ORAL DISEASES

Oral Diseases (2011) 17, 560–563 doi:10.1111/j.1601-0825.2011.01800.x

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ORIGINAL ARTICLE

Higher prevalence of periodontitis in patients with refractory arterial hypertension: a case–control study

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OBJECTIVE: The aim of this study was to assess the association of periodontitis with refractory arterial hypertension.

STUDY DESIGN: A total of 137 patients were examined. Seventy patients (mean age of 55.2 ± 9.2 years) were included in the case group, while 67 non-hypertensive subjects (mean age of 50.0 ± 7.2) served as a control group. Periodontal clinical examination included plaque index, bleeding on probing, probing pocket depth and clinical attachment loss (CAL). Patients with at least five sites with CAL ≥6 mm were considered as severe periodontitis, and with at least 30% of the sites with CAL ≥4 mm generalized chronic periodontitis.

RESULTS: The mean (±s.d.) number and percentage of sites with CAL ≥6 mm were 11 (±14) and 16.6 (±14) in the case group, and 5.7 (±9.5) and 5.8 (±9.7) in the control group ($P < 0.05$). The mean (±s.d.) percentage of sites with CAL ≥4 mm was 37 (±29.6) in the case group and 21.2 (±20) in the control group ($P < 0.05$). The significant associations with arterial hypertension were severe chronic periodontitis (OR = 4.04, 95% CI: 1.92; 8.49) and generalized chronic periodontitis (OR = 2.18, 95% CI: 1.04; 4.56).

CONCLUSIONS: Severe and generalized chronic periodontitis seem to play a role as risk indicators for hypertensive patients.

Oral Diseases (2011) **17**, 560–563

Keywords: chronic periodontitis; cardiovascular diseases; epidemiology; periodontal medicine

Introduction

Hypertension is considered a product of dynamic interaction between diverse genetic, physiological, environmental and physicosocial factors (Kakar and Lip, 2006). Recently, hypertension was associated with inflammation (Boos and Lip, 2005). Elevated inflammatory markers, such as C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) were associated with increased risk of developing hypertension (Sesso *et al*, 2003) and were significantly related to elevated blood pressures (Bautista *et al*, 2005). Inflammation and hypertension may be linked via abnormal arterial stiffness (Boos and Lip, 2005). A relationship between systemic inflammation and arterial stiffness (Vlachopoulos et al, 2005) and the elevated levels of CRP associated with arterial stiffness were observed (Hingorani *et al*, 2000; Boos and Lip, 2005).

Periodontitis is a low-grade chronic inflammatory disease of the tissues surrounding the teeth. It may cause loss of supporting connective tissue and alveolar bone, and is highly prevalent among patients over 40 years of age (Löe *et al*, 1986). Periodontitis is associated with raised systemic concentrations of CRP, fibrinogen, IL-6, and TNF-α (Loos *et al*, 2000), and periodontal treatment may decrease blood levels of these inflammatory markers (Vidal *et al*, 2009). As both periodontitis and arterial hypertension have an inflammatory component, these diseases may be associated. Few studies evaluated the association between arterial hypertension and periodontitis, with different results. Buhlin *et al* (2003) found no association between periodontitis and hypertension, but Holmlund *et al* (2006) showed the opposite. Therefore, the aim of the present study was to assess the association of primary refractory arterial hypertension with severe and chronic periodontitis.

Materials and methods

Patients

This case–control study involved 137 patients from the National Institute of Cardiology (Rio de Janeiro – Brazil). The case group included 70 patients (mean age of 55.2 ± 9.2 years) enrolled for treatment at the Hypertension Unit of the National Institute of Cardiology (Rio de Janeiro – Brazil) and diagnosed as primary refractory hypertension (from June to

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Received 4 July 2010; revised 3 November 2010; accepted 24 November 2010

December 2008). Refractory hypertension is diagnosed when blood pressure levels remain above 140 × 90 mmHg, even when the patient is engaged in a treatment program and uses three or more classes of anti-hypertensive drugs including a diuretic. The patients were under supervision of a cardiologist, and were medicated with beta-blockers, angiotensin-converting enzyme inhibitors, and a diuretic. The patients were treated in the Cardiology department for 5–8 years. The control group included 67 non-hypertensive patients (50.0 ± 7.2 years), selected from other units of the same Hospital. All case and control patients were from a low social economical class. This study was approved by the research ethical committees of Rio de Janeiro State University and the National Institute of Cardiology – Rio de Janeiro. The participants signed a highly explicative authorization document of their own free will.

