REVIEW

Oral care and nosocomial pneumonia: a systematic review

Cuidados bucais e pneumonia nosocomial: revisão sistemática

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ABSTRACT

To perform a systematic review of the literature on the control of oral biofilms and the incidence of nosocomial pneumonia, in addition to assessing and classifying studies as to the grade of recommendation and level of evidence. The review was based on PubMed, LILACS, and Scopus databases, from January 1st, 2000 until December 31st, 2012. Studies evaluating oral hygiene care related to nosocomial infections in patients hospitalized in intensive care units were selected according to the inclusion criteria. Full published articles available in English, Spanish, or Portuguese, which approached chemical or mechanical oral hygiene techniques in preventing pneumonia, interventions performed, and their results were included. After analysis, the articles were classified according to level of evidence and grade of recommendation according to the criteria of the Oxford Centre for Evidence-Based Medicine. A total of 297 abstracts were found, 14 of which were full articles that met our criteria. Most articles included a study group with chlorhexidine users and a control group with placebo users for oral hygiene in the prevention of pneumonia. All articles were classified as B in the level of evidence, and 12 articles were classified as 2B and two articles as 2C in grade of recommendation. It was observed that the control of oral biofilm reduces the incidence of nosocomial pneumonia, but the fact that most articles had an intermediate grade of recommendation makes clear the need to conduct randomized controlled trials with minimal bias to establish future guidelines for oral hygiene in intensive care units.

Keywords: Pneumonia, ventilator-associated; Oral hygiene; Chlorhexidine; Intensive care units; Evidence-based practice

RESUMO

Apresentar revisão sistemática da literatura sobre o controle do biofilme bucal e a incidência da pneumonia nosocomial, avaliando e classificando os estudos quanto ao grau de recomendação e ao nível de evidência científica. A revisão foi realizada nas bases PubMed, LILACS e Scopus, de 1º de janeiro de 2000 até 31 de dezembro de 2012. Foram selecionados os estudos que avaliaram os cuidados com higiene bucal relacionando-os com infecções nosocomiais em paciente internados em unidades de terapia intensiva, seguindo os critérios de inclusão. Foram incluídos artigos na íntegra publicados em inglês, espanhol ou português, que abordavam alguma técnica de higiene bucal, química ou mecânica, na prevenção de pneumonia, as intervenções executadas e os resultados. Após análise dos dados, os artigos foram classificados quanto ao nível de evidência e o grau de recomendação, de acordo com os critérios da *Oxford Centre for Evidence-Based Medicine*. Foram encontrados 297 resumos e, destes, 14 artigos na íntegra contemplaram nossos critérios. A maioria dos artigos incluía um grupo de estudo com uso de clorexidina e um controle com o uso de placebo para higiene bucal na prevenção de pneumonia. Quanto ao nível de evidência, todos os artigos foram classificados como B; quanto ao grau de recomendação, 12 artigos foram classificados como 2B e 2 como 2C. O controle do biofilme bucal reduz a incidência de pneumonia nosocomial, porém o nível de evidência e o grau de recomendação intermediário deixam evidente a necessidade da elaboração de estudos clínicos randomizados controlados com viés mínimo para estabelecer futuros protocolos para higiene bucal em unidades de terapia intensiva.

Descritores: Pneumonia associada à ventilação mecânica; Higiene bucal; Clorexidina; Unidades de terapia intensiva; Prática clínica baseada em evidências

INTRODUCTION

Nosocomial infections are among the main causes of mortality in seriously ill patients at Intensive Care Units (ICU), and the most frequent infections are urinary, surgical wounds, and pneumonias.[1]

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Received on: Sept 17, 2013 – Accepted on: July 21, 2014

DOI: 10.1590/S1679-45082015RW2980

The risk of developing nosocomial pneumonia (NP) increases with the use of mechanical ventilation (MV), and besides prolonging, on average, the length of hospital stay for 5 to 9 days, it rises hospital costs.[2]

