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The Intensive Care Society recommended bundle of interventions for the prevention of ventilator-associated pneumonia

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Abstract

Ventilator-associated pneumonia is an important healthcare-associated infection. Interventions for the prevention of ventilator-associated pneumonia are often used within bundles of care. Recent evidence has challenged widespread practices mandating a review of subject. This article outlines guidance for ventilator-associated pneumonia prevention.

Keywords

Ventilator-associated pneumonia, prevention, bundles, healthcare-associated infection

Introduction

Ventilator-associated pneumonia (VAP) is a common healthcare-associated infection (HCAI) occurring in 10–20% of patients mechanically ventilated in the ICU.[1,2] Although the exact attributable mortality has proved difficult to define, it has significant consequences with increased mortality, the length of ICU stay and hospital stay and an increase in healthcare costs.[3–5] Furthermore, within a global setting of worsening antimicrobial resistance, the treatment of respiratory tract infections represents a significant burden of antimicrobials in the ICU.

VAP occurs because the obtunded, endotracheally intubated patient is at risk of inoculation of the lower respiratory tract with microorganisms. The source of the potential inoculate includes the oropharynx, subglottic area, sinuses and gastrointestinal (GI) tract. Access to the lower respiratory tract occurs around the endotracheal tube (ETT) cuff.[6] Interventions to prevent VAP aim either to prevent repeated microaspiration, colonisation of upper airway and GI tract with potentially pathogenic organisms, or contamination of ventilator/respiratory equipment.

Bundles of care are evidenced-based practices that are grouped together to encourage the consistent delivery of these practices. These bundles are common in the ICU and have been developed for the prevention of VAP.[7,8] Recent evidence has challenged current widespread practice and so up to date recommendations on interventions for the prevention of VAP are needed.

Recommended bundle of interventions for the prevention of VAP

Elevation of head of bed (30°–45°)

Aspiration of oropharyngeal or gastric contents is implicated in the pathogenesis of VAP.[9] Nursing the mechanically ventilated patient in a semi-recumbent position aims to prevent aspiration of gastric content. In an observational study in which aspiration was measured using technectium (Tc)-99m labelled sulphur colloid placed into the stomach, patients who were nursed supine in comparison to those nursed at 45°, had significantly more evidence of aspiration.[10] In a randomised trial, 90 patients were either nursed in a supine position or at 45°.[11] Although the primary endpoint

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was clinically diagnosed VAP, which is highly vulnerable to bias in an unblinded trial, there were significant reductions in clinically and microbiologically diagnosed VAP (76% and 78% reductions respectively). It is, however, unusual for patients to be nursed in a fully supine position, therefore in a further randomised trial patients were nursed at either 10° (supine) or 45° (semi-recumbent).[12] The primary endpoint was the incidence of VAP, defined by a rigorous criteria based on culture of bronchoalveolar lavage (BAL) fluid. Compliance with the correct degree of elevation was poor, particularly in the semi-recumbent group. Supine patients were elevated at $14.8° \pm 7.1°$ and semi-recumbent patients at $26.5° \pm 8.2°$ by day 7. There was no significant difference in the occurrence of VAP between the two groups.

In summary, VAP is associated with nursing the patient in a supine position. While elevating the bed to 45° has been shown to reduce VAP, practically this does not appear to be achievable. The exact degree of elevation needed to prevent VAP is unclear but aiming to avoid the supine position and raising the bed to at least 30° is recommended.

Daily sedation interruption and assessment of readiness to extubate

Sedation of endotracheally intubated patients is universal to ensure patient comfort. Continuous sedation can lead to accumulation of sedatives and over-sedation, and is associated with increased duration of mechanical ventilation.[13] Since intubation and mechanical ventilation predisposes patients to VAP, reducing the duration of mechanical ventilation should reduce that time at risk for developing VAP. Two strategies that have been used to reduce the duration of mechanical ventilation are daily sedation interruption (DSI) and daily spontaneous breathing trials (SBT).

In a trial of 128 patients randomised to either DSI to the point of awakening or standard care (in which sedation was managed according to clinical discretion), the median duration of mechanical ventilation was significantly lower in patients with DSI (4.9 vs. 7.3 days, $p = 0.004$).[14] Furthermore, the ICU length of stay was shorter for the intervention group (6.4 vs. 9.9 days, $p = 0.02$). In contrast, another trial compared DSI in the context of a protocolised regimen of individualised sedation. Patients were randomised to protocolised sedation plus DSI or only protocolised sedation.[15] There was no significant difference between the two groups in time to extubation, duration of the ICU stay or duration of the hospital stay. In a recent meta-analysis of DSI, there was insufficient evidence of benefit in terms of duration of mechanical ventilation, mortality or length of the ICU or hospital stay.[16] The authors advised caution in interpreting these results as negative for DSI, since the trend is towards a reduction in these outcomes but with wide confidence intervals.

