Effectiveness of Chlorexidine in Bucal Hygiene for the Prevention of Pneumonia Associated with Mechanical Ventilation

Eficácia da Clorexidina na Higiene Bucal para Prevenção de Pneumonia Associada a Ventilação Mecânica

Eficacia de la Clorhexidina en la Higiene Bucal para la Prevención de Neumonía Asociada a la Ventilación Mecánica: Revisión Narrativa

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RESUMO

Objetivo: Analisar as evidências disponíveis sobre a eficácia da clorexidina na higiene bucal para prevenção de pneumonia associada a ventilação mecânica (PAVM). **Método:** estudo de revisão de literatura, tipo narrativa, no qual foram avaliadas as publicações referentes ao período de 2008 a 2021, indexados na Biblioteca Virtual em Saúde (BVS) no State National Library of Medicine (PubMed/MEDLINE). **Resultados:** Seleção de 18 artigos, categorizados em duas amostras de acordo com o controle do biofilme bucal, classificados em nível de evidência e sumarizados. **Conclusão:** Apesar das pesquisas sobre os cuidados orais e PAVM serem abundantes, existe uma falta de consenso em relação a frequência, aos dispositivos mecânicos e a concentração da clorexidina. Quanto ao controle químico, a clorexidina, seja na forma de gel ou como enxaguante nas concentrações de 0,12% ou 0,2%, administrados a cada doze horas reduziram a ocorrência da PAVM. Enquanto os métodos mecânico/químico mais adequados são aqueles que oferecem a escovação associada a sucção, em um mesmo dispositivo, seja escova ou esponja de sucção, ambas associadas ao uso da clorexidina.
Descritores: Clorexidina; Higiene Bucal; Unidade de Terapia Intensiva.

ABSTRACT

Objective: to analyse the available evidences on the efficacy of chlorhexidine in oral hygiene aiming to prevent cases of ventilator-associated pneumonia (VAP). **Method:** study of literature review, narrative type, in which papers from 2008 to 2021, published in the Virtual Health Library (VHL) in the State National Library of Medicine (PubMed/MEDLINE) were analysed. **Results:** Selection of 18 papers, categorized in two samples according to the control of oral biofilm, then classified by level of evidence and summarized. **Conclusion:** In spite of research on oral care and VAP being plenty, it lacks consensus regarding mechanical devices and concentration of chlorhexidine. As for chemical control, chlorhexidine, whether given as gel or mouthwash in concentration levels of 0.12% or 0.2%, being given every twelve hours, has decreased the ocurrence of VAP, while the most suitable mechanical/chemical methods are those that provide brushing and succion in the same device, whether by brush or suction sponge, both associated with the use of chorexidine.
Descriptors: Chlorhexidine; Oral Hygiene; Intensive Care Unit.

RESUMEN

Objetivo: analizar las evidencias disponibles sobre la eficacia de la clorhexidina en la higiene bucal para prevención de neumonía asociada a ventilación mecánica (NAVM). **Métodos:** estudio de revisión de la literatura, tipo narrativa, en el cual fueron evaluadas las publicaciones que hacen referencia al periodo de 2008 a 2021, indexados en la Biblioteca Virtual en Salud (BVS) de la Biblioteca Nacional Estatal de Medicina (PubMed/MEDLINE). **Resultados:** Selección de 18 artículos, categorizados en dos muestras de acuerdo con el control de biopelícula oral, clasificados por nivel de evidencia y sumariados. **Conclusión:** A pesar de que las investigaciones sobre los cuidados orales y NAVM son abundantes, hay una falta de consenso en lo que concierne a la frecuencia, los dispositivos mecánicos y la concentración de clorhexidina. Respecto al control químico, la clorhexidina, sea en la forma de gel sea como enjuague en las concentraciones de 0,12% o 0,2%, administrados a cada doce horas redujeron la ocurrencia de NAVM. Mientras los métodos mecánicos/químicos más adecuados son los que ofrecen el cepillado asociado a la succión, en un mismo dispositivo, por cepillo o esponja de succión, ambos asociados al uso de clorhexidina.
Descritptores: Clorhexidina; Higiene Oral; Unidad de Terapia Intensiva.

