

TITLE

EFFECT OF ORAL HYGIENE AND 0.12% CHLORHEXIDINE GLUCONATE
ORAL RINSE IN PREVENTING OF VENTILATOR-ASSOCIATED PNEUMONIA
AFTER CARDIOVASCULAR SURGERY

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ABSTRACT

Ventilator-associated pneumonia is a nosocomial infection of multifactorial etiology and has a negative influence on cardiovascular surgery outcomes.

OBJECTIVES: To determine the effect of tooth-brushing plus 0.12% chlorhexidine gluconate oral rinse in preventing of ventilator-associated pneumonia after cardiovascular surgery.

METHODS: In a quasi-experimental study patients undergoing heart surgery were enrolled on a protocol for controlling dental biofilm by proper oral hygiene (tooth brushing) and oral rinses with 0.12% chlorhexidine gluconate (Group 1), and were compared to a group of historical controls (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 instructed and supervised oral hygiene with tooth brushing and chlorhexidine oral rinses in patients in Group 1.

RESULTS: Each group comprised 150 patients. A lower incidence of ventilator-associated pneumonia (2.66%; 95% CI = 0.71-7.8 vs. 8.66%; 95% CI= 4.88- 14.66; $p=0.04$), and shorter hospital stay (measured in days) (9 ± 3 ; 95% CI = 8.51-9.48 vs. 10 ± 4 ; 95% CI= 9.35-10.64; $p=0.01$) were observed in Group 1. No significant differences in all-cause in-hospital death were observed between groups (5.33% vs. 4.66%; $p=1.00$). The risk for developing pneumonia after surgery was three-fold higher in Group 2 (OR 3.87; 95% CI =1.05-14.19).

CONCLUSIONS: Oral hygiene and mouth rinses with chlorhexidine under supervision of a dentist proved effective in reducing the incidence of ventilator-associated pneumonia.

KEY WORDS: ventilator-associated pneumonia- prevention – chlorhexidine – cardiovascular surgery.

INTRODUCTION:

The risk of developing post-surgical infection is a threat to early clinical recovery after cardiovascular surgery (CVS).

Ventilator-associated pneumonia (VAP) is a serious post-operative complication, and has a high impact on hospital stay and health-care costs. (1-3)

VAP occurs in 9 to 27% of patients with endotracheal intubation, resulting in an 8-fold increase in the risk of death in patients undergoing CVS. (4-5) It is therefore essential to further efforts to prevent VAP and identify predisposing risk-factors, in order to control them. (6)

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 pathophysiology of VAP, and is the most important risk factor for colonization of the oropharynx . (7-8)

Different strategies have been implemented with the aims to decrease the bacterial load by means of oral decontamination, including the use of local antiseptics. Chlorhexidine, for example, is employed on account of its high level of antibacterial, antiviral, and antifungal activity and high substantivity (ability to bind to oral tissues with subsequent slow release of antiseptic properties and therefore a long period of antibacterial action). (9-10) Although generally safe, the Chlorhexidine is not free of adverse events.

Most studies on VAP have been conducted in Intensive Care units and therefore in critically ill patients, so that in addition to heterogeneity of the underlying pathology, the patients have other risk factors for VAP including duration of endotracheal intubation and immunologic compromise. (11-12)

There is less information on VAP prevention in patients undergoing elective cardiac surgery, and therefore the efficacy of only using 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. (13-14)

The present study 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 aims to determine the effect of employing the described protocol on the incidence of VAP after major heart surgery.

The aim of the present study was to determine the effect of oral hygiene and 0.12% chlorhexidine gluconate oral rinse in preventing of ventilator-associated pneumonia after cardiac surgery.

MATERIAL AND METHODS

A quasi-experimental study was conducted in patients undergoing CVS at the Spanish Hospital of Buenos Aires between January 2011 and December 2012. The patients were subjected to an oral decontamination protocol (Group 1) and compared to historical controls (Group 2), which comprised patients who underwent CVS between January 2009 and December 2010 at the same hospital, with the same surgical team, Intensive Care Unit staff and the hospital infection control personnel during both periods of time. As a part of the inclusion/exclusion surgery criteria, all patients were given intranasal 2% mupirocin ointment twice daily for 3 days before surgery. (21-24)

A third-generation cephalosporin was administered 30 minutes before surgery and was continued for 24 hours after surgery (25-26), the habitual oral hygiene, and not subjected to the dental plaque control and 0.12% chlorhexidine gluconate oral rinse protocol.

