A review of oral preventative strategies to reduce ventilator-associated pneumonia

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ABSTRACT

Aim: This article evaluates the evidence for and efficacy of the use of mechanical hygiene and chlorhexidine in the prevention of ventilator-associated pneumonia (VAP).

Search strategies: Inclusion criteria: primary research articles; randomized controlled trials; systematic reviews. Exclusion criteria: quasi-experimental trials; opinion articles. Search Engines: PubMed; CINAHL; and EBSCO.

Background: VAP is the commonest infection found in critically ill patients who are mechanically ventilated. It is associated with increased mortality, increased length of stay in intensive care and increased costs.

Relevance to clinical practice: VAP is a health care-associated infection consistent with the presence of an endotracheal tube and mechanical ventilation for greater than 48 h. Efforts aimed at reducing infection rates include oral decontamination and mechanical hygiene to control the bacteria responsible, since there is an association between changes in bacteria found in the oropharynx and its development. Tooth brushing and the use of an oral antiseptic such as chlorhexidine gluconate are increasingly recommended in ventilator care bundles.

Conclusion: While there have been a number of studies conducted evaluating the efficacy of both approaches, there is limited evidence to support their use. The frequency of oral decontamination and mechanical hygiene interventions have not been established and chlorhexidine 2% seems to be more effective compared to weaker concentrations, but data is mainly confined to patients following cardiothoracic surgery.

Key words: chlorhexidine gluconate • critical care nursing • effectiveness of health care intervention • infection prevention • oral care • oral decontamination • oral hygiene • tooth brushing • ventilator-associated pneumonia

INTRODUCTION

An accurate diagnosis of ventilator-associated pneumonia (VAP) remains a challenge, with no consensus on a reference definition (CDC, 2012; Hunter, 2012). VAP is usually suspected if the patient was intubated and ventilated at the time or within 48 h before the onset of ventilation and uses a combination of radiological, clinical and laboratory criteria (CDC 2012). However, this definition is under review because of its subjectivity and complexity and any new definition is likely to differentiate between a ventilator-associated condition and an infection-related ventilator-associated complication (CDC, 2012). The incidence of VAP ranges from 10% to 30% (Labeau et al., 2011) with a crude mortality that may exceed 50% and is associated with increased prolonged intensive care and hospital stay, increased cost and delays in recovery (Scannapieco et al., 2003; Vincent, 2003; Chan et al., 2007; Chan et al., 2007). However, the attributable mortality, defined as the total mortality minus the mortality associated with the underlying disease process (Muscedere et al., 2010), may be much lower, somewhere in the region of 4-4% (Bekaert et al., 2011) to an absolute attributable mortality of 13.5% (Muscedere et al., 2010). Methodological issues such as the heterogeneity in studies, the associated mortality of the underlying disease and the absence of a reference standard for VAP make assessment of attributable mortality challenging (Muscedere et al., 2010; Bekaert et al., 2011). The cost of VAP has been estimated as between €9000 and €31 000 (Diaz et al. 2009). In critically ill patients and especially those who are mechanically ventilated, oral flora changes from predominantly Viridans streptococci, Haemophilus species and anaerobes (Chlebicki...
and Safdar, 2007) to a predominance of aerobic Gram-negative bacilli and *Staphylococcus aureus* predisposing them to the development of VAP (Safdar et al., 2005). The most important mechanism in the development of VAP is aspiration of oropharyngeal organisms into the distal bronchi (Chlebicki and Safdar, 2007).

The prevention of VAP needs to address three primary issues: aspiration, aerodigestive tract colonisation and contaminated equipment (Rebmann and Greene, 2010). Part of that approach is the implementation of a comprehensive oral hygiene programme. Two possible options for reducing the incidence of VAP include selective digestive decontamination (SDD) and selective oral decontamination (SOD) using oral antimicrobials. In SDD, non-absorbable antibiotics are administered topically through the oral cavity and nasogastric tubes to reduce the bacterial load in the upper GI and buccal cavity and is combined with a short course of intravenous antibiotics. This is based on the contention that the stomach is an important reservoir of bacteria that cause VAP (Safdar et al., 2005). Prophylaxis includes parenteral and enteral antimicrobials administration, and hygiene, combined with surveillance cultures of throat and rectal swabs to monitor the efficacy and compliance of enteral antimicrobials, and is termed the full four-component protocol of SDD (Silvestri et al., 2009). This treatment has received mixed reviews. There is evidence that it reduces bacteria load but it may also lead to antibiotic-resistant bacteria (CDC, 2003). However, previous meta-analyses of SDD using a combination of topical and systemic prophylactic antibiotics found a significant reduction in rates of VAP among treated patients (Liberati et al., 2009), while a systematic review found that the use of the full protocol reduced overall mortality in critically ill patients (Silvestri et al., 2009). Localized SOD in the form of bactericidal medication to the buccal cavity has also received mixed results for similar reasons and further research is required into both these treatment strategies (National Institute for Clinical Excellence, 2008). Other recommendations include elevated head of the bed, subglottic secretion drainage and closed endotracheal suctioning (Muscedere et al., 2008).

