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EFFECTIVENESS OF CHLOREXIDINE DIGLUCONATE CONCENTRATIONS IN REDUCING THE INCIDENCE OF VAP IN PATIENTS ADMITTED TO THE ICU: A CRITICAL REVIEW OF THE LITERATURE

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Abstract: The objective of this review was to identify and critically analyze the evidence in the scientific literature, through clinical trials, to compare the effectiveness of various concentrations of chlorhexidine with the same solution and the one most frequently used in the oral hygiene of hospitalized patients. The authors carried out an electronic and manual search in several databases (Pubmed, Scielo, Lilacs, Cochrane) and gray literature (Theses Bank and Google Scholar). There were no limitations regarding the year of publication or language. A total of 176 articles were selected and systematically analyzed according to the inclusion criteria that were pre-defined (clinical trials, randomized or not, in any language, conducted on sick patients, regardless of sex, age, race, admitted to hospitals, whether in the ICU or in other sectors). These articles were evaluated, the data considered relevant were extracted and a classification was made according to the quality of the methodological evidence found, with level I if it met all criteria or four (with only one B). Level II if partially met the criteria (maximum two C assessments). Level III if it followed two criteria or less (more than two Cs). The only study selected was classified as evidence level III, as it did not include the necessary information for a good quality study and, therefore, was considered to have a high risk of bias. Regarding the treatment used, the chlorhexidine solution was compared to the same product at a different concentration in the control group. Given the great variability of concentrations of this mouthwash, more research must be carried out so that there is greater certainty and standardization of which concentration proves to be most effective in preventing aspiration pneumonia in hospitalized patients.
Keywords: Oral hygiene. Chlorhexidine. Intensive care unit.

INTRODUCTION

Individuals who are admitted to Intensive Care Units (ICU), mostly due to the fact that they are extremely fragile and require intubation, do not have adequate oral hygiene during hospitalization or have precarious hygiene when there are no dental surgeons. trained professionals inserted in the hospital environment (BATISTA, SA et al., 2014). Consequently, these individuals are vulnerable to some oral conditions related to systemic diseases, medications or mechanical ventilation equipment. And, when it comes to oral infections, most of the time there is a correlation with regard to the emergence of systemic disorders such as, for example, nosocomial pneumonia (BATISTA, SA et al., 2014).

Pneumonia, an acute infection of the lungs, can bring a variety of symptoms and local and systemic signs to the patient, such as rapid and shortened breathing, cough, fatigue, fever, production of secretions and chest pain. The main causes of this lung pathology are bacteria, which, in turn, are the easiest to prevent and resolve (SCANNAPIECO, FA, 2006).

In this sense, and in the case of hospital environments, the type of pneumonia that occurs in these places, within 48 to 72 hours after the patient's hospitalization, is nosocomial. One of the risk factors for its appearance is the lack of or poor oral hygiene. Thus, one of the common causes of death among infections acquired in hospital environments is established (BARROS, JNP et al., 2022).

The bacterial colonization found in the oral cavity of hospitalized patients varies according to several factors, including the use of antimicrobials during hospitalization (BASSIN, AS; NIEDERMAN, MS, 1995). As a result, means of prevention have been the target of several studies, one of which is the adoption of non-absorbable antibiotics for topical use (FARDIN, R. et al., 2005).

Carrying out oral hygiene in ICU patients is considered a basic factor in maintaining oral health. In addition to acting in the prevention of infections, it also has the role of providing comfort to the patient (BATISTA, SA et al., 2014). With this oral hygiene action being performed frequently, there is a reduction in the occurrence of mechanical aspiration pneumonia or ventilator-associated pneumonia (VAP), since, by maintaining the patient's oral health, there is a decrease in the aspiration of potentially harmful microorganisms. causing this problem (BATISTA, SA et al., 2014).

