

PERIODONTAL DISEASE AS A RISK FACTOR FOR ASPIRATION PNEUMONIA: A SYSTEMATIC REVIEW

DOENÇA PERIODONTAL COMO FATOR DE RISCO PARA PNEUMONIA ASPIRATIVA: UMA REVISÃO SISTEMÁTICA

Adriana CAGNANI¹; Andréia Moreira de Souza BARROS¹; Luciana Luz Araújo de SOUSA¹; Luciane ZANIN¹; Cristiane de Cassia BERGAMASCHI²; Daiane Cristina PERUZZO³; Flávia Martão FLÓRIO¹

1. Department of Public Health Dentistry, São Leopoldo Mandic School of Dentistry and Research Center, Campinas, SP, Brazil. flavia.florio@slmandic.edu.br; 2. School of Pharmacy, Department of Pharmaceutical Sciences, University of Sorocaba, Sorocaba, Brazil; 3. Department of Periodontics, São Leopoldo Mandic School of Dentistry and Research Center, Campinas, SP, Brazil

ABSTRACT: The objective of this study was to systematically review the available literature, evaluating if periodontal disease is a risk factor for the development of aspiration pneumonia. The data sources were publications available between 01/01/1980 and 01/15/2011, on the following databases: MEDLINE, LILACS, Evidence Portal, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Academics. Inclusion criteria included randomized clinical trials, case-control and cohort studies, as well as cross sectional studies, in Portuguese and English. Teams of reviewers, independently and in duplicate, screened titles and abstracts of full text articles to determine eligibility. The selected articles were read in full and the variables evaluated independently and described in predetermined forms according to clinical outcomes. As a result, five studies out of 653 publications were included: three case-control studies and two cohort studies. Although these studies indicate a positive association between the presence of periodontal disease and the occurrence of aspiration pneumonia, the results must be interpreted with caution. They should not be taken as definitive conclusions due to variations in methodology and limitations, such as sample size, inadequate control of potential confounding variables, lack of calibration of periodontal measurements and inconsistent criteria for the establishment of aspiration pneumonia. There is little evidence to affirm that periodontal disease is a risk condition factor for aspiration pneumonia. Future studies are necessary to elucidate this association, as well as to establish the potential benefit of periodontal treatment with the goal of reducing the risk of developing aspiration pneumonia.

KEYWORDS: Intensive Care Units. Aspiration Pneumonia. Biofilm.

INTRODUCTION

Nosocomial pneumonia is an infection of the inferior respiratory tract, contracted by the patient in a hospital at least 48 hours after being admitted (CRAVEN et al., 2009; TORPY et al., 2007). It is often caused by *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Acinetobacter spp*, *Enterobacter spp* (JOSEPH et al., 2010). Ventilator-associated pneumonia (VAP) is the most frequent infection in intensive care units (ICUs) and its incidence may vary from 6 to 68%, with an occurrence rate of 3% per day, during the first five days under ventilation, 2% per day, from the 5th to 10th day under ventilation, and 1% per day, after this period (AMERICAN THORACIC SOCIETY, 2005). With each VAP episode, there is an increase in the length of time the patient will remain in ICU care from 4.3 to 13 days, which associates with an increase in the financial burden to the health care system (RELLO et al., 2002). The overall mortality

of ventilator-associated pneumonia episodes varies from 20 to 76% (AMERICAN THORACIC SOCIETY, 2005).

The oropharyngeal region has a special role in inferior respiratory tract infections related to severe anaerobic pulmonary infections, due to aspiration of saliva, especially in patients with periodontal disease (SCANNAPIECO, 1999). This occurs because both conditions share a common etiologic factor, the gram-negative anaerobic bacteria, leading to an immunological and inflammatory response from the host (TERPENNING, 1996). The oropharynx microbial colonization is considered the greatest source of bacteria involved in the etiology of VAP (RAGHAVENDRAN et al., 2000).

The objective of the present study was to systematically review the literature in order to evaluate if the periodontal disease is a risk factor for the development of aspiration pneumonia.

