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Evaluation of brushing efficiency in reducing oral microbiota in mechanically ventilated patients admitted to an intensive care unit

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SUMMARY

Background: Patients admitted to the Intensive Care Unit (ICU) are at greater risk of developing nosocomial infections due to their investigations, treatment and changes in the immune system. One of the most prevalent nosocomial infections is respiratory tract infection, such as hospital acquired pneumonia and ventilator-associated pneumonia (VAP). The bacteria commonly found in the oral cavity in the hospital environment are *Streptococcus viridians*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterococcus* spp., and *Klebsiella pneumoniae*. There is a need to test and define appropriate standard protocols for oral hygiene in patients undergoing mechanical ventilation in ICUs through the intervention of a dental specialist, preventing the proliferation of microorganisms into the respiratory tract, thus reducing hospitalization time, the use of antibiotics, and increased morbidity/mortality. **Objective:** This study aimed to evaluate the effectiveness of dental brushing in the reduction of the pathogenic buccal microbiota associated with mechanical ventilation in patients admitted to the Evangelical Hospital from Londrina, Paraná, Brazil. **Methodology:** The sample consisted of 90 patients (of both sexes), mean age of 65 years, under mechanical ventilation by orotracheal tube and tracheostomized patients, without suspected or confirmed diagnosis of pneumonia. Patients were randomized *** **Results:** Results showed that oral hygiene using a toothbrush by suction, with chlorhexidine gel 0.12% (Group B), was more effective than conventional hygiene using gauze soaked with chlorhexidine 0.12% (Group A) in reducing pathogenic buccal microbiota.

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Conclusions: There was a reduction of the pathogenic buccal microbiota in mechanically ventilated patients receiving oral hygiene using a toothbrush by suction with chlorhexidine gel 0.12% (Group B)

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Introduction

Patients admitted to the Intensive Care Unit (ICU) are at increased risk of developing nosocomial infections, due to their investigation, management and changes in the immune system [1–3]. One of the most prevalent nosocomial infections is respiratory, such as hospital acquired pneumonia and ventilator associated pneumonia (VAP), whose incidence increases when hospitalized patients have poor oral hygiene [4,5]. These infections are the leading causes of mortality among hospitalized patients [6,7]. Approximately 13–48% of all hospital acquired infections occur due to pneumonia in this setting [8,9]. VAP is acquired after 48–72 hours of intubation, usually by aspiration of bacterial pathogens from the oral cavity and pharynx [10]. Several routes of entry of microorganisms into the lower respiratory tract have been described, such as: aspiration of secretions from the oropharynx, exogenous inoculation of contaminated material, reflux from the gastrointestinal tract and, rarely, by hematogenous dissemination from a distant infectious focus [11].

The oral cavity undergoes continuous colonization, harboring more than 700 bacterial species, around half of all the microbiota present in the human body. In addition to the predominance of bacterial species, organisms reside in an ecosystem called biofilm, with the back of the tongue and the surfaces of the teeth being the main surfaces [12].

The constant flow of food and variety of microbial populations on the tooth surface and mucosa, allow microbial adhesion. Therefore, the oral cavity is an ideal microbial incubator and dental biofilms are potentially one of the most complex biofilms that exist in nature [13]. Studies have suggested a correlation between colonization of the oropharynx and the appearance of VAP. Within 48 hours of admission to the ICU, the oral microbiota of patients on mechanical ventilation (MV) undergoes changes, with a predominance of Gram-negative microorganisms, such as *Pseudomonas aeruginosa*, *Enterobacter* spp, *Acinetobacter baumannii*, *Klebsiella pneumoniae*; and some Gram-positive organisms, such as *Staphylococcus aureus* [14–16].

Thus, oral biofilm can act as a substrate for colonization by respiratory pathogens, and these microorganisms can be transported and aspirated into the respiratory tract, causing pulmonary infection [17–19]. Interventions to reduce bacterial colonization in the oral cavity and their potential to reduce VAP have been investigated. However, there is a need to test the quality and types of toothbrushes suitable for patients undergoing MV in ICUs with brushing techniques and protocols through the intervention of a Dentist [20]. It is known that good oral hygiene by a Dentist (following a protocol and vacuum suction brushing techniques) prevent the proliferation of microorganisms in the respiratory tract, reducing hospitalization time, the use of antibiotics and other systemic diseases [21].

