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Infection Prevention in the ICU

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This article highlights four interventions that combat healthcare-associated infections (HCAI), have a good evidence base, and are relatively inexpensive and cost-effective. However, they are not widely implemented into clinical practice.

HCAI, such as ventilator-associated pneumonia (VAP) and catheter-related bloodstream infections (CRBSI), are serious, expensive and continue to present a major challenge for intensive care units (ICU) worldwide. They have the power to undermine some of the most significant medical and surgical advances in patient care.

VAP is the most common infection occurring in mechanically ventilated patients after admission to ICU. It is associated with a modest attributable mortality (Melsen et al. 2013), increased ICU length of stay and cost. VAP also contributes significantly to the burden of antibiotic prescribing, and may add to the emergence of multi-drug resistant bacteria.

The difficulties of defining VAP may well explain some of the observed differences in incidence seen internationally. It is possible to 'define VAP away' by making the definition so specific. Partly with this in mind, the Centers for Disease Control recently suggested new definitions to reorientate the focus of surveillance from pneumonia alone to more general complications of mechanical ventilation (Klompas 2013). Introduction of high-impact interventions or bundles has gone some way to reducing VAP rates, but with no clear associated mortality reduction (Morris et al, 2011; Roquilly et al 2015).The aetiology of VAP is predominantly micro-aspiration of microbial pathogens past the endotracheal cuff of contaminated material from the oropharynx into the lower respiratory tract (Zolfaghari and Wyncoll, 2011) (see Figure 1).

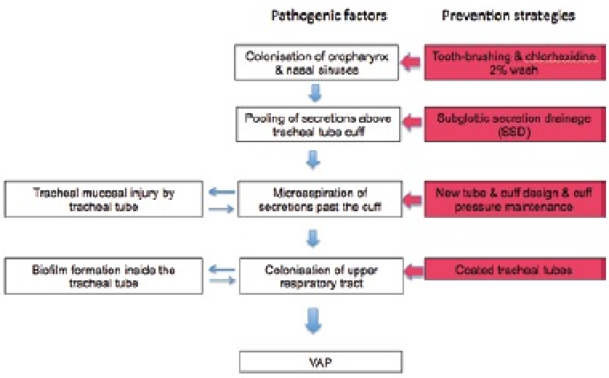

Figure 1. Diagram summarising the pathogenic processes leading to VAP (in black) and the preventative measures to combat each step (in red)
Source: Zolfaghari and Wyncoll 2011

Considerable progress has been made in the last decade in reducing CRBSI. Increased awareness and simple interventions in central venous catheter (CVC) insertion and management have reduced the number of BSI, but there is still opportunity for further improvement (Bion et al. 2013).

In a recent UK-based national survey, the prevalence of BSI was reported as 0.5%, comprising 7.3% of all HCAI detected. More than two-thirds of BSI occurred in patients with a vascular access device (Health Protection Agency 2012). There remains a considerable attributable mortality (up to 11%) and cost associated with CRBSI, including an additional ICU length of stay of between 9 and 12 days (Schwebel et al, 2012).

In this article, four simple interventions are highlighted below.

1) Subglottic Secretion Drainage (SSD)

SSD removes secretions that pool above the endotracheal tube cuff and cause micro-aspiration. Specially designed endotracheal tubes are widely available, which allow continuous or intermittent drainage of secretions via a separate lumen that opens above the cuff. The latest meta-analysis of 13 randomised controlled trials (RCT) involving ~2,500 patients, showed a reduced ICU length of stay, decreased duration of mechanical ventilation and increased time to first occurrence of VAP with SSD. There were no increased adverse events, concluding that SSD is effective for the prevention of VAP (Muscedere et al. 2011). The most recent RCT, involving 352 critically ill patients in five ICUs within a single centre, showed a 50% reduction in microbiologically-confirmed VAP with SSD. Importantly, a marked reduction in antibiotic use was also observed (Damas et al. 2015).