MATERIAL AND METHODS

Research methods to identify studies

The studies were identified by means of a bibliographical research on the databases MEDLINE, LILACS, Evidence Portal, the Cochrane Controlled Trials Library, and Google Scholar, in the period between 01/01/1980 and 01/15/2011, in both Portuguese and English. In order to obtain additional data, the authors were contacted by e-mail and registered mail. The research strategy used was a combination of the terms aspiration pneumonia, periodontal disease and nosocomial pneumonia.

Eligibility criteria for considering studies for review

Inclusion of randomized controlled trials, case-control, cohort and cross sectional studies including patients with periodontal disease and aspiration pneumonia. *Outcome measures.* We included studies that reported either of the following clinical outcomes: risk association and presence of association between periodontal disease and aspiration pneumonia.

Data extraction

The articles were read in full and the variables independently evaluated and described in

pre-determined forms according to quality (randomization and/or matching of cases and controls to control for unpaired variables, calibration, statistical adjustment) and main characteristics: type of study, methodological characteristics (inclusion and exclusion criteria, random allocation of treatment), performed interventions and clinical outcomes. The evaluations and data extraction were performed by two authors (AC and DCP). Disagreements were settled by discussions and consensus between them, and verified by a scientific consultant (FMF). Evaluation of study quality followed the guidelines for systematic reviews: Systematic Reviews – CRD's guidance for undertaking reviews in health care (CENTRE FOR REVIEWS AND DISSEMINATION, 2009).

RESULTS

Initially, 603 publications identified by electronic search were selected. After evaluating the titles, 548 publications were excluded. These publications did not evaluate periodontal disease as a risk factor for developing aspiration pneumonia. Fifty abstracts remained for further evaluation which resulted in the exclusion of 33 publications which did not meet the inclusion criteria (Table 1).

Table 1. Excluded articles based on the abstracts and main reasons for exclusion.

Reason for exclusion	Authors, year
Literature reviews=26.	Berry and Davidson, (2006); Bush and Donley, (2002); Finegold (1991); Joseph et al. (2010); Kahn et al. (2003); Kalia, (2003); Li et al. (2000); Limeback H, (1998); Mojon P, (2002); Morais et al. (2006); Oliveira & Fischer (2004); Pace and McCullough, (2010); Page (2001); Paju & Scannapieco, (2007); Patarroyo et al. (2008); Raghavendran et al.(2007); Scannapieco (1999); Scannapieco et al.(2010); Scannapieco and Mylotte (1996); Scannapieco and Rethman, (2003); Shay (2002); Taylor et al.(2000); Teng et al.(2002); Terpenning (2001); Terpenning (2005); Weidlich et al. (2008)
Systematic reviews=2.	Azarpazhooh and Leake (2006); Scannapieco et al. (2003)
Animal Studies=1.	De Bowes (1998).
Pilot studies=2.	Beck et al. (2008); Brothwell et al. (2008).
Oral hygiene protocol studies n=1.	Needleman et al., (2010).
Outcomes not related to aspiration pneumonia = 1.	Araújo and Saba-Chujfi (2008).

Full texts of 22 selected articles were evaluated for quality and key characteristics. After this evaluation 17 studies did not present the proper

variables according to the pre-established criteria (Table 2).

Table 2. Articles excluded based on the evaluation of full text and main reasons for exclusion.

Reason for exclusion	Authors, year
Microbiology research study=1.	Baba et al., (2011).
Pharmacological study=1.	Bágyi et al., (2009).
Studies with samples from pediatric and neonatal ICUs=2.	Becerra et al., (2010); Hu HB et al., (2010).
Oral hygiene protocol studies n= 4.	Bellissimo-Rodrigues et al., (2009); Shi Zongdao et al., (2010); Somal and Darby (2006); Tantipong et al., (2008).
Outcomes not related to aspiration pneumonia=9.	Liu et al., (2011); Lisboa et al., (2007); Macedo et al., (2010); Oliveira et al., (2007); Pinheiro et al., (2007); Rodrigues et al., (2009); Senpuku et al., (2003); Terpenning et al., (1993); Wong et al., (1995).

Thus 5 articles were evaluated in the present systematic review (Figure 1).

The sample size of the selected studies ranged from 80 to 697 participants, and they were distributed in three case-control studies, and two cohort studies. In the majority of the studies, the participants were hospitalized patients or patients

referred from specialized treatment centers. Two studies included patients selected from a random sample of the population. To evaluate the periodontal parameters, examiner calibration and how such was conducted are key information; however they were not clearly stated in the articles (Table 3).

