

Periodontology

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Periodontitis and nosocomial lower respiratory tract infection: preliminary findings

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Abstract

Aim: To evaluate the possible association between periodontitis and nosocomial lower respiratory tract infection (LRTI).

Material and Methods: A case–control study was conducted at a General Hospital in Feira de Santana, Bahia, Brazil. The sample consisted of 103 individuals: 22 cases (presence of nosocomial LRTI) and 81 controls (absence of nosocomial LRTI). The diagnosis of periodontitis was based on probing depth, gingival recession, clinical attachment loss and bleeding on probing. The diagnosis of nosocomial LRTI was made in accordance with established medical criteria.

Results: Invasive ventilation was much more frequent in cases (95.5%) than in controls (7.4%). An orotracheal tube was used in 81.8% of cases and in 7.4% of controls; bronchoaspiration was suspected in 81.8% of cases and in 6.2% of controls. There was no statistically significant difference in any of the clinical periodontal parameters between cases and controls. The crude odds ratio (OR) value for individuals with periodontitis having LRTI was not statistically significant [OR_{crude} = 1.70; 95% confidence interval:(0.60–4.87)]. After including age, smoking and duration of hospitalization in the logistic regression, the adjusted OR for individuals with periodontitis having LRTI was statistically significant [OR_{adiusted} = 3.67 (1.01–13.53); p = 0.049].

Conclusions: A marginal association between periodontitis and LRTI was found when smoking, age and length of hospitalization were included as covariates. Patients with LRTI had a high frequency of suspected bronchoaspiration and this could explain the possible association of periodontal disease and LRTI found in this and other studies. Additional studies are needed to further clarify the possible relationship between periodontal disease and LRTI.

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Periodontal disease has been reported to be a pre-disposing factor for several diseases and systemic conditions, for

Conflict of interest and source of funding statement

The authors declare that they have no conflict of interests.

Financial support for this research was provided by the Research Support Foundation of the State of Bahia (FAPESB) and Feira de Santana State University. example cardiovascular disease, diabetes, kidney diseases and pre-maturity and/or low birth weight (Beck et al. 1996, Grossi & Genco 1998, Li et al. 2000, López et al. 2002, Jagelaviciene & Kubilius 2006).

Among such systemic conditions, respiratory diseases are being investigated (Estes & Meduri 1995, Mojon 2002, Pineda et al. 2006). Although nosocomial pneumonia is considered to be the respiratory complaint with the best links between its aetiopathogenesis and the pathogens involved in periodontal disease (Mojon 2002, Okuda et al. 2005, Azarpazhooh & Leake 2006, Masaki et al. 2006, Mori et al. 2006, Pineda et al. 2006, Paju & Scannapieco 2007, Raghavendran et al. 2007), other respiratory diseases acquired following hospitalization, named nosocomial respiratory tract infections [nosocomial lower respiratory tract infection (LRTIs)], are also being investigated.

An interrelationship between periodontal disease and nosocomial LRTI is biologically plausible, because the bacterial proliferation of periodontal disease favours colonization of the oropharynx, thereby perpetuating the state of oral infection through inflammatory and immunological mediators. In turn, this may contribute towards greater adhesion of microorganisms in the pulmonary parenchyma, thus making this the primary locus for establishing nosocomial LRTI. Furthermore, other determinants seem to mediate this biological mechanism, for example socio-economic factors like income and education level, difficulty in accessing healthcare services, individual immune response and harmful habits like smoking, alcoholism and deficient oral hygiene (Gesser et al. 2001, Kinane 2001).

It is also known that nosocomial LRTIs are developed within the hospital environment and are not present or incubated in the individual at the time of hospitalization. It has been estimated that, in Brazilian hospitals, nosocomial LRTI accounts for approximately 10-15% of all acquired infections, and that 20-50% of all individuals affected die (Toyoshima et al. 2005). In the United States, these percentages represent >300,000 cases of nosocomial LRTI per year, resulting in 20,000 deaths and an expenditure of approximately US\$ 2 billion on hospital care (Oliveira & Fischer 2004).

Considering the relevance of this topic and the scarcity of existing investigations, the aim of the present study was to investigate the possible association between periodontitis and nosocomial LRTI.

