

# Effect of Oral Hygiene and 0.12% Chlorhexidine Gluconate Oral Rinse in Preventing Ventilator-Associated Pneumonia After Cardiovascular Surgery

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**BACKGROUND:** Ventilator-associated pneumonia (VAP) is a nosocomial infection of multifactorial etiology and has a negative influence on cardiovascular surgery (CVS) outcomes. **OBJECTIVES:** Determine the effect of toothbrushing plus 0.12% chlorhexidine gluconate oral rinse in preventing VAP after CVS. **METHODS:** In a quasi-experimental study, patients undergoing heart surgery were enrolled in a protocol for controlling dental biofilm by proper oral hygiene (toothbrushing) and oral rinses with 0.12% chlorhexidine gluconate (Group 1), and they were compared with a historical control group (Group 2), which included patients who underwent cardiac surgery between 2009 and 2010 and who received regular oral hygiene care. Seventy-two hours before surgery, a dentist provided instruction and supervised oral hygiene with toothbrushing and chlorhexidine oral rinses to patients in Group 1. **RESULTS:** Each group comprised 150 patients. A lower incidence of VAP (2.7% [95% CI 0.7–7.8] vs 8.7% [95% CI 4.9–14.7],  $P = .04$ ) and a shorter hospital stay ( $9 \pm 3$  d [95% CI 8.5–9.5] vs  $10 \pm 4$  d [95% CI 9.4–10.7],  $P = .01$ ) were observed in Group 1. No significant differences in all-cause in-hospital death were observed between groups (5.3% vs 4.7%,  $P > .99$ ). The risk for developing pneumonia after surgery was 3-fold higher in Group 2 (3.9, 95% CI 1.1–14.2). **CONCLUSIONS:** Oral hygiene and mouth rinses with chlorhexidine under supervision of a dentist proved effective in reducing the incidence of VAP. *Key words:* ventilator-associated pneumonia; prevention; chlorhexidine; cardiovascular surgery. [Respir Care 2014;59(4):504–509. © 2014 Daedalus Enterprises]

## Introduction

The risk of developing postsurgical infection is a threat to early clinical recovery after cardiovascular surgery (CVS). Ventilator-associated pneumonia (VAP) is a serious postoperative complication and has a high impact on hospital stay and health care costs.<sup>1–3</sup>

VAP occurs in 9–27% of patients with endotracheal intubation, resulting in an 8-fold increase in the risk of death in patients undergoing CVS.<sup>1,4</sup> It is therefore essen-

tial to further efforts to prevent VAP and to identify predisposing risk factors to control them.<sup>5</sup>

The patient's own flora is a primary source of microorganisms for the development of this pathology. Aspiration of microorganisms from the aerodigestive tract has been involved in the physiopathology of VAP and is the most important risk factor for colonization of the oropharynx.<sup>6,7</sup>

Different strategies have been implemented to decrease the bacterial load by oral decontamination, including the use of local antiseptics. For example, chlorhexidine is employed because of its high level of antibacterial, antiviral, and antifun-

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gal activities and high substantivity (ability to bind to oral tissues with subsequent slow release of antiseptic properties and therefore a long period of antibacterial action).<sup>8,9</sup> Although generally safe, chlorhexidine is not free of adverse events.

Most studies on VAP have been conducted in ICUs and therefore with critically ill patients, so in addition to heterogeneity of the underlying pathology, the patients have other risk factors for VAP, including duration of endotracheal intubation and immunologic compromise.<sup>10,11</sup> There is less information on VAP prevention in patients undergoing elective cardiac surgery, and therefore, the efficacy of using only local antiseptics to decrease the incidence of VAP in these patients remains unclear. Contributing to the controversy are findings supporting the use of local antibiotics to decrease the oropharyngeal microbial load, the use of which results in higher risk of bacterial resistance, allergic reactions, and increased cost.<sup>12,13</sup>

In the present study, we sought to contribute a strategy for oral decontamination in patients undergoing elective CVS, involving a protocol of oral hygiene and 0.12% chlorhexidine gluconate oral rinses under the supervision of dental professionals, with the aim to determine the effect of employing the described protocol on the incidence of VAP after major heart surgery.

## Methods

A quasi-experimental study was conducted in patients undergoing CVS at the Spanish Hospital of Buenos Aires in Argentina between January 2011 and December 2012. The patients were subjected to an oral decontamination protocol (Group 1) and compared with a historical control group (Group 2), which included patients who underwent CVS between January 2009 and December 2010 at the same hospital, with the same surgical team, ICU staff, and hospital infection control personnel during both periods of time. As part of the inclusion/exclusion surgery criteria, all patients were given intranasal 2% mupirocin ointment twice daily for 3 days before surgery.<sup>14-17</sup> A third-generation cephalosporin was administered 30 min before surgery and was continued for 24 h after surgery (the habitual oral hygiene),<sup>18,19</sup> and patients were not subjected to the dental plaque control and 0.12% chlorhexidine gluconate oral rinse protocol.