REVIEW

Introduction

Ventilatory-associated pneumonia (VAP) is defined as that which develops within 48 hours of starting mechanical ventilation (MV) and up to 48 hours after extubation. It is an infectious disease of inaccurate and multicausal diagnosis. It is one of the most common infections in Intensive Care Units (ICU), and are related to increased hospitalization time, increased morbidity and increased mortality, which significantly affects hospital costs.[1-3]

These bacterial colonization sits responsible for 15% of health care-related infections-IRAS and approximately 25% of all infections acquired in ICUs. The lower respiratory tract inoculation, at first sterile, routinely occurs by aspiration of secretions, colonization of the aerodigestive tract or the use of contaminated equipment or medications. The development of biofilm is a natural process commonly found on the surfaces of the teeth and on the back of tongue. Risk factors for VAP include prolonged intubation, enteral feeding, witnessed aspiration, paralyzing agents, underlying diseases, and age extremes.[4-7]

Considering that the microbiota of the oral cavity poses a threat to critically ill patients, some strategies to prevent colonization have been studied, such as the application of non-absorbable topical antibiotics. Although research on oral care and VAP is abundant, there is a lack of consensus regarding the technique, frequency, choice of pharmacological agent and its concentration.[6-9]

The nursing team is responsible for oral care in mechanically ventilated patients. The implementation of effective prophylactic measures are the basis for the prevention of this pneumonia, which is considered a serious pathology. In this sense, nurses should, together with the multidisciplinary team, provide continuous care to patients with complex and high-risk clinical conditions.[31]

In view of the above, we seek in evidence-based practice the theoretical framework to support this study, since its approach provides the systematic application of scientific evidence available for the evaluation of options and decision-making in the comprehensive care of the patient.[6]

In this sense, the aim of this study was to analyze the available evidence on the efficacy of chlorhexidine in oral hygiene for prevention of pneumonia associated with mechanical ventilation.

Method

This is a narrative literature review study, in which one can synthesize and summarize the information found in bibliographic research that was published in the period corresponding to the years 2008 to 2021.

As bases de dados utilizadas nas pesquisas foram: Medline, Lilacs e Pubmed. Using the descriptors of the virtual health library: Chlorhexidine, oral hygiene and intensive care unit. Data were collected in March 2019. Complete original articles, published in a nursing journal, in the Portuguese and English that addressed the theme of the study, are included. 18 articles were identified. Which were read in full, summarized and summarized for further discussion.

In the collection of bibliographic data, a form was applied that extracted from the articles important information such as objective, methodology, type of research, results, conclusions and level of evidence. The classification of the level

of evidence was performed based on the literature using evaluation criteria established between one and seven.[9-10]

• Level of evidence 1: resulting from systematic review or meta-analysis of randomized controlled trials;
• Level of evidence 2: evidence derived from at least one well-designed randomized controlled trial;
• Level of evidence 3: well-delineated clinical trials without randomization;
• Evidence level 4: well-delineated cohort and control case studies;
• Level of evidence 5: originating from a systematic review of descriptive and qualitative studies;
• Level of evidence 6: derived from a single descriptive or qualitative study;
• Level of evidence 7: from the opinion of authorities and/or report of expert committees.

Results

The study sample generated two thematic categories, which will be presented below:
• Chemical control of oral biofilm:
Of the eighteen articles contained in the sample, eight (44.4%) showed the use of Chlorhexidine at different concentrations in the prevention of VAP.
• The mechanical and chemical control of oral biofilm:
Of the eighteen articles contained in the sample, ten (55.5%) showed the use of Chlorhexidine associated with mechanical removal devices in the prevention of VAP.

As shown in Table I, we observed the main information extracted from the selected articles related to the chemical and mechanical/chemical use of chlorhexidine in the prevention of VAP, distributed according to nursing practices, classified according to publication, design, level of evidence (NE) and interventions performed.

