

Original Article

Relationship between menopause and periodontal disease: a cross-sectional study in a Portuguese population

Ricardo C Alves¹, Sérgio A Félix¹, Alberto Rodriguez-Archilla², Pedro Oliveira¹, José Brito¹, José Martins dos Santos¹

¹Center for Interdisciplinary Research Egas Moniz (CiiEM), Health Sciences Institute, Monte da Caparica, Portugal;

²School of Dentistry, University of Granada, Spain

Received May 16, 2015; Accepted July 6, 2015; Epub July 15, 2015; Published July 30, 2015

Abstract: Background: Menopause is associated with important systemic and oral changes. Many researchers have tried to evaluate the influence of hormonal changes associated with menopause in the periodontium, however results are contradictory. Objective: Evaluate the possible effects of menopause on the severity of periodontal disease and tooth loss, by considering several general, oral and periodontal parameters. Methods: 102 women with chronic periodontitis, and at least six teeth, were divided into two groups: a study group (SG) consisting of 68 menopausal women and a control group (CG) consisting of 34 premenopausal women. The participants had extensive anamnesis, made by a single senior periodontologist, which collected demographic data, medical and gynaecological history and habits. Additionally, oral and periodontal parameters including: number of teeth, plaque index, presence of calculi, probing depth, bleeding on probing, gingival recession and attachment loss were recorded. The following statistical tests were used: Chi-square, Fisher's t-test for independent samples, non-parametric Wilcoxon-Mann-Whitney, and linear multiple regression. Results: The number of teeth was significantly lower in postmenopausal women (SG 10.8 ± 5.9 , CG 6.8 ± 4.6), however, after adjusting for age, smoking and plaque index, the difference was no longer statistically significant ($P=0.169$). The attachment loss was slightly higher in the study group, although the difference is not significant (SG 4.31 ± 1.08 , CG 4.05 ± 1.28). Conclusions: Menopause does not appear to significantly influence the severity of periodontal disease and tooth loss. Other factors may exert a greater influence on the progression of periodontal disease rather than menopause itself.

Keywords: Periodontal disease, menopause, osteoporosis, oestrogen

Introduction

Menopause period is increasing and is associated with important systemic and oral manifestations [1, 2]. During menopause, gingival epithelium becomes thinner, atrophic and more prone to inflammatory changes [3], on the other hand, salivary flow rate decreases and salivary composition may be altered, contributing to the development of several oral conditions [4].

The sudden decrease in oestrogen production that occurs in menopause is considered to be the main cause of primary osteoporosis, which also affects jawbones [5, 6]. It has been suggested that this reduction in bone mineral density could contribute to periodontal disease progression [7].

Besides their effect on bone, estrogens also interfere with other periodontal tissues (gingiva and periodontal ligament) and influence host immune-inflammatory responses [8-10]. A number of studies have linked menopause with some periodontal conditions, although the different methods applied to define and assess osteoporosis, alveolar bone loss and periodontitis make it difficult to compare the results [11].

Several studies reported an improvement of the periodontal parameters [12], and tooth retention [13-15] in women undergoing hormone replacement therapy (HRT), however, contradicting results have been published [16, 17]. Furthermore, drugs that alter bone metabolism, such as estrogen and bisphosphonates, were suggested by several case-control studies as a

new approach to the treatment of periodontitis in postmenopausal patients [18].

The aim of this study was to evaluate the possible effects of menopause on the severity of periodontal disease and tooth loss, by considering several general, oral and periodontal parameters, in two groups of women with periodontitis (pre and postmenopausal).

Patients and methods

Study design

This cross-sectional study was conducted at the University Clinic of the Egas Moniz Health Sciences Institute (Almada, Portugal). Approval from this institution's ethics committee was obtained.

Women aged 35-80 years were selected, with at least 6 teeth present, diagnosis of chronic periodontitis and absence of periodontal treatments in the last year. The following patients were excluded: women with diagnosis of aggressive periodontitis; women who refused to sign the informed consent form; women who were participating in other studies.

Of the 111 patients initially screened, 8 did not meet the inclusion criteria and 1 refused to participate, resulting in a final sample of 102 participants, who were divided according to menopausal status in two groups: a study group, consisting of 68 postmenopausal women and a control group, consisting of 34 premenopausal women.

Women were considered in menopause, when they had absence of menstruation for more than 12 months, or had undergone a hysterectomy with bilateral oophorectomy [19].