Materials and Methods Study sample

A preliminary case-control study was conducted. The participants were individuals who were evaluated in the clinical wards, surgical wards or adult intensive care units (ICUs) of the Clériston Andrade General Hospital (HGCA) in Feira de Santana, Bahia, Brazil. The patients who agreed to participate or whose participation was authorized by the person responsible for the patient, after receiving information about the study, signed a statement of free and informed consent. This study was approved by the Research Ethics Committee of Feira de Santana State University, Bahia, Brazil (protocol no. 079/2007).

Out of the total of 400 individuals who were informed about the study (which was conducted between September 2007 and January 2008), 297 were excluded according to the following criteria: refusal to take part in the study (123); edentulous state (27); use of equipment that would make it impossible to conduct a periodontal examination or presence of systemic clinical signs and symptoms that would impair the periodontal examination such as delirium tremens, fever or severe angular cheilitis (90); origin in parts of HGCA other than ICUs, clinical wards or surgical wards (50); and diagnoses of LRTI acquired in the community (7).

Finally, the sample was composed of 103 participants who fulfilled the general eligibility criteria: (a) possession of at least six teeth and (b) patients attended in the ICUs, clinical wards or surgical wards of Clériston Andrade General Hospital. In addition, individuals eligible for the case group were deemed to be those who developed an LRTI after hospitalization (nosocomial LRTI), independent of the situation reported as the cause of hospitalization, with the exception of pulmonary involvement diagnosed by the medical team at HGCA. The control group consisted of individuals from the sample who did not have LRTI using the same diagnostic criteria as cases.

The initial sample size calculation used a study power of 90%, with a 95% confidence interval (CI). This was based on a review of the literature, in which a range from 1.5 to 4.0-fold greater chance that an individual would develop nosocomial LRTI if he had periodontal disease was used (Dupont 1988, Dupont & Plummer 1990). For this study, the case group (N = 22) was composed of individuals with nosocomial LRTI and the control group (N = 81) was composed of individuals without this respiratory infection.

Data collection procedures

The participants or the persons responsible for them answered a structured questionnaire that was applied by the examiner, to obtain data relating to the socio-demographic characteristics, lifestyle, medical history, dental history and clinical findings during the period of hospitalization.

Following this, the patient's oral condition was assessed clinically by a single examiner, on the hospital bed itself, under artificial light. This examiner was a general dentist, who was unaware of the respiratory diagnosis but had previously received training from an experienced specialist in periodontics. In this hospital-based pilot study, difficulties were found in the data collection procedures among the hospitalized individuals, which precluded further calibration.

In the examination of periodontal condition, the sulcus/pocket probing depth, gingival recession and bleeding on probing index were measured for all teeth, except for the third molars, and the values for clinical attachment loss were obtained. These observations were made at six different locations on each tooth (distovestibular, midvestibular, mesiovestibular, distolingual, midlingual and mesiolingual), with the aid of a Williams-type probe graduated in millimetres (Hu-Friedy, Chicago, IL, USA).

Probing depth was recorded at each location as the distance from the gingival margin to the most apical extent of probe penetration. Clinical attachment level at each site was calculated from probing depth measurements and the measurements of the location of the free gingival margin relative to the cemento-enamel junction (Ramfjord 1959). In addition, the presence of gingival bleeding was observed for 10s after removing the probe from the sulcus/pocket, following the probing depth procedure.

The examiner had access to the study participants' medical records only after this stage of periodontal examination, to check the records regarding the stated diagnosis for the respiratory system condition.

Diagnosis of periodontal disease

The diagnosis of periodontal disease was established on the clinical examination, and the classification criteria for periodontal disease established by Gomes-Filho et al. (2007) were used. In other words, individuals were deemed to have periodontitis if they presented with at least four teeth with one or more sites showing a probing depth ≥ 4 mm, attachment loss ≥ 3 mm and bleeding on probing at the same site (Gomes-Filho et al. 2007).

