Commentary

Oropharyngeal decontamination in intensive care patients: less is not more

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Abstract

Ventilator-associated pneumonia (VAP) is a common cause of morbidity, antibiotic use, increased length of stay and, possibly, increased mortality in ICU patients. Colonization of the oropharyngeal cavity with potentially pathogenic micro-organisms is instrumental in the pathogenesis of VAP, and selective oropharyngeal decontamination (SOD) with antibiotics (AB-SOD) or antiseptics, such as chlorhexidine gluconate (CHX-SOD), has been associated with reduced incidences of VAP. In a recent issue of *Critical Care* Scannapieco and colleagues investigated differences in oropharyngeal colonization between mechanically ventilated patients receiving oropharyngeal decontamination with 0.12% CHX-SOD either once or twice daily compared to placebo. CHX-SOD was associated with a reduction in *Staphylococcus aureus* colonization, but the study was underpowered to demonstrate a reduction in VAP incidence. We urgently need well-designed and adequately powered studies to evaluate the potential benefits of CHX-SOD on patient outcome in ICUs.

In this commentary we discuss the study of Scannapieco and colleagues [1] published in a recent issue of *Critical Care*.

Ventilator-associated pneumonia (VAP) frequently occurs in ICUs, with reported incidences ranging from 9% to 27% [2]. It is a leading cause of morbidity and, possibly, of mortality. As a result, many interventions have been designed and evaluated for the prevention of VAP. One of the most successful interventions in this regard is oral decontamination.

Colonization of the upper respiratory tract generally precedes the occurrence of VAP, most probably because of a reduced capacity to clear pathogens and/or an increased adherence of micro-organisms to the respiratory tract [3]. Prevention of oropharyngeal colonization has been achieved with topically applied non-absorbable antibiotics (referred to as selective oropharyngeal decontamination with antibiotics (AB-SOD)) or with topically applied chlorhexidine gluconate (CHX-SOD).

AB-SOD was associated with reduced incidences of VAP in various studies [4-6], and recently also with a better 28-day survival in a large Dutch multi-center study [7]. In that study, AB-SOD was equally effective in improving patient outcome as selective decontamination of the digestive tract (SDD), which combines AB-SOD with intestinal decontamination and 4 days of intravenous cefotaxim. The occurrence of resistance as a result of AB-SOD or SDD, however, remains of concern, especially in countries with endemic levels of antimicrobial-resistant bacteria (AMRB). Therefore, simply replacing antibiotics with antiseptics for oral decontamination might offer an effective and safe measure for ICU patients, even in settings with high levels of AMRB.

Indeed, CHX-SOD appeared effective in reducing VAP incidence in several studies [8-13]. However, the regimens used were not always carefully described and concentrations and dosing frequencies varied from 0.12% CHX twice daily to 2% CHX four times a day. In addition, patient populations varied widely: from mixed ICU populations [9,12] to surgical ICU patients [10] and patients undergoing cardiac surgery [8,11,13]. Furthermore, nasal application of CHX was used in one study [13] and CHX was combined with Colistine in another [12], and in one study effects were compared to historic controls [10]. Moreover, all individual studies published so far have been underpowered to demonstrate effects of CHX-SOD on patient survival. In a recently published systematic review and meta-analysis, CHX-SOD was associated with a significant reduction in VAP incidence of 44%, although the studies were very heterogeneous, which

AB = antibiotics; AMRB = antimicrobial-resistant bacteria; CHX = chlorhexidine; SDD = selective decontamination of the digestive tract; SOD = selective oropharyngeal decontamination; VAP = ventilator-associated pneumonia.

precludes firm conclusions about its protective effects. No reductions in overall mortality, duration of mechanical ventilation or length of stay could be demonstrated [2].

In their article, Scannapieco and colleagues [1] aimed to determine the optimal frequency of CHX-SOD to prevent VAP in trauma ICU patients. The study contains a control group (49 patients) and two intervention groups receiving CHX 0.12% either once (47 patients) or twice daily (50 patients). They conclude that the number of *Staphylococcus aureus* in dental plaque was reduced in both intervention groups, but no significant reductions were observed in the total number of respiratory pathogens or incidence of VAP. Estimated reductions in colonization were 25% and 30% in the 'twice-daily' and 'once-daily' groups, respectively. The odds ratio for developing VAP was 0.54 (95% confidence interval 0.23 to 1.25) for patients receiving CHX-SOD, which is remarkably similar to the pooled estimate from the most recent meta-analysis. Although this may suggest a beneficial effect of CHX-SOD, it cannot be demonstrated by a study of this sample size.

