Revista Brasileira de Odontologia
Brazilian Journal of Dentistry
Associação Brasileira de Odontologia - Seção Rio de Janeiro
DOI: http://dx.doi.org/10.18363/rbo.v75.2018.e1058

Aspiration Pneumonia and oral health: a critical review of literature

Nayara Perpétuo Gonçalves do Nascimento,[1] Patricia Furtado Gonçalves,[1] Dhelfeson Willya Douglas-de-Oliveira,[2] Olga Dumont Flecha[1]

[1]School of Dentistry, Faculty of Biological Sciences and Health, Federal University of Jequitinhonha Vales and Mucuri, Diamantina, MG, Brazil

[2]Departmento of Periodontology, School of Dentistry, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil

• Conflicts of interest: none declared.

Abstract

Objective: to identify evidences in the scientific literature if mechanical or chemical oral hygiene can prevent aspiration pneumonia in hospitalized patients. **Material and Methods:** it were included clinical studies indexed in Pubmed, Lilacs and Scielo databases from 2008 to 2017, following pre-determined inclusion and exclusion criteria. **Results:** twelve studies met the inclusion criteria and were reviewed. According to the quality of the evidence, three studies were evaluated as I, six as II and three as III. Regarding the treatment used, clinical researches investigating the effectiveness of different antimicrobial solutions for oral hygiene in order to reduce aspiration pneumonia in hospitalized patients. Different chlorhexidine concentrations (0.05%, 0.1%, 0.12%, 0.2%, 2%) were used, as well as other substances for mouthwash. **Conclusion:** the lack of high quality studies undermines the confidence on the effectiveness of antimicrobial solutions regarding the reduction of aspiration pneumonia. However, those studies with good methodology suggested the reduction of pneumonia by oral hygiene.

Keywords: Oral hygiene; Chlorhexidine; Aspiration pneumonia; Oral health; Intensive therapy.

Introduction

The aspiration of oral pathogens is a pathological mechanisms involved in pneumonia acquired in hospital (PAH) and it is associated with supine position, dysphagia, changes in mental status, esophageal motility disorders, vomiting, acid reflux, intubation enteral nutrition, tracheal intubation, oropharyngeal and bronchial colonization, tracheostomy and alcoholism.[1]

In sick patients, the aspiration of substances from oropharyngeal or concentrated secretions above the cuff orotracheal tube is the primary means for inoculation, in the lower respiratory tract, of oral pathogens, from dental biofilm, periodontal disease and caries.[2]

When the pathogens overcome defense mechanisms of the respiratory system, which can be mechanical (cough reflex, reflex and glottal mucociliar system), humoral (antibodies and complement system) and/or cellular (polymorphonuclear leukocytes, macrophages and lymphocytes), it can occur pneumonia.[2] It should be emphasized that patients with change in level of consciousness, a common condition in intensive care units (ICU), often aspire greater amounts of secretions from the mouth.[3]

The aspiration pneumonia has been correlated to the plaque and oropharyngeal colonization in patients receiving mechanical ventilation (MV). The endotracheal tube acts as a conductor of the oropharyngeal microorganisms to the lower respiratory tract, and these are often identified as etiological agents of nosocomial pneumonia.[4] This pneumonia can also be caused by foreign material originating in oral cavity, most commonly, scraps of food, saliva, biofilm or a combination of these.[5]

In order to reduce nosocomial pneumonia and ventilator-associated pneumonia (VAP), it has been recommended topical use of chlorhexidine (chemical agent of broad spectrum) during the care of oral hygiene in patients.[6]

A recent review showed that microorganisms of dental biofilm or associated with periodontal disease have been found in bronchoalveolar lavage samples from hospitalized patients, and that poor oral hygiene seems to be one of the most common risk factors for PAH. In edentulous individuals, oral pathogens may persist even after extraction of natural teeth; hence, tongue saburra was identified as a risk indicator for aspiration pneumonia.[5]

Oral health care seem to play an important role in the prevention of aspiration pneumonia in weak elderly. However, it is not clear what intervention is more effective in reducing the risk of aspiration pneumonia.[7] The objective of this study was to perform a critical review of clinical trials that investigated if mechanical or chemical oral hygiene can prevent aspiration pneumonia in hospitalized patients.