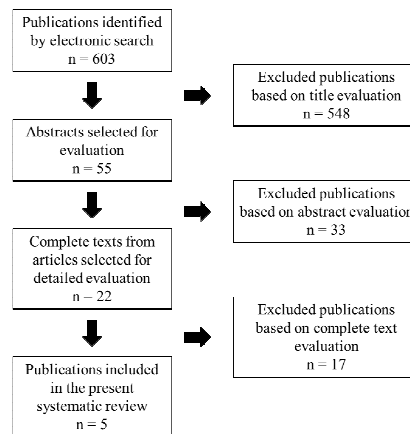


Figure 1. Selection of the articles utilized in systematic review.

Table 3. Characteristics of the studies included in this systematic review.

Source	Experimental design	n	Examiner characteristics	Calibration
Scannapieco et al (10)	Case control study	386	Not reported	Not mentioned
Terpenning et al (11)	Cohort study	358 patients from emergency rooms, infirmaries, and nursing homes	Not reported	Not mentioned
Awano et al (12)	Cohort study	697 individuals (277 men, 420 women)	Not reported	Not mentioned
El Attar et al (13)	Case control study	80	A periodontist	Not mentioned
Sharna and Shamsuddin (14)	Case control study	A group of 100 cases and 100 control, paired by race	One calibrated examiner	Not mentioned

The studies included in this review reported that all teeth were evaluated (AWANO et al., 2008; EL ATTAR et al., 2010; SCANNAPIECO et al., 1998; SHARMA and SHAMSUDDIN, 2011; TERPENNING et al., 2001). The studies by AWANO et al. (2008), EL ATTAR et al. (2010) and SCANNAPIECO et al. (1998) analyzed six sites per tooth. Scannapieco et al. (1998) and Awano et al. (2008) utilized epidemiological criteria, which are useful in planning the treatment and motivating the patients. However, El Attar et al. (2010) used epidemiological and clinical criteria, which included the use of periodontal probes to obtain periodontal measurements. The study by Sharma & Shamsuddin (2011) evaluated four sites per teeth, and used clinical and epidemiological criteria. Terpenning et al. (2001) did not report if periodontal probing was performed. With regards to the type of dental instrument utilized in the exams, two studies (EL ATTAR et al., 2010; SHARMA and SHAMSUDDIN, 2011) used the Williams periodontal probe, and the study (CENTRE FOR REVIEWS AND DISSEMINATION, 2009) used a number 5 explorer. The study by Awano et al. (2008) reported the use of a manual probe, but it did not specify the type. With regards to the periodontal criteria: i] Awano et al. (2008) used the community periodontal index [CPI]; ii] EL ATTAR et al. (2010)

and SHARMA & SHAMSUDDIN (2011) evaluated probing depth [PD]; iii] SCANNAPIECO et al. (1998) registered the periodontal index [PIn]; and, iv] in two studies (SCANNAPIECO et al., 1998; SHARMA; SHAMSUDDIN, 2011) the simplified oral hygiene index [SOHI] was calculated. Besides the measurements described above, two studies (EL ATTAR et al., 2010; SHARMA; SHAMSUDDIN, 2011) registered the gingival index [GI], plaque index [PI], and clinical attachment level [CAL]. The studies used various criteria to diagnose periodontal disease, AWANO et al. (2008) used PD; EL ATTAR et al. (2010) used CAL, and the remaining studies (SCANNAPIECO et al., 1998; SHARMA; SHAMSUDDIN, 2011; TERPENNING et al., 2001) did not disclose the criteria.

The diagnosis of aspiration pneumonia was determined by medical evaluation in two studies (SCANNAPIECO et al., 1998; TERPENNING et al., 2001). Terpenning et al. (2001) used microbiological and biochemical analyses, as well as chest X-ray to diagnose aspiration pneumonia. El Attar et al. (2010) performed microbiological analysis of the bronchoalveolar lavage [BAL]. The studies by Awano et al. (2008) and Sharma and Shamsuddin (2011) did not report their methods for diagnosing aspiration pneumonia (Table 4).