The mouth of ICU patients can serve as an important reservoir for respiratory pathogens associated with hospital-acquired pneumonia. These data suggest a new view, in which specific procedures for the control of these oral cavity pathogens should be considered in the prevention of NP.[3]

Several studies evaluated the efficiency of mouth decontamination in the prevention of nosocomial pneumonia. Two studies did this by means of a systematic literature review, both conducted in 2007,[4,5] but neither showed the level of scientific evidence or the grade of clinical recommendation. There is a great variety in methods used as to the site of development of the investigations and in intervention methods. Essentially, there are two ways to remove dental plaque and its associated microorganisms: (1) by means of mechanical and/or (2) pharmacological interventions. The need to use one of these methods was made evident when studies demonstrated that 48 hours after admission to the ICU, all the patients presented with oropharyngeal colonization by Gram-negative bacilli, which are frequent etiological agents of nosocomial pneumonia – hence, the biofilm is considered an important pool of respiratory pathogens.[2,6-8]

OBJECTIVE

To perform a systematic review of literature on the control of oral biofilm and the incidence of nosocomial pneumonia, evaluating and classifying the studies as to the grade of recommendation and level of scientific evidence.

METHODS

Planning of the systematic review sought to clarify the following guiding question: "can oral hygiene care prevent nosocomial pneumonia in patients under mechanical ventilation at the ICU?"

The selection of articles was done using three databases in the healthcare field: PubMed, LILACS, and Scopus, from January 1st, 2000, to December 31st, 2012, using the following keywords in English combined among themselves: "nosocomial pneumonia", "pneumonia associated with mechanical ventilation", "oral care", "oral hygiene", and "oral microflora".

The studies were selected after careful reading of the title and summary in order to verify if they corresponded to the guiding question. After the initial selection, the material was read in full and chosen when it covered all the following inclusion criteria: availability of the whole article; published in English; that covered some oral, chemical, or mechanical technique in prevention of pneumonia; and information about the characteristics and methodological rigor, interventions studied, and primary results found. The analysis of the articles was made by two investigators in a blind and independent manner.

The analysis of the data extracted was made descriptively, with no meta-analysis and no statistical analysis. The studies were classified as to the grade of evidence and level of significance, according to the Oxford Centre for Evidence-Based Medicine criteria (Charts 1 and 2).[9]

Chart 1. Level of Evidence - Oxford Centre for Evidence-Based Medicine

Level	Therapy/prevention etiology/damage	Prognosis	Diagnosis	Differential diagnosis/ prevalence studies	Economic/analysis decision
1a	SR studies (homogeneity*)/or RCT	SR* studies (homogeneity*) of cohort studies with controls from the start of cases; CDN† with validity in different populations	SR studies (homogeneity*) of level 1 in diagnostic studies; CDN† of 1b studies from different clinical centers	SR studies (homogeneity*) or prospective cohort studies	SR level 1 studies (homogeneity*) with economic focus
1b	Individual randomized and controlled studies with narrow confidence interval	Individual cohort studies with >80% follow-up; CDN† validated in a population group	Validation ‡ of cohort studies with good § reference standards; CDN† tested in a single center	Prospective cohort studies with good follow-up ||	Analysis based on clinical costs or alternative costs SR* of evidence including sensitivity analyses of various alternatives
1c	All died before treatment and some survived after start of treatment, but none died during treatment ¶	All died before treatment and some survived after start of treatment, but none died during treatment ¶	Absolute sensitivity ** Absolute specificity**	All or none in the case series	Estimative of analysis with absolute estimate of improvement or worsening ††

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Chart 1. Level of Evidence - Oxford Centre for Evidence-Based Medicine