Material and Methods

This literature review was performed by using a search protocol prepared by the authors (NPGN and ODF), following the criteria of the Consolidated Standards of Reporting Trials (CONSORT):[8] randomization, allocation concealment, blinding, losses in follow-up and sample size estimation. It was included clinical trials, randomized or not, conducted in sick hospitalized patients, in intensive care or in other sectors, regardless of sex, age and race. The intervention of interest was oral hygiene, without technical restrictions and the outcome was the prevention or reduc-

tion of aspiration pneumonia.

The research was conducted in Pubmed, Scielo and Lilacs databases, using the following key words in combination or not, in English and Portuguese: "oral hygiene, chlorhexidine, aspiration pneumonia, intensive care medicine, mechanical ventilation, biofilm, oral health".

For quality assessment of the trials, a criterion was adapted from Ho *et al*.,[9] based on CONSORT[8] and on the following criteria for the qualification of the methodology and classification of levels of evidence: randomization, allocation concealment, masking, losses in follow-up and sample size estimation[10] (table 1).

Table 1. Classification for assessing the quality of clinical trials

Criterion	A	B	C
Sample Size	Appropriate	Partially reported	Not mentioned
Randomization	Appropriate	Partially reported	Not mentioned
Allocation concealment	Appropriate	Partially reported	Not mentioned
Masking	Appropriate	Partially reported	Not mentioned
Losses	Appropriate	Partially reported	Not mentioned

Criterion adaptated from S.He *et al*. 2011[7] and Nogueira *et al*. 2015[9]

The criterion was considered appropriate (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 wasn't mentioned. If the clinical trial met all criteria or four, was rated as level of evidence I; if met partly the criteria (at most two evaluations C) was rated as level of evidence II; and, followed two criteria or less, was rated as level of evidence III.

A detailed evaluation of selected articles was conducted, and several items were taken into account in order to have a general notion for final evaluation. These items were: author/year, study design, sample size, objectives, criteria for inclusion, intervention, confounding factors and conclusion.

The final evaluation was made from the classification of each article according to the criteria selected. Each article was separated by table, for each assessment item. Later, they were put together in an only table for the classification of levels of evidence found.

Results

It were retrieved 91 articles. After application of the eligibility criteria, it were full read 13 manuscripts. Twelve studies were selected and included, they were published in English, from the year 2008 to 2017. One study[2] was excluded for not presenting a conclusion about the effect of oral hygiene on the incidence of VAP. Figure 1 shows the flowchart of the studies for identification, inclusion, and qualitatively analysis.