Concerning Periodontal Disease we used the criteria set by the working group of the Centres for Disease Control and Prevention (CDC) [20].

Study protocol

All participants had extensive anamnesis done by a single senior periodontologist, covering: demographics, medical history, current medication, lifestyle habits (alcohol consumption, smoking, and exercise), dental history and oral hygiene habits. Additionally, gynaecological history was collected in order to determine the

level of hormone exposure (age at menarche, number of pregnancies, number of births, age at menopause and use of oral contraceptives or hormone replacement therapy for more than 6 months).

Oral and periodontal examination

A single senior periodontologist, blinded to the groups, conducted all measurements. Before the study, this examiner was evaluated by another experienced clinician, according to the method proposed by Altman & Bland [21]. A high level of agreement for measurements of probing depth and gingival recession was found (concordance in 90%; difference ≤ 1 mm). The screening was performed on 10 volunteer patients, 15 days before the beginning of the study.

Concerning oral evaluation, World Health Organization, decayed, missing and filled teeth index (DMFT) [22] was calculated. Additionally, the presence of fixed or removable prostheses was also recorded.

Periodontal evaluation considered all completely erupted teeth, excluding third molars, retained roots and implants. The examination began by assessing the presence of supragingival calculus (absent/present) and determination of plaque index (Simplified Plaque Index) [23].

The probing depth (PD) and gingival recession (REC) were evaluated at six sites per tooth using a CP-12 graduated periodontal probe (Hu-Friedy®, Chicago, IL, USA). Simultaneously, locations with bleeding on probing after 10 seconds (BOP) were recorded. Clinical attachment level (CAL) was calculated by adding PD to REC. In addition, furcation defects were evaluated in molars and mobility was evaluated in all teeth.

Statistical analysis

Prior to analysis, all data were screened for accuracy and completeness. Data were entered into a Microsoft Office Excel 2003® (Microsoft, Seattle, USA) database. The Statistical Package for Social Sciences 17 (SPSS, Chicago, USA) was used for the statistical analysis.

Analyses were performed on a subject basis. Descriptive statistics for all variables were conducted, including: means, standard deviations, ranges and percentages.

Menopause and periodontal disease

Table 1. General characteristics of the study population (n=102)

	Study group (n=68)	Control group (n=34)	P-value
	Average (SD) or n (%)		
Age	61.2 (8.1)	44.8 (5.2)	<i>t</i> (92.9)=12.37; <i>P</i> < 0.001
Education level			χ^2 (1)=13.45; <i>P</i> < 0.001
Elementary	51 (75.0%)	13 (38.2%)	
Secondary	9 (13.2%)	13 (38.2%)	
Higher	8 (11.8%)	8 (23.5%)	
Race			<i>F</i> <i>ns</i>
Caucasian	63 (92.6%)	31 (91.2%)	
Black	5 (7.4%)	3 (8.8%)	
BMI	27.8 (5.4)	26.2 (4.9)	<i>U</i> =954.0; <i>W</i> =1549.0; <i>ns</i>
Tobacco consumption			χ^2 (1)=10.88; <i>P</i> < 0.01
Never	49 (72.1%)	13 (38.2%)	
Smokers or former smokers	19 (27.9%)	21 (61.8%)	
Alcohol consumption			χ^2 (1)=0.12; <i>ns</i>
Never	14 (20.6%)	8 (23.5%)	
Current or previous	54 (79.4%)	26 (76.5%)	
At least one dental visit in the last year	16 (23.5%)	12 (35.3%)	χ^2 (1)=1.58; <i>ns</i>

BMI–Body mass index; *F*–Fisher test; *ns*–not significant; *t*–unpaired *t*-test; *U*, *W*–non-parametric *Wilcoxon-Mann-Whitney* test; χ^2 –Chi-square test.