Table 4. Articles included according to periodontal criteria and diagnosis of aspiration pneumonia.

Source	Periodontal Criteria			
	Clinical Exam 1. Number of teeth Periodontal probe	Measurements	Diagnosis criteria for periodontal disease	Diagnosis criteria for aspiration pneumonia
Scannapieco et al. (1998)	1. All the teeth (six sites per tooth), unless it was a root. Number 5 Explorer	SOHI and PIn which corresponded to the arithmetic average of the scores	Not reported	Medical evaluation
Terpenning et al. (2001)	1. Evaluation of teeth according to oral hygiene, dental cavities, periodontal disease, number of teeth under masticatory function, and the presence of removable prosthesis. Not reported	Saliva specimens collected for evaluation of salivary constituents and salivary IgA antibodies in order to select periodontopathogens and cariogenic microorganisms. Saliva, throat mucosa, and supra and subgingival plaque samples for the detection of aerobic and anaerobic species	Not reported	Microbiological test, biochemical tests, chest x-ray, and medical evaluation

Awano et al. (2008)	1. All teeth (six sites per tooth) . Manual probe	CPI	PS>4mm	Not reported
El Attar et al. (2010)	1. All teeth (six sites per tooth). Williams periodontal probe	GI, PI, PD, CAL	Moderate and Severe chronic periodontitis (CAL \geq 3mm and < 5mm and CAL \geq 5mm respectively)	Microbiological tests of BAL
Sharma and Shamsuddin (2011)	1. All teeth (four sites per tooth) . Williams periodontal probe.	GI, PI, SOHI, CAL, PD	Not reported	Not reported

GI - gingival index; PI - plaque index; SOHI - simplified oral hygiene index; Pin - periodontal index; CAL - clinical; PS - probing depth

With regards to the statistical adjustments, one study (CENTRE FOR REVIEWS AND DISSEMINATION, 2009) performed logistic regression to adjust for confounding factors such as age, race, gender, and smoking; while another (SHARMA and SHAMSUDDIN, 2011) paired subjects according to smoking status. As for risk association, TERPENNING et al. (2001) pointed out a significant association between the presence of periodontal pathogens such as *Porphyromonas gingivalis* and *Streptococcus sobrinus* in the dental

biofilm of individuals with aspiration pneumonia [OR= 2.7, 95% IC: 1.3 – 5.3; OR= 2.3, 95% IC: 0.9 – 5.9, respectively]. For the cumulative incidence of aspiration pneumonia, in subjects with teeth, the presence of *Porphyromonas gingivalis* in the dental biofilm was strongly associated with a subsequent diagnosis of aspiration pneumonia [OR= 4.2; 95% IC: 1.6 – 11.3]. SHARMA and Shamsuddin (2011) observed that subjects with low income and respiratory disease presented periodontal disease [OR= 4.433] (Table 5).

Table 5. Articles included according to the statistical adjustments and outcomes evaluated

Authors, year	Statistical Adjustment	Risk association	Outcomes	Association
Scannapieco et al (10)	Logistic regression adjusted to age, race, gender, and smoking	Not reported		None
Terpenning et al (11)	Not reported	Presence of periodontal pathogens in the dental biofilm, such as <i>Porphyromonas gingivalis</i> : (OR= 2.7; 95% CI: 1.3-5.3) and <i>Streptococcus sobrinus</i> : (OR= 2.3; 95% CI: 0.9-5.9) was significantly high in subjects with aspiration pneumonia. In the cumulative incidence of aspiration pneumonia, the presence of <i>Porphyromonas gingivalis</i> in the dental biofilm was significant: (OR= 4.2; 95% CI: 1.6-11.3).		Positive
Awano et al (12)	Not reported	Not reported		Positive
El Attar et al (13)	Not reported	Not reported		Positive
Sharma and Shamsuddin (14)	Student <i>t</i> test and Chi-square test to compare the periodontal parameters between groups adjusted to smoking.	Subjects with low income and respiratory disease were approximately 4.4 times more likely to have poor periodontal health (OR= 4.433) when compared to the high income groups (OR=0.674)		Positive

CI = Confidence interval

DISCUSSION

Systematic reviews can be defined as the review of a clearly formulated question in an

attempt to minimize bias, using systematic and explicit methods to identify, select, critically evaluate, and summarize relevant research, with the goal of providing a broad and contemporary

understanding of the available literature (NEEDLEMAN, 2002).