In summary, the evidence that both AB-SOD and CHX-SOD reduce VAP incidence in ICU patients is accumulating. The optimal frequency and concentration for CHX-SOD remains to be demonstrated. From Scannapieco and colleagues' study we can conclude that twice daily is not necessarily better than once daily, but maybe a four times daily regimen with 2% instead of 0.12% CHX does make a difference. What we need now are well-designed and adequately powered studies to evaluate the effects of these measures on length of ICU stay and survival. If these effects were demonstrated, CHX-SOD would offer a very cheap and (ecologically) safe infection prevention measure in patient populations increasingly suffering from infections caused by AMRB.

Competing interests

The authors declare that they have no competing interests.

References

1. Scannapieco FA, Yu J, Raghavendran K, Vacanti A, Owens SI, Wood K, Mylotte JM: **A randomized trial of chlorhexidine gluconate on oral bacterial pathogens in mechanically ventilated patients.** *Crit Care* 2009, **13:**R117.
2. Chan EY, Ruest A, Meade MO, Cook DJ: **Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis.** *BMJ* 2007, **334:**889.
3. Bonten MJ, Bergmans DC, Ambergen AW, de Leeuw PW, van der Geest S, Stobberingh EE, Gaillard CA: **Risk factors for pneumonia, and colonization of respiratory tract and stomach in mechanically ventilated ICU patients.** *Am J Respir Crit Care Med* 1996, **154:**1339-1346.
4. Bergmans DC, Bonten MJ, Gaillard CA, Paling JC, van der Geest S, van Tiel FH, Beysens AJ, de Leeuw PW, Stobberingh EE: **Prevention of ventilator-associated pneumonia by oral decontamination: a prospective, randomized, double-blind, placebo-controlled study.** *Am J Respir Crit Care Med* 2001, **164:** 382-388.
5. Pugin J, Auckenthaler R, Lew DP, Suter PM: **Oropharyngeal decontamination decreases incidence of ventilator-associated pneumonia. A randomized, placebo-controlled, double-blind clinical trial.** *JAMA* 1991, **265:**2704-2710.
6. Rodríguez-Roldán JM, Altuna-Cuesta A, López A, Carrillo A, Garcia J, León J, Martínez-Pellús AJ: **Prevention of nosocomial lung infection in ventilated patients: use of an antimicrobial pharyngeal nonabsorbable paste.** *Crit Care Med* 1990, **18:** 1239-1242.
7. de Smet AM, Kluytmans JA, Cooper BS, Mascini EM, Benus RF, van der Werf TS, van der Hoeven JG, Pickkers P, Bogaers-Hofman D, van der Meer NJ, Bernards AT, Kuijper EJ, Joore JC, Leverstein-van Hall MA, Bindels AJ, Jansz AR, Wesselink RM, de Jongh BM, Dennesen PJ, van Asselt GJ, te Velde LF, Frenay IH, Kaasjager K, Bosch FH, van Iterson M, Thijsen SF, Kluge GH, Pauw W, de Vries JW, Kaan JA, *et al.*: **Decontamination of the digestive tract and oropharynx in ICU patients.** *N Engl J Med* 2009, **360:**20-31.
8. DeRiso AJ, Ladowski JS, Dillon TA, Justice JW, Peterson AC: **Chlorhexidine gluconate 0.12% oral rinse reduces the incidence of total nosocomial respiratory infection and nonprophylactic systemic antibiotic use in patients undergoing heart surgery.** *Chest* 1996, **109:**1556-1561.
9. Fourrier F, Cau-Pottier E, Boutigny H, Roussel-Delvallez M, Jourdain M, Chopin C: **Effects of dental plaque antiseptic decontamination on bacterial colonization and nosocomial infections in critically ill patients.** *Intensive Care Med* 2000, **26:**1239-1247.
10. Genuit T, Bochicchio G, Napolitano LM, McCarter RJ, Roghman MC: **Prophylactic chlorhexidine oral rinse decreases ventilator-associated pneumonia in surgical ICU patients.** *Surg Infect (Larchmt)* 2001, **2:**5-18.
11. Houston S, Hougland P, Anderson JJ, LaRocco M, Kennedy V, Gentry LO: **Effectiveness of 0.12% chlorhexidine gluconate oral rinse in reducing prevalence of nosocomial pneumonia in patients undergoing heart surgery.** *Am J Crit Care* 2002, **11:** 567-570.
12. Koeman M, van der Ven AJ, Hak E, Joore HC, Kaasjager K, de Smet AG, Ramsay G, Dormans TP, Aarts LP, de Bel EE, Hustinx WN, van der Tweel I, Hoepelman AM, Bonten MJ: **Oral decontamination with chlorhexidine reduces the incidence of ventilator-associated pneumonia.** *Am J Respir Crit Care Med* 2006, **173:**1348-1355.
13. Segers P, Speekenbrink RG, Ubbink DT, van Ogtrop ML, de Mol BA: **Prevention of nosocomial infection in cardiac surgery by decontamination of the nasopharynx and oropharynx with chlorhexidine gluconate: a randomized controlled trial.** *JAMA* 2006, **296:**2460-2466.