This figure was later corroborated by other workers. Leu *et al*. reported 9.2 days of additional hospital stay [11], and Fagon *et al*. calculated the median length of stay in the ICU for the patients that developed VAP to be 21 days, versus a median of 15 days for control patients [12]. Comparable figures were also reported for trauma patients with VAP [8].

We may conclude from this data that prevention of NP is the most important step towards reducing hospitalisation costs. A variety of measures has been suggested for prevention of NP depending on the setting and the individual risk profile, non-antibiotic strategies being the main topic of this review (Table 1). These strategies are now outlined.

Conventional infection control measures

Hand washing and use of protective gowns and gloves

Cross-contamination via the inoculation of bacteria into upper and lower airways is an exogenous mechanism in the aetiopathogenesis of NP, especially in the ICU. Bacterial contamination of respiratory equipment, condensed water in ventilator-circuit tubing, and excessive manipulation of ventilator circuits are potential sources of inoculation of highly contaminated material. Hand washing is an important yet underused measure to prevent nosocomial infections.

ICU = intensive care unit; NP = nosocomial pneumonia; VAP = ventilator-associated pneumonia.

Table 1

Non-antibiotic preventive strategies for nosocomial pneumonia in mechanically ventilated patients

Conventional infection control measures	Hand washing and use of protective gowns and gloves
	Chlorhexidine oral rinse
Strategies related to the gastrointestinal tract	Stress-ulcer prophylaxis
	Gastric overdistension: nasogastric tubes
	Enteral nutrition
Strategies related to patient placement	Semirecumbent position
	Rotational bed therapy
Strategies related to the artificial airway	Respiratory airway care
	Design of endotracheal tubes: continuous subglottic aspiration
Strategies related to mechanical ventilation	Maintenance of ventilator equipment. heat and moisture exchangers
	Adjustment of sedation
	Non-invasive mechanical ventilation

Some data indicate that an antimicrobial hand-washing agent may be more effective than a non-medicated soap in reducing the rates of nosocomial infection in the ICU [13]. Hand washing is clearly simple and should be routinely adopted based on its efficacy and low cost.

As with hand washing, the use of protective gowns and gloves during patient contact has also been found to reduce the rate of acquired nosocomial infections [14], but their use appears to be most effective when directed at specific antibiotic-resistant pathogens. The use of protective gowns and gloves during patient contact can therefore not be recommended for the routine prevention of VAP, but must be considered when handling respiratory secretions or during patient contact when the patient carries an antibiotic-resistant pathogen (for instance, methicillin-resistant *Staphylococcus aureus*).

Chlorhexidine oral rinse

Bacteria accumulated in dental plaque have been implicated as pathogens of VAP when aspirated to lower airways. Chlorhexidine is an antiseptic solution for the control of dental plaque. Oropharyngeal decontamination with chlorhexidine solution has also been shown to reduce the incidence of VAP in patients undergoing cardiac surgery [15], and has also been shown to be effective in the control of colonisation and VAP caused by antibiotic-resistant bacteria [16]. The use of preventive oral washes with chlorhexidine therefore seems reasonable in selected high-risk patients, given the easy administration and the reasonable costs.

Strategies related to the gastrointestinal tract

Stress-ulcer prophylaxis

The stomach is a reservoir of nosocomial pathogens with the potential to colonise the upper respiratory tract. When the gastric pH increases from the normal levels to pH ≥ 4, microorganisms are able to multiply to high concentrations in the stomach. The gastropulmonary route of infection has therefore been proposed as an important aetiopathogenic factor, but this issue is controversial [17–20].

Mechanically ventilated patients are at risk for stress ulcers with gastrointestinal haemorrhage, and preventive treatment with H_2-blockers, antacids or sucralfate is employed routinely. However, H_2-blockers raise the intragastric pH, which in turn enhances gastric colonisation with pathogens that can cause pneumonia. The evidence of the effects of H_2-blockers on the development of VAP is conflicting, with some studies stating a definite increased incidence of NP [21] and other studies reporting no increased risk of NP [22,23]. A recently published, large, randomised study, however, failed to identify an increased risk for pneumonia in either the sucralfate group or the ranitidine group [24]. The use of sucralfate instead of H_2-blockers, however, provides less efficient anti-ulcer prophylaxis, so the risks have to be well balanced in order to provide cost-effective treatment.