Diagnosis of nosocomial respiratory tract infection

The definition of cases and controls was done according to whether there was a diagnosis of nosocomial LRTI in the medical records of the individuals selected for this study, in accordance with the reports issued by the medical team at HGCA. The diagnosis of nosocomial LRTI was made if, within 48 h of initial hospitalization, clinical examination revealed the presence of a dull sound on percussion or crackling rales or chest radiographic evidence of new or progressive infiltration, consolidation, cavitation or pleural effusion. In addition, one of the following was required to make a diagnosis of LRTI, when necessary: (a) appearance of purulent sputum or changes in the sputum characteristics that existed at the time of hospitalization; microorganism (Pseudomonas aeruginosa, Pseudomonas sp., Klebsiella sp., E. coli, Acinetobacter baumannii, Staphylococcus aureus, Streptococcus pneumoniae, Citobacter freundi, Klebsielle pneumoniae and Citobacter amalonaticus) (b) isolated from blood culture; (c) isolated from bronchoalveolar lavage; and (d) histological evidence of pneumonia from bronchial lavage (Medeiros 1999).

Individuals were diagnosed as having suspected bronchoaspiration if lowered consciousness was accompanied by a decreased reflex cough response to respiration and swallowing (with consequent use of mechanical ventilation).

Data analysis

Following the data collection, descriptive analysis was performed on the independent variable (periodontal disease), dependent variable (nosocomial LRTI) and all the covariables considered to be of interest, as cited earlier for characterizing the individuals in the sample. For the categorical variables, simple frequencies were obtained and statistical differences were evaluated by means of the χ^2 and Fisher tests, with the significance level set at 5%. The cutoff points for categorizing the covariables were established by examining the distributions and using the mean values. In the case of continuous periodontal variables, the Mann-Whitney U-test was used to make comparisons between the groups.

Next, stratified analysis was performed to identify possible effect modifiers and confounding factors among the covariables investigated, and the crude association measurement between periodontal disease and nosocomial LRTI was obtained. For identifying potential effect modifiers, the means of the specific strata were observed in relation to

the CIs for the opposing strata and the Breslow-Day homogeneity test was applied ($\alpha = 20\%$). For the confounders, the simultaneous association between the disease (nosocomial LRTI) in the unexposed individuals (without periodontal disease) and the exposure (periodontitis) in individuals without disease (without nosocomial LRTI) was observed. For this, the statistical significance was assessed with $p \leq 0.05$ and a CI of 95%. In addition, at this stage, the criterion that variables were considered to be possible confounders if they caused a proportional difference between the crude and adjusted association measurements of at least 10% was used.

Taking into account various confounding variables, the unconditional logistic regression was used to describe the association of nosocomial LRTI as a function of the various explanatory variables.

In the logistic regression, the presence of effect-modifying covariables was investigated using the likelihood ratio test, with the significance level set at 5%. The backward strategy was used, in non-conditional-type logistic regression analysis. Theoretical and empirical bases were considered in selecting potential confounding variables, which were taken to be the factors that would produce an alteration of at least 10% in the association measurement. Thus, comparative observations of association measurements [odds ratios (OR)] and their respective CIs were made. To make statistical inferences, a 95% CI was used.

After defining the final model, its goodness of fit was determined using the Hosmer–Lemeshow test and the Akaike information criterion (AIC), and its discriminating strength was determined by means of calculating the area under the ROC curve.

The data analysis was performed using statistical software programs SPSS, version 10 (SPSS Inc., Chicago, IL, USA), Epi-Info, version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA), R, version 2.3.1, (Bell Laboratories, Vienna, Austria).

Results

Descriptive analysis

The general characteristics of the case and control groups, relating to sociodemographic characteristics, medical history during hospitalization and preexisting systemic diseases, are presented in Table 1. Most of the results presented, for example medical data from evaluations of heart diseases, kidney diseases, allergies, etc., did not demonstrate any statistically significant differences, except for three covariables that were strongly associated with LRTI: type of ventilation, type of invasive ventilation and suspected bronchoaspiration. The invasive type of ventilation was much more frequent in the case group (95.5%) than in the control group (7.4%). Among the types of invasive ventilation, an orotracheal tube was used in around 81.8% and 7.4% of the cases and controls, respectively. Further-