Table 2. Hormonal history

	Study group (n=68)	Control group (n=34)	P-value
	average (SD) or n (%)		
Age of menarche	12.8 ± 1.6	12.34 ± 1.70	<i>U</i> =858.0; <i>W</i> =1386.0; <i>ns</i>
Age of menopause	49.3 ± 5.6	----	----
No. of pregnancies	2.7 ± 1.8	2.4 ± 2.4	<i>U</i> =979.5; <i>W</i> =1574.5; <i>ns</i>
No. of births	1.8 ± 1.2	1.7 ± 1.1	<i>U</i> =1133.5; <i>W</i> =1728.5; <i>ns</i>
Years of oral contraceptive use	9.3 ± 10.2	10.6 ± 11.0	<i>U</i> =927.5; <i>W</i> =3205.5; <i>ns</i>
Reproductive years	36.7 ± 5.8	33.2 ± 5.8	<i>t</i> (99)=2.85; <i>P</i> < 0.01
Years of estrogen exposure	37.8 ± 6.0	9.0 ± 10.8	<i>U</i> =28.5; <i>W</i> =623.5; <i>P</i> < 0.001
Type of menopause		----	----
Physiological	57 (83.8%)		
Surgical	11 (16.2%)		
HRT users	18 (26.5%)	----	----
Years of HRT use	1.8±2.9	----	----

ns–not significant; *t*–unpaired *t*-test; *U*, *W*–non-parametric *Wilcoxon-Mann-Whitney* test.

For qualitative variables (nominal and ordinal), Chi-square test and Fisher's exact test were used. For quantitative variables (discrete or continuous) nonparametric *Wilcoxon-Mann-Whitney* and *t* test for independent samples were used. For some variables, linear multiple regression analysis were performed in order to control the effect of possible confounding factors.

A significance level of $\alpha=0.05$ was set for all tests (*P* < 0.05).

Results

The general characteristics of the study population are summarized in **Table 1**. The majority of the women are Caucasian (92.2%), overweight or obese (SG 70.6%, CG 52.9%; no significant differences in body mass index between groups) and, as expected, the average age in the study group is higher than in the control group (61.2 ± 8.0 vs. 44.8 ± 5.2). Smokers and former smokers in the control group are almost twice than in the study group (SG 27.9%, CG

Menopause and periodontal disease

Table 3. Oral measurements and dental hygiene routines

	Study group	Control group	<i>P</i> -value
	(n=68)	(n=34)	
	Average (SD) or n (%)		
DMFT index	17.8 (6.9)	16.7 (5.5)	<i>t</i> (100)=0.86; <i>F ns</i>
Last dental visit			<i>F ns</i>
≤ 1 year	16 (23.5%)	12 (35.3%)	
> 1 year	52 (76.5%)	22 (64.7%)	
Previous periodontal treatment			
None	43 (63.2%)	21 (61.8%)	<i>F ns</i>
Dental prophylaxis	19 (27.9%)	12 (35.3%)	<i>F ns</i>
Scaling and root planing	-----	-----	-
Periodontal surgery	1 (1.5%)	-----	<i>F ns</i>
Other	18 (26.5%)	4 (11.8%)	<i>F ns</i>
Brushing			<i>F ns</i>
Once per day	14 (20.6%)	7 (20.6%)	
More than once per day	54 (79.4%)	27 (79.4%)	
Flossing			<i>F ns</i>
Never/occasionally	61 (89.7%)	26 (76.5%)	
One or more times per day	7 (10.3%)	8 (23.5%)	
Mouthwash use			<i>F ns</i>
Never/occasionally	38 (55.9%)	15 (44.1%)	
One or more times per day	30 (44.1%)	19 (55.9%)	

DMF-Decayed Missing Filled index; *F*-Fisher test; *ns*-not significant; *t*-unpaired *t*-test; χ^2 -Chi-square test.

61.8%) and the number of packs/year is significantly higher in the same group (SG 3.0 ± 8.3 , CG 7.5 ± 10.7 , $P < 0.001$). However, if we consider non-smokers and former smokers together the difference is less pronounced (SG 89.7%, CG 61.75%).

Concerning hormonal history (**Table 2**), the age of menarche is similar in both groups (SG 12.8, CG 12.3 years), and the mean age at menopause was 49.3 ± 5.6 years. On average, women were in menopause for 11.8 years (SD 9.4 yrs), and in 83.8% of cases menopause occurred naturally. Regarding pregnancies, births, and use of oral contraceptives no significant differences were observed, although women in the study group used (on average) oral contraceptives for fewer years.

Regarding oral hygiene habits, frequency of dental visits and type of previous periodontal treatments, no differences were observed between groups (**Table 3**).

In the study group the most commonly used drugs to treat/prevent osteoporosis were: bis-

phosphonates (11.7%), followed by HRT (4.4%). If we consider the previous use of HRT, the percentage increases to 26.5%. Only 4 women (5.9%) used calcium supplements and none took vitamin D.

