



Review Article

Non-Pharmacological Prevention of Ventilator Associated Pneumonia

Luis Aurelio Díaz,^a Mireia Llauradó,^b Jordi Rello,^{b,c} and Marcos I. Restrepo^{d,*}^aGeisinger Health System, Danville, Pensilvania, United States^bCIBER de Enfermedades Respiratorias (CibeRes), Hospital Universitario Joan XXIII, Tarragona, Spain^cInstitut d'Investigació Sanitària Pere Virgili (IISPV), Universitat Rovira i Virgili, Tarragona, Spain^dVERDICT, South Texas Veterans Health Care System Audie L. Murphy Division, University of Texas Health Science Center at San Antonio, Division of Pulmonary and Critical Care Medicine, San Antonio, Texas, USA

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ABSTRACT

Ventilator-associated pneumonia (VAP) is the first cause of mortality due to nosocomial infections in the intensive care unit. Its incidence ranges from 9% to 67% of patients on mechanical ventilation. Risk factors are multiple and are associated with prolonged stays in hospital and intensive care units. Additional costs for each episode of VAP range from €9,000 to €31,000.

Thus, its prevention should be considered as a priority. This prevention could decrease associated morbidity, mortality, costs, and increase patient safety.

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Prevención no farmacológica de la neumonía asociada a ventilación mecánica

RESUMEN

La neumonía asociada a ventilación mecánica es la primera causa de mortalidad por infecciones nosocomiales en la unidad de cuidados intensivos. Su incidencia oscila entre el 9 y el 67% de los pacientes que requieren ventilación mecánica. Hay múltiples factores de riesgo asociados y aumenta significativamente la estancia en la unidad de cuidados intensivos y en el hospital. El coste adicional por cada neumonía asociada a ventilación mecánica oscila entre 9.000 y 31.000 €.

Por tanto, su prevención debe considerarse una prioridad. Ésta podría disminuir tanto la morbimortalidad asociada como el coste de la atención, y mejorar la seguridad del paciente.

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Introduction

Ventilator-associated pneumonia (VAP) is the leading cause of mortality attributable to nosocomial infections and has the greatest impact on morbidity and mortality of patients hospitalised in the intensive care unit (ICU).¹⁻⁴ Its incidence ranges from 9 to 67% of patients intubated and from 4.4 to 15.2 cases per 1,000 days of mechanical ventilation (MV) are reported.⁵

Risk factors for VAP are numerous and are divided into modifiable and non modifiable^{2,6,7} (Table 1). These are further classified as early or late, depending on whether they develop in the first 4 days of MV or later.^{8,9} The organisms responsible for early VAP are those that usually produced community-acquired pneumonia, and those responsible for late VAP are usually multiresistant organisms.^{10,11}

The attributable mortality, which is influenced by a large number of factors, may be higher than 50%, and is higher still in the group of patients with bacteraemia or infections by *Pseudomonas aeruginosa* or *Acinetobacter* sp.¹²⁻¹⁶

* Corresponding author.

E-mail address: restrepom@uthscsa.edu (M.I. Restrepo).

Several authors have shown an increase in ICU stay due to VAP of between 4.3 and 13 days.^{13,14,17} The cost for each VAP is estimated between €9,000 and €31,000.^{2,3,13,18}

Several authors have reported a decrease of 44.5 to 59% in the incidence of VAP by applying the Ventilator Bundle, which is a group of simple interventions applied jointly, as well as a reduction in days of MV and stay in ICU and in hospital.¹⁹⁻²¹

Blot et al,²² in the EVIDENCE study, conducted a questionnaire on knowledge of the guidelines for VAP prevention among nursing professionals. Respondents obtained an overall score of 41.2% correct responses.

Different studies have assessed the compliance with these guidelines. Rello et al²³ reported a breach of non-pharmacological guidelines by 19.6% of medical staff. The most common causes of non-compliance were disagreement with the results of the trials, unavailability of resources, and cost. With regard to nurses, Ricart et al²⁴ reported a 22.3% lack of adherence to guidelines. The most common reasons were the unavailability of resources, patient discomfort, disagreement with the results of trials, fear of side effects, and cost.

