SUNSTAR AWARD: RESEARCH

B. Söder M. Yakob Risk for the development of atherosclerosis in women with a high level of dental plaque and severe gingival inflammation

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© 2007 The Authors. Journal compilation © 2007 Blackwell Munksgaard Abstract Introduction: Chronic infection and inflammation are considered to be risk factors in the development of cardiovascular diseases; the chronic inflammatory and microbial burden caused by the dental plaque in these individuals may predispose them to atherosclerotic process. Aims: The aims were to study the involvement of a high level of dental plaque, severe gingival inflammation and periodontitis in the development of early atherosclerotic process in women. Methods: Forty-six randomly chosen women with periodontitis and 21 periodontally healthy women were subjected to a comprehensive clinical oral examination, including oral hygiene status and level of gingival inflammation. Atherosclerotic risk factor analysis and carotid ultrasonography were performed. Common carotid artery intima-media thickness (IMT) and lumen diameter were measured and intima-media area (cIMA) was calculated. The following statistical methods were used: analysis of variance, chi-squared tests and multiple logistic regression analysis. Results: There were highly significant differences between the patients and controls in the amount of dental plaque, gingival inflammation as well as bleeding on probing and pocket depth. The mean values of IMT and cIMA were significantly higher in women with periodontal disease than in controls. Multiple logistic regression analysis identified periodontitis as a principal-independent predictor of both the common carotid artery cIMA and IMT. Conclusions: The present results indicate that a high amount of dental plaque, severe gingival inflammation as well as periodontitis seem to be associated with the

development of atherosclerotic lesions in women already at its early and subclinical stages.

Key words: atherosclerosis; dental plaque; gingival inflammation; periodontitis; women

Introduction

Periodontal disease is characterized by a chronic infection and inflammation in the periodontal tissue, leading to the destruction of bone surrounding the teeth and, ultimately, to tooth loss (1, 2). It is estimated that 15-35% of the adult population in the industrialized countries suffers from this multifactorial illness (3-5). Periodontal disease is initiated by a biofilm of bacteria on the teeth that may trigger an immunoinflammatory response in the adjacent host tissues. (1, 6). Tobacco smoking is an important risk factor in the development of periodontitis and increases the severity of the periodontal diseases (7, 8) although bacterial pathogens are required to initiate the process of the disease. However, it has become evident that without inflammatory host reaction, the presence of bacterial pathogens alone is not sufficient to cause destruction of the tissue that occurs in the course of periodontitis. In individuals with constitutional 'proinflammatory' traits, the reaction to bacteria may lead to an excessive host response, resulting in general inflammatory reaction (9, 10). The presence of gingivitis and periodontitis in young women may reflect the underlying weakness of the host defence system and increased proinflammatory reactivity in the affected individuals. As chronic infection and inflammation are considered to be risk factors for the development of cardiovascular disease, the chronic inflammatory and microbial burden caused by dental plaque in these individuals may predispose them to atherosclerotic process.

The atherosclerotic cardiovascular disease is the most common cause of mortality among women in Sweden accounting for as much as 45% of the deaths each year in the Swedish female population (11–13). In addition, seen from the international perspective, there is a high mortality from the coronary artery disease among Swedish women, the coronary event rate expressed as event per 100 000 women being 2.3 times higher in Sweden than, for example, in Italy (14).

Apart from age, gender, use of tobacco, high blood pressure and high blood lipid content, over 200 other risk factors for atherosclerotic cardiovascular disease have been discussed in the literature (15). The results of several studies performed during the last two decades have indicated that also oral diseases, and especially periodontitis, may possibly act as risk factors for the development of cardiovascular disease (7, 16-24).

The aims of the present study were to study the involvement of a high level of dental plaque, severe gingival inflammation and periodontitis in the development of early atherosclerotic process in women.

Materials and methods

Study participants

The baseline cohort was selected in 1985 using the registry file of all inhabitants of the Stockholm metropolitan area and consisted of 3273 individuals. Of these 1585 were women aged 30–40 years and born on the 20th of any month between 1945 and 1954. In this cross-sectional study, 46 women were randomly chosen from the group of individuals in whom the presence of periodontal disease was documented. At the same time, 21 periodontally healthy women were randomly selected not having periodontitis.

The Ethics Committee of the Karolinska University Hospital at Huddinge approved the study. All the subjects gave their informed consent to participate.

Clinical examination and questionnaire

In all the subjects, the following clinical oral health parameters were recorded: (i) the number of remaining teeth excluding third molars, (ii) gingival inflammation around every tooth with Gingival Index (25) and (iii) oral hygiene status using the dental Plaque Index (26) on six surfaces of all teeth excluding third molars. Pocket depth and attachment level were determined with a periodontal probe and recorded to the nearest higher millimetre of six sites of each tooth on all teeth excluding third molars. Wisdom teeth were excluded due to the frequent occurrence of pseudo-pockets around these teeth. At the time of the oral examination, blood samples were taken after 12 h of overnight fasting for the analysis of total plasma cholesterol. Blood pressure was measured and 12-lead electrocardiogram was also recorded.