An alternative strategy to SDD is oral decontamination and effective oral hygiene. They may be thought of as a continuum from the use of antibiotics, antiseptics, such as chlorhexidine and povidone-iodine through to the use of toothbrushes alone and combinations thereof. The CDC (2003) stated that planned, structured oral hygiene programmes will reduce the rate of nosocomial pneumonia in ventilated intensive care patients (Schleder et al., 2002). They advocate a combined approach of frequent tooth brushing and the use of antiseptics. They also recommend the use of subglottic suction to clear the oropharynx of pooled secretions. Recent guidelines recommend that all ventilator care bundles include oral antisepsis (NICE, 2008). The use of antiseptics is shown to be more effective in targeting localized sites and is not associated with the same incidence of bacterial resistance as drug therapy (Chan et al., 2007). Antiseptics are broad spectrum antibacterial agents that control plaque formation and inhibit the growth of bacteria (Grap et al., 2004), as opposed to antibiotics which are bactericidal. In addition to the use of antiseptics, mechanical tooth brushing is also a method to reduce bacteria in the buccal cavity. There are various methods of providing oral care including the use of sponge swabs, toothbrushes, electric as well as manual and the more advanced suction toothbrush. This article will evaluate the efficacy of mechanical hygiene and oral decontamination in reducing the incidence of VAP.

While oral care is considered by nurses as important and is prioritized, it is perceived as a difficult and unpleasant task, with oral status deteriorating irrespective of interventions (Binkley et al., 2004; Rello et al., 2007).

### SEARCH STRATEGIES

The following inclusion criteria were used: primary research articles; randomized controlled trials (RCTs); systematic reviews; limited from 2007 to 2012. Exclusion criteria: quasi-experimental trials; opinion articles. The following electronic data bases were searched using combinations of the keywords oral hygiene, oral care, oral decontamination, VAP, chlorhexidine and tooth brushing, PubMed, CINAHL, EBSCO and EMBASE. This yielded a total of six systematic reviews, two meta-analyses, two papers which claimed to be both and four RCTs which were primarily used in this literature review.

### MECHANICAL HYGIENE

Tooth brushing is recommended as the first stage in an oral hygiene regime to loosen dental plaque and mechanically remove it with the secondary effect of reducing the protective biofilm generated by the bacteria residing there. Subsequent treatment using antiseptics may follow to combat the bacterial loading. Oropharyngeal suctioning and other VAP preventative strategies may also help in the reduction of VAP. Regular oral hygiene has only a minimal effect on reducing plaque (Jones et al., 2011).

Patients arrive in critical care units with pre-existing oral hygiene issues including high levels of dental plaque (Jones et al. 2011). This predisposes
to the development of VAP as plaque is bacteria laden. The first to identify the link between oral hygiene and VAP was Scannapieco et al. (1992). They determined that the rate of dental plaque and/or buccal cavity colonization by bacteria was significantly higher in intensive care patients than those who attended a dental clinic. In subsequent comparison between tracheal aspirate cultures and dental plaque, Scannapieco et al. (1992) demonstrated a correlation between the two suggesting that the bacteria which grow on dental plaque contribute to the colonization of the respiratory tract proposing that dental plaque could be an important reservoir for bacterial growth (Fourrier et al., 2000). Jones et al. (2011) further support the findings of Scannapieco et al. (1992). In a prospective study Fourrier et al. (2000) examined the incidence of dental plaque in patients admitted to intensive care, the rate of plaque growth and the incidence of colonization of the plaque by bacteria. The bacteria were either present on admission or developed during patients’ stay. Over a 10-day period of data collection there was an increase in plaque formation and the loading of plaque by bacteria increased. Similar to Scannapieco et al. (1992), Fourrier et al. (2000) and later El-Solh et al. (2004) established a positive correlation between a positive buccal culture and a significant increase in nosocomial respiratory infections indicating that bacterial buccal load may be a source of infection in intensive care patients.