The aim of this study was to compare the effectiveness of two different brushing techniques in the reduction of pathogenic oral microbiota associated with MV in patients admitted to the ICU of the Hospital Evangélico (HEL), located in the municipality of Londrina, Paraná, Brazil. The statistical analysis also aimed to determine the incidence between groups, age group and hospitalization period.

Methodology

Criteria for selection, inclusion and exclusion of the sample

The study involved 90 critically ill patients, based on a sample calculation of 63% (N=82) with a difference of 9.4% [22], to obtain a statistical power of 80% and an alpha error of 5%. The clinical team screened all patients admitted to the ICU daily to identify those who were mechanically ventilated for over 48 hours without suspicion or diagnosis of pneumonia. Patients were only included after 48 hours of ventilation or tracheostomy tube insertion, since according to some studies, this is the minimum time for the formation of biofilms on the tube surfaces [23,24]. Relatives of eligible patients were approached for participation and included after providing informed consent. Informed consent was given by the immediate relatives of the patients hospitalized in the Intensive Care Unit (ICU), who had the responsibility of authorizing patients' admission to said unit. Inclusion criteria was as follows – (i) Adult patients (over 18 years old), (ii) Under mechanical ventilation via endotracheal tube or tracheostomy, and (iii) Ventilated for at least 48 hours. Exclusion criteria included – (i) Allergy to chlorhexidine, (ii) Suspected or confirmed pneumonia diagnosis, and (iii) Ventilated for less than 48 hours.

During recruitment and screening, information was collected on each patient's medical conditions and medications. Patients were enrolled regardless of their underlying medical conditions, provided they met the inclusion criteria listed above. We did not exclude patients based on specific diagnoses or drug regimens. However, patients' medical conditions and medications were noted and taken into consideration during the analysis to account for potential influences on the study outcomes.

Design of the study

A prospective randomized clinical trial was carried out comparing "existing standard of care" oral hygiene with the protocol under investigation. The existing standard of care oral hygiene consisted of gauze soaked in 0.12% chlorhexidine digluconate, applied with a wooden spatula (Group A). The protocol under investigation consisted of cleaning with a toothbrush connected to vacuum suction, using a sachet containing 3g of 0.12% chlorhexidine gel (Group B). The study was conducted from February

to August 2017, in the adult ICUs of the Evangelical Hospital, in the city of Londrina, Paraná, Brazil. The Evangelical infrastructure has three adult general medicine ICUs; ICU-1, ICU-2 and OCU. ICU-1 has 24 beds. ICU 2 has 10 beds and the OCU has seven beds, totaling 41 beds. The study was approved by the Internal Research Committee (CIP, AEBEL) of the Evangelical Hospital. Following consent of this committee, it was approved by the Ethics Committee on Human Research, via Plataforma Brazil, with Opinion number 1.902.398.

Oral hygiene protocols

Group A: Consisted of 45 patients, the conventional routine hygiene involved daily use of gauze soaked in 0.12% chlorhexidine digluconate, together with a wooden spatula, administered twice daily, in the morning and evening. When introduced into the oral cavity, back-and-forth movements were performed in the buccal regions of the posterior teeth bilaterally and in the anterior region. In the mucosal, palatal, lingual and occlusal regions, the spatula was introduced as far as possible, remembering that the oral cavity was not aspirated before and after cleaning.

Group B: Consisted of 45 patients, evaluated during a period of 30 days, with a hygiene frequency of twice a day (morning and evening), with a suction toothbrush. This brush was soaked in 0.12% chlorhexidine gel. After this period, the brush was connected to the HEL vacuum system, aspirating all saliva and debris present. The 0.12% chlorhexidine gel was inserted in a few portions, thus effectively initiating brushing. At the end of each cleaning, the oral cavity was aspirated to avoid the presence of debris, preventing aspiration of the patients.