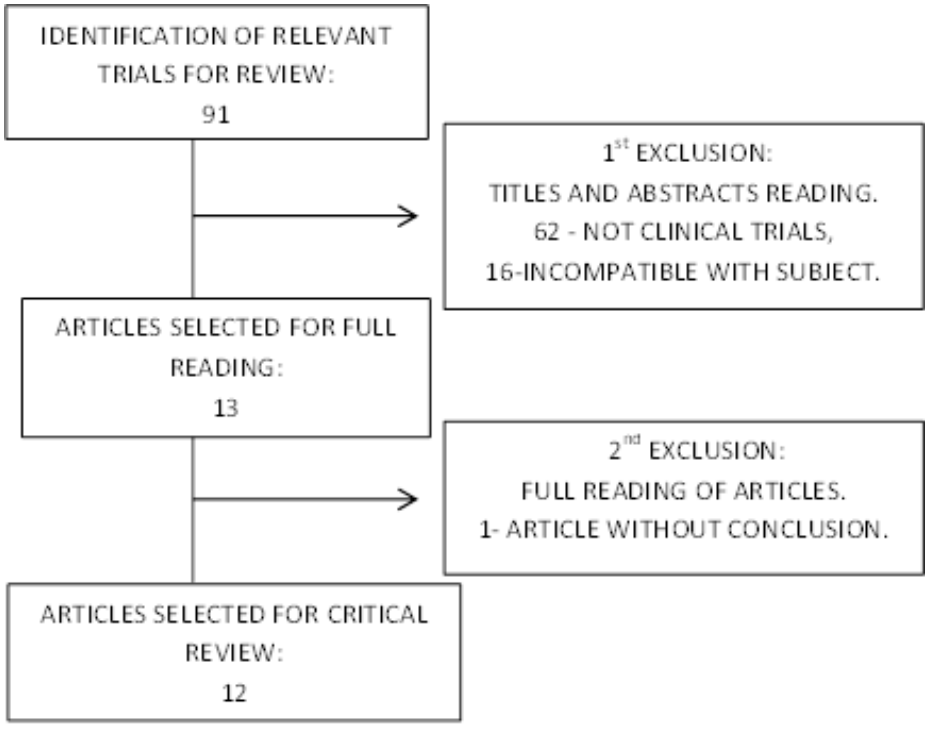

Figure 1. Flowchart of selection and inclusion of articles

The Table 2 presents a summary of the 12 selected studies and the classification given in accordance with the levels of evidence.[8-11] it is important to note the vast heterogeneity of the variables, and the samples have different sizes. There are several types of interventions used, as well as, the inclusion criteria.

Table 2. Summary of selected studies

Author/Year	Design	Sample	Objective	Inclusion criteria	Intervention	Confunding factors	Conclusion	Evidence
Sharif-Abdullah *et al*. 2016[12]	Duble-blinding, controlled, randomized parallel	35 subjects > 65 years	Effect of CHX 0.2% and thymol in hospitalized patients	Pacients older than 65 years, no prothesis	OH and CHX 0.2% in intervention group, and thymol in control group	NM	CHX 0.2% reduced oral colonization. Easy and economical OH	I
Scannapieco *et al*. 2009[13]	Randomized, double-blinding	547 subjects > 18 years	Frequency of CHX 0.12% in reducing respiratory pathogens	Purulent secretion, leukocytosis, chest X-ray	OH with CHX and MB, separated or combined	NM	CHX reduced viable amount of S. aureus, in ICU-MV. The CHX didn't reduce total amount of PR.	I
Vidal *et al*. 2017[4]	Randomized prospective	213 subjects > 18 years	OH by MB with gel CHX 0.12% reduce VAP incidence	Fever, leukocytosis, chest X-ray, PRS	Mouthwash with CHX 0.12% in the control group and MB x CHX in the intervention group	Yes: heart patients	Patients undergoing MB reduced duration on VAP	I
Nobahar *et al*. 2016[14]	Randomized clinical trial	68 subjects > 18 years	Effect of HP on the incidence of VAP	Patients under MV > 48 hs, no IC for oral use, nor the head elevation 30°	HP group x placebo group with saline	Smoking and drug abuse	VAP reduction was more effective with HP	II
Azimi *et al*. 2016[15]	Clinical study, randomized, double-blinded	39 subjects > 15 years	Evaluate effects of 0.2% CHX, matriarch and SS	Patients with ET tube or NG, MV > 48, no antibiotic treatment prior to hospitalization, no sensitivity to BA.	Mouthwash with 0.2% CHX and matriarch in the experimental group. In the control group SS.	NM	Mouthwash with CHX 0.2% reduces bacterial colonization	II
Hollaar et al.2015[16]	Randomized clinical trial, controlled, multi-center	500 subjects > 65 years	Assess application of 0.05% CHX on VAP reduction	Disabled patients with symptoms of disfagias .	Application of 0.05% CHX	NM	Reducing the risk of developing pneumonia	II
Klarin *et al*. 2008[17]	Randomized	50 subjects >18 years ou mais	Compare the pro biotic LP299 efficiency with CHX 0.1%	Chest x-ray, cultures AT occurring after 48 hours of MV	Oral MB followed by mouthwash with 0.1% CHX and application of emulsion of LP 299	NM	No differences were found between 0.1% CHX and LP299	II
Naiktari et al. 2014[18]	Clinical study, multi-center, double-blinding, randomized.	120 subjects > 20 a 65 years de idade	Compare effectiveness of mouthwash with trifala x 0.2% CHX	Hospitalized patients + plaque + calculus and clinical signs of IG.	Mouthwash with CHX, distilled water and trifala divided into groups.	NM	Trifala is effective as CHX 0.2%	II
Tantipong *et al*. 2008[19]	Randomized	207 subjects > 18 years ou mais	Efficacy of oral decontamination with 2% CHX or normal SS.	Temperature, leukocytosis, purulent aspirate	Oral decontamination with CHX 2% in a group and normal in other SS	NM	CHX 2% solution is an effective method in preventing VAP in patients receiving MV	II