In a systematic review Scannapieco et al. (2003) examined the association between periodontal disease and bacterial pneumonia in high-risk patients such as those with chronic lung disease and intensive care patients. They indicated that bacteria grow on the plaque deposits on teeth and develop a biofilm, and suggest that this helps to protect them from topical antiseptic and antibiotic use (El-Solh et al., 2004; Kishimoto, 2007). They concluded that the data imply the development of nosocomial pneumonia in high-risk patients such as intensive care patients may be linked to poor oral hygiene. They claim that the incidence of nosocomial pneumonia through the removal of dental plaque may be reduced by improving oral hygiene either through mechanical approaches such as tooth brushing or by chemical means such as the use of antiseptics.

Kishimoto (2007) advocates the use of tooth brushing to reduce the incidence of bacteria. Tooth brushing is more advantageous compared to antiseptic use alone as tooth cleaning mechanically removes dental plaque, thus removing the environment that promotes bacterial growth. It also prevents the development of the protective biofilm. This enables subsequent treatment by antiseptic drug therapies to be more effective.

In a randomized controlled clinical trial, Munro et al. (2009) examined the effectiveness of chlorhexidine over tooth brushing. They found that chlorhexidine significantly reduced the incidence of VAP \(p > 0.006\) as measured by the clinical pulmonary infection score (CPIS) whilst tooth brushing had no effect on development of VAP. The CPIS tool is a method of determining VAP. It is non-invasive and is dependent on measurement of physiological variables. There are criticisms of the CPIS tool in that it is not sensitive as a predictor of VAP (Zilberberg and Shorr, 2010). The study mentions the sampling of tracheal aspirate for culture, but did not report culture outcome. Patients received other VAP protective strategies which may have confounded the results.

In a single blinded RCT, Pobo et al. (2009) compared the effectiveness of electric tooth brushing to standard oral care on the incidence of VAP and secondary outcomes such as ventilator free days, length of stay, antibiotic free days and hospital mortality. Patients in both study arms received a number of additional elements that are recommended in the prevention of VAP, such as head elevation \(\geq 30^\circ\), monitoring of endotracheal cuff pressure and stress ulcer prophylaxis. The study concluded that the use of electric toothbrush combined with chlorhexidine mouthwash did not reduce the incidence of VAP.

Utilizing both manual cleaning techniques using proprietary oral swabs and electric toothbrushes, and VAP measured via the CPIS tool, in a single randomized pilot study Yao et al. (2011) determined that there was a significant reduction in VAP. The experimental group also received an elevated head position \(30–45^\circ\) and oropharyngeal suctioning both before and after brushing but it is not clear whether the control group also received these interventions.

In a study by Needleman et al. (2011), two groups received identical care with the exception of a powered toothbrush in the experimental group whilst the control group received oral hygiene with the use of sponge and no toothbrush. The study intended to assess the effectiveness of the use of an electric toothbrush on dental plaque. They concluded that powered toothbrushes are highly efficient at removing dental plaque and reducing the pathogens associated with VAP \(p = 0.006\). They recommend the use of powered toothbrushes to remove VAP-associated pathogens and to explore further the direct impact on the incidence of VAP.

It is not clear from the literature the frequency of tooth brushing that is required, whether toothpaste should be used and if so what type and whether
electric tooth brushes are more effective than manual, since it is generally not made explicit if toothpaste was used during tooth brushing. The Needleman et al. (2011) study used chlorhexidine at the time of tooth brushing whilst Yao et al. (2011) used water. There is evidence that toothpaste interacts with chlorhexidine rendering it ineffective and that a separation of 2 h between the use of tooth brushing and chlorhexidine rinse is recommended (Kolahi and Soolari, 2006). There is no consensus in the literature as to the optimal frequency of tooth brushing for effectively reducing the incidence of VAP with recommendations ranging from two (Yao et al., 2011) to four times a day. Further research is required to establish the frequency and duration of tooth brushing as well as use and type of toothpaste.

**ORAL DECONTAMINATION**

Daily oral care with chlorhexidine has been recently added to the ventilator care bundle because of its inhibitory properties on dental plaque formation and gingivitis and based on recent evidence (Institute for Health Care Improvement, 2012). It is a pharmacological strategy to control oral colonization by VAP organisms (Brennan et al., 2004). In Europe, chlorhexidine is widely used by nurses in oral hygiene in the form of mouthwashes or gels (Jones et al., 2004; Rello et al., 2007) but less so in the USA, where only 17% of nurses surveyed used this product (Binkley et al., 2004). This is likely because the use of an antiseptic agent is optional in guidelines used for the prevention of VAP (CDC, 2003) but also because these are not consistently or uniformly implemented (Cason et al., 2007) and the optional use of antiseptics in oral hygiene continues (Johnson et al., 2012).