Inclusion criteria: Patients scheduled for CVS requiring sternotomy. All patients in Group 1 signed an informed consent form. Exclusion criteria: Patients requiring emergency surgery, patients who died within the first 48 hours after surgery, patients presenting infection prior to surgery, patients receiving antibiotic therapy during 30 days prior to surgery, patients receiving immunosuppressive therapy or who were hypersensitive to chlorhexidine gluconate, totally edentulous patients.

The study was conducted in compliance with international standards of data protection and confidentiality, as stated in the declarations of Helsinki, Tokyo, and subsequent documents.

The 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. (15-16)

The patients were evaluated by a team of calibrated dentists who determined oral health status and specific dental treatment needs prior to 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. (17) 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 around 10 to 15 seconds, ensuring that each tooth is brushed on each surface. Hygiene was complemented with dental floss and interdental brushes, and cleaning partial dentures as required. The patients rinsed their

mouth with 0.12% chlorhexidine gluconate every 12 h for 3 days. (18-20) All patients underwent pre-surgery profilaxis as described above.

The endpoint of the study was development of VAP; cases of VAP diagnosed within 48 hours of intubation or 72 hours after extubation, were included. Criteria for diagnosis of VAP were evidence of new lung infiltrate in chest X-rays in addition to at least two of the following: leukocytosis, fever, or purulent tracheobronchial secretion. (27-28) All patients had a High Resolution Computed Tomography scan as an adjuvant diagnostic tool.

All infections occurring post-surgery were recorded, and VAP pathogens were identified at the bacteriology and microbiology laboratory of the hospital.

Statistical analysis

The differences between groups were analyzed using Chi square test and Fisher's test; independent risk factors that could 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% confidence intervals (CI). All statistical analyses were performed using SPSS version 17. Sample size was calculated in accordance with the formula of sample size with the hypothesis testing for difference of frequency mean of two independent groups (group 1: 1.5% and group 2: 8.66%). Significance level of $\alpha=5\%$ and a power of 80% were used. Based on these considerations, a total of 123 patients in each group were required.

RESULTS

Two-hundred and ten patients scheduled for elective CVS were studied. However, according to inclusion/exclusion criteria, one-hundred and fifty of these patients were enrolled on a protocol for oral decontamination under the supervision of a dentist

(Group 1) and compared to 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 post-operative infection was recorded; a lower incidence of VAP was observed in Group 1 (2.66 %; 95% CI = 0.71-7.8) as compared with Group 2 (8.66%; 95% CI = 4.88- 14.66) (p=0.04).

On average, the risk of developing VAP after surgery was three-fold higher in patients who did not receive oral decontamination (OR 3.8; 95% CI =1.05-14.19).

As regards the remaining infections, no significant differences were observed between groups as shown in Table 2.

A significant decrease in length of hospital stay was observed in Group 1 (9 ± 3 ; 95% CI = 8.51-9.48) as compared to Group 2 (10 ± 4 ; 95% CI = 9.35-10.64) (p=0.01).

The pathogens identified in VAP patients are shown in Table 3.

No significant differences in all-cause in hospital death were observed between groups: 5.33% (n=8) and 4.66% (n=7) (p=1.00) for patients receiving and not receiving oral decontamination, Group 1 and Group 2; respectively.

DISCUSSION

The present study shows 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 (more than 70 years of age), perioperative transfusions, previous heart surgery, emergency surgery, intraoperative inotropic support, endotracheal reintubation, and duration of mechanical ventilation support, with the incidence of VAP reaching 45.9% after 48 h (6); 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. (29-30) Great effort has been devoted to identifying the risk factors of VAP, in an attempt to diminish the incidence and consequences of this disease. (31-33) Aspiration of bacteria from the upper digestive tract has been identified as a key mechanism in the pathogenesis of VAP. (34) 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. (35) The host defense mechanisms in the critically ill are diminished, generating a suitable environment for the adhesion of microorganisms to epithelial cells in the mouth and pharynx. (36) 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. (37-38)

The present study showed that chlorhexidine gluconate effectively diminished the bacterial load of the dental plaque reducing its pathogenic potential and oral decontamination effectively decreased the incidence of VAP in patients hospitalized in intensive care unit. These data are in agreement with the effects shown by others. (39-41)

Though not critically ill and not usually requiring mechanical ventilation support for more than 24 h, patients undergoing elective cardiac surgery are likely to develop VAP.