Gastric overdistension: nasogastric tubes

Providing adequate enteral nutritional support to intensive care patients is an important point in the prevention of NP. It has been suggested, however, that placement of a nasogastric tube in the stomach may facilitate the reflux of bacteria from the gut, and hence may be a risk factor for the development of VAP [25]. The nasogastric tube does impair the closure of the upper oesophagus sphincter [26] and some investigators have suggested the use of smaller nasogastric tubes [27].

Gastric overdistension may facilitate the reflux of bacteria from the gut and should be avoided by reduction using narcotics and anticholinergic agents, monitoring gastric residual volumes after intragastric feeding, using gastric prokinetic agents (e.g. metoclopramide) and, when necessary, supplying

enteral feeding via nasojejunal intubation [28–30]. Gastric overdistension has especially to be avoided when non-invasive mechanical ventilation is applied. However, the effectiveness of this intervention awaits validation in clinical trials.

Nutritional support

By impairing host defence, malnutrition has been shown to be a major contributing factor to the development of pneumonia [27,31]. Providing adequate nutritional support to intensive care patients is therefore important for the prevention of NP. However, as already pointed out, enteral feeds may encourage bacterial colonisation and may increase the risk of NP by increasing the pH in the stomach. The acidification of the enteral nutrient may result in decreased bacterial colonisation of the stomach in critically ill patients. Enteral nutrition is generally preferred to parenteral feeding and is associated with fewer septic complications [32]. In addition, enteral feeding could increase the risk of NP when the patient remains in a supine body position [33].

Montecalvo *et al*. suggested the use of orojejunal feeding, bypassing the stomach, as a better method of nutrition in ICU patients [34]. However, this measure is associated with increased costs due to the catheter and the control measures required. As a general recommendation, early enteral nutrition should be provided to patients in the ICU, initially supplemented by parenteral nutrition when enteral nutrition can only be tolerated in low volumes [32].

The use of immune enhancing feeds enriched with a variety of nutrients including amino acids, arginine, glutamine, and nucleotides has recently been associated with fewer acquired infections [35]. However, whether this measure is cost-effective remains to be proven.

Strategies related to patient placement

Semirecumbent body position of patients

Aspiration of upper-airway secretions is common, even in healthy adults, in the supine position. Two studies with a radioactive-labelled gastric content showed that reflux can be reduced and subsequent aspiration avoided by positioning mechanically ventilated patients in a semirecumbent position [36,37]. An elevated head position (>30° angle) was also a protective factor of NP in an epidemiological study [38], and Kollef demonstrated that a supine body position during the first 24 hours of mechanical ventilation was an independent risk factor of mortality in patients with NP [5]. It has also been documented, in a randomised clinical trial, that a persistent semirecumbent body position reduced the incidence of NP in intubated and mechanically ventilated patients, but without a significant decrease in morbidity or mortality [33].

If there is no contraindication to the manoeuvre, the head of the bed should be elevated at an angle of 30–45° for those patients receiving mechanical ventilation and having an enteral tube in place.

Postural changes by rotating beds

Kinetic therapy that changes the patient's position may also prevent VAP by enhancing pulmonary drainage. Automated position changes during the first 5 days in the ICU reduced the incidence of early NP in both traumatic patients and non-traumatic patients [39,40]. However, this form of automated position changes does not reduce significantly the number of days of mechanical ventilation, the length of the ICU stay or the hospital stay, or the in-hospital mortality. The rotating beds method is also much more expensive than that of standard ICU beds, which limits the use of this system.

Strategies related to the artificial airway

Respiratory airway care

Not only gross aspiration, but also micro-aspiration to lower the airway can facilitate the development of NP despite the presence of an artificial airway. It is therefore important to maintain an adequate tube cuff pressure to reduce micro-aspiration. Rello *et al*. found a higher risk for VAP in patients with cuff pressures less than 20 cmH_2O [41]. Maintaining cuff pressure is clearly simple and should be routinely adapted based on its efficacy and low cost.