A total of five articles were analyzed in this systematic review, distributed in three case-control studies, and two cohorts. Terpenning et al. (2001) found evidence that the presence of periodontal bacteria is an important risk factor for aspiration pneumonia. Awano et al. (2008) concluded that a larger number of teeth with PD > 4 mm were an independent predictor of mortality due to pneumonia. El Attar et al. (2010) and Sharma and Shamsuddin (2011) suggested an association between poor periodontal health and the risk of developing nosocomial pneumonia and respiratory disease.

When evaluating periodontal measurements, variations may occur within an examiner or between examiners. Such problems can be minimized or even avoided by proper calibration of the examiners (EKLUND et al., 1996). Methods of calibration and the characteristics of the examiners are critical in clinical studies; however they were not clearly stated in the articles evaluated in this review. In order to clarify this and other questionable facts from the articles included in this review, the authors were contacted by e-mail and registered letter to obtain additional data. The reply rate however was null.

There is significant variation in the way periodontal parameters are reported in the literature. Some studies report full-mouth measurements, others only a single quadrant, or specific teeth, and even selected sites are evaluated (SOUZA, 2004). In this systematic review, variations were found regarding the criteria used in the clinical examination. Some studies (AWANO et al., 2008; EL ATTAR et al., 2010; SCANNAPIECO et al., 1998; SHARMA and SHAMSUDDIN, 2011) reported that the periodontal exam involved probing of all teeth. Other studies (AWANO et al., 2008; EL ATTAR et al., 2010; SCANNAPIECO et al., 1998) analyzed 6 sites per tooth, disagreeing with the study by Sharma and Shamsuddin (2011) that evaluated four sites per tooth. In the study by TERPENNING et al. (2001) there was no report of periodontal probing during clinical examination.

When evaluating oral health conditions with a periodontal index, a study aims at applying a simple and reproducible method which can be used at a large scale (KINGMAN and ALBANDAR, 2002). However, this simplification might lead to mistakes in the evaluation of the disease and differences between studies. Even though the criteria based on clinical attachment level [CAL] has been referred to in the literature as the most

applied method (LÓPEZ et al., 2002), only El Attar et al. (2010) used this index.

Several factors can interfere with periodontal probing, such as: pressure applied to the probe by the operator, variability rate among examiners, inflammatory status of the tissue, pain threshold, local factors, presence of calculus, and factors related to the instrument (BIDDLE et al., 2001). None of the studies reviewed here reported the precautions taken to minimize these interferences, which is fundamental for the accurate diagnosis of periodontal disease.

The early diagnosis of VAP is essential and it is directly associated with the reduction in mortality rates (KOLLEF et al., 2008). In this systematic review, two studies (SCANNAPIECO et al., 1998; TERPENNING et al., 2001) performed medical evaluations. The microbiological evaluation consists of a diagnostic strategy, by an invasive method known as bronchoalveolar lavage [BAL], in association with a fibrobronchoscopy. This method should be performed according to a standardized technique for patients under mechanical ventilation (CONTRERAS et al., 2011). Terpenning et al. (2001) performed microbiological tests, but did not provide a detailed protocol. El Attar et al. (2010) utilized the BAL technique. Even though biochemical tests have no value in the etiological definition, they contribute with the evaluation of the organic dysfunction and have implications on the prognosis (AMERICAN THORACIC SOCIETY, 2005). However, only the study by TERPENNING et al. (2001) performed these tests, and included the evaluation of chest X-rays which, even though has a low positive predictive value, plays an important role in the diagnosis (SAN PEDRO, 2001).

Blood culture analysis was only included in one study (Terpenning et al., 2001). A positive blood culture test is used as a diagnostic criterion, because the probability of isolating the same etiological agent in BAL is 26%, with a positive predictive value of 73% (RELLO et al., 2001). Studies by AWANO et al. (2008) and SHARMA & SHAMSUDDIN (2011) did not report the criteria used to establish the diagnosis of aspiration pneumonia. In order to obtain reliable results, the studies should have performed a careful evaluation of the signs, risk factors and conditions for specific etiological agents, and established their severity. In the study by El Attar et al. (2010) the medical evaluation, biochemical tests, and chest x-ray could have been added as diagnostic criteria, assisting in the diagnosis. The study by SCANNAPIECO et al. (1998) could have supplemented the diagnostic criteria by including microbiological and

biochemical tests, and chest x-rays, since the results of these tests will change the prognosis of the condition.