Table 1 - Distribution of nursing practices related to oral biofilm control, classified according to publication, design, evidence level (EL) and interventions performed. 2021

Nursing Practice	Authors/Title/Country/Year of publication	Design	EL	Intervention
Dental biofilm chemical control	Souza AF, Guimarães AC, Ferreira EF. Evaluation of the implementation of new protocol of oral hygiene in an intensive Care center for prevention of pneumonia associated with mechanical ventilation. Brazil, 2013.[12]	Experience Report	6	Replacement of 0.05% cetylpyritinichloride solution with 0.12% chlorhexidine solution
	Guimarães GR, Queiroz APG, Ferreira ACR. Establishment of a Protocol of Oral Hygiene in Hospitalized Patients in the ICU of Husf.Brazil, 2016.[13]	Prospective study	4	Chlorhexidine at 0.12% of 12/12H (PerioPlak,REYMER)
	Chen Y, Mao E, Yang Y, Zhao S, Zhu C, Wang X, Jing F, Sheng H, Zhu C, Wang X, Jing F, Sheng H. Prospective Observational Study To Compare Oral	Prospective study	4	Metronidazole 0.08 every 12hours X Chlorhexidine 0.2% 12/12H

	Topical Metronidazole Versus 0.2% Chlorhexidine Gluconate To Prevent Nosocomial Pneumonia. China, 2016.[14]			
	Bosca I, Berar C, Marincean AM, Petrisor C, Ionescu D, Hagau N. The Impact of 0.5% Chlorhexidine Oral Decontamination on the Prevalence of Colonization and Respiratory Tract Infection in Mechanically Ventilated Patients. Preliminary Study. Romênia, 2013.[15]	Cohort study	4	Chlorhexidine 0.5% 6/6H X 12/12H
	Tang H, Chao C, Leung P, Lai C. An Observational Study to Compare Oral Hygiene Care With Chlorhexidine Gluconate Gel Versus Mouthwash to Prevent Ventilator-Associated Pneumonia.Taiwan, 2017. [16]	Prospective study	4	Mouthwash with 0.2% Chlorhexidine 3 times a day X 0.2% Chlorhexidine Gluconate gel 3 times a day
Mechanical and chemical control of dental biofilm	Cabov T., Macan D., Husedžinović I., Skrlin-Šubić J. Sestan-Crnek S., Perić B., Kovač Z., Golubović V. The impact of oral health and 0.2% chlorhexidine oral gel on the prevalence of nosocomial infections in surgical intensive-care patients: a randomized placebo-controlled study. Croácia. 2010.[17]	Double-blind randomized clinical trial	2	Chlorhexidine gel 0.2% 3 times a day X Placebo Gel 3 times a day.
	Chlorhexidine decreases the risk of ventilator-associated pneumonia in intensive care unit patients: a randomized clinical trial. Turkey. 2012. [18]	Double-blind randomized clinical trial	2	Saline solution 4 times a day X chlorhexidine 0.12% 4 times a day
	Triamvisit S., Maneewan C., Bunturat P., Wongprasert W., Limpassatan K., Kasatpibal N., Euathrongchit J. Results of an Evidence-Based Care Bundle for Reducing Ventilator-Associated Pneumonia (VAP) in Neurosurgical Patients. Thailand. 2016. [19]	Prospective study	4	Chlorhexidine 0.12% 4 times a day
Mechanical and chemical control of dental biofilm	Vidal CFL, Vida KL, Monteiro JGM, Cavalcanti A, Trindade AP, Oliveira M, Godoy M, Coutinho M, Sobral PD, Dutra P, Vilela BG, Leandro MA, Montarroyos U, Ximenes RA, Lacerda H. Impact of Oral Hygiene Involving Toothbrushing Versus Chlorhexidine in the Prevention of Ventilator-Associated Pneumonia: A Randomized Study. [20]	Prospective, randomized study	2	0.12% clx solution every 12 hours X Toothbrush and clx gel 0.12% every 12 hours
	Chacko R, Rajan A, Lionel P, Thilagavathi M, Yadav B, Premkumar J. Oral Decontamination Techniques and Ventilator-associated Pneumonia. India, 2017. [21]	Double-blind randomized clinical trial	2	Sponge with CLX 0.2%, 3x per day X toothbrush, Yankauer disposable suction catheter and a disposable syringe. 0.2% chlorhexidine gluconate
	Chacko R, Rajan A, Lionel P, Thilagavathi M, Yadav B, Premkumar J. Oral Decontamination Techniques and Ventilator-associated Pneumonia. India, 2017. [21]	Double-blind randomized clinical trial	2	Sponge with CLX 0.2%, 3x per day X toothbrush, Yankauer disposable suction catheter and