Table 1
Risk factors for ventilator-associated pneumonia^{2,6,7}

Modifiable factors	
1. Supine position	
2. Gastric distension	
3. Contamination of ventilator tubing	
4. Frequent transfers of the patient	
5. Low tracheal cuff pressure	
Non-modifiable factors	
1. Male gender	
2. Subjects older than 60	
3. Acute respiratory distress syndrome in adults	
4. Multiorgan failure	
5. Coma	
6. Chronic obstructive pulmonary disease	
7. Tracheotomy	
8. Reintubation	
9. Neurosurgery	
10. Head injury with intracranial pressure monitoring	

At least 2 multicentre studies have evaluated the performance of non-pharmacological measures and found high compliance, although there are differences between them, as shown in Table 2.^{25,26}

To conclude, the importance of disseminating preventive measures of VAP in order to improve results is evident.

In this article we review non-pharmacologic measures, which are cheaper and are mostly easy to implement, given the importance of dissemination to improving the consequences of VAP (Table 3).^{27,28}

General Measures for Infection Control

These measures have been aimed at preventing cross-transmission and to optimize the use of invasive devices.²⁹⁻³¹ Among the strategies to prevent VAP are a program of strict infection control that includes education of the healthcare team, proper disinfection of hands, the use of barrier methods and a microbiological surveillance protocol.^{2,32,33}

Hand Hygiene

The VAP-causing organisms, in particular gram-negative bacilli and *Staphylococcus aureus*, are those of the hospital environment and transmission to patients often occurs after colonisation of the hands of health-care personnel.³⁴⁻³⁶

The guidelines for hand hygiene in health facilities of the Centres for Disease Control and Prevention report that, according to several observational studies, compliance with hand washing recommendations among health care workers is low, around 40%.³⁰ Bonten et al^{37,38} reported that compliance with this measure is lower among physicians (nurses: 40%; physicians: 25%). However, the use of alcoholic solutions has increased compliance (48 to 66%) and has decreased the rate of nosocomial infections (from 17 to 9.9%).³⁹

Appropriate Ratio of Health Personnel

Needleman et al⁴⁰ found a strong association between a greater number of care hours per head nurse and a decrease in the incidence of 5 side effects -urinary tract infection, high digestive haemorrhage, nosocomial pneumonia, shock or cardiac arrest and "failure to

Table 2
Comparison of compliance with non-pharmacologic measures^{25,26}

	Overall		University hospitals		Non-university hospitals		Hospital beds				ICU beds			
							> 500		= 500		> 10		= 10	
	R (n = 24)	S (n = 28)	R (n = 9)	S (n = 15)	R (n = 14)	S (n = 13)	R (n = 4)	S (n = 14)	R (n = 20)	S (n = 14)	R (n = 16)	S (n = 14)	R (n = 8)	S (n = 14)
Change of respiratory tubing = 72h	96.5	71	100	80	93	62	100	79	95	64	100	79	94	64
Hot water humidifiers/humidity	57	96	67	100	47	92	50	100	55	93	50	100	56	93
Use of open suction equipment	26	96.6	45	93	7	100	0	93	25	100	12.5	100	25	92
Use of open and closed suction equipment	59		45		73		75		60		62.5		62.5	
Subglottic suction equipment	41	0	22	0	60	0	0	0	55	0	56	0	25	0
Daily endotracheal cuff pressure control	74	58	67	47	81	69	25	43	85	71	75	43	75	71
Inclined position	75.5	92.5	78	93	73	92	75	93	75	93	100	93	62	93
Non-invasive ventilation as first line of treatment	75.5	70	78	71	73	69	75	77	75	64	75	69	75	71

Values are expressed as percentages. R: De Rosa et al;²⁶ S: Smith et al;²⁵ ICU: Intensive Care Unit.