A confounding variable is a variable that will change the relationship between the exposure factor and the outcome. However, it is not an intermediary link in the causality chain between exposure and outcome (RELLO et al., 2001). One of the steps of a study involving randomization and/or matching of cases and controls is to control for unpaired variables (NEEDLEMAN et al., 2005). Proper sample randomization to prevent systematic errors was done in several studies (AWANO et al., 2008; SCANNAPIECO et al., 1998; SHARMA and SHAMSUDDIN, 2011). Sharma & Shamsuddin (2011) randomized and paired the study subjects. El Attar et al (2010) did not control for confounding variables.

Another way of controlling unpaired variables is by using the statistical adjustment model. Scannapieco et al. (1998) and Sharma and Shamsuddin (2011) performed statistical adjustment for smoking. Nevertheless, the study (CENTRE FOR REVIEW AND DISSEMINATION, 2009) did not report the odds ratio [OR] nor found evidence to support the association between periodontal disease and smoking, disagreeing with Sharma & Shamsuddin (2011). Terpenning et al. (2001) reported the OR, however controlling of confounding variables were not reported, especially in the case of a multifactorial disease such as periodontitis (PAGE and KORNMAN, 1997). The study by Awano et al. (2008) evaluated the relation between oral hygiene standards and mortality rate

by pneumonia in the elderly, and suggested a positive association, but did not report an OR. El Attar et al. (2010) did not report the implementation of statistical adjustment or an OR.

Although four studies analyzed in the present review found positive associations between periodontal disease and aspiration pneumonia, such results must be carefully interpreted. They should not be taken as definitive conclusions, due to methodological variations and limitations, such as sample size, inadequate control of potential confounding factors, lack of calibration, and inconsistent criteria for the diagnosis of aspiration pneumonia.

Conclusions of a systematic review have two implications: a clinical implication, which allows one to recommend or not the use of a certain intervention; and a research implication, which allows one to recommend future research studies to elucidate new questions towards the same clinical condition. Thus, it becomes clear the importance of systematic reviews as guidelines not only for research purposes for planning future studies, but also for the clinical practice in assisting with decision making.

The studies analyzed in this systematic review indicate that periodontal disease is a risk factor for the development of aspiration pneumonia. It is noteworthy that only five studies were included and for this reason future studies are necessary to elucidate this association as well as to establish the potential benefit of periodontal treatment with the goal of reducing the risk for developing aspiration pneumonia.

RESUMO: O Objetivo do estudo foi revisar sistematicamente a literatura disponível, avaliar se a doença periodontal é um fator de risco para o desenvolvimento de pneumonia por aspiração. As fontes de dados foram publicações disponíveis entre 01/01/1980 e 15/01/2011, nas seguintes bases de dados: Medline, Lilacs, Evidence Portal, Cochrane Central Register de Ensaios Controlados (CENTRAL) e Google Academics. Os estudos de seleção foram ensaios clínicos randomizados, estudos de caso-controle e coorte, assim como estudos transversais, em Português e Inglês. Equipes de revisores, independente e em duplicado fez os títulos de telas e resumos e do texto completo para determinar a elegibilidade. Os artigos selecionados foram lidos na íntegra e as variáveis avaliadas de forma independente e descrito em formas pré-determinadas de acordo com os resultados clínicos. Como resultado, cinco estudos de 653 publicações foram incluídos: três estudos de caso-controle, um estudo de coorte e um estudo prospectivo, com análise retrospectiva de dados. Embora esses estudos indicam uma associação positiva entre a presença de doença periodontal e a ocorrência de pneumonia aspirativa, os resultados devem ser interpretados com cautela. Eles não devem ser tomados como conclusões definitivas devido a variações nas metodologias e limitações, tais como tamanho da amostra, controle inadequado de potenciais variáveis de confusão, a falta de calibração das medições periodontais e sem critérios consistentes para o estabelecimento de pneumonia por aspiração. Há pouca evidência para afirmar que a doença periodontal é um fator condição de risco para pneumonia aspirativa. Futuros estudos são necessários para elucidar essa associação, bem como para estabelecer o potencial benefício do tratamento periodontal com o objetivo de reduzir o risco de desenvolver pneumonia por aspiração.