Scannapieco *et al*. 2012[20]	Clinical trial randomized, controlled	547 subjects > 18 years	Effects of 0.12% CHX and CHX alone or only in MB	Temperature, white blood cell count, secretion	Oral care	NM	MB did not reduce the incidence of VAP, and the combination of MB + CHX not provided more benefits than CHX	III
Tuon *et al*. 2017[21]	Prospective, randomized, controlled, duble-blinding	16 subjects >18 years	Incidence of PB associated with VAP and PD in patients treated with CHX	Hospitalized patients with MV > 48 hs, anterior and posterior teeth	Group with CHX 2% X placebo group	NM	CHX reduziu 2% incidência de colonização de S. aureus	III
Estaji *et al*. 2016[22]	Randomized	30 subjects > 18 a 65 years.	Evaluate effectiveness of CHX 2% with brushing of teeth	Intubated, without OL, and coagulopathy, prostheses	Groups with toothbrushes and groups with chlorhexidine 2%	NM	Using the toothbrush has remarkable impact in reducing oral lesions	III

ET- endotracheal. CHX – chlorhexidine. MB – mechanical brushing. PD – periodontal disease. NM – not mentioned. OH – oral hygiene. SS –saline solution. OL – oral lesions. PRS – purulent respiratory secretions. PB – pathogenic bacteria. VAP – ventilation-associated pneumonia. MV – mechanical ventilation. PH – hydrogen peroxide.

The trials had evidence levels I, II, or III according to the rating scale for assessing the quality of randomized clinical trials. The twelve articles that fully or partly filled the inclusion criteria inclusion were randomized clinical trials, four presented allocation concealment, eight reported masking, two cited confounding factors, seven mentioned losses in follow-up. Seven studies explained the sample calculation. Only three clinical trials received evidence level I, six received II and three were rated III (table 3). Studies that was rated as level of evidence I, may be considered to have low risk of bias; those with evidence of level II, have moderate risk of bias; and the qualified as III, can carry high risk of bias.

Table 3. Methodological evaluation of included articles

Author/year	Sample size	Randomization	Allocation concealment	Masking	Losses	EL
Sharif-Abdullah *et al*. 2016[11]	YES=A	YES (in block=A)	YES=A	YES (TB=A).	YES=A	I
Scannapieco *et al*. 2009[13]	YES=A	YES (computer=A)	YES=A	YES (TB=A)	YES=A	I
Vidal *et al*. 2017[4]	NM=C	YES (envelope=A)	YES =A	YES (DB=A).	YES=A	I
Nobahar *et al*. 2016[14]	NM=C	YES (coin=A)	YES=A	YES (DB=A)	NM=C	II
Azimi *et al*. 2016[15]	YES=A	YES (NC=B)	NM=C	YES (DB=A)	NM=C	II
Hollaar *et al.*2015[16]	YES=A	YES (NC=B)	NM=C	NM=C	YES=A	II
Klarin *et al*. 2008[17]	NM=C	YES (NC=B)	NM=C	YES (SB=A)	YES=A	II
Naiktari *et al.* 2014 [18]	YES=A	YES (NC=B)	NM=C	YES (SB=B)	YES=A	II
Tantipong et al. 2008[19]	YES=A	YES (NC=B)	NM=C	NM=C	YES=A	II
Scannapieco *et al*. 2012[20]	YES= A	YES (PB=A)	NM=C	NM=C	NM=C	III
Tuon *et al.* 2017[21]	NM=C	YES (NC=B).	NM=C	NM=C	NM=C	III
Estaji *et al.* 2016 [22]	NM=C	YES (PB=A)	NM=C	YES (SB=B)	NM=C	III

PB = permuted block SB= simple-blinding DB = duble-blinding TB = triple-blinding
NC = Not clear EL = evidence level NM = not mentioned

Discussion

Studies have reported that oral hygiene in sick patients prevents infections and secondary diseases such as aspiration pneumonia. However, there are few clinical trials in the literature evaluating the effectiveness of oral hygiene in the prevention of this condition. The main prevention cited by the revised studies is the oral hygiene through mouthwash with antimicrobials and/or mechanical brushing.[4,12-22]

The studies of Vidal *et al*.,[4] Sharif-Abdullah *et al*.[12] and Scannapieco *et al*.[13] had evidence level I and followed almost every criteria.[8] A estudy[4] did not report the sample calculation which is very important to determine the amount needed to compose the sample in order to obtain valid results, but, no more than enough.[23] In the study of Vidal et al.,[4] there was a significant reduction in the duration of mechanical ventilation and tendency to reduce the incidence of VAP and duration time of staying in the ICU, although this last result without statistic significance. The authors compared the tooth brushing with and without chlorhexidine 0.12%. The authors[4] concluded that more studies would be needed to define the ideal oral hygiene, dental plaque index, which is important to evaluate before and after the intervention to compare its reduction in oral cavity and the effect of the intervention, the observation of the impact of measures of oral hygiene, mainly in the hospital mortality rates and ITU.