Postmenopausal women had fewer teeth than the premenopausal women ($P < 0.01$), but the reason for teeth loss was similar in both groups (**Table 4**). The major reason for tooth loss was the extraction in consequence of tooth decay (SG 48.5%, CG 58.8%). The number of teeth lost for periodontal reasons was slightly higher in the study group, although the difference is not significant (SG 14.7%, CG 5.95%).

In relation to periodontal parameters (**Table 5**), the amount of bacterial plaque is greater in the control group ($P < 0.01$), whereas the number of sextants with calculus is similar in both groups.

Gingival recession is slightly higher in the study group (SG 1.06 ± 0.81 ; CG 0.78 ± 0.70) and also attachment loss (SG 4.31 ± 1.08 , CG 4.05 ± 1.28), although the difference is not significant.

Concerning the other periodontal parameters there are no differences between groups, except for a higher percentage of sites with PD > 4 mm, in the control group ($P < 0.05$).

Discussion

The mechanisms that could explain the relationship between periodontal disease and menopause are not fully understood. Some studies have shown a relationship between decreased bone mineral density and tooth loss [24-26] and/or deterioration of certain periodontal parameters [13, 24, 26], while others have failed to demonstrate such relationship [27, 28].

Menopause and periodontal disease

Table 4. Comparison of the number of teeth in premenopausal and postmenopausal women

	Study group (n=68)	Control group (n=34)	P-value
Subjects with missing teeth n (%)	66 (97.1%)	34 (100%)	F ns
No. of missing teeth (average ± SD)	10.8 ± 5.9	6.8 ± 4.7	U=710.5; W=1035.5; P < 0.01
Reason for loss n (%)			
Periodontal	10 (14.7%)	2 (5.9%)	F ns
Decay	33 (48.5%)	20 (58.8%)	F ns
Fracture	3 (4.4%)	10 (29.0%)	F ns
Other	21 (30.9%)	10 (30.9%)	F ns
Unknown	1 (1.5%)	1 (2.9%)	F ns

F-Fisher test; ns-not significant; U, W-non-parametric Wilcoxon-Mann-Whitney test.

Table 5. Distribution of periodontal variables in pre and postmenopausal women

	Study group (average ± SD)	Control group (average ± SD)	P-value
Plaque index	40.08 ± 20.24	51.41 ± 20.69	U=770.5; W=3116.5; P < 0.01
No. of sextants with calculus	2.38 ± 2.25	2.97 ± 2.59	U=1038.0; W=3384.0; ns
CAL	4.31 ± 1.08	4.05 ± 1.28	t (100)=1.09; ns
PD	3.25 ± 1.70	3.25 ± 0.69	U=1144.0; W=3490.0; ns
REC	1.06 ± 0.81	0.78 ± 0.70	U=875.5; W=1470.5,0; ns
Deepest pocket	7.1 ± 2.1	7.0 ± 1.6	U=1105,0; W=3451,5; ns
No. of locations PD ≥ 4	34.1 ± 20.8	45.7 ± 25.2	t (100)=-2,47; P < 0.05
No. of locations PD ≥ 6	9.3 ± 13.3	11.8 ± 11.9	U=941,0; W=3287,0; ns
No. of locations CAL ≥ 5	35.64 ± 21.62	33.92 ± 26.89	U=1050; W=1645; ns
No. of locations with BOP	37.75 ± 22.19	38.48 ± 22.76	t (100)=-0.16; ns
Tooth mobility	0.89 ± 0.59	0.75 ± 0.56	U=1124.5; W=1719.5; ns
Furcation lesions*	0.22 ± 0.58	0.17 ± 0.43	U=1128.0; W=1723.0; ns

*only for molars; CAL-clinical attachment loss; F-Fisher test; ns-not significant; PD-probing depth; REC-gingival recession; t-unpaired t-test; U, W-non-parametric Wilcoxon-Mann-Whitney test.

In our study, nearly all women had at least one missing tooth, and the number of missing teeth was higher in the group of postmenopausal women (10.8 ± 5.9 vs. 6.8 ± 4.6; P < 0.01). The difference in the number of missing teeth (from all causes) observed in postmenopausal and premenopausal women could suggest a possible effect of menopause on tooth loss. However, it is conceivable that age, smoking and the accumulation of plaque may play a role as confounders on the relationship between menopause and missing teeth. Multiple regression analysis is the best way to assess such relationship after adjusting for those confounders simultaneously [29].

