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LESS IS MORE IN INTENSIVE CARE

Less daily oral hygiene is more in the ICU: no

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Oral care in the intensive care unit (ICU) is a basic need, but oral care regimens vary, ranging from daily tooth brushing to applying antiseptics or antibiotics around the clock. While tooth brushing may be considered a standard procedure strategies with antiseptics or antibiotics have gained more ground in the past decades because of their beneficial effect on ICU-acquired infections and, for selective decontamination using antibiotics, also mortality [1–3].

The most widely used antiseptic for oral hygiene in European ICU patients in is chlorhexidine digluconate (CHX) [4]. Chlorhexidine reduces the incidence of ventilator-associated pneumonia (VAP), but not mortality and it was long thought to be of minimal risk. CHX had already been widely used in dental care and commercially available mouth rinses and was adopted in VAP bundles, for example in Scotland and Belgium [5, 6]. A meta-analysis suggested that a higher CHX concentration would be more effective at preventing VAP than the 0.12% and 0.2% concentrations that were commonly used, although there were no head-to-head comparisons included [7].

The good news lasted until meta-analyses indicated a possible increase in mortality associated with oral chlorhexidine, with most studies using 0.12/0.2% [8, 9]. Also, 4 times daily application of a CHX 2% *solution* led to oral mucosal side effects in a multicenter cluster-randomized trial and was therefore replaced by CHX 1% *gel* [10]. Although the CHX 1% gel did not lead to side effects, there was no difference between that intervention versus standard oral care with CHX 0.12/0.2% in preventing ICU-acquired bacteremia or mortality [11]; two endpoints for which interventions cannot bias the outcome assessment, as opposed to VAP. Is oral care with chlorhexidine not so safe and effective after all?

There are a few important side notes on these negative effects. First, regarding oral mucosal side effects, CHX 2% is ten times as strong as concentrations that are regularly used [4] and seems too aggressive for use in critically ill, intubated patients. In this respect "less is more". Second, as to yet, it remains unknown *how* CHX mouthwash (0.12/0.20%) increases mortality; is it chemical damage following micro-aspiration? And third, the vehiculum and method of application may also matter; a solution may be more easy to micro-aspirate than a gel or toothpaste and each may contain different other components. These side notes require additional research and until results of future studies such as the CHORAL study are available [12], the potential beneficial effects of CHX come with potential detrimental effects. As a result, the European Society of Intensive Care Medicine refrained from a recommendation concerning CHX use in the most recent VAP guideline [13].

Fortunately, there is more to oral care in the ICU than CHX, and there is every reason to assume that changing the microbiome in the oral cavity by oral care *can* prevent infections. It has been shown that there are similarities between bacteria in the mouth and in the respiratory tract [14] and colonization of the respiratory tract by Gram-negative bacteria is associated with development of ICU-acquired infections (Fig. 1) [15]. Breaking this chain is an important aim of oral care.

Mind the *O* in SOD

Selective oropharyngeal decontamination (SOD) aims to do just that with a mouthpaste consisting of nystatin, colistin and tobramycin, applied 4 times daily after regular oral care with tooth brushing. It's the 'leanest' version of selective decontamination, a strategy that aims to prevent overgrowth of potentially pathogenic microorganisms using high-dosages of topical, non-absorbable, bactericidal antibiotics. SOD is more effective at

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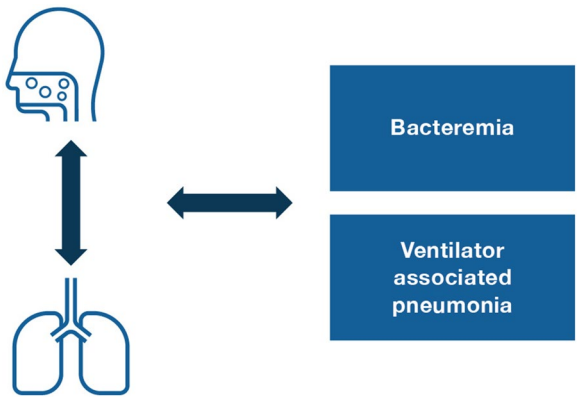

Fig. 1 There are similarities between bacteria in the mouth and in the respiratory tract and colonization of the respiratory tract by Gram-negative bacteria is associated with development of ICU-acquired infections

preventing ICU-acquired bacteremia (OR 0.68 [95% CI 0.53–0.86]) and 28-day mortality (adjusted OR 0.86 [95% CI 0.74–0.99], NNT = 23) than standard care without topical antibiotics [2]. When compared to selective digestive tract decontamination (SDD), the latter was found to be more effective than SOD in preventing bacteremia (crude proportions 4.5% vs 5.9% of patients, $P = 0.001$) and 28-day mortality (adjusted OR 0.85 [95% CI 0.77–0.93]) [3]. However, in a previous study [2], SOD reduced 28 day mortality by 2.9% (and SDD by 3.5%), compared to standard care without decontamination, which is a remarkable achievement given that SOD consist of just one component (antibiotic mouthpaste) and SDD of two additional components (gastro intestinal antibiotic suspension and an intravenous third-generation cephalosporin during the first four days in ICU). This indicates that oral decontamination has the potential to prevent infections and improve patient outcome.

Thus far, SOD and SDD were not associated with increases in antibiotic resistance in three large multicenter cluster-randomized trials (CRT) [2, 3, 11] and reduced colonization with Gram-negative bacteria resistant to third-generation cephalosporins and carbapenems [16]. They have only proven effects on patient outcome in settings with low-to-moderate levels of antibiotic resistance [2, 17].