The studies of Sharif-Abdullah *et al*.[12] and Scannapieco *et al*.[13] had similar conclusions in reducing oral colonization by bacterias. The first one used chlorhexidine 0.2%,[12] and the second one[13] used chlorhexidine 0.12%. Both[12,13] reported that the use of chlorhexidine reduced oral colonization. A estudy[13] reported the reduction only of *S. aureus* and other[12] stated positive effect in reducing oral colonization when compared with oral care routine.

All studies with level of evidence I[4,12,13] reported losses in follow-up. When there are losses of contact with some participants, the researchers cannot complete the collection of data as planned.[24] Studies can be affected by clearances, withdrawals and losses of participants, which could void the initial equivalence of the experimental and control groups. To manage these deviations, two strategies are commonly used: the principle of analysis by intention to treat (ITT) states that any person must be parsed as if he'd followed completely the project programmed; and protocol analysis (per-protocol = PP) that proposes to include only those volunteers who joined the designated intervention and concluded the following default, without any deviation of the main protocol.[10] Studies that reported losses, did not mention they were administered.

The studies of Nobahar *et al*.,[14] Azimi *et al*.,[15] Hollaar *et al*.,[16] Klarin *et al*.,[17] Naiktari *et al*.,[18] and Tantipong *et al*.,[19] had evidence level II. Only Nobahar *et al*.[14] presented the allocation concealment, which is a method used to ensure that the random sequence of subjects selected for intervention/control groups is followed and kept hidden until the time of the intervention, thus avoiding, bias selection. This technique prevents the researchers, unconsciously or not, to determine in advance which participants will be allocated to a certain group.[24]

Clinical trials in which the sequence of allocation was improperly hidden can produce larger estimates of treatment effects than the tests in which the authors report adequate concealment. The conduct for the generation of sequence has a smaller role in preventing bias than the conduct for concealment. Having a random (unpredictable) sequence should make little difference without adequate concealment.[10]

Only the studies of Hollaar *et al*.[16] and Tantipong *et al*.,[19] among the classified as II, were masked. This is an important element in a clinical trial, because intentionally not knowing the treatment of each individual is receiving avoids subjectivities, bias and prejudices, which could introduce bias.[25] However, regarding the randomization of the studies with evidence level II, the only one clear enough was the study of Nobahar *et al*.[14] Randomization is a search strategy used to increase the validity of clinical trials that assess the effect of interventions.[26]

Two studies[4,14] mentioned confounding factors that are able to influence both the dependent and independent variable. These factors (for example, baseline characteristics, prognostic factors or concomitant interventions) can generate bias in the estimated effect of intervention.[24] Oral hygiene is a major preventive factor to parkinsonian which can be susceptible to aspiration and colonization of bacilli and bacteria that are the main responsible for the development and severity of aspiration pneumonia.[27]

The studies that had evidence level III were of poor quality, without enough data, unable to consider any evidence and at high risk of bias.

Clinical trials compared or investigated the effectiveness of an antimicrobial for oral hygiene of patients, and their impact in the prevention of pneumonia. According to Amaral *et al*.,[28] in patients admitted to ICU, oral hygiene is usually precarious, also, there is reduced salivary flow by use of some drugs, which contributes to the increase of biofilm, and consequently its complexity, favoring the oral colonization by respiratory pathogens.

It is difficult to compare the studies due to the diversity of interventions and results for each test. Over the different chlorhexidine concentrations (2%, 0.12%, 0.05%, 0.2%, 0.1%), other substances were used for mouthwashes such as hydrogen peroxide, Thymol, matriarch, probiotic *bacteria Lactobacillus plantarum 299*, saline solution, and trifala.