Level	Therapy/prevention etiology/damage	Prognosis	Diagnosis	Differential diagnosis/ prevalence studies	Economic/analysis decision
2a	SR (homogeneity*) of cohort studies	SR (homogeneity*)/ or other retrospective cohort studies or group. Control levels of evidence of the randomized groups of clinical trials	SR (homogeneity*) level 2 diagnostic studies or with better levels of evidence	SR (homogeneity*) of 2b and studies with better levels of evidence	SR (homogeneity*) of studies with economic focus with level of evidence 2 or with better levels of evidence
2b	Individual cohort studies (including low quality randomized studies, that is, <80% of follow-up)	Retrospective cohort studies or of follow-up of control group patients treated by randomized clinical trials; derived from CDN† that used regression analysis ‡‡	Exploratory cohort studies ‡ with good § reference standard (gold standard); derived from CDN† With regression analysis of data ‡‡	Retrospective cohort studies, or with poor follow-up	Analysis based on costs or limited alternatives of review of simple study evidence, including analysis of sensitivity of various alternatives
2c	Outcome studies; ecological studies	Outcome studies		Ecological studies	Outcome or auditing studies
3a	SR (homogeneity*) of case-control studies		SR (homogeneity*) of 3b	SR (homogeneity*) of 3b	SR (homogeneity*) of 3b
3b	Individual case-control studies		Nonconsecutive studies or without applying the gold standard of reference	Nonconsecutive cohort study or very limited population	Analysis based on limited cost alternatives, data from very poor estimates, but incorporating sensitivity analysis
4	Case series (or cohort studies with poor quality or case control-studies §§)	Series of cases (with poor prognostic quality), cohort studies***	Case-control studies that depend on the gold standard	Series of cases or studies that substitute the gold standard	Decision analysis with sensitivity analysis
5	Opinion of specialists without specifying a critical evaluation or one based on studies of physiology or initial principles	Opinion of specialists without specifying a critical evaluation or based on studies of physiology or initial principles	Opinion of specialists without specifying a critical evaluation or based on studies of physiology or of initial principles	Opinion of specialists without specifying a critical evaluation or based on studies of physiology or of initial principles	Opinion of specialists without specifying a critical evaluation or based on studies of physiology or of initial principles

SR: systematic reviews; RCT: randomized clinical trials; CDN: clinical decision norms; * Systematic review (SR), with homogeneity, means to be free of heterogeneous variation. † Clinical decision norms (CDN) represented graphically by algorithms or score systems, which provide an estimate of diagnosis or prognosis. ‡ Validating specific diagnostic tests previously based on evidence, studies with data collection and analysis (using regression analysis) to find factors that may be considered significant. § Good standard – called the "gold standard", are independent tests applied blindly and objectively to all patients. | | Good follow-up (> 80%) in studies with differential diagnosis, with adequate follow-up time: in an acute situation (1-6 months) and in chronic cases (1-5 years). ¶ When all the patients died before undergoing treatment, but now some survive with the start of treatment, or when some patients died before treatment became available, but none died during the treatment.** There is absolute specificity (negative result) when it excludes the diagnosis. There is absolute sensitivity (positive test) when the test defines the diagnosis. †† Estimates of treatments of better value are clearly those that have low costs. The estimate of a lower value treatment may be a good option, but more expensive; it can also be a bad option with equal costs or even more expensive. ‡‡ Validation studies test the quality of a specific diagnosis, based on prior evidence. An exploratory study collects data and uses regression analysis to identify factors that might be significant. §§ Cohort studies (with poor quality) failed in defining the comparison between the groups and/or failed in measuring exposure and outcome (they should preferentially be blinded); they failed to identify the control group and confounding factors; the follow-up was not sufficiently long to evaluate the outcome; the follow-up of the patients was not complete. Case-control studies (with poor quality) failed to clearly define the comparison between the groups, failed to measure exposure and outcome (preferentially should be blinded), failed to identify the control group and confounding factors. *** Cohort studies, with focus on diagnosis are considered poor in quality when there is bias in sample selection; measurement of outcome occurs only in <80% of the patients that conclude the study; when the outcomes are determined, but not blinded, and there is no objectivity or correction of confounding factors.