Table 3
Prevention of Ventilator-Associated Pneumonia (VAP). Summary of non-pharmacological measures

Non-pharmacologic measures	ATS/IDSA 2005 ¹	CDC 2003 ²	ETF 2001 ²⁷	CCCS 2004 ²⁸	Comments and recommendations
General measures for infection control	Yes	Yes	Yes	Not specified	Yes. Group education microbiological monitoring
Adequate ratio of health personnel	Yes	Not specified	Not specified	Not specified	Yes. An adequate nurse-patient ratio (1:1) is proposed as well as an ICU-trained respiratory therapist
Avoid unnecessary inpatient transfers	Not specified	Not specified	Not specified	Not specified	If necessary, take measures to prevent VAP
Use of non-invasive mechanical ventilation	Yes	Yes	Yes	Not specified	Yes. Alternative for decompensated COPD, hypoxemic respiratory failure and some immunocompromised patients
Early disconnection from mechanical ventilation	Yes	Not specified	Not specified	Not specified	Yes. Termination of daily sedation, implement guidelines for early extubation
Endotracheal/orogastric intubation	Yes	Yes	Yes	Yes	Yes. Orotracheal and orogastric intubation
Prevention of formation of biofilm or biolayer	Not specified	Not specified	Not specified	Not specified	Should be investigated
Drainage of subglottic secretions	Yes	Yes	Should be investigated	Yes	Yes. Especially in ICUs where the incidence of VAP is high
Tracheal cuff pressure control	Yes	Not specified	Yes	Not specified	Yes. At least 20cmH ₂ O. However, there may be leakage of secretions
Avoid changing or handling the respirator tubing	Yes	Yes	Yes	Yes	Yes. Only change them when they are visually contaminated
Inclined position	Yes	Yes	Yes	Yes	Yes. Maintains 30-45° all the time
Kinetic beds	Not specified	Should be investigated	Not specified	Yes	Yes. Indicated for postoperative and neurological patients
Enteral nutrition	Yes	Not specified	Should be investigated	Not specified	Yes, as early as possible
Gastric or post-pyloric enteral nutrition		Post-pyloric	Not Specified	Should be investigated	Not specified
Gastric if there is no evidence of alteration of gastrointestinal motility					

ATS/IDSA: American Thoracic Society/Infectious Diseases Society of America; CCCS: Canadian Critical Care Society; CDC: Centers for Disease Control and Prevention; COPD: chronic obstructive pulmonary disease; ETF: European Task Force; ICU: Intensive care unit.

rescue" (death of a patient associated with a complication)- and hospital stay.

Cho et al,⁴¹ in a retrospective study that included 124,204 patients, concluded that the overload of work for the nursing staff contributes to errors in infection control measures such as hand disinfection and isolation of patients infected with multiresistant organisms.

The involvement of respiratory therapists facilitates the success of educational programs as well as the implementation of protocols to reduce the incidence of VAP.⁴² The recommended nurse:patient ratio is 1:1. Furthermore, skilled respiratory therapists should intervene in the ICU in order to share responsibilities and work together.

Avoiding Unnecessary Inpatient Transfers

It is often necessary to move the MV patients from the ICU to other areas of the hospital for diagnostic tests and treatments. Patients may remain in a supine position for long periods of time and the ventilator tubing is often manipulated, which facilitates the aspiration of contaminated secretions. The intra-hospital transfer of patients with MV increases the risk of developing VAP.

At least 2 studies report that of patients who had at least one transfer out of ICU, 24-26% had VAP, while only 4-10% of non-transferred patients had VAP ($p = 0.001$).^{43,44} Nevertheless, no pathophysiological cause has been established that explains these findings. It is recommended that when transfer of these patients is necessary, preventive measures are taken such as suspending enteral nutrition 4h prior to transfer, preventing ventilator tubing manipulation that can lead to aspiration of condensation into the lower airway and, if not contraindicated, transferring the patient in an inclined position.