Sample collection

One mL of saliva was collected before and after the cleaning performed in Group A (Figure 1) and Group B (Figure 2) in a single session. The saliva was collected from between the canine and first molar of the lower arch of each volunteer research patient, using sterile pipettes (LABMATEpro), before and after aspiration (Group B) and before and after standard hospital hygiene (Group A).

Isolation and identification of microorganisms

Saliva samples were seeded on culture media for bacterial isolation for qualitative and semiquantitative evaluation of

microorganisms. Plating was always performed with 0.1 ml of each sample for semi-quantitative comparison. The culture medium used was CHROMagar Orientation (PLASTLABOR), which has a wider application as a general nutrient medium for the isolation of various microorganisms, facilitating and speeding up the identification of some Gram-negative and Gram-positive bacteria by contrasting colony morphology. Cultural characteristics of bacteria on chromogenic agar were strain-dependent.

Randomization

Enrolled participants were randomly allocated to Group A or Group B using a computer-generated random number sequence. Allocation was concealed in sequentially numbered opaque envelopes that were opened after obtaining informed consent. After applying the eligibility criteria, included patients were randomly assigned to one of the defined research groups. A biostatistician, who did not participate in any stage of this study, was responsible for generating the random allocation sequence, as well as organizing and distributing the participants into the groups. Participants in both groups had similar baseline characteristics in terms of age, gender, severity of illness scores, and comorbidities. We believe this strengthened the randomized study design and supports the validity of comparing the intervention effects between the groups.

Blinding

Blinding was not possible, the dental surgeon performing the oral hygiene had to know to which group each patient belonged. However, the Physicians who confirmed the diagnosis of VAP and the Microbiologists who evaluated the presence of pathogens in the oral specimens did not know to which group each participant belonged.

Statistical analysis

Analysis of residual normality and homogeneity between data variances were performed using the Shapiro-Wilk and Hartley tests, respectively. If the value of the Shapiro-Wilk Test was > 0.05 , the data was normal; and if it was < 0.05 , the data significantly deviated from a normal distribution. Hartley's test assumes the data for each group are normally distributed, and that each group has an equal number of members. A multiple-



Figure 1. Oral hygiene kit (Group A).



Figure 2. Oral hygiene kit (Group B).

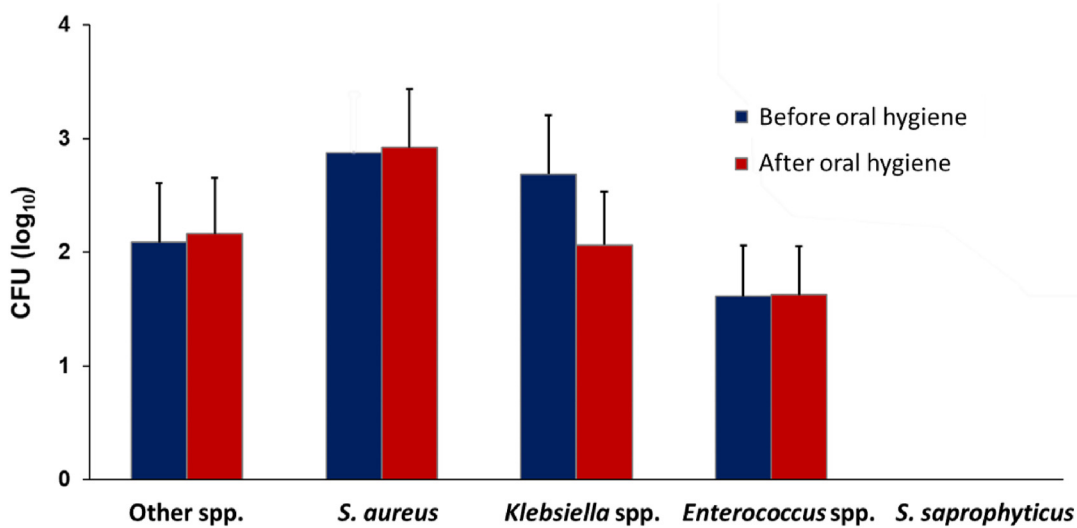


Figure 3. Quantification of CFU of microorganisms before and after cleaning (Group A). CFU of other spp., *Staphylococcus aureus*, *Klebsiella* spp., *Enterococcus* spp., *Staphylococcus saprophyticus*.

comparison correction test i.e. The Bonferroni test was used when several dependent or independent statistical tests were being performed simultaneously. Means were compared using Wilcoxon's t-test and Mann Whitney (to determine a confidence interval for difference between two population medians). Paired ($P < 0.05$), unpaired and chi-squared tests were performed using the R software program version 3.3.1.