Chart 2. Grade of Recommendation Oxford Centre for Evidence-Based Medicine

A	Consists in level 1 studies. A study with strong recommendation in choice; levels of evidence for routinely recommending medical management are excellent. The benefits outweigh the damage. There is good evidence to support the recommendation.
B	Consists in levels 2 and 3 studies or generalization of level 1 studies. A study that recommends the action; significant evidence is found in the outcome, and the conclusion that there is benefit in the choice of the action relative to the risks of the damage. There is reasonable evidence to support the recommendation.
C	Consists of level 4 studies or generalization of levels 2 or 3 studies. Finds minimal satisfactory evidence in outcome analysis, but concluded that the benefits and the risks of the procedure do not justify generalization of the recommendation. There is insufficient evidence, whether against or in favor.
D	Consists of level 5 studies or any inconclusive study. Studies with poor quality. There is evidence to discard the recommendation.

RESULTS

Of the 297 summaries first found, 14 articles met the criteria established in this systematic review (Figure 1). Most of the articles included a study group with the use of chlorhexidine and a control group with the use of a placebo. Nine articles concluded that the use of topical chlorhexidine reduced the incidence of NP. Four articles still had not determined statistically significant differences among the groups. Nevertheless, one observed a delay in the establishment of the NP, and another studied toothless patients. As to level of evidence, all the articles were classified as B; as to grade of recommendation, 12 articles were classified as 2B and two articles as 2C (Table 1).

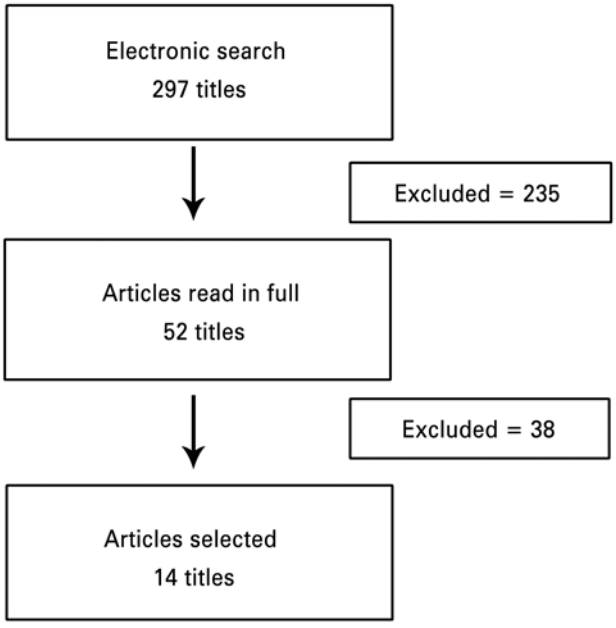

Figure 1. Flow chart of the search strategy

Table 1. Description of the articles included in this review

Authors	Objective	Type of study	Population (n/type of ICU)	Intervention	Control	Results	Level of evidence	Grade of recommendation
Munro et al.[6]	To describe the effects of CHX, toothbrush, and their combination in the development of MVAP in ICU patients under MV	RCT	547/Mixed ICU	(1) 0.12% CHX solution twice a day (2) toothbrush three times a day (3) 0.12% CHX two times a day + toothbrush three times a day	Control group along with usual care	CHX reduces MVAP, but brushing does not	B	2C
Pobo et al.[7]	To evaluate the addition of the electric toothbrush to oral hygiene in order to reduce MVAP	RCT with single blinding	147/Mixed ICU	0.12% CHX solution every 8 hours	Electric toothbrush	The addition of the electric toothbrush to standard hygiene with 0.12% CHX is not effective in preventing MVAP	B	2B
Scannapieco et al.[8]	To determine the minimum frequency (one or two times a day) of 0.12% CHX to reduce oral colonization by pathogens in patients under MV	RCT double-blind	175/Trauma ICU	0.12% CHX one or two times a day	Placebo	The use of 0.12% CHX reduces the number of *Staphylococcus aureus*, but does not reduce the proportional number of Pseudomonas, actinobacteria or enteral species in the bacterial plaque	B	2B
Tantipong et al.[11]	To determine the efficacy of oral decontamination with a solution of 2% CHX for the prevention of MVAP	RCT	207/Mixed ICU	CHX 2% solution four times a day	Saline solution	Oral decontamination with 2% CHX is an effective and safe method for prevention of MVAP	B	2C
Houston et al.[12]	To evaluate the efficacy of oral use of 0.12% CLX in decreasing colonization of the respiratory tract and hospital-acquired pneumonia in patients submitted to cardiac surgery	ECR	591/Surgical ICU	0.12% CHX solution two times a day	Listerine	Rates of MVAP were lower in patients treated with CHX	B	2B