Use of Non-invasive Ventilation (NIV)

Intubated patients have up to 21 times greater risk of acquiring nosocomial pneumonia than patients without an artificial airway.⁴⁵ In addition to the depression of patient's immune system defences, the insertion of an endotracheal tube is an invasive manoeuvre that can cause injury to the tracheal mucosa and eliminate the cough reflex. This leads to the accumulation of subglottic secretions generated by bacterial inoculants and facilitates their entry into the lungs.⁴⁶⁻⁴⁸

The guidelines of the American Thoracic Society/Infectious Disease Society of America recommend NIV as an alternative for patients with acute exacerbations of chronic obstructive pulmonary disease or hypoxemic respiratory failure, and for some immunocompromised patients with respiratory failure, pulmonary infiltrates and fever. The evidence shows a resulting decrease in the incidence of nosocomial pneumonia and mortality.^{1,49,50}

The use of NIV to prevent reintubation after failed extubation is a measure being challenged. In a multicentre study in 37 centres in 8 countries, results showed that the application of NIV to patients with extubation failure did not prevent the need for reintubation nor reduced mortality. However, the time of reintubation was higher in patients treated with NIV.⁵¹ Nevertheless, this may be an alternative for extubation in patients with hypercapnia.⁵²⁻⁵⁵

Early Disconnection from Mechanical Ventilation

Although it is not always possible to avoid endotracheal intubation, there must be a strategy for its withdrawal. The reduction of MV time can reduce the incidence of VAP significantly and also reduce costs.^{56,57} Uncontrolled studies have

shown that following a protocol aimed at early extubation of ventilated patients decreases the duration of MV.⁵⁸⁻⁶¹ Marelich et al⁴² published the results of a controlled clinical trial in 385 patients in which respiratory therapists and nurses applied a protocol for early extubation, which reduced the time of MV by 2.33 days. That same year, a meta-analysis was published that recommended the use of protocols for early withdrawal of MV with the participation of nurses and respiratory therapists in its implementation.⁶² These strategies, including daily interruption of sedation (despite being a pharmacological measure) and following a protocol for early extubation, have been shown to shorten the time of MV.^{42,62-65}

Endotracheal/Orogastric Intubation

It has been shown that the insertion of catheters or tubes that prevent the drainage of the sinuses for more than 48h encourages the development of nosocomial sinusitis.^{66,67} Holzapfel et al⁶⁸ showed that, compared with nasotracheal intubation, endotracheal intubation was associated with a lower incidence of VAP. The use of the oropharyngeal airway for endotracheal intubation and orogastric tube insertion is recommended, given the decline in the incidence of sinusitis and VAP.⁶⁹⁻⁷² A controlled clinical study showed that a systematic search for maxillary sinusitis in patients intubated via the nasotrachea may reduce the incidence of VAP.⁷² However, a systematic search for sinusitis in patients with endotracheal intubation is not recommended, since the literature is inconclusive.^{67,73}

Prevention of Biofilm or Biolayer Formation

In 1986, Sottile et al⁷⁴ described the presence of a biofilm or biolayer, consisting of an aggregate of bacteria formed on the inside of the endotracheal tube that protects the organisms from the action of antibiotics and the patient's defenses. Feldman et al⁷⁵ studied the colonisation of endotracheal tubes of patients with MV and found that all tubes had a biofilm in the distal third. Adair et al⁷⁶ investigated the antibiotic resistance of endotracheal tube biofilm and pulmonary organisms in VAP, and concluded that 70% of patients with VAP had the same organisms in the biofilm of the tube and in tracheal secretions.

Another strategy is to prevent or reduce the formation of biofilm, which has been accomplished by the design of silver-coated endotracheal tubes.⁷⁷ Silver prevents the formation of the biofilm, has a bactericidal action, reduces bacterial load and decreases inflammation.⁷⁷ Rello et al⁷⁸ reported that the use of silver-coated endotracheal tube was safe, delayed the colonisation of the endotracheal tube, reduces the formation of biofilm and decreases the bacterial load. They concluded that controlled trials are needed to establish the efficacy of the device in the prevention of VAP. In November 2007, the Food and Drug Administration approved the sale of silver-coated endotracheal tubes. In a controlled clinical trial with 2003 patients intubated for more than 24 hours, Kollef et al⁷⁹ concluded that those with whom silver-coated endotracheal tubes were used had a lower incidence of microbiologically proven VAP ($p = 0.03$). Furthermore, the development of VAP was delayed with silver-coated endotracheal tubes as compared to similar non-silver tubes ($p = 0.005$).