Results

The results demonstrate no significant reduction in the number of colony forming units (CFU) before and after cleaning (Group A). This was the case for *S. aureus* ($P=0.92$), *Klebsiella* spp. ($P=0.14$), *Enterococcus* spp. ($P=0.93$), *S. saprophyticus* ($P=1$) and among other bacterial species ($P=0.7$), (Figure 3).

Within Group B, a significant reduction in CFU was observed before and after hygiene. This included *S. aureus* ($P=0.03$) before sanitizing with $4.04 \text{ Log}_{10} \text{ CFU mL}^{-1}$ and after sanitizing with $2.53 \text{ Log}_{10} \text{ CFU mL}^{-1}$. Analyzing *Klebsiella* spp. ($P<0.001$) showed effects in decreasing CFU from

3.36 before sanitization to $1.42 \text{ Log}_{10} \text{ CFU mL}^{-1}$ after sanitization (Figure 4).

Comparing the sanitization protocols, there was a statistical difference in the reduction of CFU in other spp. ($P=0.007$) between Group A ($2.16 \text{ Log}_{10} \text{ CFU mL}^{-1}$) and Group B ($0.53 \text{ Log}_{10} \text{ CFU mL}^{-1}$) (Figure 6).

In both groups, there was a predominance of the male gender, Group A showed 25 men (55%) and Group B 31 men (69%). The mean age in Group A was 63 years and in Group B the mean was 65 years old (not statistically different).

In the present study, no significant differences were found between the length of stay of the two groups; there was only a reduction of three days of hospitalization between the groups, with Group A having a mean length of stay of 36 days, and group B, 33 days (Figure 7).

Discussion

Oral hygiene of hospitalized patients is known to be an issue [25,26]. The presence of Dentistry in this environment is