| Table 1. | General | characteristics | of the | study | population |
|----------|---------|-----------------|--------|-------|------------|
|----------|---------|-----------------|--------|-------|------------|

| Characteristics | Cases | Controls | <i>p</i> * |
|----------------------|------------|------------|------------|
| | N = 22 | N = 81 | |
| | [N (%)] | [N (%)] | |
| Age | | | |
| ≤35 years | 14 (63.6%) | 44 (54.3%) | |
| >35 years | 8 (36.4%) | 37 (45.7%) | 0.44 |
| Sex | | | |
| Female | 8 (36.4%) | 34 (42.0%) | |
| Male | 14 (63.6%) | 47 (58.0%) | 0.63 |
| Race (self-reported) | | | |
| White | 3 (13.6%) | 15 (18.5%) | |
| Black | 19 (86.4%) | 66 (81.5%) | 0.76 |
| Conjugal situation | | | |
| Married/stable union | 13 (59.1%) | 36 (44.4%) | |
| Single/divorced/ | 9 (40.9%) | 45 (55.6%) | 0.22 |
| separated/widowed | | | |
| Education | | | |
| >4 years | 16 (72.7%) | 46 (56.8%) | |
| ≤4 years | 6 (27.3%) | 35 (43.2%) | 0.17 |
| Place of residence | | | |
| Feira de Santana | 17 (77.3%) | 45 (55.6%) | |
| Other cities | 5 (22.7%) | 36 (44.4%) | 0.06 |

Table 1. (Contd.)

| Characteristics | Cases | Controls | p^* |
|---|------------------------|-------------|-------|
| | N = 22 | N = 81 | |
| | [N (%)] | [N (%)] | |
| Family income (in MMS - | minimum monthly salari | es) | |
| $\leq 1 \text{ MMS}$ | 18 (81.8%) | 64 (79.0%) | |
| >1 MMS | 4 (18.2%) | 17 (21.0%) | 1.00 |
| Present occupation | | | |
| Employed | 8 (36.4%) | 25 (30.9%) | |
| Unemployed | 14 (63.6%) | 56 (69.1%) | 0.62 |
| Hypertension | | | |
| Yes | 6 (27.3%) | 21 (25.9%) | |
| No | 16 (72.7%) | 60 (74.1%) | 0.90 |
| Diabetes | × , | | |
| Yes | 5 (22.7%) | 8 (9.9%) | |
| No | 17 (77.3%) | 73 (90.1%) | 0.14 |
| Allergy to drugs | | | |
| Yes | 3 (13.6%) | 12 (14.8%) | |
| No | 19 (86.4%) | 69 (85.2%) | 1.00 |
| Cardionathy | 19 (00.170) | 0) (03.270) | 1.00 |
| Ves | 0 (0) | 10 (12 3%) | |
| No | 22(100%) | 71(87.7%) | 0.11 |
| Asthma | 22 (100 %) | /1 (07.770) | 0.11 |
| Astillia Vos | 1 (4 50%) | 2(2.70/) | |
| I CS | 1(4.5%) | 3(3.7%) | 1.00 |
| INO Liver diseases | 21 (93.3%) | 78 (90.5%) | 1.00 |
| Liver diseases | 1(4.507) | 1(1.207) | |
| I es | 1(4.5%) | 1(1.2%) | 0.29 |
| INO IV: 1 I: | 21 (95.5%) | 80 (98.8%) | 0.58 |
| Kidney diseases | 5 (00 70) | | |
| Yes | 5 (22.7%) | 6 (7.4%) | 0.05 |
| No | 17 (77.3%) | 75 (92.6%) | 0.05 |
| Bone diseases | | | |
| Yes | 0 (0) | 11 (13.6%) | |
| No | 22 (100%) | 70 (86.4%) | 0.11 |
| Blood abnormalities | | | |
| Yes | 0 (0) | 4 (4.9%) | |
| No | 22 (100%) | 77 (95.1%) | 0.57 |
| Neoplasia | | | |
| Yes | 0 (0) | 4 (4.9%) | |
| No | 22 (100%) | 77 (95.1%) | 0.57 |
| Time between hospitalization | on and data collection | | |
| ≤5 days | 12 (54.5%) | 60 (74.1%) | |
| >5 days | 10 (45.5%) | 21 (25.9%) | 0.07 |
| Type of ventilation | | | |
| Non-invasive | 1 (4.5%) | 75 (92.6%) | |
| Invasive | 21 (95.5%) | 6 (7.4%) | 0.00* |
| Type of invasive ventilation | n | | |
| Not applicable | 1 (4.5%) | 75 (92.6%) | |
| Orotracheal tube | 18 (81.8%) | 6 (7.4%) | |
| Tracheostomy | 3 (13.7%) | 0 (0) | 0.00* |
| Suspected bronchoaspiration | n | ~ (~) | |
| Yes | 18 (81.8%) | 5(6.2%) | |
| No | 4 (18.2%) | 76 (93.8%) | 0.00* |
| | . (10.270) | | 0.00 |