Our inclusion criteria included patients scheduled for CVS requiring sternotomy. All patients in Group 1 signed an informed consent form. Our exclusion criteria included patients requiring emergency surgery, patients who died within the first 48 h after surgery, patients presenting infection before surgery, patients receiving antibiotic therapy during 30 days before surgery, patients receiving immunosuppressive therapy or who were hypersensitive to chlorhexidine gluconate, and totally edentulous patients.

## QUICK LOOK

### Current knowledge

Ventilator-associated pneumonia (VAP) is an expensive complication following cardiovascular surgery (CVS) that portends a poor outcome. The impact of oral hygiene and toothbrushing on the incidence of VAP has met with mixed results.

### What this paper contributes to our knowledge

Compared with a historical control, toothbrushing plus 0.12% chlorhexidine gluconate oral rinse regimen reduced the incidence of VAP in patients following CVS compared with a standard antibiotic regimen.

This study was conducted in compliance with international standards of data protection and confidentiality, as stated in the Declarations of Helsinki and Tokyo and subsequent documents. This study was approved by the Ethics Committee of the Spanish Hospital of Buenos Aires.

The logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation) was calculated and used as a predictor of operative mortality.<sup>20,21</sup>

Patients were evaluated by a team of calibrated dentists who determined oral health status and specific dental treatment needs before surgery. The patients were then enrolled in a protocol for oral decontamination, which consisted of instructing the patient on oral hygiene using the modified Bass technique.<sup>22</sup> The latter consists of tipping the toothbrush at a 45° angle and brushing no more than 3 teeth at a time using gentle vibratory/circular movements for ~10–15 s, ensuring that each tooth is brushed on each surface. Hygiene was complemented with dental floss and interdental brushes, and partial dentures were cleaned as required. The patients rinsed their mouths with 0.12% chlorhexidine gluconate every 12 h for 3 days.<sup>23-25</sup> All patients underwent presurgery prophylaxis as described above.

The end point of the study was development of VAP; cases of VAP diagnosed within 48 h of intubation or 72 h after extubation were included. Criteria for diagnosis of VAP were evidence of a new lung infiltrate on chest x-ray and at least two of the following: leukocytosis, fever, or purulent tracheobronchial secretion.<sup>26,27</sup> All patients had a high-resolution computed tomography scan as an adjuvant diagnostic tool. All infections occurring after surgery were recorded, and VAP pathogens were identified at the bacteriology and microbiology laboratory of the hospital.

## Statistical Analysis

Differences between groups were analyzed using chi-square test and Fisher exact test; independent risk factors that could

Table 1. Characteristics of the Study Population

Patient Characteristics	Receiving Oral Decontamination ( <i>n</i> and % of Patients), Group 1 ( <i>n</i> = 150)	No Oral Decontamination ( <i>n</i> and % of Patients), Group 2 ( <i>n</i> = 150)
Mean age ± SD, y	62.3 ± 12.4 (95% CI 60.7–63.8)	63.10 ± 9.3 (95% CI 62.0–64.1)
Men	112 (81.3)	129 (86)
Mean EuroSCORE ± SD	4.7 ± 1.8 (95% CI 4.4–4.9)	4.6 ± 1.8 (95% CI 4.3–4.8)
Surgical procedure		
Coronary bypass	66 (44)	68 (45.3)
Bypass with pump	21 (14)	25 (16.66)
Valve replacement	38 (25.3)	35 (23.3)
Combined	18 (12)	9 (14)
Thoracic aortic artery	4 (2.7)	5 (3.3)
Bentall-De Bono	3 (2)	3 (2)
Diabetes	22 (14.7)	21 (14)
COPD	9.33 (14)	12 (8)
Active smoker	9 (6)	11 (7.3)
Mean EF ± SD	51 ± 14.3 (95% CI 49.1–52.8)	50 ± 13.2 (95% CI 48.4–51.5)
Previous myocardial infarction	18 (12)	19 (12.7)
Renal clearance < 60 ml/min*	5 (3.3)	6 (4)
Peripheral arteriopathy	11 (7.3)	13 (8.7)
Postoperative re-operation	15 (10)	16 (10.7)
> 24 h of inotropic support	11 (7.3)	14 (9)
Mean duration of mechanical ventilation ± SD, h	12.8 ± 10.4 (95% CI 11.4–14.3)	13.4 ± 10.2 (95% CI 12.1–14.6)