Age is correlated with the number of missing teeth (P < 0.001) and smoking habits (P=0.005) and correlation is stronger with menopausal condition (P < 0.001), which is also associated with smoking (P=0.028). Multiple regression

analysis shows that after adjustment for age, smoking and plaque index, the number of missing teeth is no longer influenced by menopausal status (P=0.169). The quality of the fit was poor, as expressed by an adjusted R2 of 0.177, which means that factors other than those included in the model may play a role in tooth loss. Moreover, the multiple regression analysis of the same data, after removing menopause as a predictor, also shows that smoking, plaque index and age are significant predictors of missing teeth, with observed powers of 45.5, 71.0 and 98.7%, respectively.

The use of missing teeth as a surrogated measure of periodontal disease has several limitations [30] because tooth loss is a complex phenomenon and reflects cumulative conditions of oral health over time [31]. In a large prospective study, LaMonte et al. observed that periodontal disease was responsible for 13% of

teeth lost during a five-year follow-up period, although the mean number of teeth lost was quite small [32]. In our study, tooth loss due to periodontitis occurred in 14.7% of all patients, although some cases may have been included in the other/unknown category. It is important to note that differences at periodontal level between the two groups do not justify the discrepancy in the number of missing teeth.

One of our inclusion criteria was the absence of periodontal treatment in the last year, in order to minimize potential differences caused by active therapy. As a matter of fact, only a minority of the women (37.3%) had ever had some kind of periodontal treatment, being these usually limited to a simple scale and polishing (93.1%). The extent and severity of periodontal disease were not exclusion criteria, since it was sought to evaluate this relationship in all types of chronic periodontitis.

The lack of a universally agreed definition of periodontal disease hampers the comparison of the existing studies. On the other hand, there is no single variable that entirely expresses the full complexity of the phenomenon of periodontal disease progression and that justifies our analysis on more than one parameter. The average attachment loss gives an indication of the severity of the disease, while the number of teeth with pockets gives an idea of the extent of it, however, we must not forget that the attachment loss, considered the “gold standard” in the diagnosis of periodontal disease, is a measure of its past evolution.

The control group presented a greater plaque score ($P < 0.01$), however, the amount of visible calculi was similar in both groups. It is somewhat curious the difference found on plaque score, since no significant differences were found on oral hygiene habits reported by subjects in both groups. This may be due to a tendency to omit behaviours considered less appropriate.

The attachment loss was slightly higher in the study group (4.31 ± 1.08 vs. 4.05 ± 1.28), although the difference is not significant. Since the mean values of probing depth are similar, this difference can be attributed to the fact that the study group had a greater tendency for gingival recession (1.06 ± 0.81 vs. 0.78 ± 0.70). However is important to note that gingival

recession may be associated with other causes beyond periodontal disease. In the remaining periodontal parameters, there are no significant differences indicating a greater extent or severity of the disease in the study group. In contrast, other authors have observed an association between menopausal status and attachment loss. In a study of 46 menopausal women and 15 premenopausal, Pallos et al. observed significant differences in attachment loss and alveolar bone loss. Still, when comparing oestrogen sufficient menopausal women and oestrogen deficient women for the same parameters, no significant differences were found [33].

When comparing results from different studies it is important to consider the age of the studied populations. In our study, the mean age of participants was 61.2 ± 8.0 years. Results from studies in younger populations typically revealed negative results since it is unlikely to find a significant degree of disease (osteoporosis or periodontal) at these ages. On the other hand, the fact that the majority of patients in our study have a high BMI, may contribute to increased peripheral conversion of estrogens, providing a protective effect difficult to estimate.

Some studies observed an increased teeth retention [14, 15], reduction of gingival inflammation, and reduction of attachment loss in women on HRT treatment, suggesting a protective role of estrogens in periodontal disease progression [12, 13, 34, 35]. We also conducted a comparison between women who used bisphosphonates or HRT and those who did not use (data not shown), but no statistically significant differences were observed for periodontal parameters, probably due to the small number of users.

The fact that we have opted for a complete periodontal examination, rather than a partial recording protocol and the fact that the measurements were made by a single blinded examiner are strong points of this study.

Regarding limitations, it is important to note that the determination of menopausal status and HRT use is based on anamnesis and subject to errors, however, it continues to be widely used, since the determination of hormone levels is costly and time consuming. Moreover, an isolated measurement of hormone levels does

not reveal the oestrogen life exposure. Some studies show a high degree of concordance between self-reported data regarding the use of HRT and medical records [14].