Two types of suction-catheter systems are available: the open, single-use system, and the closed, multiple-use system. The risk of VAP appears to be similar with both systems [30]. The main advantages of the closed, multiple-use catheters are lower costs, because daily changes are not needed [42], and decreased environmental cross-contamination.

Prolonged nasal intubation (>48 hours) should be avoided because nosocomial sinusitis may predispose the patient to pneumonia through the aspiration of infected secretions from the nasal sinuses [43], and using an endotracheal tube involves no extra cost. In cases where nasal intubation cannot be avoided (e.g. maxillar surgery), early tracheostomy may still be a cost-effective measure to prevent NP.

Re-intubation is a risk factor for VAP, as has been shown in a case–control study [44]. Careful evaluation during the weaning trial of the patient's ability to sustain spontaneous breathing might therefore reduce the number of extubation failures, and thus may also prove to be a cost-effective measure.

Design of endotracheal tubes

Stagnant oropharyngeal secretions pooled above the cuff can easily gain access to lower airways when the pressure of the cuff decreases spontaneously or there is a temporal deflation of the cuff, providing a direct route for tracheal colonisation and bolus aspiration from the oropharynx. Endotracheal tubes with an extra lumen designed to continuously suction secretions pooled above endotracheal tube cuffs are available. Continuous subglottic suctioning has been found able to decrease the incidence of NP in mechanically ventilated

Table 2

Non-antibiotic preventive strategies for nosocomial pneumonia in mechanically ventilated patients according to their effectiveness based on criteria of the Centers for Disease Control (CDC) [30] and of the European Task Force on ventilator-associated pneumonia (Task Force) [65]

	CDC	Task Force
Do not routinely change the breathing circuit more frequently than every week	Recommended	Not controversial
Humidification system: heat and moisture exchangers versus heated humidification	Unresolved	Still controversial
Avoid in-line nebulisers	Not mentioned	Still controversial
Handwashing	Recommended	Not controversial
Chlorhexidine oral rinse	Not mentioned	Not mentioned
Multiple-use, closed-system suction catheter or the single-use, open-system catheter	Unresolved	Still controversial, should be investigated
Semirecumbent body position	Recommended	Not controversial
Nasojejunal enteral nutrition	Unresolved	Should be investigated
Small-bore tubes for enteral feeding	Unresolved	Should be investigated
Orotracheal instead of nasotracheal intubation	Unresolved	Not controversial
Continuous suction of subglottic secretions	Unresolved	Still controversial, should be investigated
Cuff pressure optimisation	Not mentioned	Not controversial
Stress ulcer prophylaxis	Unresolved	Still controversial, should be investigated
Avoid gastric overdistension	Recommended	Not mentioned
Kinetic beds	Unresolved	Not mentioned
Avoid deep sedation paralytic medication	Not mentioned	Not controversial
Non-invasive mechanical ventilation	Not mentioned	Not controversial, should be investigated

patients [45], and its cost-effectiveness has recently been proven [46].

It has been suggested that biofilm formation in the tracheal tubes is a source of persistent bacterial lung colonisation [47] because the film acts as a reservoir for infecting pathogens. However, the contribution of the endotracheal tube biofilm for the pathogenesis of VAP is controversial [48,49], especially if the magnitude of the problem is related to that of other risk factors of VAP. Nevertheless, it may be of crucial importance to the pathogenesis of recurrent VAP [50,51]. Prevention of biofilm formation could be a necessary step in the successful prophylaxis of VAP. Silver-coated endotracheal tubes are able to prevent bacterial colonisation, which is a requisite for biofilm formation [52], but further investigations are needed.