Among antiseptic mouthwashes, chlorhexidine, an antimicrobial agent, is highly effective and generally used as the gold standard over others (ELDRIDGE, KR et al., 1998). In this sense, it presents several benefits, which: it has good substantivity, that is, it can act against several pathogenic agents such as gram-positive bacteria, gram-negative bacteria and yeasts, and therefore can reduce bacterial colonization (DAI, W. et al., 2022). It also presents low rates of undesirable effects, low local and systemic toxicity (ELDRIDGE, KR et al., 1998). Furthermore, it has good substantivity, that is, effectiveness even after approximately 12 hours of application (ZAND, F. et al., 2017). When combined with salivary glycoprotein, chlorhexidine reduces adsorption protein on the tooth surface and prevents the formation of bacterial plaque (DAI, W. et al., 2022). Chlorhexidine is also beneficial for the healing and regeneration of oral tissue, its mechanism of action occurs with its dissociation, thus generating cations and anions of chlorhexidine and the combination of the bacterial cell wall with a negative charge, produces a detoxifying effect. sterilization (DAI, W. et al., 2022). Furthermore, chlorhexidine can also bind to

bacterial extracellular polysaccharide, which prevents bacteria from easily attaching to the cell membrane and thus helping to decrease bacterial proliferation (DAI, W. et al., 2022).

Being indicated for individuals with motor limitations and mental disabilities, it will play a fundamental role in reducing pathologies and problems with oral health (ELDRIDGE, KR et al., 1998). Furthermore, the topical use of this mouthwash, when used in patients undergoing mechanical ventilation, appears to reduce colonization of the oral cavity, being precisely associated with a decrease in the occurrence of aspiration pneumonia due to mechanical ventilation (BERALDO, CC; ANDRADE, D. DE., 2008).

According to the results of research by Nascimento (2018), there are several concentrations of chlorhexidine found in investigative studies, namely 0.02%, 0.05%, 0.1%, 0.12%, 0.2% and 2%, which makes any discussion regarding the effectiveness in preventing aspiration pneumonia in hospitalized patients difficult. However, amid this variety, there is still no consensus regarding the ideal concentration of this mouthwash for oral hygiene in hospitalized patients (BERALDO, CC; ANDRADE, D. DE., 2008). Given the above, the main objective of this study was to compare the effectiveness of various concentrations of chlorhexidine and the one most frequently used in the oral hygiene of hospitalized patients.

MATERIAL AND METHOD

The methodology was developed following the PICO Strategy. The clinical questioning was prepared according to the PICO acronym: Population = patients regardless of age or sex, hospitalized with VAP; Intervention = use of 0.12% chlorhexidine. Comparison/Control = chlorhexidine in different concentrations. Outcomes = effectiveness of chlorhexidine in reducing the incidence of VAP. The question asked was: "What is the most effective concentration of chlorhexidine for mouthwash in hospitalized patients with VAP?"

The searches were carried out in the Pubmed, Scielo, Lilacs, Cochrane databases and in the gray literature (Theses Bank and Google Scholar) with pre-determined inclusion and exclusion criteria, with keywords obtained from DECS and MeSH, isolated or combined., in English "oral hygiene", "chlorhexidine" and "intensive care unit".

Clinical trial studies were included, randomized or not, in any language, conducted on sick patients, regardless of sex, age, race, admitted to hospitals, whether in the ICU or in other sectors. The intervention of interest was performing oral hygiene using chlorhexidine comparing concentrations and the outcome to be evaluated was the effectiveness of chlorhexidine in the oral hygiene of hospitalized patients.

A detailed and complete analysis of the articles chosen for the study was carried out and several aspects were taken into consideration to carry out the final evaluation. These aspects were: author/year, study design, sample size, objectives, inclusion criteria, interventions, material used and its concentration, conclusions and level of evidence.

The quality assessment of the trials was carried out in accordance with the CONSORT checklist (MOHER, D. et al. 2010) and based on the following criteria for qualifying the methodology and classifying levels of evidence: sample calculation, randomization, concealment of allocation, masking and losses to follow-up (BELÉM, L. et al. 2021) (Table 1).

Criteria	A	B	W
Sample calculation	Adequate	Partially reported	Not mentioned
Randomization	Adequate	Partially reported	Not mentioned
Allocation Concealment	Adequate	Partially reported	Not mentioned
Masking	Adequate	Partially reported	Not mentioned
Follow-up losses	Adequate	Partially reported	Not mentioned

Table 1. Classification for assessing the quality of clinical trials

Source: adapted from Belém. Ludmila M*et et et* 2021

Author! Year	Study design	Sample Size	Goal	Inclusion Credits	Interventions	Conclusion
Zand *et al.*, 2017	ECR	**114** patients	Compare 2 concentrations of CHX in reducing oropharyngeal colonization and VAP among patients admitted to the ICU	Age to 18 years, with tracheal tube on mechanical ventilation for at least 48 hours, without diagnosis of pneumonia upon admission, without allergy to CHX, trauma or oral inflammation, immune disorders and first time in the ICU	CHX 0.2%	CHX 2% was more effective than CHX 0.2% in reducing oropharyngeal colonization and incidence of VAP

Figure 01. Flowchart: selection and inclusion of articles

The criterion was considered adequate A when reported by the authors and explained, if it was only mentioned and not explained it was established as B and C if it was not even mentioned. If the trial met all criteria or four (with only one B), it was assessed as level of evidence I, if it partially met the criteria (at most two C assessments) it was assessed as level of evidence II and if it followed two criteria or less (more than two C), was evaluated as level of evidence III (BELÉM, L. et al. 2021).