To conclude, the oral care paradigm continues to shift. CHX may not be as harmless as first thought, and beneficial effects such as a reduction in VAP have thus far not been translated in improved survival. Selective decontamination with antibiotics has been shown to reduce the incidence of bacteremia *and* mortality without negative effects on ICU-ecology, at least in settings with low-to-moderate levels of antibiotic resistance. Most important, the relative importance of the *O* in SOD, in terms of effectiveness compared to SDD, does confirm that oral care matters and that less *pathogenic bacteria* in the oral cavity is in fact more, even in terms of survival.

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Compliance with ethical standards

Conflicts of interest
The authors declare that they have no conflict of interests.

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References

1. Hua F, Xie H, Worthington HV, Furness S, Zhang Q, Li C (2016) Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. Cochrane Datab Syst Rev 10:CD008367. https://doi.org/10.1002/14651858.CD008367.pub3
2. de Smet AM, Kluytmans JA, Cooper BS, Mascini EM, Benus RF, van der Werf TS et al (2009) Decontamination of the digestive tract and oropharynx in ICU patients. N Engl J Med 360(1):20–31. https://doi.org/10.1056/NEJMoa0800394
3. Oostdijk EAN, Kesecioglu J, Schultz MJ, Visser CE, de Jonge E, van Essen EHR et al (2014) (2017) Notice of retraction and replacement: Oostdijk et al. Effects of decontamination of the oropharynx and intestinal tract on antibiotic resistance in ICUs: a randomized clinical trial. JAMA 312(14):1429–1437. https://doi.org/10.1001/jama.2017.1282
4. Rello J, Koulenti D, Blot S, Sierra R, Diaz E, De Waele JJ et al (2007) Oral care practices in intensive care units: a survey of 59 European ICUs. Intensive Care Med 33(6):1066–1070. https://doi.org/10.1007/s00134-007-0605-3
5. Care SI (2012) VAP Prevention Bundle; Guidance for Implementation. NHS National Services Scotland/Crown
6. Jadot L, Huyghens L, De Jaeger A, Bourgeois M, Biarent D, Higuet A et al (2018) Impact of a VAP bundle in Belgian intensive care units. Ann Intensive Care 8(1):65. https://doi.org/10.1186/s13613-018-0412-8
7. Labeau SO, Van de Vyver K, Brusselaers N, Vogelaers D, Blot SI (2011) Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and meta-analysis. Lancet Infect Dis 11(11):845–854. https://doi.org/10.1016/s1473-3099(11)70127-x
8. Klompas M, Speck K, Howell MD, Greene LR, Berenholtz SM (2014) Reappraisal of routine oral care with chlorhexidine gluconate for patients receiving mechanical ventilation: systematic review and meta-analysis. JAMA Internal Med 174(5):751–761. https://doi.org/10.1001/jamainternmed.2014.359
9. Price R, MacLennan G, Glen J (2014) Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. BMJ (Clin Res Ed) 348:g2197. https://doi.org/10.1136/bmj.g2197
10. Plantinga NL, Wittekamp BH, Leleu K, Depuydt P, Van den Abeele AM, Brun-Buisson C et al (2016) Oral mucosal adverse events with chlorhexidine 2% mouthwash in ICU. Intensive Care Med 42(4):620–621. https://doi.org/10.1007/s00134-016-4217-7
11. Wittekamp BH, Plantinga NL, Cooper BS, Lopez-Contreras J, Coll P, Mancebo J et al (2018) Decontamination strategies and bloodstream infections with antibiotic-resistant microorganisms in ventilated patients:

a randomized clinical trial. JAMA 320(20):2087–2098. https://doi.org/10.1001/jama.2018.13765
12. Dale CM, Rose L, Carbone S, Smith OM, Burry L, Fan E et al (2019) Protocol for a multi-centered, stepped wedge, cluster randomized controlled trial of the de-adoption of oral chlorhexidine prophylaxis and implementation of an oral care bundle for mechanically ventilated critically ill patients: the CHORAL study. Trials 20(1):603. https://doi.org/10.1186/s13063-019-3673-0
13. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H et al (2017) International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT). Eur Respir J 50:3. https://doi.org/10.1183/13993003.00582-2017
14. Sands KM, Wilson MJ, Lewis MAO, Wise MP, Palmer N, Hayes AJ et al (2017) Respiratory pathogen colonization of dental plaque, the lower airways, and endotracheal tube biofilms during mechanical ventilation. J Crit Care 37:30–37. https://doi.org/10.1016/j.jcrc.2016.07.019
15. Frencken JF, Wittekamp BHJ, Plantinga NL, Spitoni C, van de Groep K, Cremer OL et al (2018) Associations between enteral colonization with gram-negative bacteria and intensive care unit-acquired infections and colonization of the respiratory tract. Clin Infect Dis 66(4):497–503. https://doi.org/10.1093/cid/cix824
16. Plantinga NL, Wittekamp BHJ, Brun-Buisson C, Bonten MJM (2020) The effects of topical antibiotics on eradication and acquisition of third-generation cephalosporin and carbapenem-resistant Gram-negative bacteria in ICU patients; a post hoc analysis from a multicentre cluster-randomized trial. Clin Microbiol Infect 26(4):485–491. https://doi.org/10.1016/j.cmi.2019.08.001
17. Plantinga NL, de Smet A, Oostdijk EAN, de Jonge E, Camus C, Krueger WA et al (2018) Selective digestive and oropharyngeal decontamination in medical and surgical ICU patients: individual patient data meta-analysis. Clin Microbiol Infect 24(5):505–513. https://doi.org/10.1016/j.cmi.2017.08.019