Drainage of Subglottic Secretions

One of the main mechanisms of development of VAP is bacterial colonisation of the oropharynx and aspiration of subglottic

secretions.⁸⁰ The presence of the endotracheal tube leads to the accumulation of secretions from the oropharynx or gastrointestinal tract above the endotracheal tube cuff⁴⁶ and, despite adequate control of cuff pressure, there may be aspiration.⁸¹ It is therefore logical that continuous suctioning of subglottic secretions could prevent the onset of VAP. For this purpose, an endotracheal tube with an additional dorsal canal was designed to allow continuous or intermittent aspiration of subglottic secretions (HI-LO Evac-tube, Mallinckrodt, Hazelwood, Missouri, USA). At least 5 controlled clinical trials and a meta-analysis have shown a decrease in the incidence of VAP, especially early onset, but not in mortality, ICU stay or time of MV.⁸²⁻⁸⁵ It is important to note that the back channel for aspiration of secretions can become clogged. Rello et al⁴⁷ observed a dysfunction in continuous aspiration of secretions in the tube in 34% of patients. Furthermore, a recent publication that investigated the cause of this dysfunction found that the most common cause was prolapse of the tracheal mucosa through the subglottic suction port, which exposes the patient to the risk of tracheal injury in that area.⁸⁶ This study was conducted in patients with continuous aspiration of subglottic secretions, so it remains to be seen whether this dysfunction occurs with intermittent suction.

Based on limited evidence, there is the Microcuff™ endotracheal tube, which incorporates an ultra-thin polyurethane cuff (7 μ , as compared to 50 μ in conventional cuffs) and provides a better airway seal, thereby reducing the formation of folds when the cuff is inflated.⁸⁷ On the other hand, the SealGuard Evac endotracheal tube (Mallinckrodt) incorporates a polyurethane cuff and suction of subglottic secretions.⁸⁸ A prospective, randomised study of 280 patients compared the conventional tube with the SealGuard Evac endotracheal tube (Mallinckrodt), and found a significant 3-fold decrease in the incidence of early and late VAP using intermittent subglottic secretion drainage.⁸⁸

In a randomised study, Bouza et al⁸⁹ compared conventional suction of subglottic secretions continuously in patients undergoing cardiac surgery, and concluded that patients with more than 48 hours of MV and subglottic suctioning had a lower incidence of VAP ($p = 0.03$) and a decrease in the use of antibiotics ($p < 0.001$).

Endotracheal Cuff Pressure Control

Several central features of the endotracheal tube include sealing the airway in such a way that does not allow air leakage, not compromising the perfusion of the tracheal mucosa, and preventing the passage of subglottic secretions to the lower airway.^{47,90,91} Conventional high-volume, low pressure endotracheal cuffs cannot prevent microaspiration even with pressures up to 60cmH₂O.⁹² Despite automatic pressure control of the balloon, there may be passage of secretions into the lower airway.⁸¹ Given the available information, we recommend keeping the endotracheal cuff balloon pressure between 20 and 30cmH₂O, although microaspiration prevention is not ideal, since cuff pressures above 30cmH₂O can cause tracheal injury.^{1,6,93-97}

Prevent Changes or Manipulations of the Ventilator Tubing

The condensation that appears in the ventilator tubing that uses humidifiers, especially hot water, runs the risk of contamination. Craven et al⁹⁸ showed a higher incidence of VAP in patients whose ventilator circuits were changed every 24 hours as compared with those for whom the change was made at 48h. Kollef⁹⁹ then reported

that changing ventilator tubing every 7 days did not increase the incidence of VAP, but it did increase costs.