				a disposable syringe. 0.2% chlorhexidine gluconate
	Conley P, McKinsey D, Graff J, Ramsey AR. Does an Oral Care Protocol Reduce Vap in Patients With a Tracheostomy? United States, 2013. [22]	Prospective study	4	Brushing with toothpaste and applying Chlorhexidine Gluconate solution 0.12% every 12 hours
	Cutler RL, Sluman P. Reducing ventilator associated pneumonia in adult patients through high standards of oral care: A historical control study. England, 2014. [23]	Historical Control	4	Brushing with toothpaste and 1% chlorhexidine.
	Munro CL, Grap MJ, Jones DJ, Deborah J, McClish DK, Sessler CN.Chlorhexidine, Toothbrushing, and Preventing Ventilator-Associated Pneumonia in Critically Ill Adults. United States, 2009. [24]	Randomized, controlled study with double experimental design.	2	Chlorhexidine 0.12% with swsow 2 times a day X Brushing 3 times a day X Brushing + chlorhexidine X Usual oral care.
	Lev A, Aied AS, Arshed S. The effect of different oral hygiene treatments on the occurrence of ventilator associated pneumonia (VAP) in ventilated patients. Israel, 2015. [25]	Prospective, controlled study.	4	Suction brush + baking soda + 1.5% hydrogen peroxide + mouth hydration X Chlorhexidine sponge.
Mechanical and chemical control of dental biofilm	Zhao L, Liu L, Chen J, Yang C, Nie J, Zhang M. Ventilator bundle guided by context of JCI settings can effectively reduce the morbidity of ventilator-associated pneumonia. China, 2017. [26]	Prospective, controlled study	4	Cotton with Chlorhexidine X Chlorhexidine suction sponge

Discussion

Chlorhexidine is an antimicrobial that has effective action against plaque, gingivitis and is biocompatible with the tissues of the oral cavity, being considered the gold standard in the lineage of oral antiseptics. Its use in selective decontamination of the oropharynx may reduce the incidence of pneumonia, as it inhibits bacterial colonization. However, it can lead to resistance of microorganisms and should only occur in high-risk situations.[10,30-31]

The eighteen articles reported that the use of chlorhexidine in the prevention of VAP has been widely studied, however, being implemented as a chemical agent or associated with a mechanical method for control of oral biofilm, fragmenting the articles into two categories.

In the first category, eight articles studied chlorhexidine as a chemical agent in the prevention of VAP. Of these, three (37.5%) used it twice a day, one (12.5%) compared the use of chlorhexidine administered four times a day versus twice a day, two (25%) analyzed its use three times a day and two (25%) investigated chlorhexidine administered four times a day.[11-18]

Chlorhexidine concentrations were also observed in the eight articles, and three (37.5%) used chlorhexidine at 0.12%, four (50%) used chlorhexidine concentration at 0.2% and one (12.5%) used chlorhexidine at 0.5%.[11-18]

Researchers compared 0.08% metronidazole with 0.2% chlorhexidine, both applied every 12 hours, in 873 intensive care patients, in addition to a standard care protocol for pneumonia prevention. The eligible patients were divided into 4 periods: period M (metronidazole at 0.08%) and period C (chlorhexidine at 0.2%), which was fractionated into three moments C1, C2 and C3. The occurrence of VAP in patients intubated during period M was 62.5%, decreasing significantly to 47.6%, 36.7%, and 17.2% per year in the 3 subsequent years. Making evident the importance of the use of chlorhexidine in the prevention of VAP.[13]

The antimicrobial effects of 0.5% chlorhexidine administered every 6 hours and every 12 hours were studied in the ICU with mechanically ventilated patients and realized that no significant differences were found between these approaches. However, the sample composed of only 30 patients limits the relevance of this study. [14]

