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## Letters to the Editor

## Dental care and hospital mortality in ICU patients



Dear Editor,

Maintaining oral health in critically ill patients is important, as poor oral hygiene is associated with unfavorable outcomes such as pneumonia. However, cleaning the oral cavity in critically ill patients, especially those on mechanical ventilation, is a particular challenge as there is a lack of scientific basis regarding the appropriate technique, frequency of care, and preferred supplies and products.<sup>1–3</sup> In this regard we read with interest the article by Ribeiro and colleagues and applaud their repeated efforts to explore and stress the importance of thorough dental care in critically ill patients.<sup>4</sup> By means of a quasi-experimental study with interrupted time-series, the authors assessed the impact of thrice weekly dental care in intensive care unit (ICU) patients compared with standard oral care by nurses mainly based on chlorhexidine mouthwashes. Pre-intervention mortality rates ranged from 32% to 36% and in the intervention period, a drop to 28% was observed ( $P = .015$ ). The authors hypothesized that the reduction in mortality could be explained by diminished periodontal inflammation leading to a decreased likelihood of primary bloodstream infection, ischemic myocardial infarction, and stroke. Unfortunately, data to support this explanation were not collected.

Alternatively, Ribeiro et al. assume that the reduced use of chlorhexidine mouthwashes may have contributed to the decreased mortality rate. In recent years the safety of chlorhexidine oral care has been repeatedly questioned. Chlorhexidine mouthwashes have been associated with an increased risk of mortality in meta-analysis of randomized trials as in large cohort studies executed either in ICUs or hospital-wide.<sup>5–8</sup> These observations led to a plea for prudent use of antiseptic mouthwashes<sup>9</sup> and initiatives to safely de-adopt the practice from the daily routine.<sup>10</sup> However, the exact pathogenic mechanism remains unclear. At first it was assumed that micro aspiration of chlorhexidine in intubated patients triggered pulmonary complications. Indeed, in endotracheally intubated patients micro aspiration of subglottic secretions along the cuff is nearly unavoidable as any change in patient position causes deviations in cuff pressure and the manipulations associated with oral care may, at least theoretically, trigger microaspiration.<sup>11,12</sup> However, as the link between chlorhexidine oral care and mortality was also observed in non-ICU patients<sup>6</sup>, this hypothesis appeared unlikely. Ribeiro and colleagues assume that the increased mortality may be triggered by oral mucositis as they reported in a previous study in which they assessed the value of additional dental care in ICU patients receiving chlorhexidine-based oral care.<sup>13</sup> Oral mucositis induced by chlorhexidine mouthwashes appeared associated with increased mortality (adjusted OR 6.1, 95% CI 2.0–19.1). We believe however, that their analysis includes a bias

since higher chlorhexidine concentrations were applied in patients with greater disease severity (2% vs 0.12%), constituting an inherent trigger for mucositis.<sup>14</sup> Additionally, adjustments for severity of disease were based on admission data while patients may have acquired oral mucositis later in the ICU course.

We believe that the mortality associated with chlorhexidine oral care is caused by a disturbance of the nitric oxide (NO) homeostasis.<sup>15</sup> NO is a key-messenger molecule in multiple physiological processes such as, among more, relaxation and permeability of the microcirculation and inhibition of platelet aggregation.<sup>16</sup> The oral microbiome has an essential role in the provision of NO by reducing nitrate to nitrite. By eradicating the oral bacterial flora, antiseptic mouthwashes interrupt the nitrate-nitrite-NO pathway resulting in a state of deficient NO bioavailability. As such, antiseptic mouthwash leads to a condition of suboptimal NO bioavailability, which put patients at risk for ischemic heart events and sepsis. This pathogenic mechanism is supported by Steitieh and Amin, who reported resolution of angor pectoris after cessation of chlorhexidine oral care and Parreco et al. who observed significantly higher rates of ICU-acquired sepsis in patients exposed to chlorhexidine mouthwashes.<sup>5,17</sup>

When it comes to infection prevention and control, it is important to recognize that the interruption of the nitrate-nitrite-NO pathway by eradicating oral bacteria is evident with all broad-spectrum oral antiseptics, and not exclusively with chlorhexidine.<sup>15</sup> Therefore, we recommend being cautious with antiseptic mouthwashes in general and to restrict this practice to evidence-based indications as described in the dental care protocol described by Ribeiro and colleagues.

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Conflicts of interest: None.

Patrick M. Honore PhD  
Elsa da Palma Afonso MSc  
Stijn Blot PhD\*

<sup>a</sup> Intensive Care Unit Department, Faculty of Medicine of the  
Université Libre de Bruxelles, Brugmann University Hospital, Brussels,  
Belgium

<sup>b</sup> Department of Internal Medicine and Pediatrics, Ghent University,  
Ghent, Belgium

<sup>c</sup> Senior Lecturer, School of Nursing and Midwifery, Anglia Ruskin  
University, Cambridge, UK

\* Address correspondence to S. Blot, PhD, Ghent University, Campus  
UZ Gent, Corneel Heymanslaan 10, 9000 Ghent, Belgium.  
E-mail address: [stijn.blot@UGent.be](mailto:stijn.blot@UGent.be) (S. Blot).

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## Customizing the indication of chlorhexidine mouthwash for critically ill patients: A reply letter to Honore P.M. and colleagues



Dear Editor,

We read with great interest the comments performed by Honore and colleagues<sup>1</sup> about our recently published article addressing the impact of a dental care intervention on the in-hospital mortality of critically ill patients.<sup>2</sup> We do agree with them that there is now enough evidence for not routinely using oral topical chlorhexidine

among hospitalized patients, for the purpose of preventing health-care-associated infections.<sup>3–5</sup> Unfortunately, in Brazil, chlorhexidine mouthwashes are still largely used, especially in the intensive care setting, despite all the evidence of its negative impact on mortality.

On the other hand, our results point in the direction that chlorhexidine topical cautious application may do more good than harm to a specific subset of critical patients. We are talking here about people with intra-oral infectious diseases, such as deep caries, oral abscesses, or periodontal disease, for example. In most of these cases, the oral microbiome has long been deeply compromised, and, therefore, the negative impact of using chlorhexidine on that would be offset by its positive impact on controlling the oral infection and inflammation. Among our last study population, chlorhexidine was used in approximately one-third of all oral hygiene procedures (723/2136) performed by dentists. In such cases, dentists managed to focus the antiseptic application on the source(s) of infection, rather than generally applying it in the whole oral cavity.

If we do parallel thinking with systemic antibiotic use, similar outcomes are found. We mean, if adequate antibiotics are prescribed to patients with a treatable infectious disease, a clear clinical benefit is produced in most cases. However, when prophylactic antibiotics are prescribed for long periods of time, superinfections with *C. difficile*, yeasts, and multidrug-resistant microorganisms frequently arise, and no clinical benefit is obtained for the patient.<sup>6,7</sup>

So, in conclusion, our perception goes in the direction that “one size does not fit all”, and a customized approach is the best way to go when considering the use of chlorhexidine mouthwash among critically ill patients.

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Wanessa Teixeira Bellissimo-Rodrigues, DDS, PhD  
Mayra Gonçalves Meneguetti, RN, PhD  
Anibal Basile-Filho, MD, PhD  
Fernando Bellissimo-Rodrigues, MD, PhD\*

<sup>a</sup> Department of Social Medicine, Ribeirão Preto Medical School,  
University of São Paulo. Ribeirão Preto, São Paulo, Brazil