the clinical examination *versus* 37% of the control group. The individuals in the case group reported that periodontitis, together with caries, was the main cause of 63.6% of the tooth losses that had occurred. On the other hand, in the control group, such findings accounted for around 86.4% of the losses.

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The distribution of the variables relating to periodontal condition is presented in Table 3. There was no statistically significant difference in any of the clinical periodontal parameters evaluated between the case and the control groups.

Logistic regression analysis

The principal association measurements are presented in Table 4. The crude OR value for individuals with periodontitis having LRTI was not statistically significant [OR_{crude} = 1.70; 95% CI: (0.60– 4.87)]. After including age, smoking and duration of hospitalization in the logistic regression, the adjusted OR reached statistical significance [OR_{adjusted} 3.67 (1.01–13.53); p = 0.049].

After obtaining the final model, the goodness-of-fit test (Hosmer–Lemeshow) was applied. It was seen that the model presented a good fit (p = 0.81).

Discussion

According to the findings from this study, and in the light of the particular limitations within the nature of this type of investigation, a possible association between periodontal disease and LRTI acquired while hospitalized was marginally statistically significant only when smoking, age and duration of hospitalization were included in the logistic regression model. From an epidemiological point of view, the association measurements obtained need to be treated with caution, considering the limits imposed by the structure of the study design.

The literature on this topic still presents controversies and, in the light of the complex aetiologies of both periodontal disease and nosocomial LRTI, some authors (Pineda et al. 2006, Page 2001) have regarded the biological mechanism linking these two events with scepticism, without finding any association between them. Nevertheless, other studies (Beck et al. 1996, Gomes 2001, Grap et al. 2003, Almeida et al. 2006, Bágyi et al. 2006, Masaki et al. 2006) have been conducted and have presented a statistically significant asso-

Clériston Andrade General Hospital, Feira de Santana, Bahia, Brazil, 2007 (n = 103).

**p*-value. Statistical significance: $p \leq 0.05$.

more, bronchoaspiration was suspected in 6.2% of the individuals in the control group, while in the case group the frequency of this suspicion was 81.8%. The mean age among the study participants was 35.1 years, with a median of 32 years, range from 13 to 78 years, and prevalence of individuals aged 35 years or under.

With regard to characteristics relating to oral condition and lifestyle in the case and control groups (Table 2), no statistically significant difference between the covariables investigated was seen, thus demonstrating homogeneity between the groups. Out of the total number of individuals investigated, 50% of the case group presented periodontitis in

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Table 2. Oral condition and lifestyle characteristics of the study population