Considering the exclusive approach of chlorhexidine at 0.12% every 12 hours, two articles had different results. In one study, chlorhexidine gluconate at 0.12% in the oral hygiene protocol incorporated in the VAP prevention bundle had a significant impact on reducing the rates of this respiratory infection from 33.3% to 3.5%. On the other hand, the use of 0.12% chlorhexidine gluconate (Perioplak, REYMER) every 12 hours in mechanically ventilated patients did not significantly decrease the incidence of pneumonia. However, the researchers reported that this procedure is a challenge for the nursing team because they are involved in the execution of oral hygiene daily, however, this care was not prioritized in the daily routine of nursing in this ICU.[11-12]

Chlorhexidine at 0.2% administered three times a day was the subject of two studies, both of which showed a decrease in the incidence of nasocomal infections, shorter hospitalization time and lower mortality rate. The value of the gel was cheaper than that of the solution, making it the best choice, as it proved to be more effective, and cheaper in addition to having less time from the nursing team. [15-16]

Analyzing the results obtained in two studies, it was observed that the topical use of chlorhexidine every four hours reduces the incidence of VAP. Researchers implemented the Suandok Neurosurgical Critical Care Bundle (SNCCB) protocol, which uses chlorhexidine at 0.12% every six hours, in addition to other measures. And they reduced the rate of VAP per 1,000 days of ventilation from 39.55% to 13.3%.[17-18]

A randomized, controlled, double-blind study was conducted with 61 patients aiming to compare oral hygiene with saline solution (n=32) and oral hygiene with 0.2% chlorhexidine (n=29), both administered four times a day. The rate of VAP in the group using saline was 68.8%, contrasted with 41.4% of the group that used chlorhexidine.[17]

In the second category, ten articles were studied regarding the chemical and mechanical control of oral biofilm performed by the intensive care nursing team.[19-28]

Researchers conducted a prospective randomized study to verify whether oral hygiene through more chlorhexidine brushing in 0.12% gel reduces the incidence of VAP, MV time, time of hospitalization and icu mortality rate, when compared to oral hygiene only with chlorhexidine, a solution of 0.12%, without brushing, in mechanically ventilated adult individuals. The sample consisted of

213 patients, 108 were randomized to the control group and 105 to the intervention group. The results showed that, among patients submitted to tooth brushing, there was a significant reduction in MV time and tendency to reduce the incidence of VAP and length of icu stay, although without statistical significance.[19]

In order to evaluate oral hygiene with brushing and toothpaste twice a day, brushing with chlorhexidine gel at 1% four times a day and oromouth aspiration in patients undergoing mechanical ventilation, a historical control study was conducted with 1,087 patients, showing a 50% reduction in the occurrence of VAP. Researchers evaluated the effects of oral hygiene using toothbrushing with toothpaste associated with 0.12% chlorhexidine solution every 12 hours and Suction by Yankauer catheter. The sample consisted of 75 patients and the results showed that this method did not significantly reduce the occurrence of VAP.[21]

On the other hand, a prospective, randomized, 'double-blind' study was conducted with 212 randomized patients in 02 groups, the control group with 106 patients using Chlorhexidine 0.2% and the experimental group, also with 106 patients using a toothbrush with 0.2% chlorhexidine associated with the Yankauer disposable suction catheter and disposable syringe. No difference was found between the methods. However, the use of strict exclusion criteria made episodes of VAP in the study population substantially lower, possibly compromising the analysis of the results. [20]

The relationship between oral hygiene and the reduction of VAP rates was also researched by a randomized, controlled study with a double design that distributed 547 patients in four groups, the first used 0.12% chlorhexidine with oral swa dome twice a day, the second performed brushing three times a day, the third combined brushing three times a day with chlorhexidine every twelve hours and the fourth used the usual care. The article showed that chlorhexidine 0.12% with oral swawas effective in reducing VAP, that brushing did not reduce the incidence of VAP and that the combined use of brushing and chlorhexidine did not provide additional benefit over the use alone of chlorhexidine.[23]

The implementation of a global hygiene regimen was investigated in 90 patients divided into two groups, the first (study group, n=45) implemented a global hygiene regimen with suction brush, sodium bicarbonate, 1.5% hydrogen peroxide and mouth moisturizer, while the second (control group, n=45) underwent conventional treatment with sponge and chlorhexidine at 0.2%. The incidence of VAP in the study group was 8.9% compared to 33.3% in the control group. Evidencing that global hygiene effectively reduces the occurrence of VAP. However, the non-blind nature of the study has the potential to introduce.[26]