The aspiration pneumonia was defined by most studies as acquired pneumonia after 48 hours in hospital stay post

intubation for mechanical ventilation. The diagnosis was diversity in several studies and involved temperature, leukocytosis, chest x-rays, tracheal aspirates. And it pathogenesis is related to aspiration of bacteria from cavity and upper airway to the lungs due to low immunity of the host and biofilms that are reservoirs for microorganisms. The literature indicates oral health as an important factor in preventing and/or improving the patient's systemic health, indicating that oral amendments can be considered hotbeds for systemic spread of pathogens, especially in patients with compromised health.[29]

Articles with evidence level I or II presented a variety of objectives and conclusions, making it difficult to establish a comparison. There is no standardized methodology that allows it. Nevertheless, those that aimed to compare the reduction of pneumonia incidence or microbial reduction,[12,14,16,18,19] didn't present statistically significant conclusion that the oral hygiene can reduce the incidence of aspiration pneumonia, except the study of Vidal*et al*.[4] These results agree with a systematic review on oral hygiene and pneumonia in children in ICU[11] which concluded that there is no scientific evidence to support the use of oral hygiene isolated with chlorhexidine to prevent PVA. Overall, there are no well-established protocols that aim the best method of oral hygiene for children admitted to ICU.

Many patients who are admitted to hospital present oral hygiene deficiency and oral problems such as caries, periodontal disease, calculus, which become focus of infection and can overcome the immunological defenses of the weak patient, achieving blood and reaching other organs. To prevent systemic infections of odontogenic origin, Dentistry comes changing history of curative treatments only for preventative care, looking at the patient as a whole and seeking the best quality of service, not only in offices, but extending to hospital environments.[30]

Assuming oral microorganisms are involved in the origin of aspiration pneumonia, this question arises: if oral hygiene measures reduce the risk inherent of oral biofilm. Whereas mechanical hygiene measures appear to reduce the incidence of pneumonia, the use of chemical agents alone yielded little improvement in the incidence of upper respiratory tract infections.[31] It is recommend tooth brushing after every meal, cleaning removable dentures once a day and professional oral health care once a week as the best scheme to reduce the incidence of aspiration pneumonia.[7] The reviewed studies[4,12-22] presented reduced oral colonization through oral hygiene with mouthwash and mechanical brushing, emphasizing the study of Estaji *et al*.,[22] that reported remarkable impact using toothbrush in reducing oral lesions.

An important finding of this review showed that appropriate oral health care decreased the amount of potential respiratory pathogens, and suggested a reduction in the risk of aspiration pneumonia, consequently, an improvement in the reflection of swallowing and cough reflex sensitivity. However, it still remains the question of what is the most effective intervention in reducing the incidence of aspiration pneumonia in the elderly. An individualized approach based on the assessment of the risk of aspiration pneumonia may be the best guide to determine the content of a program for prevention of oral health more intensive.[7]

Studies with humans are limited by ethical questions that respect and protected the health of the participants. Some groups of people are considered vulnerable, and need special attention, for example, the hospitalized patients. These patients often cannot give or refuse consent for themselves, due to the situation in which they are.[29] Therefore, the few researches in sick patients, often due to the low availability due to vulnerability of patients and the priorities of family and health professionals engaged in the rehabilitation of the health and comfort of patients.

Another important aspect to be addressed herein are the hospital costs of nosocomial infections. The time of hospitalization can be increased by up to nine days because of nosocomial pneumonia, raising costs up to $40000, summing more than U $1.2 billion/year for the health system of the United States.[32] Thus, the aspiration pneumonia impact both the patient's health, worsening their condition and may lead to death, and, every institution, increasing the length of stay of patients and consequently the hospital costs.

This review was limited due to low methodological quality of the included studies. The strong point of the review was detailed and critical evaluation of the items considered important to a good level of evidence of clinical trials included. There is a need for further studies to be carried out with a good methodological quality, containing more foundations and scientific evidence on the subject. It is important to have a clarification on the subject, which could lead to hospitals, nursing homes and homes for the elderly to control hospital infection and reduce to the number of deaths by secondary infections, with professional interaction between doctors, dentists and health officers in these institutions.

Conclusion

In this study, it could be concluded that there are need for more studies to ensure evidence that antimicrobial solutions can reduce the aspiration pneumonia, however, studies with good levels of evidence suggest that this may happen with the oral hygiene care, which brings benefits to the patient and every institution, by reducing the mortality rate and the hospital costs. Also, it is important dentists stay in the hospital, promoting professional interaction and a better quality of life to the patient.