| Cases | Controls | p^* |
|------------|--|---|
| N = 22 | N = 81 | |
| [N (%)] | [N (%)] | |
| | | |
| 1 (4.5%) | 12 (14.8%) | |
| 21 (95.5%) | 69 (85.2%) | 0.28 |
| | | |
| 9 (40.9%) | 35 (43.2%) | |
| 13 (59.1%) | 46 (56.8%) | 0.85 |
| | | |
| 7 (31.8%) | 32 (39.5%) | |
| 15 (68.2%) | 49 (60.5%) | 0.51 |
| . , | . , | |
| 11 (50%) | 30 (37.0%) | |
| 11 (50%) | 51 (63.0%) | 0.27 |
| | | |
| 8 (36.4%) | 16 (19.8%) | |
| 14 (63.6%) | 65 (80.2%) | 0.10 |
| . , | . , | |
| 6 (27.3%) | 25 (30.9%) | |
| 16 (72.7%) | 56 (69.1%) | 0.74 |
| | | |
| 3 (13.6%) | 6 (7.4%) | |
| 19 (86.4%) | 75 (92.6%) | 0.40 |
| | | |
| 9(40.9%) | 35 (43.2%) | |
| 13 (59.1%) | 46 (56.8%) | 0.84 |
| × / | · · · · · | |
| 11 (50%) | 49 (60.5%) | |
| 11 (50%) | 32 (39.5%) | 0.40 |
| | | |
| 16 (72.7%) | 66 (81.5%) | |
| 6 (27.3%) | 15 (18.5%) | 0.38 |
| - () | - () | |
| 14 (63.6%) | 57 (86.4%) | |
| 2 (9.1%) | 9 (13.6%) | 1.00 |
| | Cases N = 22 [N (%)] 1 (4.5%) 21 (95.5%) 9 (40.9%) 13 (59.1%) 7 (31.8%) 15 (68.2%) 11 (50%) 11 (50%) 8 (36.4%) 14 (63.6%) 9 (40.9%) 13 (59.1%) 11 (50%) 11 | Cases N = 22 Controls N = 81 [N (%)] N = 81 [N (%)] 1 (4.5%) 12 (14.8%) 21 (95.5%) 69 (85.2%) 9 (40.9%) 35 (43.2%) 13 (59.1%) 46 (56.8%) 7 (31.8%) 32 (39.5%) 15 (68.2%) 49 (60.5%) 11 (50%) 30 (37.0%) 11 (50%) 51 (63.0%) 8 (36.4%) 16 (19.8%) 14 (63.6%) 65 (80.2%) 6 (27.3%) 25 (30.9%) 16 (72.7%) 56 (69.1%) 3 (13.6%) 6 (7.4%) 19 (86.4%) 75 (92.6%) 9(40.9%) 35 (43.2%) 13 (59.1%) 46 (56.8%) 11 (50%) 32 (39.5%) 16 (72.7%) 66 (81.5%) 11 (50%) 32 (39.5%) 16 (72.7%) 66 (81.5%) 11 (50%) 15 (18.5%) 14 (63.6%) 57 (86.4%) 2 (9.1%) 9 (13.6%) |

Clériston Andrade General Hospital, Feira de Santana, Bahia, Brazil, 2007 (n = 103). *p-value. Statistical significance: $p \le 0.05$.

[†]Excluding 22 individuals who reported that they had not lost any teeth.

Table 3. Distribution of periodontal condition variables among case group (presence of LRTI) and control group (absence of LRTI)

| Characteristics | Cases | Controls | p^* |
|------------------|---------------|---------------|-------|
| | N = 22 | N = 81 | Ĩ |
| Bleeding on pro | obing index | (%) | |
| Median | 6.0 | 12 | |
| Mean \pm SD | 10.8 ± 9.9 | 18.2 ± 18.3 | |
| Range | 0 to 28 | 0 to 98 | 0.14 |
| Probing depth (| (mm) | | |
| Median | 3.3 | 2.7 | |
| Mean \pm SD | 3.4 ± 1.4 | 3.0 ± 1.1 | |
| Range | 1.8 to 7.2 | 1.2 to 5.4 | 0.46 |
| Clinical attachr | nent loss (m | m) | |
| Median | 3.1 | 2.5 | |
| Mean+SD | 3.6 ± 1.7 | 3.1 ± 1.3 | |
| Range | 1.8 to 7.8 | 1.2 to 6.0 | 0.31 |

Feira de Santana, Bahia, Brazil, 2007 (n = 103). *p-value. Statistical significance: $p \le 0.05$. LRTI, lower respiratory tract infection; SD, standard deviation. *Table 4.* Association measurements between nosocomial lower respiratory tract infection (LRTI) and periodontal disease

| LRTI | Unadjusted OR (95% CI) | Adjusted OR* (95% CI) |
|---------|---------------------------|--------------------------|
| Overall | 1.70 (0.60-4.87) | 3.67 (1.01–13.53) |

Feira de Santana, Bahia, Brazil, 2007. *Adjusted for duration of hospitalization, age and smoking.