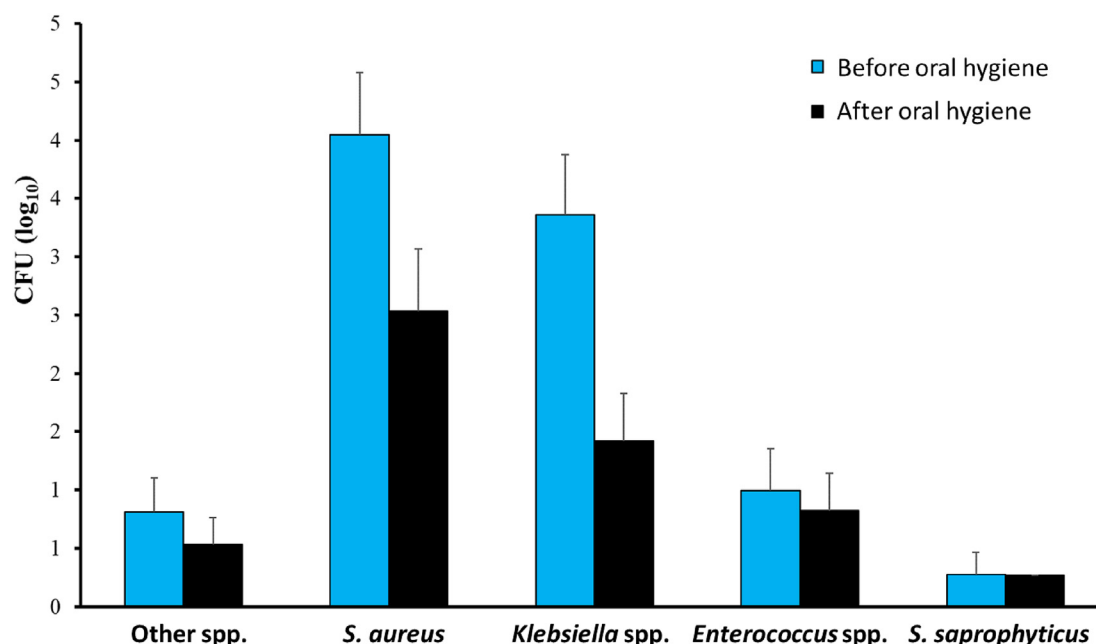


Figure 4. Quantification of CFU of microorganisms before and after sanitization (Group B). CFU of other spp., *Staphylococcus aureus*, *Klebsiella* spp., *Enterococcus* spp., *Staphylococcus saprophyticus*. * Statically significant difference ($P < 0.05$).

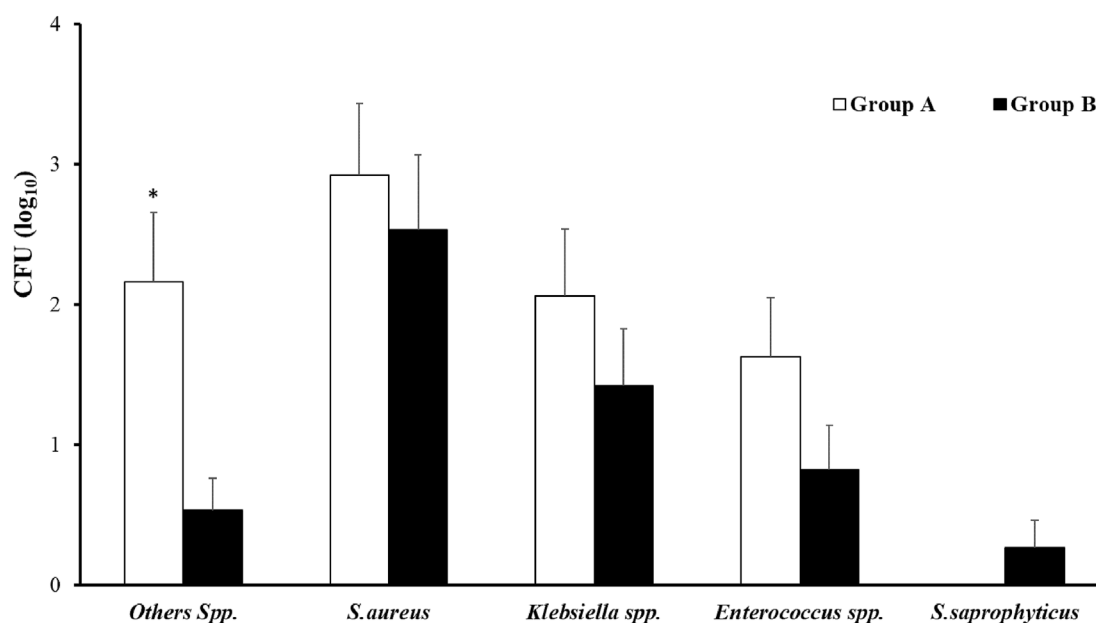


Figure 5. Quantity of oral bacteria (CFU) upon the implementation of oral hygiene protocols in Group A and Group B patients. Statistically significant ($P < 0.05$) difference was found between other spp., *S. aureus*, *Klebsiella* spp., *Enterococcus* spp., and *S. saprophyticus*.

necessary to evaluate the presence of oral biofilm, periodontal disease, presence of caries and oral lesions that are precursors to nosocomial infections, trauma and other oral pathologies that represent risk or discomfort to hospitalized patients. It is known that oral care, when properly performed, greatly reduces the incidence of pneumonia associated with the use of MV in ICU patients [27].

Figures 4 and 5 show the prevalence of CFU of respiratory bacterial pathogens such as *S. aureus*, *Klebsiella* spp.,

Enterococcus spp., and other species of bacteria in the saliva of the patients studied, before and after oral hygiene, corroborating the data reported in the literature [28–31]. Group A, which consisted of brushing with spatula, gauze, and 0.12% chlorhexidine, was less effective in reducing CFU than the oral hygiene method performed in Group B, associated with suction brushing and 0.12% chlorhexidine gel.