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Table 1. Description of the articles included in this review

Authors	Objective	Type of study	Population (n/type of ICU)	Intervention	Control	Results	Level of evidence	Grade of recommendation
Grap et al.[13]	To document the efficacy of a single application of CHX in the oral cavity immediately after intubation on the oral microbiota and MVAP	RCT	34/Mixed ICU	0.12% CHX solution two times a day	Usual care Bicarbonate four times a day	Use of CHX during post-intubation may attenuate or retard the development of MVAP	B	2B
Belissimo-Rodrigues et al.[14]	To evaluate the efficacy of the oral application of a solution of 0.12% CHX for the prevention of respiratory infection in the ICU	RCT double-blind	194/Mixed ICU	0.12% CHX solution three times a day	Placebo	0.12% CHX does not impede respiratory tract infection, but can retard its appearance	B	2B
Lorente et al.[15]	Comparar a incidência de PAVM de pacientes críticos que receberam cuidados bucais com e sem escovação manual dos dentes	RCT	436/Mixed ICU	Group A corresponded to 0.12% CHX without mechanical brushing Group B corresponded to 0.12% CHX with mechanical brushing		There were no statistically significant results	B	2B
Fourrier et al.[16]	To compare the incidence of MVAP in critically ill patients who received oral care with and without manual brushing of the teeth	RCT with single blinding	60/Mixed ICU	0.2% CHX gel three times a day	Usual care Bicarbonate four times a day	Decontamination with 0.2 % CHX decreased oral bacterial colonization and can reduce the incidence of infections in patients under MV in the ICU	B	2B
Fourrier et al.[17]	To document the efficacy of decontamination of the dental plaque and oral cavity with use of CHX on the rates of hospital-acquired bacteremia and respiratory infections acquired in the ICU	RCT double-blind	228/Mixed ICU	0.2% CHX gel three times a day	Placebo	Decontamination of bacterial plaque and gums with CHX reduced the colonization of the oropharynx by aerobic pathogens in ventilated patients, but was insufficient in reducing respiratory infections	B	2B
Panchabhai et al.[18]	To evaluate if 0.2% CHX reduces the incidence of MVAP in the ICU	RCT	512/General ICU	0.2% CHX solution two times a day	0.01% potassium permanganate	The use of 0.2% CHX did not reduce the incidence of NP in ICU patients, but meticulous oral cleaning decreased the risk of developing it	B	2B
Berry et al.[19]	To test two oral hygiene strategies on the effects of microbial colonization of the dental plaque with respiratory pathogens (primary result) and incidence of pneumonia associated with mechanical ventilation (secondary outcome)	RCT double-blind	225/Mixed ICU	Group B corresponded to sodium bicarbonate Group C corresponded to 0.2% CHX two times a day and irrigation with sterile water*	Group A corresponded to sterile water	There was no significant difference between the groups	B	2C
Özçaka et al.[20]	To evaluate if oral scraping with 0.2% CHX decreases the risk of MVAP in patients in the ICU	RCT double-blind	66/ Respiratory ICU	0.2% CHX solution	Saline solution	The development rate of pneumonia in the control group was greater than in the study group	B	2B
Koeman et al.[21]	To determine the effect of decontamination of the oral cavity with CHX or CHX + colistin on the incidence of MVAP	RCT double-blind	257/Mixed ICU	2% CHX (1) CHX + colistin (2)	Placebo	Topical decontamination with CHX or CHX + colistin reduces the incidence of MVAP	B	2B