CI, confidence interval; OR, odds ratio.

ciation between these two diseases. Thus, in the current study, the difference between the case and the control groups with bronchoaspiration is the most interesting finding and may be a possible explanation for the present and other previous studies that show a significant association. It would therefore be interesting to see whether oral organisms could be found in alveolar lavage either by culturing or, better, by real-time PCR, but this was not the aim of the present study.

It is important to emphasize that this study was preliminary and, although the initial findings showed a marginally statistically significant association between periodontitis and LRTI when age, smoking and duration of hospitalization were included in the logistic regression model, the study had low power. Based on the results of this study a sample size of 120 cases and 240 controls would be required to obtain 90% power with a CI of 95%.

It should be noted that due to the retrospective case–control design of this study, the diagnosis of periodontal disease was made within seven days after diagnosing the lung infection. Prospective designs would be more appropriate for future studies to determine whether a temporal relationship exists between the presence of periodontal disease and subsequent development of LRTI. Moreover, the use of radiographs to establish a diagnosis of periodontitis would be helpful (Kinane, 2001), but this was not possible in this preliminary study (Kinane 2001).

In view of this limitation, the criteria proposed by Gomes-Filho et al. (2005) were adopted with the aim of ensuring greater methodological rigour in diagnosing periodontitis. Moreover, these criteria have been compared with others (Gomes-Filho et al. 2007) that have commonly been used in studies in the literature on periodontal medicine, and have been shown to be very specific for diagnosing periodontal disease, independent of complementary radiographic examinations, for investigations in which it was not possible to use radiography as a routine examination. Measurements of probing depth, attachment loss and bleeding on probing were made at the same sites for all the teeth present, with six measurements per tooth. However, for operational reasons, it was not possible to obtain data for evaluating the plaque index, which has been considered important in some studies (Scannapieco 1999, Mojon 2002). Within this topic, no studies in which complete periodontal examinations were performed on individuals with nosocomial LRTI were found. Furthermore, it is emphasized that none of these measurements of periodontal condition showed a statistically significant difference between the case and the control groups, probably because of the sample size. On the other hand, descriptively, there was a higher

frequency of worse conditions in the case group than in the control group, for example with regard to probing depth and clinical attachment level. Moreover, these were the criteria that defined the presence of periodontitis (dichotomous variable), according to Gomes-Filho et al. (2007) in the subitem of periodontal disease diagnosis.

In describing the oral conditions of the individuals analysed, it was found that the main causes of self-reported tooth loss were periodontitis and/or caries, in both the case and the control group. However, it needs to be stated that tooth loss is not a reliable predictor for periodontitis, considering that it is known that these losses may have been influenced by other nonperiodontal causes, such as caries, trauma, etc.

With regard to measurement of the effect (nosocomial LRTI), it is important to make some points concerning the procedures used for diagnosing this infection at Clériston Andrade General Hospital (HGCA), given that they have their own form of clinical definition. In the ICU, individuals are radiographed every day (posteroanterior chest radiography) and the images are evaluated jointly by the doctors and physiotherapists who are on duty in the ICU every day and directly caring for these patients. On these radiographs, lung transparency, anatomical components and the area of the heart are assessed. If there are any zones on the images that are suggestive of abnormalities, diagnostic hypotheses are raised until the pathology of the case has been determined.

Likewise, clinical symptoms are assessed every day using descriptors such as chest expansibility, ventilation patterns, pulmonary auscultation, fever, oxygen saturation, cough reflexes and presence and quality of secretions. Microbiological examinations of tracheal secretions, pulmonary infiltrate and secretions expelled are sometimes performed. In fact, the term LRTI is adopted to speak in general terms about the bronchopulmonary pathological conditions that are encountered during patient evolution, in medical bulletins. Nonetheless, the specific pathological condition affecting each individual, such as aspiration pneumonia or atelectasis, is defined in that patient's medical file. Aspiration pneumonia consists of pneumonia acquired following bronchoaspiration of the oropharyngeal substrates, while atelectasis is a clinical condition with a physiopathological presentation of collapsed areas in the lungs (Azeredo 2002).