Appropriate procedures must be implemented to drain condensation and prevent medical personnel from facilitating movement of condensation to the lower airway due to patient movements or by the nozzles.¹⁰⁰⁻¹⁰² As a result, it is recommended to change them when they are visually contaminated with blood, vomit or purulent secretions.^{1,103,104}

With regard to hot water humidifiers and heat and moisture exchangers, the latter can reduce the build-up of condensation and the colonisation of the tubing, but has not been associated with a decreased incidence of VAP.^{103,105,106}

Inclined Position

At least 3 radioactive tagging studies of stomach contents have shown that gastric reflux and subsequent aspiration in patients with MV could be avoided by placement in an inclined position.^{92,107,108} The supine position facilitates the aspiration of subglottic secretions, especially when the patient is receiving enteral nutrition.^{92,109,110} Drakulovic et al¹¹⁰ demonstrated the benefit of the inclined position (45°), which decreased the rate of orogastric aspiration and the incidence of VAP (3 times less).^{110,111} A tendency toward decreased mortality was observed as compared with the neutral supine position (0°).¹¹⁰ Recently, Van Nieuwenhove et al.,¹¹² in a controlled clinical trial, questioned the feasibility of keeping patients in an inclined position (45°) continuously and its usefulness in preventing VAP. In Holland 221 patients from four ICUs were randomised into 2 groups: one with the head at 45° and the other at 10°. The goal of maintaining the head at 45° for 85% of the time was not achieved, and the difference obtained between the 2 groups (28 versus 10°) did not prevent the development of VAP.

The inclined position is recommended, especially in patients receiving enteral nutrition, due to the low cost that this intervention requires, its easy implementation and its established efficacy.

Kinetic Beds

Patients hospitalised in the ICU are, due to confinement to bed, at greater risk of pulmonary complications (atelectasis, poor handling of secretions, etc.). The use of kinetic beds has been proposed, which allows continuous rotation of these patients in order to decrease the incidence of VAP. Controlled clinical trials have shown a reduced risk of VAP in surgical and neurosurgical patients, but not in medical patients.^{113,114} However, there are barriers to the use of these beds: the higher cost, the possibility of disconnection of intravenous catheters and the difficulty in controlling pressure zones.¹¹³

Enteral Nutrition

It is well known that malnutrition in critically ill patients causes damage to the immune system, dysfunction of the respiratory impulse and respiratory muscle weakness, leading to prolonged ventilator dependency and increased morbidity and mortality,¹¹⁵ in addition to being associated with a longer hospital stay.^{115,116} Although no controlled clinical trials demonstrate significant and permanent gains in important clinical outcomes such as duration of mechanical ventilation, the ICU stay and

mortality, nutritional support is considered an integral component of what should be the optimal treatment of patients in the ICU.^{117,118}

However, this treatment is not without complications. Enteral nutrition has been considered a risk factor for VAP because of the possibility of aspiration of gastric contents.^{2,92,109,117,119,120} A recent publication describes the establishment and monitoring of an enteral nutrition protocol, including the inclined position (> 30°), which achieved the goal of enteral nutrition in 85% of patients (78% before the protocol) and the incidence of VAP was reduced from 6.8 to 3.2 per 1,000 days of MV.¹²¹

In a systematic review of the medical literature that compared enteral with parenteral nutrition in critically ill patients with respect to case development, there was no statistically significant difference in mortality, but there was a significant increase in infectious complications such as VAP, aspiration pneumonia, urinary tract infections, bacteraemia, intra-abdominal abscesses and catheter-associated sepsis, as well as increases in costs.^{122,123}

A recent meta-analysis of 11 controlled clinical trials conducted in the ICU, which evaluated mortality, the risk of aspiration and pneumonia, found no significant differences in the evolution and concluded that, in critically ill patients without evidence of gastrointestinal dysmotility, the use of post-pyloric nutrition not associated with clinical benefits.¹²⁴

Conclusions

This article reviews the evidence related to non-pharmacologic measures that have demonstrated an impact on the prevention of VAP. It is recommended to implement some of these interventions jointly to achieve better results.

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Conflicts of Interest

Dr. Restrepo is a speaker for Ortho-McNeil-Janssen, Johnson & Johnson, Pfizer, Inc. and Covidien BARD. He also belongs to the advisory committee of Ortho-McNeil-Janssen and Johnson & Johnson.

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