Periodontal examination

Both test and control groups received a periodontal examination that included (i) plaque index, considered as present or absent, (ii) bleeding on probing (BOP), considered as present or absent (iii) probing pocket depth (PPD), and (iv) clinical attachment loss (CAL). All teeth, except third molars were probed in six sites, using a periodontal probe with controlled pressure (Hawe 'click-probe'; Hawe-Neos Dental ®, Zurich, Switzerland) that allows a controlled pressure on probing of 20–25 g/F. The same examiner collected the data of all patients, using a structured interview and medical registers. All patients were examined by the same calibrated examiner (FV) (kappa = 0.91). Patients with periodontitis should have at least four sites with CAL ≥4 mm. Patients with severe chronic periodontitis should have at least five sites with CAL ≥6 mm according to Preshaw (2009), while patients with generalized chronic periodontitis should have at least 30% sites with CAL ≥4 mm (Armitage, 1999).

Statistical analysis

All statistical analyses were carried out using Statistical Package for Social Sciences (SPSS 11.0, Chicago, IL, USA) with a significance level of 5% ($P < 0.05$). Age, number of teeth, percentage of plaque, body mass index, percentage of BOP, PPD, CAL, systolic and diastolic blood pressure were expressed by means and standard deviation, and comparisons between groups performed using Student's *t* test. Gender, race, smoking, alcohol drinking problems, family history of arterial hypertension, history of acute myocardial infarction, and stroke were presented by frequency distribution, and comparisons between groups performed using chi-squared test. To assess the association of periodontitis with arterial hypertension, two models of logistic regression test were performed. Both models included gender (male), race (black/non-black), diabetes (yes or no), alcohol drinking problems (yes or no), and smoking (yes or no) as risk indicators. Severe chronic periodontitis (yes or no) was included only in the first model and generalized chronic periodontitis (yes or no) was included only in the second model as risk indicators. The power calculation indicated that with 65 subjects in each group, the study would have 80% power to observe differences between case and control groups considering prevalences of 50% and 25% of severe chronic periodontitis in the case and control groups, respectively.

Results

There was no statistical difference between case and control groups regarding gender, race, smoking, diabetes, and alcohol habits. However, there was a significantly higher frequency of patients with family history of arterial hypertension, history of acute myocardial infarction and stroke in the case group. The mean age, systolic and diastolic blood pressures were significantly higher in the case group; however, the mean body mass index was similar in both case and control groups (Table 1).

There were significantly less teeth in the case group when compared with the control group. There were higher numbers of sites with plaque, BOP, CAL ≥6 mm in the case group, when compared with the control group (Table 2). Of all patients, 44.3% and 26.9% had generalized chronic periodontitis in the case and control groups, respectively ($P < 0.05$), while 61.4% and 28.4% of the patients were diagnosed as severe chronic periodontitis in the case and control groups ($P < 0.05$).

The odds ratio (OR) for the presence of severe chronic periodontitis was OR = 4.04 (95% CI: 1.92; 8.49). Other significant association was generalized chronic periodontitis (OR = 2.18, 95% CI: 1.04; 4.56). Gender, race, diabetes, alcohol drinking problems, and smoking were not significant risk indicators for this sample (Table 3).