Although incorporated into some recent VAP prevention bundles (Department of Health 2010) SSD uptake into clinical practice has been sluggish. This is possibly due to previous conflicting clinical trial evidence, concerns over endotracheal tube design and the higher acquisition cost associated with these tubes (~10 Euros versus 1 Euro). With newer generation tubes, early concerns about increased stiffness and size have been overcome. Similarly, concerns over suction damage to the tracheal mucosa have been mitigated, now that intermittent suctioning is possible because of more effective cuff design. Hopefully with novel innovation and more compelling evidence, the implementation of SSD may become more widespread (Zolfaghari and Wyncoll 2011).

2) Continuous Cuff Pressure Control

Maintaining correct endotracheal tube cuff pressure is important in intubated patients, as low pressures (< 20mmHg) predispose to micro-aspiration and high pressure (>30mmHg) causes tracheal ischaemia. Despite routine manual control of cuff pressure with a manometer, in one study only 18% of patients had cuff pressures within normal range throughout an eight-hour period. Under-inflation was observed in 54% of patients, with at least a single over-inflation in 73% (Nseir et al 2009). Manual checking of cuff pressure may cause deflation or over-inflation, and aspiration of secretions frequently occurs during this manoeuvre. Devices are now available which control cuff pressure continuously and automatically; they are easy to use and save staff time. A RCT, proofof- concept study, showed continuous cuff pressure control resulted in reduced microaspiration as measured by tracheal pepsin aspirates, reduced tracheobronchial bacterial counts and reduced VAP (Nseir et al. 2011). A previous underpowered RCT showed a nonsignificant, 24% reduction in VAP, between intermittent and continuous cuff pressure monitoring (Valencia et al. 2007). The most recent 284-patient, pseudo-randomised trial, suggested that continuous cuff pressure control, compared with intermittent control using a manometer, reduced VAP by 49%, particularly when used in conjunction with SSD (Lorente et al. 2014).

A number of continuous cuff pressure monitors are available. These may be pneumatic (Nosten®, Leved, St-Maur, France, used in Nseir 2011) or electronic (VBM Medizintechnik GmbH, Sulz am Neckar, Germany, used by Lorrente 2014). A recent study of 64 patients showed the pneumatic device was effective in controlling cuff pressure in patients intubated for more than 48 hours with reduced incidence of cuff under-, or over-inflation (Jaillette et al. 2013). Improving technology may increase the use of continuous cuff pressure monitoring, with the availability of modules incorporated into the ventilator (Hamilton Medical Inc., Bonaduz, Switzerland) or disposable devices (Portex®, Smiths Medical St Paul, MN, USA). This is an evolving area. Devices used to regulate the cuff pressure, and also the endotracheal tube cuff itself, may be important in determining the effectiveness of cuff pressure monitoring.

Selective digestive tract decontamination and selective oropharyngeal decontamination have a good evidence base, and are associated with a reduction in hospital mortality (de Smet et al. 2009). However, there remains an ongoing fear about its introduction and widespread systemic antibiotic use, particularly with the increasing emergence of highly resistant gramnegative infections (Klompas 2015).

3) Chlorhexidine-Impregnated Dressings

CRBSIs may increase mortality and ICU length of stay. They also have a considerable financial impact, costing approximately $24,000 per infection (Schwebel et al. 2012). Implementation of evidence-based ‘bundles’ for insertion of CVCs and their subsequent management has reduced the rate of CRBSI. Chlorhexidine gluconate-impregnated dressings release chlorhexidine on to the skin and reduce bacterial colonisation of the skin at the catheter insertion site, reducing extraluminal infection. Large multi-centre RCTs involving nearly 8,000 catheters have shown that chlorhexidine gluconate-impregnated sponges and dressings (Timsit et al. 2009; 2012) reduce CRBSI. A recent meta-analysis identified nine studies, including 6,067 patients and 11,214 catheterisations, showing that use of chlorhexidine-impregnated dressings prevents catheter colonisation and CRBSI by 48% and 45% respectively. The benefit is greatest in short-term catheters where the extra-luminal route of infection predominates (Safdar et al. 2014). These data suggest the use of such dressings, alongside usual preventative measures, should be incorporated into best practice guidelines. A dressing or sponge costs approximately 5 Euros; when weighed against the attributable cost of CRBSI, it is difficult to justify not using them.