\* Renal clearance was calculated using the Cockcroft-Gault equation.  
 Combined = coronary bypass and valve replacement  
 Bentall-De Bono = replacement of the ascending aorta and the aortic valve  
 EF = ejection fraction

influence the incidence of VAP were determined using multivariate logistic regression analysis (variables are shown in Table 1). Statistical significance was set at  $\alpha < 0.05$  (95% CI). All statistical analyses were performed using statistics software (SPSS 17, SPSS, Chicago, Illinois). Sample size was calculated in accordance with the formula of sample size with the hypothesis testing for difference in frequency mean of two independent groups (Group 1, 1.5%; and Group 2, 8.7%). A significance level of  $\alpha = .05$  and a power of 80% were used. Based on these considerations, a total of 123 patients in each group were required.

**Results**

We studied 210 patients scheduled for elective CVS. However, according to the inclusion/exclusion criteria, 150 of these patients were enrolled in a protocol for oral decontamination under the supervision of a dentist (Group 1) and compared with a group of 150 patients receiving CVS in previous years, with no oral decontamination before surgery (Group 2). The characteristics of the population, as well as the type of surgery, are shown in Table 1.

The presence of postoperative infection was recorded. A lower incidence of VAP was observed in Group 1 (2.7%,

95% CI 0.7–7.8) compared with Group 2 (8.7%, 95% CI 4.9–14.7) ( $P = .04$ ).

On average, the risk of developing VAP after surgery was 3-fold higher in patients who did not receive oral decontamination (3.9, 95% CI 1.1–14.2). No significant differences were observed between groups regarding the remaining infections, as shown in Table 2. The pathogens identified in VAP patients are shown in Table 3.

A significant decrease in length of hospital stay was observed in Group 1 ( $9 \pm 3$  d, 95% CI 8.5–9.5) compared with Group 2 ( $10 \pm 4$  d, 95% CI 9.4–10.6) ( $P = .01$ ). No significant differences in all-cause in-hospital death were observed between groups: 5.3% ( $n = 8$ ) and 4.7% ( $n = 7$ ) ( $P > .99$ ) for patients receiving (Group 1) and not receiving (Group 2) oral decontamination, respectively.

**Discussion**

The present study showed that the oral hygiene protocol was associated with a lower incidence of VAP. Our patient population was at low risk of developing VAP, which increases with age (> 70 y of age), perioperative transfusions, previous heart surgery, emergency surgery, intraoperative inotropic support, endotracheal re-intubation, and

Table 2. Postoperative Infections

Nosocomial Infections	Receiving Oral Decontamination (n and % of Patients), Group 1 (n = 150)	No Oral Decontamination (n and % of Patients), Group 2 (n = 150)	P
VAP	4 (2.7)	13 (8.7)	.04
Urinary infection	19 (12.7)	16 (10.7)	.71
Superficial incisional surgical site infection	10 (6.7)	18 (12)	.59
Deep incisional surgical site infection	8 (5.3)	12 (8)	.57
Deep sternal surgical site infections	5 (3.3)	10 (6.7)	.28

VAP = ventilator-associated pneumonia

Table 3. VAP Pathogens Identified in Each Group

	Receiving Oral Decontamination, Group 1 (n = 4)	No Oral Decontamination, Group 2 (n = 13)
<i>Klebsiella pneumoniae</i>	2	3
<i>Pseudomonas aeruginosa</i>	0	4
<i>Staphylococcus aureus</i>	2	3
<i>Escherichia coli</i>	0	2
<i>Streptococcus viridans</i>	0	1

VAP = ventilator-associated pneumonia

duration of mechanical ventilation support, with the incidence of VAP reaching 45.9% after 48 h.<sup>5</sup> However, differences between groups receiving and not receiving oral decontamination were detected.

VAP as a nosocomial infection prolongs hospital stay and increases mortality and medical costs.<sup>3,28</sup> Great effort has been devoted to identifying the risk factors of VAP in an attempt to diminish the incidence and consequences of this disease.<sup>29-31</sup>

Aspiration of bacteria from the upper digestive tract has been identified as a key mechanism in the pathogenesis of VAP.<sup>32</sup> The normal flora of the oral cavity can comprise a variety of up to 350 bacterial species that have the potential to colonize different oral surfaces.<sup>33</sup> The host defense mechanisms in critically ill patients are diminished, generating a suitable environment for the adhesion of microorganisms to epithelial cells in the mouth and pharynx.<sup>34</sup> Tackling dental biofilm (bacterial plaque) formation by optimizing oral hygiene and performing oral decontamination in critically ill patients is an essential strategy for decreasing the incidence of VAP.<sup>35,36</sup>

The present study showed that chlorhexidine gluconate effectively diminished the bacterial load of dental plaque, reducing its pathogenic potential, and oral decontamination effectively decreased the incidence of VAP in patients hos-

pitalized in ICUs. These data are in agreement with the effects shown by others.<sup>37-39</sup>

Although not critically ill and not usually requiring mechanical ventilation support for > 24 h, patients undergoing elective cardiac surgery are likely to develop VAP. For example, this study found a decreased incidence of VAP with oral hygiene and chlorhexidine gluconate oral rinses 72h before surgery and therefore before endotracheal intubation.