Since the study population is not representative of the Portuguese population, this data should not be extrapolated to the general population. It is possible that the methodology used tended to accrue individuals more concerned with their health and with easier access to health care system. Thus, additional studies with larger samples and longer periods of observation are needed in order to confirm or exclude the role of menopause on periodontal disease course.

Conclusions

When comparing pre and postmenopausal women we did not observe significant differences for periodontal parameters and teeth loss.

The relationship between menopause and periodontal disease is difficult to establish due to the multitude of factors involved. If any relationship is found, it will always be less significant comparing to other well-known risk factors of periodontal disease.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Pedro Oliveira, Instituto Superior de Ciências da Saúde Egas Moniz, Centro de Investigação Interdisciplinar Egas Moniz, CiiEM, Quinta da Granja, Monte de Caparica 2829-511 Caparica, Portugal. Tel: 00351 936983136; Fax: 00351 212946868; E-mail: pedromaoliveira@hotmail.com

References

- [1] Vitiello D, Naftolin F, Taylor HS. Menopause: Developing a rational treatment plan. *Gynecol Endocrinol* 2007; 23: 682-691.
- [2] Friedlander AH. The physiology, medical management and oral implications of menopause. *J Am Dent Assoc* 2002; 133: 73-81.
- [3] Forabosco A, Criscuolo M, Coukos G, Uccelli E, Weinstein R, Spinato S, Botticelli A, Volpe A. Efficacy of hormone replacement therapy in postmenopausal women with oral discomfort. *Oral Surg Oral Med Oral Pathol* 1992; 73: 570-574.
- [4] Yalcin F, Gurgan S, Gurgan T. The Effect of Menopause, Hormone Replacement Therapy (HRT), Alendronate (ALN), and Calcium Supplements on Saliva. *J Contemp Dent Pract* 2005; 2: 10-17.
- [5] Becker C. Pathophysiology and clinical manifestations of osteoporosis. *Clin Cornerstone* 2006; 8: 19-27.
- [6] Lerner UH. Bone Remodeling in Post-menopausal Osteoporosis. *J Dent Res* 2007; 85: 584-595.
- [7] Wactawski-Wende J. Periodontal diseases and osteoporosis: association and mechanisms. *Ann Periodontol* 2001; 6: 197-208.
- [8] Mariotti A. Estrogen and extracellular matrix influence human gingival fibroblast proliferation and protein production. *J Periodontol* 2005; 76: 1391-1397.
- [9] Shu L, Guan SM, Fu SM, Guo T, Cao M, Ding Y. Estrogen modulates cytokine expression in human periodontal ligament cells. *J Dent Res* 2008; 87: 142-147.
- [10] Liang L, Yu JF, Wang Y, Ding Y. Estrogen Regulates Expression of Osteoprotegerin and RANKL in Human Periodontal Ligament Cells Through Estrogen Receptor Beta. *J Periodontol* 2008; 79: 1745-1751.
- [11] Mascarenhas P, Gapski R, Al-Shammari K, Wang HL. Influence of sex hormones on the periodontium. *J Clin Periodontol* 2003; 30: 671-681.
- [12] Reinhardt RA, Payne JB, Maze CA, Patil KD, Gallagher SJ, Mattson JS. Influence of estrogen and osteopenia/osteoporosis on clinical periodontitis in postmenopausal women. *J Periodontol* 1999; 70: 823-828.
- [13] Ronderos M, Jacobs DR, Himes JH, Pihlstrom BL. Associations of periodontal disease with femoral bone mineral density and estrogen replacement therapy: cross-sectional evaluation of US adults from NHANES III. *J Clin Periodontol* 2000; 27: 778-786.
- [14] Grodstein F, Colditz GA, Stampfer MJ. Postmenopausal hormone use and tooth loss: a prospective study. *J Am Dent Assoc* 1996; 127: 370-377.
- [15] Taguchi A, Sanada M, Sueti Y, Ohtsuka M, Nakamoto T, Lee K, Tsuda M, Ohama K, Tanimoto K, Bollen AM. Effect of estrogen use on tooth retention, oral bone height, and oral bone porosity in Japanese postmenopausal women. *Menopause* 2004; 11: 556-562.
- [16] Civitelli R, Pilgram TK, Dotson M, Muckerman J, Lewandowski N, Armamento-Villareal R, Yokoyama-Crothers N, Kardaris EE, Hauser J, Cohen S, Hildebolt CF. Alveolar and postcranial bone density in postmenopausal women receiving hormone/estrogen replacement therapy: a randomized, double-blind, placebo-con-