PALAVRAS-CHAVE: Unidades de Cuidados Intensivos. Pneumonia aspirativa. Biofilme dental.

REFERENCES

- AMERICAN THORACIC SOCIETY. Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. **Am J Respir Crit Care Med.** v. 171, n. 4, p. 388-416, 2005. <http://dx.doi.org/10.1164/rccm.200405-644ST>
- AWANO, S.; ANSAI, T.; TAKATA, Y.; SOH, I.; AKIFUSA, S.; HAMASAKI, T. Oral health and mortality risk from pneumonia in the elderly. **J Dent Res.** v. 87, n. 4, p. 334-339, 2008. <http://dx.doi.org/10.1177/154405910808700418>
- BIDDLE A. J.; PALMER R. M.; WILSON R. F.; WATTS T. L. Comparison of the Validity of Periodontal Probing Measurements in Smokers and Nonsmokers. **J Clin Periodontol.** v. 28, n. 8, p. 806-812, 2001. <http://dx.doi.org/10.1034/j.1600-051X.2001.280813.x>
- CENTRE FOR REVIEWS AND DISSEMINATION. Systematic Reviews. CRD's guidance for undertaking reviews in health care. Available online at: http://www.york.ac.uk/inst/crd/pdf/Systematic_Reviews.pdf. 2009. Access on 14 jan. 2012.
- CONTRERAS, P.; MILET, B.; CORIA, P. Evaluation of quantitative cultures of endotracheal aspirates for pediatric ventilator-associated pneumonia diagnosis: analytic, prospective study. **Rev Chilena Infectol.** v. 28, n. 4, p. 349-356, 2011.
- CRAVEN, D. E.; CHRONEOU A.; ZIAS, N.; HJALMARSON, K. I. Ventilator-associated tracheobronchitis: the impact of targeted antibiotic therapy on patient outcomes. **Chest.** v. 135, n. 2, p. 521-528, 2009. <http://dx.doi.org/10.1378/chest.08-1617>
- EKLUND, S. A.; MOLLER, I. J.; LECLERCQ, M. H. Calibrating examiners for oral health epidemiological surveys. Geneva: **World Health Organization (WHO/ORH/Epid.93.1)**. 1996.
- EL ATTAR, M. M.; ZAGHLOUP, M. Z.; ELMENOUFR, H. S. Role of periodontitis in hospital-acquired pneumonia. **East Mediterr Health J.** v. 16, n. 5, p. 563-569, 2010.
- JOSEPH, N. M.; SISTLA, S.; DUTTA, T. K.; BADHE, A. S.; PARIJA, S. C. Ventilator-associated pneumonia: A review. **Eur J Intern Med.** v. 21, n. 5, p. 360-368, 2010. <http://dx.doi.org/10.1016/j.ejim.2010.07.006>
- KINGMAN, S.; ALBANDAR, J. M. Methodological aspects of epidemiological studies of periodontal diseases. **Periodontol 2000.** n. 29, v. 1, p. 11-30, 2002. <http://dx.doi.org/10.1034/j.1600-0757.2002.290102.x>
- KOLLEF, K. E.; SCHRAMM, G. E.; WILLS, A. R.; REICHLEY, R. M.; MICEK, S. T.; KOLLEF, M. H. Predictors of 30-day mortality and hospital costs in patients with ventilator-associated pneumonia attributed to potentially antibiotic-resistant Gram-negative bacteria. **Chest.** v. 134, p. 281-287, 2008. <http://dx.doi.org/10.1378/chest.08-1116>
- LÓPEZ, N. J.; SMITH, P. C.; GUTIERREZ, J. Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial. **J Periodontol.** v. 73, n. 8, p. 911-924, 2002. <http://dx.doi.org/10.1902/jop.2002.73.8.911>
- NEEDLEMAN, I. G. A guide to systematic reviews. **J Clin Periodontol.** n. 29, v. 3, p. 6-9, 2002. <http://dx.doi.org/10.1034/j.1600-051X.29.s3.15.x>
- NEEDLEMAN, I.; MOLES, D. R.; WORTHINGTON, H. Evidence based periodontology, systematic reviews and research quality. **Periodontol 2000.** v. 37, n. 1, p.12-28, 2005. <http://dx.doi.org/10.1111/j.1600-0757.2004.37100.x>