There are reports showing that oropharyngeal cleansing with 0.2% chlorhexidine solution was similar in antimicrobial properties to oral cleansing with potassium permanganate. Moreover, published results regarding the efficacy of a local antiseptic and oral hygiene in preventing VAP are controversial.<sup>40,41</sup>

The prospective, randomized, and controlled trial conducted by Segers et al<sup>42</sup> to determine the efficacy of chlorhexidine gluconate in decreasing nosocomial infection after cardiac surgery showed a lower incidence of deep surgical site infections and lower respiratory tract infections, including tracheobronchitis and VAP, in chlorhexidine gluconate-treated patients. In contrast with other reports, analysis of postoperative infections showed similar percentages of surgical site infections in both groups.<sup>42</sup>

The guidelines of the Centers for Disease Control and Prevention recommend topical application of oral 0.12% chlorhexidine during the preoperative period in adults undergoing CVS (level II evidence).<sup>27</sup>

The meta-analysis by Tantipong et al<sup>43</sup> showed that oral antiseptic prophylaxis significantly reduced the incidence of VAP. According to the meta-analysis by Pineda et al,<sup>44</sup> which included four studies, the use of chlorhexidine as a local antiseptic of the oral cavity did not result in a lower incidence of VAP.<sup>45</sup> In contrast, our observations are in agreement with other reports showing that oral decontamination effectively decreased the incidence of VAP.<sup>46-48</sup>

We found no differences in mortality, which is similar to the results reported by Segers et al<sup>42</sup> and Chan et al.<sup>36</sup> This finding may be associated with the low expected mortality of our group of patients as predicted by EuroSCORE, which was below 5%.<sup>36</sup> A study reported in the literature found that the use of intravenous and topical antibiotics in ICU patients receiving mechanical ventilation for > 48 h resulted in lower mortality.<sup>49</sup> The patients studied herein received prophylactic intravenous antibiotic therapy in keeping with current recommendations, and this likely explains the similar mortality in patients receiving and not receiving oral decontamination.<sup>50</sup>

The decontamination strategies and the pathologies found in patients requiring mechanical ventilation are varied. Different oral decontamination protocols have been used, and they have ranged from the use of oral hygiene and local antiseptics to topically applied antibiotics. In addition, other strategies involve decontamination of the aerodigestive tract and intravenous antibiotic prophylaxis. The differences among

studies regarding the choice and use of these strategies would account for discrepancies among results, which in turn contribute to sustaining the controversy.

Patients undergoing CVS are a special group within the wide spectrum of patients, and the use of oral decontamination in those subjects has also yielded controversial results.<sup>51,52</sup> Prevention of VAP should focus on optimizing the host's defenses to avoid the pathogens that get through the defense barriers. Examination of the oral cavities of patients undergoing CVS provides an excellent opportunity to reduce the risk of nosocomial infection.

The results of the present study further highlight the need to maximize resources by optimizing hygiene and local antisepsis with chlorhexidine to decrease the oral pathogen load preoperatively. The protocol used in the present study was designed for this purpose, and its use reduced the incidence of VAP.

One of the limitations of our research is that it is not a prospective randomized case-control study. A group of historical controls who had similar characteristics, who were treated at the same center but at a previous time, and who did not receive oral decontamination because the chlorhexidine gluconate oral rinse was not implemented at that time were compared with a group of patients enrolled in the study protocol and assessed prospectively. The present study design was based on current scientific evidence of the benefits of decontamination with chlorhexidine before surgery in reducing the risk of VAP. We consider it unethical to conduct a clinical trial study in which a group of patients would be denied the chance to decrease the bacterial plaque load before a high-risk procedure, as is the case of cardiac surgery.

### Conclusions

Oral hygiene and chlorhexidine gluconate oral rinses before elective cardiac surgery proved effective in reducing the incidence of postoperative VAP. The clinical implications are that the lower incidence of VAP in patients undergoing elective CVS resulted in a shorter hospital stay but had no significant impact on mortality, which must be analyzed in a larger study sample. In view of the safety, simplicity, and efficacy of the protocol described herein, it would seem suitable as a prevention strategy to be used preoperatively in patients undergoing elective CVS.

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