In a trial combining DSI with SBT, in comparison with standard sedation practice and SBT, patients in the intervention arm had more days without mechanical ventilation at 28 days (14.7 vs. 11.6 days) and shorter duration of the ICU length of stay (median 9.1 vs. 12.9 days) and hospital stay (median 14.9 vs. 19.2 days).[17]

The protocolised approach to judging when a patient is ready to wean and ultimately to tolerate extubation has been the subject of meta-analysis. Blackwood et al.[18] examined trials that compared weaning protocol interventions to standard care. Protocolised weaning was associated with a 25% (95% CI 9–39%) reduction in the mean duration of mechanical ventilation.

Trials of sedation and weaning protocols predominantly focus on duration of the mechanical ventilation and ICU stay. In a prospective before-after study of a nurse-led sedation protocol, there were significantly fewer episodes of VAP amongst patients with the nurse-led protocol (6% vs. 15%).[19] Furthermore in another non-randomised, before-after study of an intervention of spontaneous awakening trials and SBT to determine the preventability of ventilator-associated events (VAE), spontaneous awakening trials and SBT were associated with a significant reduction in duration of mechanical ventilation and a reduction in VAE risk per episode of mechanical ventilation (odds ratio (OR) 0.63, 95% CI 0.42–0.97) and infection-related ventilator-associated complications (OR 0.35, 95% CI 0.17–0.71).[20] Although this study determines the preventability of a clinical entity that does not solely represent VAP, it further highlights that reducing time on mechanical ventilation limits the time that the patient is at risk of its complications.

In conclusion, there is sufficient evidence to support a strategy of DSI to prevent over-sedation and liberation from mechanical ventilation through SBT.

Use of subglottic secretion drainage

Secretions are potentially able to bypass the ETT cuff, especially when it is deflated. Secretions that pool above the ETT but below the vocal cords are a potential source of pathogens that could cause VAP. Since conventional suction methods cannot access this area, ETT tubes that have a designated suction catheter for this space allows this pool to be drained.

The benefits of subglottic secretion drainage (SSD) have been analysed in three meta-analyses with a consistent signal of a reduction in VAP. Dezflulian et al. demonstrated a relative risk reduction of 0.51 (95% CI 0.37–0.71) and excluding one trial that was the predominant source of heterogeneity, SSD reduced the duration of mechanical ventilation by 2 days (95% CI 1.7–2.3) and length of the ICU stay by 3 days (95% CI 2.1–3.9).[21] The reduction in VAP was also demonstrated in another meta-analysis with

a relative risk reduction of 0.56 (95% CI 0.45–0.69) with an effect that reduced early-VAP but not late-VAP.[22] In a further meta-analysis of 13 RCTs with no heterogeneity (I^2 0%), the risk ratio for VAP was 0.55 (95% CI 0.46–0.66) for SSD.[23] This meta-analysis also found a reduced length of the ICU stay of 1.52 days (95% CI –2.94 – −0.11). In a recent RCT performed subsequent to the meta-analyses, SSD was associated with not only a reduction in microbiologically confirmed VAP but also a reduction in the percentage of days in the ICU on antibiotic therapy.[24]

SSD remains an intervention for the prevention of VAP with a consistent signal of reducing VAP rates and is therefore recommended in this bundle.

Avoidance of scheduled ventilator circuit changes

Humidified gases condense in the ventilator circuitry and are at risk of becoming contaminated. Frequent changes of the circuit is a risk factor for the development of VAP.[25] This may be due to the increased manipulation of the ventilator tubing causing contaminated secretions to enter the bronchial tree via the ETT lumen. Several studies have aimed to determine the optimum interval at which tubing should be changed. In an observational study of separate periods of circuit changes every 2 days, 7 days or 30 days, the highest VAP rate occurred at 2 days and the lowest at 7 days.[26] In two RCTs, one using heat humidification[27] and another using heat moisture exchange filters,[28] routine 7-day circuit changes were compared to no routine changes, in which circuits were changed at the clinicians discretion if faulty or visibly soiled. There were no significant differences in VAP between the two-trial arms in either trial. The cost implications were significant, with 247 circuit changes occurring in the 7-day group at a cost of $7410 in comparison to 11 circuit changes in the group with no routine changes, at a cost of $330.[27]

The evidence suggests that frequent circuit changes are associated with an increased incidence of VAP, probably due to the excessive manipulation of the ventilator circuit. Changing the ventilator circuit only when clinically indicated such as visible soiling or when faulty, does not increase the incidence of VAP and would result in significant cost savings compared to routine changing of circuit.