- PAGE, R. C.; KORNMAN, K. S. The pathogenesis of human periodontitis: an introduction. **Periodontology** **2000**. v. 14, n. 1, p. 9-11, 1997. <http://dx.doi.org/10.1111/j.1600-0757.1997.tb00189.x>
- RAGHAVENDRAN, K.; MYLOTTE, J. M.; SCANNAPIECO, F. A. Nursing home-associated pneumonia, hospital-acquired pneumonia and ventilator-associated pneumonia: the contribution of dental biofilms and periodontal inflammation. **Periodontol** **2000**. v. 44, n. 1, p. 164-177, 2007. <http://dx.doi.org/10.1111/j.1600-0757.2006.00206.x>
- RELLO, J.; OLLENDORF, D. A.; OSTER, G.; VERA-LLONCH, M.; BELLM, L.; REDMAN, R. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. **Chest**. v. 122, n. 6, p. 2115-2121. 2002. <http://dx.doi.org/10.1378/chest.122.6.2115>
- RELLO, J.; PAIVA, J. A.; BARAIBAR, J.; BARCENILLA, F.; BODI, M.; CASTANDER, D. International Conference for the Development of Consensus on the Diagnosis and Treatment of Ventilator-associated Pneumonia. **Chest**. v. 120, n. 3, p. 955-970, 2001. <http://dx.doi.org/10.1378/chest.120.3.955>
- SAN PEDRO, G. Are quantitative cultures useful in the diagnosis of hospital-acquired pneumonia? **Chest**. v. 119, n. 2, p. 385-390, 2001. http://dx.doi.org/10.1378/chest.119.2_suppl.385S
- SCANNAPIECO, F. A. Role of oral bacteria in respiratory infection. **J Periodontol**. v. 70, n. 7, p. 793-802, 1999. <http://dx.doi.org/10.1902/jop.1999.70.7.793>
- SCANNAPIECO, F. A.; PAPANDONATOS, G.D.; DUNFORD, R. G. Associations between oral conditions and respiratory disease in a national sample survey population. **Ann Periodontol**. v. 3, n. 1, p. 251-256, 1998. <http://dx.doi.org/10.1902/annals.1998.3.1.251>
- SHARMA, N.; SHAMSUDDIN, H. Association Between Respiratory Disease in Hospitalized Patients and Periodontal Disease: A Cross-Sectional Study. **J Periodontol**. v. 82, n. 8, p. 1155-1160, 2001. <http://dx.doi.org/10.1902/jop.2011.100582>
- SOUZA, S. L. S.; TABA JÚNIOR, M. Cross-sectional evaluation of clinical parameters to select high prevalence populations for periodontal disease. The site comparative severity methodology. **Braz Dent J**. v. 15, n. 1, p. 46-53, 2004. <http://dx.doi.org/10.1590/S0103-64402004000100009>
- TERPENNING, M. S. The ten most common questions about aspiration pneumonia. **Infect Dis Clin Pract**. v. 5, p. 42-46, 1996. <http://dx.doi.org/10.1097/00019048-199601000-00009>
- TERPENNING, M. S.; TAYLOR, G. W.; LOPATIN, D. E.; KERR, C. K.; DOMINGUEZ, B. L.; LOESCHE, W. J. Aspiration pneumonia: dental and oral risk factors in an older veteran population. **J Am Geriatr Soc**. v. 49, n. 5, p. 557-563, 2001. <http://dx.doi.org/10.1046/j.1532-5415.2001.49113.x>
- TORPY, J. M.; LYNM, C.; GLASS, R. M. Ventilator-associated pneumonia. **JAMA**. v. 297, n. 14, p. 1616, 2007. <http://dx.doi.org/10.1001/jama.297.14.1616>