The subjects answered a questionnaire concerning health problems, medication, occurrence of stroke or coronary artery disease in siblings or parents before the age of 65, dental visits, use of tobacco, marital status, socioeconomic data and education.

Radiograms

A full-mouth set of 14 Kodak Ektaspeed periapical radiograms was obtained from each patient. Percentage of remaining bone on radiographs was determined by a method described by Wouters *et al.* (27).

Carotid B-mode ultrasonography

Carotid arteries were examined bilaterally with a duplex scanner (Aspen, Acuson, Mountain View, CA, USA) using a 7 MHz linear array transducer. At the department of laboratory medicine, division of clinical physiology, Karolinska Institutet, Karolinska University Hospital, Huddinge, Sweden. Carotid intima-media thickness (IMT), calculated carotid intima-media area (cIMA) and carotid lumen were determined on each patients using a method earlier described (19, 28–34).

Statistical methods

Analysis of variance (ANOVA), chi-square tests and multiple logistic regression analysis with backwards elimination of nonsignificant variables were performed using the SPSS[®] software package, version 14.0 (SPSS Inc. Chicago, IL, USA). All *P*-values are two-tailed, and confidence intervals were calculated at the 95% level.

Results

The demographic data and risk factors of the studied women are presented in Table 1. As can be seen from Table 1, the study group did not differ regarding age, occurrence of hypertension, body mass index, atherosclerotic disease and plasma cholesterol. The relative number of individuals with higher education was greater in controls, whereas smoking dominated in the patient group.

The results of oral examination are presented in Table 2. As can be seen from Table 2, there were highly significant differences between the patients and the controls in amount of dental plaque as well as gingival inflammation.

The measured IMT as well as calculated cIMA B-mode variables were significantly greater in the patients than in controls, bilaterally (Table 3), but not carotid lumen diameter. In a multiple logistic regression model analysis for IMT (Table 4) age and periodontitis appeared to be principal-independent predictors associated with 7.08-times the odds of increased IMT for age and 6.05-times the odds of increased IMT for periodontitis. In a multiple logistic regression model analysis for cIMA periodontitis, age and heredity for atherosclerotic disease appeared to be principal-independent predictors associated 5.41-times the odds of increased cIMA for periodontitis, 4.78-times the odds for age and 4.01-times the odds for heredity for atherosclerotic disease (Table 5).

Discussion

The study addresses the issue of periodontitis in women as a risk factor for atherosclerosis and future risk for coronary heart

	Patients (<i>n</i> = 46) number, mean ± SD	Controls ($n = 21$) number, mean \pm SD	P-value
Age (years)	54.7 ± 2.9	53.5 ± 2.7	NS
Education (compulsary/higher)*	22/22	2/19	<0.01
Smoking (yes/no)	22/24	4/17	<0.05
Number of visits to the dentist last 5 years	6.0 ± 4.1	4.9 ± 1.4	NS
Number of visits to the hygienist last 5 years	5.4 ± 5.3	2.4 ± 3.5	<0.05
BMI (kg m^{-2})	24.8 ± 4.3	23.1 ± 2.6	NS
Heredity for arteriosclerotic disease (yes/no)	19/27	4/15	NS
Diabetes mellitus (yes/no)	2/44	0/21	NS
Hypertension (yes/no)*	16/28	5/16	NS
Plasma cholesterol (mmol L ⁻¹)*	5.8 ± 1.0	5.5 ± 0.6	NS

Table 1. Demographic data and risk factors for females

*Systolic pressure >140 mm Hg, diastolic pressure >90 mm Hg or ongoing antihypertensive therapy.

BMI, body mass index.

	Patients ($n = 46$) mean \pm SD	Controls $(n = 21)$ mean ± SD	<i>P</i> -value
Dental Plaque Index (PLI)	0.4 ± 0.5	0.2 ± 0.2	<0.05
Gingival Index (GI)	1.1 ± 0.9	0.3 ± 0.3	<0.001
Pocket depth (mm)	2.7 ± 0.8	2.1 ± 0.3	<0.001
Loss of attachment (mm)	3.2 ± 0.9	2.1 ± 0.5	<0.001
Number of teeth with pocket depth ≥5 mm	8.0 ± 5.5	0.2 ± 0.4	<0.001
Percentage of bleeding on probing (BOP %)	36.0 ± 22.7	20.4 ± 13.5	<0.01
Percentage of remaining bone on radiographs	84.9 ± 5.2	92.8 ± 1.8	<0.001
Number of missing teeth	3.0 ± 2.2	0.7 ± 1.1	<0.001

Table 2. Clinical oral and radiographic data in females with periodontal diseases and controls