A meta-analysis of seven RCTs evaluating the effectiveness of topical chlorhexidine use in reducing incidences of VAP compared to placebo or standard care for its prevention, concluded that it is effective (Chlebicki and Safdar, 2007). Overall the reduction in VAP was 9-11% in the treatment group compared with 11-81% in the comparison group. However, in a sub-group analysis, this effect was seen more clearly in cardiothoracic patients who accounted for 443 of 805 patients in the studies reviewed. One explanation for this is that these patients tend to be intubated and ventilated for a much shorter time. In one study comprising of 127 patients, a 2% solution was compared to a usual concentration of 0.12% or 0.2%. This could have confounded the results in favour of the intervention because there is evidence that a 2% solution is much more effective than weaker ones (Chan et al., 2007).

In a systematic review and meta-analysis of eleven RCTs totalling 3242 patients, seven trials totalling 2144 patients Chan et al., (2007) evaluated the effectiveness of antiseptic oral decontamination concluding that chlorhexidine was not effective in trials using 0.2% concentration but was effective at 2%. Similar to the study by Chlebicki and Safdar (2007), medical patents derive a more modest effect, suggesting that specific surgical or trauma patients often have fewer comorbidities compared to medical or mixed patients. They suggest that more evidence is needed before firm conclusions can be made on the full effect of oral decontamination. This is one of the two studies relied on by the Institute for Health Care Improvement (2012) in making recommendations in relation to chlorhexidine use.

A more recent systematic review and meta-analysis concluded that there is strong evidence to support the use of chlorhexidine in the prevention of VAP, particularly in cardiosurgical patients at 2% but the protective effect was less strong at lesser concentrations and in mixed patient population (Labeau et al., 2011). However, at present the recommended concentration for use in patients is 0.12% indicating guidelines need revision (Institute for Health Care Improvement, 2012). In contrast, Pileggi et al. (2011) showed a significant (31%) reduction in VAP even using the lowest concentration of chlorhexidine but with lower efficacy in non-specialized intensive care units (ICUs). However, in this meta-analysis of 28 RCTs, this was not statistically significant and there was no overall reduction in mortality. The conclusions from these systematic reviews and meta-analyses are that cardiosurgical patients benefit more from the use of chlorhexidine and that the currently recommended concentration is likely to be ineffective.

Under the auspices of the Canadian Critical Care Society comprehensive VAP clinical practice guidelines were developed by carrying out a comprehensive review of RCTs and systematic reviews of RCTs (Muscedere et al., 2008). The evidence base is only sufficiently strong to indicate that chlorhexidine should be considered since it may decrease the incidence of VAP. These were published before the latest meta-analysis. However, one of the studies that this recommendation is based on used 2% chlorhexidine as well as bed elevation, making it difficult to conclude that reductions in the incidence of VAP were due to the use of chlorhexidine alone. In an RCT (Scannapieco et al., 2009) reported a reduction in the number of *S. aureus* using chlorhexidine in a concentration of 0.12% but its use did not reduce the total number of potential pathogens. Gram-positive pathogens such as *S. aureus* are more sensitive to chlorhexidine than Gram-negative ones.
Studies analysing the effectiveness of chlorhexidine in reducing VAP suffer from a number of methodological issues. There is substantial clinical heterogeneity, with different patient populations, concentration and frequency of application of chlorhexidine and definition of VAP (Chlebicki and Safdar, 2007). The effectiveness of 0.12% chlorhexidine formulations remains equivocal with studies reporting reductions, absence of effect as well as increases in anaerobic Gram-negative bacilli while 0.12% chlorhexidine formulations at frequencies of up to three times daily appears to be uniformly ineffective (Lam et al., 2012). Sample sizes tend to be small and blinding is problematic and often not reported. While there is some evidence that at concentrations of 2% chlorhexidine may have some benefit, patients often receive multi-faceted interventions such as use of the semirecumbent position, stress ulcer prophylaxis and subglottic drainage which may confound trial results.