Discussion

The diagnosis of VAP remains a challenge with a wide range of diagnostic criteria used. The evidence considered for these recommendations includes studies with differing diagnostic criteria for VAP. It is beyond the scope of this work to grade the quality of the evidence in this very broad area of interventions. Furthermore, the range of methods used to diagnose VAP in the UK ICUs varies widely.[29] The method of respiratory sampling can influence the rate of VAP within an ICU, with a diagnostic strategy based on clinical judgement and endotracheal aspirate being associated with an over-diagnosis of VAP in comparison to a strategy based on BAL sampling.[30] This has significant implications for antibiotic therapy and efforts to improve antibiotic stewardship in a time of growing concern over antimicrobial resistance.

Recent evidence has called into question the widespread use of oral chlorhexidine to decontaminate the oropharynx. Oral chlorhexidine use has been associated with a reduction in respiratory tract infections in the ICU in high profile meta-analyses.[31,32] These meta-analyses included RCTs in both cardiac surgery and general ICU patients, and are heavily influenced by large trials that show benefit in cardiac surgery patients.[33–35] In a meta-analysis by Klompas et al.,[36] cardiac surgery patients accounted for 51% of patients. In non-cardiac patients, the reduction in VAP was not significant with a relative risk of 0.78 (95% CI 0.60–1.02). Analysis of mortality endpoints demonstrated a non-significant trend towards an increase in mortality with chlorhexidine use in non-cardiac surgery patients with a relative risk of 1.13 (95% CI 0.99–1.29). In another recent meta-analysis, three strategies of decontamination, selective decontamination of the digestive tract, selective oral decontamination and oral decontamination with chlorhexidine, were analysed for mortality endpoints in general ICU patients.[37] Decontamination with oral chlorhexidine was associated with an increase in mortality with an odds ratio of 1.25 (95% CI 1.05–1.50). The reason for the possible increase in mortality is unclear.

In light of this recent evidence, the ICS does not recommend the use of oral chlorhexidine in non-cardiac surgery patients. Furthermore, the National Institute for Health and Care Excellence (NICE) has recently withdrawn its VAP prevention recommendations in light of this new evidence.[7]

There is a paucity of evidence on outcomes for tooth brushing alone, since many studies have been performed in the context of chlorhexidine use as standard care.[38] Oral hygiene remains important in ventilated patients in order to remove dental plaque (which may lead to gingivitis or dental caries), for patient comfort, and to promote a 'normal' microbial community. Oral hygiene should continue to be provided despite stopping using chlorhexidine. Concerns exist that toothbrushing could lead to both transient bacteraemia and aspiration. Bacteraemia occurred in 23% of 98 individuals in an observational study,[39] and 93% of these resolved within 20 min of toothbrushing. While toothbrushing in the ICU patients is under-researched, there is no clear signal of adverse outcome from toothbrushing.[38] In the absence of a clear evidence base for optimal oral care, removal of dental plaque and other debris from teeth, tongue and oral mucosa with a foam swab or a toothbrush appears unlikely to be harmful. Pragmatically,

minimising the amount of water on the brush or swab may reduce the volume of any material aspirated.

Gastrointestinal stress ulcer prophylaxis (SUP) has been included in other VAP bundles.[7,8] Raising the pH of the stomach contents promotes colonisation with potentially pathogenic organisms and so SUP remains a balance of risk between GI bleeding and developing VAP. Clinically important bleeding has been demonstrated to occur in 1.5% of patients, with risk factors identified as respiratory failure and coagulopathy.[40] There is a suggestion that the rate of GI bleeding has fallen in recent years with changing ICU practices.[41] In a meta-analysis that aimed to determine the effects of enteral feeding on SUP, the enterally fed subgroup did not have a significant benefit in reducing GI bleeding (OR 1.26, 95% CI 0.42–3.7) and furthermore there was in increased risk of developing VAP (OR 2.81, 95% CI 1.20–6.56).[42] In an observational study of two 15-month periods during which SUP was used in only one, there was no significant difference in GI bleeding, VAP or mortality.[43]

Despite the low incidence of GI bleeding, proton pump inhibitors (PPI) are widely used.[44] Meta-analysis of PPI in comparison to histamine H2 receptor blockers (H2RB) has not demonstrated a difference in terms of reduction in GI bleeding.[45] In a large pharmacoepidemiological observational study of 35,312 mechanically ventilated patients receiving PPI or H2RB, PPI use was associated with more GI bleeding compared to H2RB (5.9% vs. 2.1%), more VAP (38.6% vs. 27%) and more *Clostridium difficile* (3.8% vs. 2.2%).[46]

There is insufficient evidence to give a clear recommendation of the use of SUP and the potential protective benefits of enteral feeding. We therefore recommend consideration of the risk profile of GI bleeding in each patient with judicious use of SUP in patients considered to be at risk of GI bleeding.

Summary

This bundle of interventions for the prevention of VAP aims to highlight interventions, which if implemented consistently, could reduce VAP rates. Importantly this update does not recommend the use of oral chlorhexidine outside of cardiac surgery patients. The change in the use of oral chlorhexidine should act as a word of caution that these recommendations are bounded by current evidence and best practice at the time of writing and so will be subject to change as further developments are made in this field.

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