Analyzing the results obtained in two articles, it was observed that the use of chlorhexidine sution sponge in oral hygiene of adult patients, under mechanical ventilation, reduced the incidence of VAP, with statistically significant results. In one study researchers distributed 899 patients in two periods. Period 1 (n=425) used foam with chlorhexidine, while period 2 (n=474) used the suction sponge and chlorhexidine. In patients in period 1, the incidence of VAP was 12.8%, compared to 8.5% in period 2. However in period 1 the annual costs were calculated at US$ 475.00 and in period 2 at US$ 12,882.00. However, in the hospital where the study was conducted, for each VAP infection, the expenditure was approximately US$ 37,920.00.[26]

On the other hand, a study conducted by a group of researchers to evaluate oral hygiene with cotton soaked in chlorhexidine confronting as a suction sponge device soaked in chlorhexidine, both associated with a ventilatory budle guided by the Joint Commission International (JCI). The incidence of bad breath, dirt residue and plaque were significantly lower in the group that used the sponge with suction and chlorhexidine. Bad breath 10% versus 40%, dirt residue 16.7% versus 70%, plaque 3.3% versus 30%. Vap cases per thousand days of MV were reduced from 17 to 3.5 cases. The study concludes that the ventilation package can in fact reduce vame morbidity and oral care as the suction sponge and chlorhexidine can effectively improve oral hygiene.[25]

The electric brush was another object of investigation among the researches analyzed. A randomized double-blind longitudinal prospective study compared oral hygiene with chlorhexidine (GS) versus oral hygiene with chlorhexidine associated with electric brush (GR). A total of 147 patients were included in the study, 73 in the chlorhexidine standard group and 74 in the raspall group (chlorhexidine + electric brush). The incidence of VAP per 1000 days of mechanical ventilation was 25.89 days in the standard group and 20.68 days in the raspall group, so there is a tendency to decrease the occurrence of VAP in the raspall group.[28]

On the other hand, in this prospective, simple-blind randomized study, 147 patients were divided into two groups. The first, standard group (n=73), performed oral care with chlorhexidine at 0.12% every 8 hours, the second group brushed teeth (n=74), used oral care standards plus electric brush. An episode of VAP was documented in 73.3% of the toothbrush group compared to 55.6% in the standard group. The intervention was simple and safe, but was not effective in preventing VAP.[27]

Oral care in intensive care is extremely important, considering the immobility imposed on the mechanically ventilated patient and the microbial diversity of the oral cavity, enabling high rates of VAP. In order to reduce the incidence of VAP, the National Agency for Sanitary Surveillance - ANVISA, recommends the use of chlorhexidine at 0.12%.[4]

VaP is associated with increased costs in health, morbidity and mortality, therefore, other studies are needed, in larger groups, with greater statistical relevance that investigates the use of oral chlorhexidine associated, or not, with other devices and that require adequate time from the nursing team, because due to the complexity of this patient audience, the nursing professional will often be overloaded, as well as the financial cost to the institution.

Conclusion

The narrative review allowed the construction of a synthesis of practices related to oral hygiene of critically ill patients. The number of publications allowed comparing a diversity of practices related to the reduction of oral biofilm aiming to reduce the incidence of VAP.

Although research on oral care and VAP is abundant, there is a lack of consensus regarding the frequency, mechanical devices and chlorhexidine concentration.

As for chemical control, chlorhexidine, either in the form of gel or as a rinse at concentrations of 0.12% or 0.2%, administered every twelve hours

reduced the occurrence of VAP. Despite the lack of uniformity regarding the number of times the procedure should be performed and the concentration of the drug to be used, these results show that the institutions seek to use the latest evidence on the use of this antimicrobial.

In view of the findings of this review, the most appropriate mechanical/chemical methods are those that offer brushing associated with suction, in the same device, be it brush or suction sponge, both associated with the use of chlorhexidine.

It was evident that brushing, in isolation, did not bring benefits in reducing infection, however the isolated use of chlorhexidine proved beneficial in reducing VAP.

Regarding clinical practice, we can affirm that this review collaborates with the implementation of new protocols aimed at improving oral care in the prevention of VAP in critically ill patients.

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