**FUTURE DIRECTIONS**

The role that biofilm has in the development of VAP warrants further investigation as it may be a more significant contributory factor than oropharyngeal contamination. The evidence that secondary to colonization with bacteria, endotracheal tubes are a source of VAP is further supported by evidence that silver-coated endotracheal tubes significantly reduce the incidence of VAP (Dallas and Kollef, 2009). However, more robust clinical trials are needed to establish the efficacy of such tubes in preventing VAP. It may be more accurate to refer to the problem not as VAP but as endotracheal-tube-associated pneumonia since the problem is the ETT and not the ventilator (Safdar et al., 2005).

VAP is the most formidable of all infections that are dealt with in ICU and needs a multi-faceted approach (Safdar et al., 2005). Combining an antibacterial approach with something that prevents mucus from binding to the tube is one such possibility. This is consistent with the conclusion that the most effective way to prevent VAP is to decrease the duration of intubation and mechanical ventilation (Rebmann and Greene, 2010), more specifically the duration of tracheal intubation (Hunter, 2012). The most effective claim that can be made in relation to the routine use of chlorhexidine is that it shows a decreased trend in the prevention of VAP but there is evidence that it is more effective in cardiosurgical patients and at a strength of 2%. The protective effect is less strong at lesser concentrations and in mixed patients.

There is a trend now of just using chlorhexidine and assuming that it will fix the problem of oropharyngeal contamination (Safdar et al., 2005). If oral decontamination is used then it should be in addition to other evidence-based preventative measures such as hand hygiene, control of antibiotic use, strategies that speed up extubation and having a culture of surveillance (Wiener-Kronish and Dorr, 2008) as well as more specific recommendations such as those contained in ventilator care bundles. Although the evidence is not strong, the use of ventilator care bundles is currently recommended as best practice in reducing the incidence of VAP (Lawrence and Fulbrook, 2011). Elevation of the head of the bed of between 30 and 45° is also recommended (How-to Guide, 2012) as part of such bundles. The semirecumbent position may be associated with a decreased incidence of VAP (Mucedere et al., 2008). While antiseptic oral decontamination is inexpensive and relatively safe, it may yet have a role in reducing the incidence of VAP but that role has yet to be fully evaluated. There is concern that given time and antimicrobial use, resistance will inevitably emerge (Dallas and Kollef, 2009). It is likely that chlorhexidine may simply delay the development of VAP rather than prevent it and may explain its greater effectiveness in cardiothoracic patients (Dallas and Kollef, 2009). A multi-faceted approach is essential.

**CONCLUSION**

VAP continues to be a leading cause of mortality and morbidity in patients hospitalized in the ICU. It is also linked to increased length of stay and consequently increased costs. Ventilator care bundles have been developed in an attempt to reduce the incidence of VAP. Central to such an initiative is mechanical hygiene and oral decontamination.

Patients are admitted to the ICU with oral hygiene issues such as bacteria growing on dental plaque contributing to the development of VAP. Mechanical hygiene is an attempt to remove plaque. There is some evidence that tooth brushing is effective at removing plaque and that electric toothbrushes are more effective compared to standard oral care. However, the frequency of such an intervention and the use or not of toothpaste has not been established.

There is some evidence supporting the use of chlorhexidine in reducing the incidence of VAP but this effect is strongest in cardiosurgical patients. If oral decontamination is to be incorporated into ventilator care bundles current research suggests that a 2% concentration is more effective compared to lesser concentrations.

Current studies suffer from a number of methodological issues that make it difficult to evaluate the
efficacy of mechanical hygiene and oral decontamination. These include heterogeneous populations, inconsistency in the definition of VAP, small sample sizes and patients receiving multi-faceted interventions. Future research investigating the efficacy of mechanical hygiene and oral decontamination should consistently define VAP, include a more homogenous population and control for such variables as bed elevation and sub-glottic drainage since it is difficult to come to conclusions when more than one intervention is made.

WHAT IS KNOWN ABOUT THIS TOPIC

- Ventilator-associated pneumonia is associated with increased mortality, increased stay in intensive care and prolonged hospital stay.
- Plaque formation and the loading of plaque by bacteria is increased in critically ill patients.
- The incidence of nosocomial pneumonia through the removal of dental plaque may be reduced by improving oral hygiene.

WHAT THIS PAPER ADDS

- In relation to mechanical removal, patients receive other VAP protective strategies which may confound results.
- Chlorhexidine in concentrations of 2% seem to be more effective.
- Mechanical hygiene and oral decontamination strategies are less effective in patients with comorbidities.
- Methodological issues make it difficult to evaluate the efficacy of mechanical hygiene and oral decontamination strategies.

REFERENCES