References

1. Pássaro L, Harbarth S, Landelle C. Prevention of hospital-acquired pneumonia in non-ventilated adult patients: a narrative review. Antimicrob Resist Infect Control. 2016;14(5):43.
2. Meinberg MC, Cheade MF, Miranda AL, Fachini MM, Lobo SM. Uso de clorexidina 2% gel e escovação mecânica na higiene bucal de pacientes sob ventilação mecânica: efeitos na pneumonia associada a ventilador. Rev Bras ter Intensiva. 2012;24(4):369-74.
3. Morais TMN, Silva A, Avi ALRO, Souza PHR, Knobel E, Camargo LFA. A importância da atuação odontológica em pacientes internados em unidade de terapia intensiva. Rev bras ter intensiva. 2006;18(4):12-417.
4. de Lacerda Vidal CF, Vidal AK, Monteiro JG Jr, Cavalcanti A, Henriques AP, Oliveira M, et al. Impact of oral hygiene involving toothbrushing versus chlorhexidine in the prevention of ventilator-associated pneumonia: a randomized study. BMC Infect Dis. 2017;17(1):112.
5. Müller F. Oral hygiene reduces the mortality from aspiration pneumonia in frail elders. J Dent Res. 2015;94(3):14S-16S.
6. Hollaar VRY, van der Putten GJ, van der Maarel-Wierink CD, Bronkhorst EM, de Swart BJM, Creugers NHJ. The effect of a daily application of a 0.05% chlorhexidine oral rinse solution on the incidence of aspiration pneumonia in nursing home residents: a multicenter study. BMC Geriatr. 2017;17(1):128.
7. van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Oral health care and aspiration pneumonia in frail older people: a systematic literature review. Gerodontology. 2013;30(1):3-9.
8. Moher D, Hopewell S, Schulz KF, Montori V, Gøtsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol, 2010;63:(1)37.
9. He S, Wang Y, Li X, Hu D. Effectiveness of laser therapy and topical desensitising agents in treating dentine hypersensitivity: a systematic review. J Oral Rehabil. 2011;38(5):348-58.
10. Flecha OD, Douglas de Oliveira DW, Marques LS, Gonçalves PF. A commentary on randomized clinical trials: How to produce them with a good level of evidence. Perspect Clin Res. 2016;7(2):75-80.
11. Nogueira EB, Cortine AAO, Daher A, Costa LR. Higiene oral e pneumonia em crianças em Unidade de Terapia Intensiva: revisão sistemática, Rev Assoc Paul Cir Dent. 2015;69(1):14-9.
12. Sharif-Abdullah SS, Chong MC, Surindar-Kaur SS, Kamaruzzaman SB, Ng KH. The effect of chlorhexidine in reducing oral colonisation in geriatric patients: a randomised controlled trial. Singapore Med J. 2016;57(5):262-6.
13. Scannapieco FA, Yu J, Raghavendran K, Vacanti A, Owens SI, Wood K, Mylotte JM. A randomized trial of chlorhexidine gluconate on oral bacterial pathogens in mechanically ventilated patients. Crit Care. 2009;13(4):R117.
14. Nobahar M, Razavi MR, Malek F, Ghorbani R. Effects of hydrogen peroxide mouthwash on preventing ventilator-associated pneumonia in patients admitted to the intensive care unit. Braz J Infect Dis. 2016; 20(5):444-50.
15. Azimi M, Jouybari L, Moghadam S, Ghaemi E, Behnampoor N, Sanagoo A, Hesam M. Antimicrobial effects of chlorhexidine, matrica drop mouthwash (chamomile extract), and normal saline on hospitalized patients with endotracheal tubes. Iran J Nurs Midwifery Res. 2016;21(5):458-63.
16. Hollaar V, van der Maarel-Wierink C, van der Putten GJ, de Swart B, de Baat C. Effect of daily application of a 0.05% chlorhexidine solution on the incidence of (aspiration) pneumonia in care home residents: design of a multicentre cluster randomised controlled clinical trial. BMJ Open. 2015;5(12):007889.
17. Klarin B, Molin G, Jeppsson B, Larsson A. Use of the probiotic Lactobacillus plantarum 299 to reduce pathogenic bacteria in the oropharynx of intubated patients: a randomised controlled open pilot study. Crit Care. 2008;12(6):R136.