Strategies related to mechanical ventilation

Maintenance of ventilator equipment: heat and moisture exchangers

Although transmission of bacteria via the respirator equipment was identified as a cause of pulmonary infections more than 15 years ago, current systems are rarely a major source of bacteria. The frequency of ventilator circuit change has not been shown to be beneficial [53]. Heat and moisture exchangers reduce the incidence of VAP by minimising the development of condensate within ventilator circuits [54], they are well tolerated by most patients, and they are easy to use. Heat and moisture exchangers should therefore be preferred to heated-water humidificators.

Sterile water should be used for rinsing nebulisation devices and other semicritical respiratory-care equipment after they have been cleaned and/or disinfected because of the risk of nosocomial transmission of *Legionella* spp. [55,56].

Adjustment of sedation

Aspiration is an important aetiopathological factor in patients with coma and an altered level of consciousness, and can significantly contribute to the development of lung infections [57,58]. Accordingly, sedative agents in patients with mechanical ventilation should be adjusted to the individual patient in order to adjust the level of sedation and the duration of sedation. A strategy based on daily interruption of

sedative-drug infusions until the patients were awake decreased the duration of mechanical ventilation and the length of stay in the ICU [59]. The use of excessive sedation could be reduced in this way.

Non-invasive mechanical ventilation and other ventilation strategies

Several recent investigations have attempted to examine directly the influence of eliminating tracheal intubation on the incidence of NP. Nourdine *et al*. report an observational cohort study to determine the influence of different types of ventilatory support on the occurrence of NP. Based on their study results, the use of non-invasive positive pressure ventilation, adjusted for severity of the illness, was associated with a lower risk of NP [60].

Brochard and coworkers, in a case–control study in France, compared the use of non-invasive ventilation in chronic obstructive pulmonary disease exacerbation and in cardiogenic pulmonary oedema with the use of conventional mechanical ventilation in an historical control population. They concluded that non-invasive mechanical ventilation is associated with a lower risk of nosocomial infections, with less antibiotic use, with a shorter length of ICU stay, and with lower mortality [61].

The benefits of non-invasive mechanical ventilation in terms of NP reduction rate have been demonstrated in different pathologies. Previous studies by Nava *et al*. in patients with chronic obstructive pulmonary disease [62] and by Antonelli *et al*. in patients with acute hypoxic respiratory failure [63] also demonstrated a lower incidence of NP. In immunosuppressed patients with pneumonitis and acute respiratory failure, early initiation of non-invasive ventilation has reduced the rate of endotracheal intubation and hospital mortality [64].

These studies suggest that prevention strategies should include efforts aimed at eliminating or at least reducing the frequency of tracheal intubation. Further investigation is needed in intubated patients regarding the impact of different ventilatory patterns, such as high or low tidal volumes, on the incidence of NP

Summary

A variety of measures for the prevention of NP have been reviewed according to their mode of action. However, the effectiveness also has to be taken into account. We shall therefore again present the reviewed measures in tabular form, according to the efficacy as it has been proposed by the Centers for Disease Control in 1994 [30] and by the European Task Force on ventilator-associated pneumonia in 2001 [65] (Table 2).

The Centers for Disease Control report comprises three classes of evidence: recommended strategies are based on strong rationale and suggestive evidence, suggested strategies may be supported by suggestive clinical or epidemiologic studies, and no recommendations are given for practices for which insufficient evidence or consensus regarding efficacy exists. The European Task Force Report attempted to ask three questions related to the prevention of NP: what is not controversial?, what is still controversial?, and what should be investigated? In Table 2, preventive measures are exposed according to their effectiveness following the aforementioned consensus.

Conclusion

The appropriate use of the discussed techniques can reduce the incidence of NP in ICU patients. While simple and effective methods without extra cost, such as hand washing or placing the patients in a semirecumbent position, should be part of routine practice, the use of more invasive and expensive preventive measures should be used only in patients who are at high risk of NP.

The impact on the incidence of NP of the nursing personal resources has not been previously evaluated and has not been included in the present review. The effectiveness of a combination of several of the proposed measures is also something to be evaluated in the future. The results of ongoing research may strengthen our preventative capabilities and help to limit further the number of patients who currently develop NP, with a reduction in medical care costs.

Competing interests

None declared.

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