

# Letter to the Editor

## Selective digestive decontamination is superior to oropharyngeal chlorhexidine in preventing pneumonia and reducing mortality in critically ill patients

A descontaminação digestiva seletiva é superior à clorexidina via orofaringe na prevenção de pneumonia e na redução da mortalidade em pacientes criticamente enfermos

### To the Editor:

We welcome the review article entitled “Nosocomial pneumonia: importance of the oral environment” by Amaral et al., as they unequivocally acknowledge the two fundamentals of pneumonia prevention in patients requiring treatment in the ICU.<sup>(1)</sup> First, pathogens in the oropharynx cause lower airway infections, and second, eradication of oropharyngeal pathogens prevents lower airway infections. The authors advocate pharmacological interventions to prevent pneumonia, including “decontamination with the administration of systemic antibiotics” and “local decontamination with the topical use of oral antiseptic and toothbrushing”. We were surprised by the ready dismissal of the issue of selective digestive decontamination (SDD), since the authors cited only one randomized controlled trial (RCT) using oropharyngeal decontamination with 2% gentamicin, polymyxin B and vancomycin, whereas the use of chlorhexidine was widely supported.

The issue of SDD has been addressed in 60 RCTs and 10 meta-analyses including only RCTs (Chart 1). In all meta-analyses in which pneumonia was the endpoint, SDD using parenteral, as well as enteral (oropharyngeal and intestinal), antimicrobials has consistently been shown to reduce the number of cases of pneumonia. The parenteral component effectively controls primary endogenous pneumonias caused by “normal” bacteria, whereas the enteral antimicrobials reduce secondary endogenous pneumonias due to “abnormal” bacteria, including *Pseudomonas* spp. and *Acinetobacter* spp. Although the authors are concerned about *Actinomyces* spp., this microorganism cannot be considered to be among the potential agents of pneumonia in mechanically ventilated ICU patients. Nevertheless, *Actinomyces* spp. are covered by the SDD antimicrobials. In 8 of the 10 meta-analyses, mortality was the outcome measure. There was a consistent survival benefit in all meta-analyses that assessed the

full SDD protocol with parenteral and enteral antimicrobials, assuming that the sample size was sufficient. Opinion leaders have expressed concerns regarding resistance, and, despite the fact that those concerns are based on low level evidence, this has hindered the implementation of SDD. Resistance was not a clinically relevant problem in the 60 RCTs evaluating SDD.<sup>(2)</sup> Two large Dutch RCTs in which the endpoint was resistance demonstrated that the carriage of and infection with multiresistant aerobic gram-negative bacilli were significantly lower after SDD than after the standard therapy.<sup>(3)</sup>

The use of selective oropharyngeal decontamination (SOD) alone, rather than the full SDD protocol, has recently been advocated. However, a recent meta-analysis demonstrated that SOD significantly reduces lower respiratory tract infections but does not reduce mortality.<sup>(4)</sup>

In their review, Amaral et al. focused most of their attention on the role that the oropharyngeal application of antiseptics, mainly chlorhexidine, plays in the prevention of ventilator-associated pneumonia (VAP). This preventive policy has been studied in several RCTs, with opposite results. To our knowledge, there have been only 5 meta-analyses of oral antiseptics,<sup>(5)</sup> the majority of which concluded that oral antiseptics seem to be effective in reducing VAP. However, results from RCTs of oral antiseptics and from meta-analyses should be interpreted with caution. Two thirds of the population included in the meta-analyses were cardiac surgery patients who had received no more than two days of mechanical ventilation.<sup>(6)</sup> Such patients should not be included in a meta-analysis in which the endpoint is VAP. In addition, the differences in terms of the definition of lower respiratory tract infections, as well as in the dosages and applications of antiseptics (e.g., chlorhexidine vs. povidone iodine; 0.12% vs. 2% chlorhexidine; use of solution, spray, gel or paste), might have influenced the results. In summary, it seems that oral antiseptics are

**Chart 1** – Efficacy of selective digestive decontamination in ten meta-analyses evaluating only randomized controlled trials.

Authors	Year	Lower airway infection	Bloodstream infection	MODS	Mortality <sup>a</sup>
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Vandenbroucke-Grauls et al. <sup>(7)</sup>	1991	0.12 (0.08-0.19)			0.92 (0.45-1.84)
D'Amico et al. <sup>(8)</sup>	1998	0.35 (0.29-0.41)			0.80 (0.69-0.93)
Liberati et al. <sup>(9)</sup>	2004	0.35 (0.29-0.41)			0.78 (0.68-0.89)
Safdar et al. <sup>(10)</sup>	2004				0.82 (0.22-2.45)
Silvestri et al. <sup>(11)</sup>	2005		0.89 (0.16-4.95)		
Silvestri et al. <sup>(12)</sup>	2007		0.63 (0.46-0.87)		0.74 (0.61-0.91)
Silvestri et al. <sup>(13)</sup>	2008				
Gram negative		0.07 (0.04-0.13)	0.36 (0.22-0.60)		
Gram positive		0.52 (0.34-0.78)	1.03 (0.75-1.41)		
Silvestri et al. <sup>(14)</sup>	2009				0.71 (0.61-0.82)
Liberati et al. <sup>(15)</sup>	2009	0.28 (0.20-0.38)			0.75 (0.65-0.87)
Silvestri et al. <sup>(16)</sup>	2010			0.50 (0.34-0.74)	0.82 (0.51-1.32)

MODS: Multiple organ dysfunction syndrome. <sup>a</sup>The meta-analyses by Vandenbroucke-Grauls et al.<sup>(7)</sup>, Safdar et al.<sup>(10)</sup> and Silvestri et al.<sup>(16)</sup> showed an impact on mortality. However, due to small sample size, the differences were not significant.

effective in preventing lower respiratory tract infection only in patients who receive mechanical ventilation for 48 h or less. The question of whether oral antiseptics are useful in preventing late-onset VAP requires further investigation. Furthermore, oral antiseptics have not been shown to significantly reduce mortality.

We believe SDD to be the only strategy that is associated with a survival benefit. We wonder why these authors chose to ignore this intervention in their review.

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