The research, reading of articles, selection and critical evaluation of the selected studies was carried out by two previously trained evaluators (JHLB) and (RSC). In case of doubt, a third evaluator (ODF) was consulted to reach a consensus.

RESULTS

Initially, 176 articles were found, 155 through electronic search and 21 through manual search. After applying the eligibility criteria, 1 article was separated for full and critical reading, the synopsis of which is found in Table 2.

Figure 1 shows the flowchart for identifying, tracking and including articles for critical review.

The only article that met the inclusion criteria for this study had level III evidence according to the criteria established to evaluate the quality of randomized clinical trials (Chart 3).

DISCUSSION

VAP is pneumonia that occurs in patients who are mechanically ventilated through an endotracheal tube or tracheostomy for at least 48-72 hours. Several studies have also shown a relationship between dental plaque colonization and respiratory disease. Fortunately, the incidence of VAP is reduced by identifying risk factors and improving prevention methods. Oral hygiene is basic and special nursing care that helps to provide comfort to patients and prevent VAP, and may include mechanical and pharmacological interventions (ZAND, F. et al., 2017).

When properly designed, conducted and reported, the randomized clinical trial represents the gold standard study in the evaluation of health interventions. However, it can produce biased results if there is no methodological rigor (FLECHA, OD et al., 2016). The study evaluated in this review may have a high risk of bias, as it does not report sufficient information contained in a good quality study.

In the selected article, the method for carrying out the sample calculation was not mentioned, which represents the possibility

that the authors did not obtain an adequate number of participants. The sample calculation is very important to determine the quantity necessary to compose the sample in order to obtain valid results (NASCIMENTO, NPG DO et al., 2018).

Randomization was graded A, as it was performed based on a computer-generated randomization table. However, allocation concealment and blinding were also not mentioned regarding how and if they were carried out. Trials in which the allocation sequence is inadequately concealed may produce higher estimates of treatment effects than trials in which authors report adequate concealment (SCHULZ, KF, 1996).

The development of the study can be affected by absences or losses of participants and to compensate for these deviations, one of the strategies commonly used is Intention-to-Treat Analysis, using the last observation made or the worst possible result (FLECHA, OD et al., 2016). In the study evaluated, 16 deaths were reported (9 in the 0.2% chlorhexidine group and 7 in the 2% chlorhexidine group). They are not even included in the flowchart and it was also not explained how these losses were treated, which means that there is a possibility that the study result was not consistent with reality, as there is a chance of reducing the power of comparison (NASCIMENTO, NPG DO et al., 2018).

Some of the greatest difficulties in carrying out clinical trials on patients admitted to the ICU are due not only to the resistance to acceptance, on the part of those responsible, for patients to undergo studies, as well as the difficulty in evaluating various intra-oral parameters due to the limitation imposed by intubation devices.

In the study conducted by Keijser JAM et al., (2003), where volunteer participants did not receive mechanical removal of plaque, but only rinsed with CHX solutions twice a day for three days, the results revealed that the effectiveness of mouthwash for 30 seconds with a 15 ml 0.12% solution was equivalent to rinsing for 60 seconds with a 10 ml 0.2% solution. The authors concluded that a 30-second rinse time was sufficient for CHX in a 0.12% solution to be effective.

The most commonly used method was through mouthwash, twice a day, using 10 ml of chlorhexidine at a concentration of 0.2%. Further research revealed that when reducing the concentration of the product and increasing the volume of solution, the amount of drug used was practically the same, and the ability to combat bacterial plaque remained similar, resulting in fewer side effects. As a result, the 0.12% concentration with 15 ml mouthwashes began to be widely used and the recommended time at this concentration would be 1 minute (FARDIN, R. et al., 2011).