Discussion

The results of this study showed that hypertensive patients had significantly higher percentage of sites with plaque, BOP, number and percentage of sites with CAL ≥6 mm, but significantly lower number of teeth. Holmlund *et al* (2006), in a cross-sectional study in Sweden, with a sample of 4254 patients, showed an increased number of diseased pockets (PPD ≥5 mm) in patients with hypertension, similar to our results. However, the number of teeth was similar in both groups. Buhlin *et al* (2002) evaluated 50 patients with severe periodontitis and 46 periodontally healthy patients, and found difference in the prevalence of hypertension among the groups. A National Survey in Sweden showed an association of bleeding gums with hypertension (Buhlin *et al*, 2003). None of these two studies (Buhlin *et al*, 2002, 2003) made reference to the prevalence of periodontal clinical parameters. These results are difficult to compare as they had different methodologies to characterize periodontal disease. Buhlin *et al* (2002) diagnosed hypertension by a questionnaire, and all periodontal parameters were self-reported. Holmlund *et al* (2006) used bone loss and BOP to describe periodontal disease. Our study used CAL. Both bone loss and CAL estimate the accumulated exposure to periodontal inflammation, and seems to reflect the chronic characteristic of periodontitis. In accordance,

Table 1 Frequency of male, blacks, smokers, diabetes, family history of arterial hypertension (AH), history of acute myocardial infarction, history of stroke, alcohol drinking problems, and mean (s.d.) age, body mass index, systolic and diastolic blood pressure in the case and control groups

Variable	*Case group (n = 70)*	*Control group (n = 67)*
Age in years (s.d.)	55.2 (9.2)*	50 (7.1)
Male (%)	34.3	34.3
Black (%)	28	21
Smokers (%)	37	27
Diabetes (%)	7.5	17
Alcohol drinking problems (%)	25.7	31.4
Family history of AH (%)	71.4*	25
History of acute myocardial infarction (%)	21.4*	1.5
History of stroke (%)	20*	1.5
Body mass index (s.d.)	29 (5.3)	28.9 (4.4)
Systolic BP mmHg (s.d.)	176 (30.6)*	122 (4.9)
Diastolic BP mmHg (s.d.)	107 (19.6)*	78 (5.3)

*$P < 0.05$.

Table 2 Mean (s.d.) number of teeth, percentage of sites with plaque, percentage of bleeding on probing (BOP), number of sites with clinical attachment loss (CAL) ≥6 mm, percentage of sites with CAL ≥4 mm and CAL ≥6 mm in case and control groups

Clinical parameters	*Case group (n = 70)*	*Control group (n = 67)*
Number of teeth	15.1 (8.2)*	19.6 (6.5)
% sites with plaque	60.1 (22.5)*	51.1 (27.3)
% sites with BOP	33.7 (19.5)*	25 (21.5)
Number of sites CAL ≥6 mm	11 (14)*	5.7 (9.5)
% sites CAL ≥4 mm	37 (29.6)*	21.2 (20)
% of sites CAL ≥6 mm	16.6 (21.9)*	5.8 (9.7)

*$P < 0.05$.

Holmlund *et al* (2006) and our study presented similar results related to the frequency of bone and attachment loss. Although Buhlin *et al* (2003) showed association between BOP and hypertension, BOP gives more information about ongoing periodontal inflammation, and may be not appropriated to diagnose periodontitis.

The results of this study showed that the OR for the association between arterial hypertension and severe chronic periodontitis and generalized chronic periodontitis were 4.04 and 2.18, respectively. These results are higher than those presented by Holmlund *et al* (2006) (OR = 1.32). As mentioned before, the differences in these results may be related to differences in the populations studied and methodologies applied.