*All the patients had their teeth brushed with brushes and tooth paste. ICU: intensive care unit; CHX: chlorhexidine; MVAP: mechanical ventilation-associated pneumonia; MV: mechanical ventilation; RCT: randomized clinical trial; HAI: hospital-acquired infection; NP: nosocomiaal pneumonia.

DISCUSSION

Various aspects compromise mouth hygiene in ICU patients favoring microbial growth, such as difficulty and/or impossibility of self-care, presence of the orotracheal tube, which hinders access to the mouth, and the consequent formation of the biofilm and dental plaque.[10] Thus, mouth decontamination takes on extreme importance in preventing nosocomial pneumonia of patients in the ICU.[2] However, there are many methods used besides the diversity of centers in which the studies are carried out, which makes the adequate interpretation and use of intervention methods difficult.

Chlorhexidine is a wide-spectrum cationic antiseptic agent that includes Gram-negative and Gram-positive bacterial, such as oxacillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus sp*., which may persist chemically active in tissues for up to 6 hours.[11,22] In literature, there is a great variety of treatment regimens using chlorhexidine, including variations in concentration: 0.12%,[6-8,14-15] 0.2%,[16-20] and 2%.[11,21] No study evaluated in this review performed comparisons correlating the different concentrations of chlorhexidine and the incidence of nosocomial pneumonia. The most studied solution was 0.12% chlorhexidine (7 of 14 studies), and in some articles, it served as control for another method of evaluation.[7,15] The 2% concentration was the most effective in preventing NP, but only two studies evaluated this concentration – one of them, as study with a 2C level of recommendation.

Some articles compared isolated chemical removal using 0.12% chlorhexidine, and associated with mechanical removal using an electric and manual toothbrush.[6,7,15] The results of the addition of dental brushing were not significant for the prevention of MV-associated pneumonia. Tooth brushing alone did not reduce pneumonia associated with mechanical ventilation; the combination of brushing with chlorhexidine also showed no additional benefits when compared to the use of chlorhexidine alone. Additionally, during brushing, dislocation of the dental plaque may occur, supplying a large number of microorganisms translocated from the mouth to the subglottic secretions of the lungs, contraindicating the mechanical removal of bacterial plaque with dental brushes, with recommendation only for chemical removal with 0.12% chlorhexidine.[6]

The diversity of patients and of ICUs is an important factor that should be considered in the analysis of NP incidence, taking into consideration the type of ICU and the profile of the patients. The percentage of NP varied from a minimum of 7% in a group that used mechanical brushing to control biofilm[15] to a maximum of 68.8% in the control group.[20] A reduction superior to 40% in incidence of pneumonia was found in five studies,[6,9,14,18,19] but only one article [17] showed an elevation in the incidence of NP (17.5% in the placebo group *versus* 18.4% of the treated group).

CONCLUSION

The control of oral biofilm reduces the incidence of nosocomial pneumonia. Oral hygiene using a 0.12% solution of chlorhexidine, and not dental brushing, seems to be the most effective hygiene method. This concentration of chlorhexidine does not harm the oral mucosa and no dislocation of the dental biofilm towards the posterior oropharynx occurs when mechanical brushing is done.

The fact that most of the articles presented an intermediate B and 2B level of evidence and grade of recommendation, respectively, makes clear the need for conducting randomized controlled clinical trials with a minimal bias, due to the need for intensive care services having at their disposal valid protocols for the effective application of oral care and consequent reduction of nosocomial pneumonia.

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