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ASSOCIATIONS BETWEEN ORAL BIOFILM, PERIODONTAL DISEASE, AND SYSTEMIC HEALTH

WITH A FOCUS ON ATHEROSCLEROSIS
AND BREAST CANCER

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i sal 4 U, plan 4, Institutionen för odontologi, Alfred Nobels Allé 8, Huddinge

Måndagen den 13 februari 2012, kl 09:00

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Stockholm and Helsinki 2012

ABSTRACT

The general hypothesis of this series of studies was that oral infections, particularly periodontal disease, by triggering inflammatory reactions detrimentally affect systemic health where inflammations are known to play a role in the pathogenesis, namely cardiovascular disease and cancer. Consequently, the general aim was to study the association between oral biofilm and certain oral micro-organisms, periodontal disease, and selected inflammatory markers with a focus on atherosclerosis and breast cancer (BC).

In *Study I*, the aim was to examine the involvement of a high amount of dental plaque, severe gingival inflammation and periodontal disease in the development of early atherosclerotic lesions in women. The carotid arteries were examined with ultrasonography. Periodontal disease appeared to be a principal independent predictor in the development of atherosclerotic process women with periodontal disease. Our findings indicated that a high amount of dental plaque, severe gingival inflammation as well as periodontal disease seemed to be associated with the development of atherosclerotic lesions in women already at the early subclinical stage. In *Study III*, the aim was to examine early atherosclerotic changes in carotid arteries and relate the findings to the serum levels of high-sensitivity C-reactive protein (hsCRP) in subjects whose periodontal status have been followed for at least 18 years. Women had significantly lower hsCRP values and significantly higher high-density lipoprotein (HDL) cholesterol values than men. Nevertheless, women with periodontal disease had significantly more atherosclerotic lesions than women without periodontal disease. Increased levels of hsCRP could not discriminate the patient group from the control group for either men or women. Periodontal disease was identified as the major independent predictor of increased carotid artery lesions. Hence, periodontal disease might nevertheless present a risk for atherosclerotic disease, particularly in women, irrespective of low hsCRP levels.

In *Study II*, the aim was to evaluate the incidence of BC in subjects with periodontal disease and the characteristic tooth loss in a 16-year prospective investigation. Participants diagnosed with periodontal disease and BC had significantly more missing molars when compared with subjects with periodontal disease but without BC. The difference in the prevalence of BC in subjects with periodontal disease and with or without any missing molar in the mandible was significant. Thus, chronic periodontal disease indicated by missing molars seemed to be associated with the incidence of BC.

In *Study IV*, the aim was to investigate in subjects with and without periodontal disease the levels of salivary albumin, total protein, and matrix metalloproteinases-8 (MMP-8), with or without the simultaneous presence of specific periodontal micro-organisms detected by polymerase chain reaction (PCR) in gingival crevicular fluid (GCF). The presence of both *Treponema denticola* and *Tannerella forsythia* associated with increased MMP-8 concentration in GCF. Furthermore, the presence of *T. denticola* associated with increased albumin and total protein concentrations in saliva. In *Study V*, the aim was to assess the association between site-specific subgingival micro-organisms and the levels of MMP-8 and MMP-9 at test sites. *T. denticola* was significantly more present at test sites in patients compared with the control group. Furthermore, the site -specific presence *T. denticola* in GCF appeared to increase the release of MMP-8 and MMP-9 at test sites. Thus, the results from *Studies IV* and *V* confirmed the assumption that periodontal micro-organisms might indeed trigger an inflammatory host-response.

Summing up, periodontal disease was found to be associated with subclinical atherosclerotic lesions and also a higher incidence of BC. Furthermore, *T. denticola* associated with increased salivary albumin, total protein as well as with higher levels of MMP-8 and MMP-9 in GCF, indicating a possible inflammation triggering capacity of the oral biofilm. Thus, our findings did confirm our primary hypotheses. The associations indicate that periodontal disease might pose a threat to systemic health.

Keywords: periodontal disease, periodontitis, oral biofilm, dental plaque, inflammation, atherosclerosis, breast cancer, gingival crevicular fluid, matrix metalloproteinase, C-reactive protein, carotid plaque, micro-organisms, salivary proteins, *Treponema denticola*

ISBN 978-91-7457-646-7