Based on this preliminary study, it is suggested that future studies should (1) have sufficient sample size to achieve adequate statistical power, (2) have a prospective design and (3) be carefully controlled for factors such as age, smoking history, length of hospitalization and bronchoaspiration, which may be prominent risk factors, confounders or effect modifiers in the possible association between periodontal disease and LRTI.

Several studies (Scannapieco 2003, Bopp et al. 2006, Senol et al. 2007, Siempos & Falagas 2007) have cited deficiencies in oral hygiene as a predictive factor for aspiration pneumonia, which in fact is one of the possible clinical manifestations of LRTI. The stimulus given towards implementing programmes that emphasize the importance of oral care within the hospital environment, for controlling medical factors that have already been recognized through research, has not been proportional to the public health interest in reducing the mortality rates due to respiratory infections. The findings from the present study therefore emphasize the preventive importance of instituting oral care protocols among bedridden individuals (Limeback 1998, Terpenning et al. 2001, Ferozali et al. 2007, Siempos & Falagas 2007) whether they are institutionalized in clinics for elderly people or for individuals with neurological disorders, or whether they are hospitalized.

Also with regard to the criteria for identifying possible characteristics that might have influenced the final result for the association measurement in the present pilot study, the covariables of age, smoking habit and duration of hospitalization were retained in the model while conducting the logistic regression analysis because they were identified as possible confounding factors. It was also decided to make adjustments only for the abovementioned covariables, given that the type of invasive ventilation presented collinearity with these covariables and could have interfered with the final findings. Although the variable of type of ventilation was seen to be one of the major risk factors for LRTI from the univariate analysis of this study, thus corroborating the findings in the medical literature (Craven et al. 1986, Kollef 2004), it was not retained in the model after logistic regression analysis, even

after confirmation of confounding factors, for the following reasons: (1) its categories were seen to be unbalanced between cases and controls because of the relatively small sample size of the study and (2) Its CI measurements were extremely wide [OR = 262.5; 95% CI:(29.92-2308.52)], thus indicating imprecision. The same can be said in relation to variable of bronchoaspiration: the although this too presented an association with LRTI in the univariate analysis [OR = 68.40; 95% CI: (16.67-280.61)],the logistic regression analysis did not confirm it as a confounding factor for LRTI. Nonetheless, its relevance to the discussion of this topic is recognized. In summary, in view of the small sample size and an imbalance between cases and controls regarding these important confounding factors for LRTI, the final adjusted model only included the three variables mentioned earlier as associated factors, in order to avoid overcontrol by the remaining variables.

Finally, this study contributes towards ratifying the need for additional research on this topic, given that these two diseases are recognized as serious public health problems. This study increases the body of evidence regarding the influence of oral health on systemic conditions. For future studies, the possibility of using bacteriological correlations for greater confidence in the results should be considered, because periodontal disease and systemic diseases may also occur simultaneously without a causal relationship between them (Slots 1998).

Conclusions

A marginally statistically significant association between periodontitis and nosocomial LRTI was found in the current study only when age, smoking and length of hospitalization were included in the statistical model. Patients with LRTI had a high frequency of bronchoaspiration and this could explain the possible association of periodontal disease and LRTI found in this and other studies. Additional studies are needed to further clarify the possible relationship between periodontal disease and LRTI: these studies should be prospective in design, have an appropriate sample size, account for confounding factors and effect modifiers and include microbial assessment.

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Clinical Relevance

Scientific rationale for the study: To study the possible association between periodontitis and nosocomial LRTI.

Principal findings: A marginal association between periodontitis and LRTI was found when smoking, age and length of hospitalization were included in the analysis; bronchoaspiration could explain the possible association of periodontal disease and LRTI.

Practical implications: Additional studies are needed to further clarify the possible relationship between

periodontal disease and LRTI; these studies should be prospective in design, have appropriate sample size, account for confounding factors and effect modifiers, and include microbial assessment. This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.