For instance, this study found a decreased incidence of VAP with oral hygiene and the chlorhexidine gluconate oral rinses, seventy-two hours 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. (42-43)

The prospective, randomized, controlled trial conducted by Segers et al 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. (44)

The Guidelines of the Centers for the Control and Prevention of Diseases recommend topical application of oral 0.12% chlorhexidine during the preoperative period in adults undergoing CVS (level II evidence). (28)

The meta-analysis by Tantipong et al showed that oral antiseptic prophylaxis significantly reduced the incidence of VAP. (45)

According to the meta-analysis by Pineda et al, 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. (46-47) In contrast, our observations are in agreement with other reports showing that oral decontamination effectively decreased the incidence of VAP. (48-50)

Our results showed no differences in mortality which are similar to that reported in other studies by Segers (44) and Chan et al (38). This finding may be associated with the low expected mortality of our group of patients, as predicted by the EuroSCORE, which was below 5%. (38)

A study reported in the literature found the use of intravenous and topical antibiotics in intensive care unit patients receiving mechanical ventilation for more than 48 h to result in lower mortality. (51)

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. (52)

The decontamination strategies and the pathologies found in patients requiring mechanical ventilation are varied. Different oral decontamination protocols have been used, and have ranged from including 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 these subjects has also yielded controversial results. (53-54) Prevention of VAP should focus on optimizing the host's defenses in order to avoid the pathogens to get through the defense barriers. Examination of the oral cavity 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 in order to decrease the oral pathogen load preoperatively. The protocol used in the present study was designed for this purpose, and allowed reducing the incidence of VAP.

Among the limitations to our study is the fact that it is not a prospective randomized case-control study. We compared a group of historical controls, with similar characteristics, treated at the same Center but at a previous time, not receiving oral decontamination because the chlorhexidine gluconate oral rinse was not implemented at

that time, to 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 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 ventilator associated pneumonia.

CLINICAL IMPLICATIONS:

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 cardiovascular surgery.

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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TABLES

Table 1

CHARACTERISTICS OF THE STUDY POPULATION

PATIENT CHARACTERISTICS	Receiving oral decontamination Group 1 (n=150)	No oral decontamination Group 2 (n=150)
Mean age in years (SD)	62.3 ± 12.4 (CI 95% 60.7-63.8)	63.10 ± 9.3 (CI 9 5% 62.0-64.1)
Men	112 (81.33)	129 (86)
Mean EuroSCORE (SD)	4.7 ± 1.8 (CI 95% 4.4-4.9)	4.6 ± 1.8 (CI 95 % 4.3-4.8)
Surgical Procedure:	66 (44)	68 (45.33)
Coronary Bypass		
Bypass with pump	21 (14)	25 (16.66)
Valve replacement	38 (25.33)	35 (23.33)
Combined *	18 (12)	9 (14)
Thoracic Aortic Artery Bentall Bono †	4 (2.66)	5 (3.33)
3 (2)		3 (2)
Diabetes	22 (14.66)	21 (14)
COPD ‡	9.33 (14)	12 (8)
Active Smoker	9 (6)	11 (7.33)
Mean EF§ (SD)	51 ± 14.3 (CI 95% 49.1-52.8)	50 ± 13.2 (CI 95 % 48.4-51.5)
Previous myocardial infarction	18 (12)	19 (12.66)
Renal clearance < 60ml/min ¶	5 (3.33)	6 (4)
Peripheral arteriopathy	11 (7.33)	13 (8.66)
Post-operative Reoperation	15 (10)	16 (10.66)
> 24 h Inotropic support	11 (7.33)	14 (9)
Mean duration of Mechanical ventilation in hours (SD)	12.8 ± 10.4 (CI 95% 11.4-14.3)	13.4 ± 10.2 (CI 95% 12.1-14.6)

* Combined: Coronary bypass and valve replacement

† Bentall Bono: Replacement of the ascending aorta and of the aortic valve

‡ COPD: Chronic obstructive pulmonary disease

§ EF: Ejection fraction

¶ Renal clearance was calculated using the Cockcroft-Gault equation

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 value
VAP	4 (2.66)	13 (8.66)	0.04
Urinary infection	19 (12.66)	16 (10.66)	0.71
Superficial incisional surgical site infection*	10 (6.66)	18 (12)	0.59
Deep incisional surgical site infection†	8 (5.33)	12 (8)	0.57
Deep sternal surgical site infections ‡	5 (3.33)	10 (6.66)	0.28

* Superficial incisional surgical site infection

† Deep incisional surgical site infection

‡ Deep sternal surgical site infections

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>Pseudomona aeruginosa</i>	0	4
<i>Srephylococcus auerus</i>	2	3
<i>Escherichia coli</i>	0	2
<i>Streptococcus viridans</i>	0	1