18. Naiktari RS, Gaonkar P, Gurav AN, Khiste SV. A randomized clinical trial to evaluate and compare the efficacy of triphala mouthwash with 0.2% chlorhexidine in hospitalized patients with periodontal diseases. J Periodontal Implant Sci. 2014;44(3):134-40.
19. Tantipong H, Morkchareonpong C, Jaiyindee S, Thamlikitkul V. Randomized controlled trial and meta-analysis of oral decontamination with 2% chlorhexidine solution for the prevention of ventilator-associated pneumonia. Infect Control Hosp Epidemiol. 2008;29(2):131-6.
20. Scannapieco FA, Binkley CJ. Modest reduction in risk for ventiltor-associated pneumonia in critically ill patients receiving mechanical ventilation following topical oral chlorhexidine. J Evid Based Dent Pract. 2012;12(3):15-7.
21. Tuon FF, Gavrilko O, Almeida S, Sumi ER, Alberto T, Rocha JL, Rosa EA. Prospective, randomised, controlled study evaluating early modification of oral microbiota following admission to the intensive care unit and oral hygiene with chlorhexidine. J Glob Antimicrob Resist. 2017;8:159-6.3
22. Estaji Z, Alinejad M, Hassan Rakhshani M, Rad M. The Comparison of Chlorhexidine Solution and Swab With Toothbrush and Toothpaste Effect on Preventing Oral Lesions in Hospitalized Patients in Intensive Care Unit. Glob J Health Sci. 2015;8(5):211-6.
23. Editorial. Importância do Cálculo Amostral em Pesquisa Científica [Editorial]. Rev Cir Traumatol Buco-Maxilo-Fac. 2005;(7):5.
24. Reis FB, Lopes AD, Fallopa F, Ciconneli RM. A importância da qualidade dos estudos para a busca da melhor evidência. Rev Bras Ortop. 2008;43(6):209-16
25. Rodrigues, MlV. "Estudos "cegos" ou "mascarados"?. Medicina (Ribeirao Preto. Online) 2000;33(1):1-2.
26. Ferreira JC, Patino CM, Randomização: mais do que o lançamento de uma moeda, J Bras Pneumol. 2016;42 (5):310-0.
27. Gasparim AZ, Jurkiewicz AL, Marques JM, Santos RS, Marcelino PCO, Junior FH, et al. Deglutition and Cough in Different Degrees of Parkinson Disease. Rev Intl Arch Otorhinolaryngol. 2011;15(2):181-8.
28. Amaral SM, Cortês AQ, Pires FR. Pneumonia nosocomial: importância do microambiente bucal. J Bras Pneumol. 2009;35(11):1116-24.
29. Morais MI. Vulnerabilidade do doente versus autonomia individual. Rev. Bras. Saúde Matern. Infant. 2010;10(2):331-6.
30. Lima, DCd, Saliba, NA, Garbin, AJI, Fernandes, LA, Garbin, CAS. A importância da saúde bucal na ótica de pacientes hospitalizados. Ciência & Saúde Coletiva [Internet]. 2011;16(1):1173-80.
31. El-Solh AA. Association between pneumonia and oral care in nursing home residents. Lung. 2011;189(3):173-80.
32. Fonseca B, Bocassanta ACS, Bozza A, Fosquiera EC, Microrganismos bucais no desenvolvimento da pneumonia aspirativa por ventilação mecânica em pacientes de unidade de terapia intensiva - revisão de literatura. Rev Uningá. 2017;2(30):37-43.

Mini Curriculum and Author's Contribution

1. Nayara Perpétuo Gonçalves do Nascimento – Dentistry undergraduate student. Contribution: bibliographic review, data acquisition, writing the work.
2. Patricia Furtado Gonçalves – DDS and PhD. Contribution: co-advisor, conception and design, data acquisition, writing the work.
3. Dhelfeson Willya Douglas-de-Oliveira – DDS and MSc. Contribution: methodological review of the article, data acquisition, formatting tables and responsible for submission.
4. Olga Dumont Flecha – DDS and PhD. Contribution: Advisor, data acquisition and interpretation, writing work, final approve.

Submitted: 11/27/2017 / Accepted for publication: 12/14/2017

Corresponding Author
Dhelfeson Willya Douglas-de-Oliveira
E-mail: dhodonto@hotmail.com