4) Chlorhexidine Daily Washes

Patient colonisation with multi-drug-resistantorganisms (MDRO) such as MRSA, MSSA, *E. coli* and *Klebsiella* may lead to HCAIs. Although improved awareness, screening and recognition of these bacteria have been effective in reducing their prevalence, daily washing of all patients with chlorhexidine cloths may improve this further. Chlorhexidine gluconate has antiseptic and residual antibacterial activity. Its use may decrease the cutaneous microbial burden, preventing secondary environmental contamination. Decontamination of the skin reduces the entry of organisms into the blood through CVCs and may reduce hospital-acquired BSI. A multi-centre RCT of 7,700 patients found that daily washing with chlorhexidine-impregnated cloths significantly reduced hospital-acquired BSI, and also the presence of MDRO (Climo et al. 2013). Similar results have been seen amongst paediatric ICU populations, where a 36% reduction in BSI was observed with daily chlorhexidine bathing in 4,947 children greater than two-months old (Milstone et al. 2013). A large, multi-centre, cluster RCT compared screening and isolation, targeted, and universal decontamination, to prevent infection in the ICU. Nearly 75,000 patients from 74 different ICUs were enrolled and randomised into each of the three groups. Decontamination was achieved by daily bathing with chlorhexidine-impregnated cloths and intranasal mupiricin. Universal decontamina- tion reduced rates of MRSA, clinical isolates and BSI from any pathogen more effectively than in the other groups (relative risk reduction 37% and 47% respectively; Huang et al. 2013).

Interestingly a recent randomised, crossover study looked at 9,340 patients in a single centre, and found no benefit from daily chlorhexidine bathing in the reduction of CRBSIs, catheter-associated urinary tract infections, VAP or *Clostridium difficile* infection (Noto et al. 2015). It is important to note though that the effectiveness of chlorhexidine bathing against urinary tract infections, VAP and *clostridium difficile* infection is limited, and their use as clinical end-points is therefore very unconventional. Genuine concerns exist as to chlorhexidine resistance, allergy and the added cost (Pittett and Angus 2015). However, the current benefits, particularly where MDRO incidence is high, would appear to override these concerns.

Recent national evidence-based guidelines for preventing HCAI in the UK now recommend consideration of chlorhexidine-impregnated sponge dressing and daily bathing with chlorhexidine in patients with CVCs to prevent CRBSI (Loveday et al. 2014).

Cost-Effectiveness

Considerable financial investment in sophisticated ventilators in the ICU, to optimise ventilator support and minimise adverse effects, may well be justifiable given the significance and value of human life. At the vital interface between these two is the endotracheal tube. For a comparatively small cost, this interface can be improved to incorporate features that may reduce the risk of VAP. The cost-effectiveness of these interventions can be calculated assuming one knows the baseline event rate (Wyncoll and Camporota, 2012). Assuming a baseline VAP rate of 8% and an intervention that reduces VAP by 45% (such as SSD by Muscedere 2011), the number needed to prevent one VAP is just 28. Additional money spent to prevent an episode of VAP to achieve costneutrality (assuming VAP cost of ~13,000 Euros) in this example is calculated as ~350 Euros per patient per 10 days of mechanical ventilation (Wyncoll and Camporota, 2012); the cost of an endotracheal tube capable of SSD is less than 15 Euros.

Conclusion

HCAIs remain serious and expensive. This paper highlights four simple interventions that could make a substantial difference in reducing the burden of secondary infection within the ICU. These interventions do not work in isolation, but when used in conjunction with good, basic infection control measures and ‘bundles’ of care, may provide simple and cost-effective solutions.

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