Menopause and periodontal disease

- trolled trial. *Arch Intern Med* 2002; 162: 1409-1415.
- [17] Tarkkila L, Kari K, Furuholm J, Tiitinen A, Meurman JH. Periodontal disease-associated micro-organisms in peri-menopausal and postmenopausal women using or not using hormone replacement therapy. A two-year follow-up study. *BMC Oral Health* 2010; 10: 10.
- [18] Kochman RH, Kochman T, Stabholz A, Celinkier DH. Bisphosphonate and estrogen replacement therapy for postmenopausal periodontitis. *Isr Med Assoc J* 2004; 6: 173-7.
- [19] Streckfus CF, Baur U, Brown LJ, Bacal C, Metter J, Nick T. Effects of estrogen status and aging on salivary flow rates in healthy Caucasian women. *Gerontology* 1998; 44: 32-39.
- [20] Page RC, Eke PI. Case definitions for use in population-based surveillance of periodontitis. *J Periodontol* 2007; 78: 1387-1399.
- [21] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307-310.
- [22] WHO. Oral Health Surveys, Basic Methods. 4th edition. WHO; 1997.
- [23] O'Leary TJ, Drake RB, Naylor JE. The plaque control record. *J Periodontol* 1972; 43: 38.
- [24] Renvert S, Berglund J, Persson RE, Persson GR. Osteoporosis and periodontitis in older subjects participating in the Swedish National Survey on Aging and Care (SNAC-Blekinge). *Acta Odontol Scand* 2011; 69: 201-207.
- [25] Nicopoulou-Karayianni K, Tzoutzoukos P, Mitsea A, Karayiannis A, Tsiklakis K, Jacobs R, et al. Tooth loss and osteoporosis: the osteodent study. *J Clin Periodontol* 2009; 36: 190-197.
- [26] Inagaki K, Kurosu Y, Yoshinari N, Noguchi T, Krall EA, Garcia RI. Efficacy of periodontal disease and tooth loss to screen for low bone mineral density in Japanese women. *Calcif Tissue Int* 2005; 77: 9-14.
- [27] Famili P, Cauley J, Suzuki JB, Weyant R. Longitudinal study of periodontal disease and edentulism with rates of bone loss in older women. *J Periodontol* 2005; 76: 11-15.
- [28] Earnshaw SA, Keating N, Hosking DJ, Chilvers CE, Ravn P, McClung M, Wasnich RD. Tooth counts do not predict bone mineral density in early postmenopausal Caucasian women. EPIC study group. *Int J Epidemiol* 1998; 27: 479-483.
- [29] Rosner B. *Fundamentals of Biostatistics*, Duxbury Thompson Brooks/Cole. 6th edition. 2006.
- [30] Geurs NC, Lewis CE, Jeffcoat MK. Osteoporosis and periodontal disease progression. *Periodontol* 2000 2003; 32: 105-110.
- [31] Krall EA, Garcia RI, Dawson-Hughes B. Increased risk of tooth loss is related to bone loss at the whole body, hip, and spine. *Calcif Tissue Int* 1996; 59: 433-437.
- [32] LaMonte MJ, Hovey KM, Genco RJ, Millen AE, Trevisan M, Wactawski-Wende J. Five-year changes in periodontal disease measures among postmenopausal females: the Buffalo OsteoPerio study. *J Periodontol* 2013; 84: 572-584.
- [33] Pallos D, Ceshin A, Victor G, Bulhões R, Quirino M. Menopausa: fator de risco para a doença periodontal? *Rev Bras Ginecol Obstet* 2006; 28: 292-7.
- [34] Haas AN, Rosing CK, Oppermann RV, Albandar JM, Susin C. Association among menopause, hormone replacement therapy, and periodontal attachment loss in southern Brazilian women. *J Periodontol* 2009; 80: 1380-1387.
- [35] Lopez-Marcos JF, Garcia-Valle S, Garcia-Iglesias AA. Periodontal aspects in menopausal women undergoing hormone replacement therapy. *Med Oral Patol Oral Cir Bucal* 2005; 10: 132-141.