Lecomte et al. [32], mention that suction brushing associated with chlorhexidine used in ICU patients, has benefits in reducing

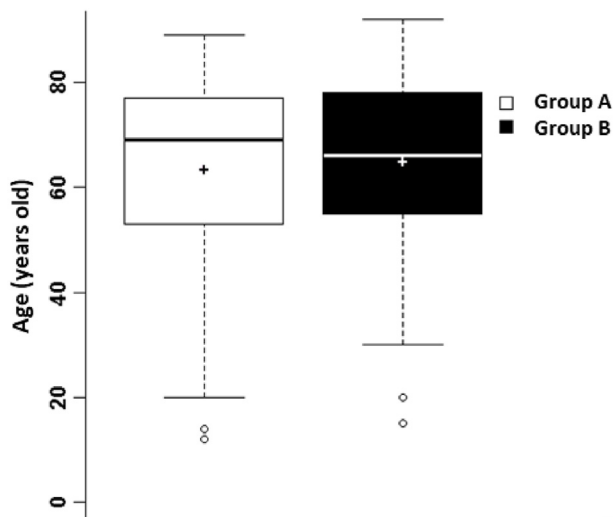


Figure 6. Mean age of the patients ($P= < 0.01$).

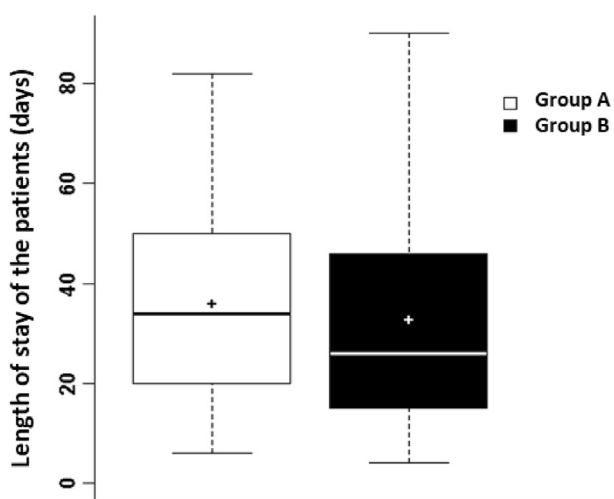


Figure 7. Mean length of stay ($P= > 0.01$).

pathogenic microorganisms for the prevention of VAP. These suction toothbrushes tend to be more efficient at removing dental plaque and removing debris and secretions, hence a significant reduction was found in the present study in Group B patients.

Oral hygiene involving brushes, toothpaste and 0.12% chlorhexidine provides removal of tongue coating and significantly reduced pneumonia and length of stay of compromised patients in the hospital environment [33–35].

This study has limitations, firstly it is small, single center and therefore findings are not readily generalizable to other institutions. Secondly, we were able to demonstrate the impact of oral hygiene techniques on the buccal microbiota, but not on the incidence of VAP itself and this should be an area for further study.

Conclusions

Our results demonstrate that oral hygiene using a suction toothbrush with 0.12% chlorhexidine gel proved to be more effective than conventional hygiene (using gauze soaked in 0.12% chlorhexidine) at reducing the CFU of potentially

pathogenic organisms in patient saliva. There was a reduction in the pathogenic oral microbiota in patients receiving the oral hygiene method under study in the ICU of the Evangelico Hospital. In the present investigation, we did not find significant impact of length of stay of the patients in the hospital. This study confirmed that tooth brushing with chlorhexidine based regimes is vital in dental care. Decay of human dental structures and inflammatory degeneration of the alveolar bone are attributed to oral biofilms. In addition, lifespan of dental prostheses and restoratives are negatively affected by oral biofilms on artificial materials. Poor brushing habit favors the deposition and lingering sugars and other food particles on teeth surfaces which in turn results in the proliferation and biofilm formation by pathogenic microbes. Therefore, oral brushing has significant importance in reducing the oral biofilms and enhancing the oral health, in addition to its' potential impact on VAP incidence.

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Conflict of interest statement

All authors report no conflicts of interest relevant to this article.

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Patient consent

Written consent gained from patient/next of kin for use of anonymized photographs within manuscript. Consent retained by authors.

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