Table 3. Ultrasonographic B mode variables

	Patients (<i>n</i> = 43*) (mean ± SD)	Controls (<i>n</i> = 21) (mean ± SD)	<i>P</i> -value
Common carotic	d artery IMT (mm)		
Right side	0.65 ± 0.11	0.60 ± 0.09	≤0.05
Left side	0.67 ± 0.11	0.58 ± 0.08	<0.001
Common carotic	d artery lumen (mm)		
Right side	5.70 ± 0.55	5.48 ± 0.48	NS
Left side	5.55 ± 0.55	5.42 ± 0.37	NS
Common carotic	d artery cIMA (mm ²)		
Right side	13.9 ± 3.16	11.4 ± 2.44	<0.05
Left side	12.2 ± 2.85	10.9 ± 1.9	<0.01

*In three cases, measurements of the B-mode variables listed in the table could not be successfully performed because of a local plaque formation or other technical reasons.

cIMA, carotid intima-media area; IMT, intima-media thickness.

disease by evaluating the relationship between periodontitis and occurrence of early atherosclerotic changes in carotid arteries in patients without any symptoms of overt atherosclerotic disease. The present results clearly identify periodontitis as a principal-independent predictor of carotid arterial wall thickness and calculated cross-sectional arterial wall area, i.e. two ultrasonographic measures of preclinical atherosclerosis.

Regarding the reliability of the obtained results, it can be pointed out that the patients and the controls were randomly chosen to avoid selection bias and to ensure normal distribution of the sampled variables. The same experienced dental examiner performed all dental examinations, whereas dental radiograms were evaluated blind by another experienced examiner blinded to the results of the clinical examination. The carotid sonography was performed and evaluated by the same experienced and blinded sonographer. Hence, the methodological biases were minimized. It can be emphasized that the B-mode-derived carotid IMT is a well-established variable, reflecting early atherosclerosis and its value in studies of early stages of this disease and various vascular risk factors has been well documented (32, 33) as well as cIMA (28, 31).

Women run considerably lower risk than men of being afflicted affected by cardiovascular diseases. Women seem to be subjected to myocardial infarctions 10 years later than men, i.e. the risk for myocardial infarction in women is the same as that

Table 4. The results of multiple logistic regression analysis of the relationship between common carotid artery IMT (bilaterally) as a dependent variable and several independent variables (periodontal diseases, age, BMI, heredity for arteriosclerotic disease, hypertension, diabetes, plasma cholesterol, smoking and education) in females

Dependent variable	Explaining variable	β	χ^2 -value	P-value	Odds ratio	95% confidence interval
Common carotid artery IMT (bilaterally)	Age Periodontal disease	1.96 1.80	9.10 5.46	0.003	7.08	1.98–25.25
Common carolid artery INT (bilaterally)	Periodonial disease	1.80	5.46	0.019	6.05	1.34-27.35

BMI, body mass index; IMT, intima-media thickness.

Table 5. The results of multiple logistic regression analysis of the relationship between common carotid artery cIMA (bilaterally) as a dependent variable and several independent variables (periodontal diseases, age, gender, BMI, heredity for atherosclerotic disease, hypertension, diabetes mellitus, plasma cholesterol, smoking and education) in women

Dependent variable	Explaining variable	β	χ^2 -value	P-value	Odds Ratio	95% confidence interval
Common carotid artery	Periodontal disease	1.69	4.82	0.028	5.41	1.20-24.43
cIMA (bilaterally) Age Heredity for ather	Age	1.57	5.72	0.017	4.78	1.33-17.25
	Heredity for atherosclerotic disease	1.39	4.36	0.037	4.01	1.09-14.74

BMI, body mass index; cIMA, carotid intima-media area.

of a 10-year younger men (11, 35). Female sex hormones, oestrogens, are considered to protect women from cardiovascular diseases (35). Women have better oral hygiene with lower amount of dental plaque and periodontitis than men (36) and the results of their smaller inflammatory and microbial burden might therefore also retard the subsequent effect on the vessel wall. In some situation, younger women seem to have an extremely high risk for death. Vaccarino *et al.* (37) found that younger women with myocardial infarction are at greater risk for death than men. The heredity for arteriosclerotic disease was correlated to cIMA and therefore it seems important for the therapist e.g. the dental hygienist, to ask women with periodontitis the question about the family history of coronary heart disease (38, 39).

Consequently, we have shown the involvement of high level of dental plaque, severe gingival inflammation and periodontitis in the development of atherosclerotic process in women already at its early and subclinical stage. This may create basis for new approaches for prophylactic treatment given by the dental hygienist in the view of atherosclerotic diseases and the cost it means to society.

Conclusion

The present results indicate that a high amount of dental plaque, severe gingival inflammation as well as periodontitis seem to be associated with the development of atherosclerotic lesions in women already at its early and subclinical stage.

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