Some strengths of the current study were carrying out a broad electronic and manual search for articles on clinical trials in several databases. Furthermore, the standardization of important items for a good level of evidence of the clinical trials found and their critical evaluation. On the other hand, the outcome of this review, initially, is that many studies were found according to the keywords, but excluded due to not meeting the inclusion criteria, as the majority compare chlorhexidine with several other solutions, such as saline solution, placebo, emulsions, among others. Unfortunately, literature on the subject is scarce. Therefore, this review study was limited, as only 01 article was included.

Prolonged use of chlorhexidine in high concentrations can cause side effects such as changes in taste and peeling of the oral mucosa. In contrast, lower concentrations are preferred because they have the same preventive effect and greater clinical safety.

Due to the great variability of concentrations of this mouthwash, more research must be

carried out so that there is greater certainty and standardization of which concentration proves to be most effective in preventing aspiration pneumonia in hospitalized patients.

CONCLUSION

There is not enough evidence to answer the study question due to low methodological quality and high risk of bias.

REFERENCES

1- BASSIN, A. S.; NIEDERMAN, M. S. New approaches to prevention and treatment of nosocomial pneumonia. In: **Seminars in Thoracic and Cardiovascular Surgery**. 1995. p. 70-77.

2- BATISTA, Simone Alves et al. Alterações orais em pacientes internados em unidades de terapia intensiva. **Revista Brasileira de Odontologia**, v. 71, n. 2, p. 156, 2015.

3- BELÉM, Ludmila M. et al. Uso da laserterapia no tratamento de pacientes com paralisia de Bell: revisão crítica da literatura. **Revista Portuguesa de Estomatologia, Medicina Dentária e Cirurgia Maxilofacial**, v. 62, n. 2, p. 81-86, 2021.

4- BERALDO, Carolina Contador; ANDRADE, Denise de. Higiene bucal com clorexidina na prevenção de pneumonia associada à ventilação mecânica. **Jornal Brasileiro de Pneumologia**, v. 34, p. 707-714, 2008.

5- DAI, Weiying et al. Meta-analysis of the efficacy and safety of chlorhexidine for ventilator-associated pneumonia prevention in mechanically ventilated patients. **Evidence-Based Complementary and Alternative Medicine**, v. 2022, 2022.

6- DO NASCIMENTO, Nayara Perpétuo Gonçalves et al. Aspiration Pneumonia and oral health: a critical review of literature. **Rev. Bras. Odontol**, v. 75, p. e1058, 2018.

7- **ELDRIDGE, Kathrine R. et al. Eficácia de um enxaguatório bucal com clorexidina sem álcool como agente antimicrobiano. The Journal of prótese dentária**, v. 80, n. 6, pág. 685-690, 1998.

8- FARDIN, Rafaela Fiorotti et al. Avaliação in vitro das diferentes concentrações de clorexidina no controle da placa dental bacteriana. **Revista Brasileira de Pesquisa em Saúde/Brazilian Journal of Health Research**, v. 13, n. 2, 2011.

9- FLECHA, Olga Dumont et al. A commentary on randomized clinical trials: How to produce them with a good level of evidence. **Perspectives in clinical research**, v. 7, n. 2, p. 75, 2016.

10- KEIJSER, Jan AM et al. Comparação de 2 enxaguatórios bucais de clorexidina disponíveis comercialmente. **Revista de Periodontia**, v. 74, n. 2, pág. 214-218, 2003.

11- MOHER, David et al. Explicação e elaboração do CONSORT 2010: diretrizes atualizadas para relatar ensaios randomizados de grupos paralelos. **Revista Internacional de Cirurgia**, v. 10, n. 1, pág. 28-55, 2012.

12- MONTEIRO, Catarina Luzia dos Santos José. A importância da capacitação do cirurgião-dentista no atendimento ao paciente de UTI. **Revista Fluminense de Odontologia**, 2019.

13- SCANNAPIECO, Frank A. Pneumonia em pacientes não deambuladores: o papel das bactérias orais e da higiene oral. **The Journal of the American Dental Association**, v. 137, p. S21-S25, 2006.

14- SCHULZ, Kenneth F. Ensaios randomizados, natureza humana e diretrizes para relatórios. **The Lancet**, v. 9027, pág. 596-598, 1996.

15- ZAND, Farid et al. Os efeitos do enxágue oral com clorexidina 0,2% e 2% na colonização orofaríngea e pneumonia associada à ventilação mecânica em adultos' unidades de terapia intensiva. **Jornal de cuidados intensivos**, v. 40, p. 318-322, 2017.