The association between periodontitis and cardiovascular diseases (CVD) was studied in case–control (Matilla *et al*, 1993), cross-sectional (Arbes *et al*, 1999), and longitudinal studies (DeStefano *et al*, 1993; Joshipura *et al*, 1996, 2003), suggesting that periodontitis might be a risk factor for coronary heart disease (CHD). The measures of CVD varied among studies, including myocardial infarction, death from CHD, stroke, and hypertension (DeStefano *et al*, 1993; Matilla *et al*, 1995; Joshipura *et al*, 1996, 2003). The causal relationship between periodontal disease and CVD may be difficult to prove, as both diseases share risk factors, such as smoking, genetics, and diabetes. The most likely explanation for the association of periodontitis with hypertension is related to low-grade chronic inflammation (Beck *et al*, 1996). Atherosclerosis has been considered as a dynamic and progressive disease arising from a combination of endothelial disfunction, thrombosis and inflammation (Libby, 2002). Inflammation was also related to endothelial dysfunction (Bautista, 2003). By impairing the capacity of the endothelium to generate vasodilating factors, particularly nitric oxide, elevated cytokines may cause endothelial dysfunction, chronic impaired vasodilation, and hypertension (Bautista, 2003). Inflammation was also associated with increased arterial stiffness, a predictor of primary coronary events in hypertensive patients (Hingorani *et al*, 2000). Periodontitis is a chronic inflammatory disease of the supportive tissue of the teeth that may lead to tooth loss. It was shown that periodontitis patients have elevated levels of systemic inflammation markers, such as CRP, IL-1, IL-6, fibrinogen, and TNF-α (Ebersole *et al*, 1997; Loos *et al*, 2000; Slade *et al*, 2000). On the other hand, periodontal treatment decreased plasma levels of these inflammatory markers (Tonetti *et al*, 2007; Vidal *et al*, 2009). Therefore, periodontitis, as a chronic inflammatory disease, may be associated with atherosclerosis and hypertension. The possibility that hypertension may be an inflammatory disease may have implications for therapeutic strategies to decrease the morbidity and mortality of hypertension.

Case–control studies have inherent limitations to determine a causal relationship between periodontitis

Table 3 Multiple logistic regression analysis of the factors associated with arterial hypertension, including severe chronic periodontitis (Model 1), generalized chronic periodontitis (Model 2), race, smoking, gender, diabetes, and alcohol drinking problems

	Model 1		*Model 2*	
Associated factors	*OR*	*95% CI*	*OR*	*95% CI*
Severe chronic periodontitis (yes × no)	4.04*	1.92;8.49	–	–
Generalized chronic periodontitis (yes × no)	–	–	2.18*	1.04;4.56
Race (black × non-black)	1.13	0.48;2.66	1.46	0.65;3.30
Smoking (yes × no)	1.25	0.53;2.93	1.23	0.54;2.81
Gender (male)	1.07	0.49;2.36	1.02	0.48;2.18
Diabetes (yes × no)	2.42	0.72;8.09	2.32	0.72;7.41
Alcohol drinking problems (yes × no)	1.44	0.52;3.98	1.41	0.53;3.75

*$P < 0.05$.

and hypertension, as they can often identify risk indicators, but quite often cannot include important confounding factors. In our study, adjustment for race, smoking and diabetes could be performed. However, adjustment for other risk factors such as hyperlipidemia and life-long exposure to tobacco could not be performed. Further studies including longitudinal and interventional ones are necessary to evaluate a possible causal relationship between periodontitis and arterial hypertension.

In conclusion, patients with arterial hypertension had higher frequency of number and percentage of sites with CAL >6 mm, and lower number of teeth. Moreover, severe and generalized chronic periodontitis were risk indicators for hypertensive patients. There are indications that inflammation may be an important component linking both conditions. Larger epidemiological studies, longitudinal and intervention clinical trials are necessary to confirm the association between periodontitis and arterial hypertension.

Acknowledgements

The authors are grateful to Dr Constante Ramos, Dr Marcelo Barros, and Dr Ana Beatriz Lima, from the National Institute of Cardiology, for their assistance in the study. The authors declare that there are no conflicts of interest in this study. Funding for this study were available from Rio de Janeiro State Research Foundation (FAPERJ, grant no E-26/111439/2008), Brazil, and resources of Rio de Janeiro State University.

Author contributions

Dr Fabio Vidal examined all patients, while Dr Ivan Cordovil designed the cardiological part of the study. Dr Figueredo was responsible for the design of study and review of the draft paper. Dr Ricardo Fischer was responsible for the design, analyses of the data, and drafting the paper.

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