Periodontal care may improve systemic inflammation

Arnon Blum, MD
Eran Front, DMD*
Aviva Peleg, MSc

Department of Internal Medicine A, *Periodontal Unit, Baruch-Padeh Poriya Medical Center, Lower Galilee 15208 Israel.

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Abstract

Background: Periodontitis is an infectious chronic insidious disease of the tooth supporting structures that causes a general inflammatory response. The aims of the study were to determine whether periodontitis is associated with markers of general inflammation high-sensitivity (hs) C-reactive protein (CRP) leading to cardiovascular disease, and whether proper management of the periodontal disease would improve inflammation and thus, may prevent cardiovascular disease in the future.

Methods: This was a prospective case-controlled pilot study. Nine patients (3 women, 6 men; 40 ± 5 yr) took part. All had severe periodontitis, without systemic disorders, and were all treated conservatively without surgical intervention. All had a 2nd visit after 3 months of treatment at the Outpatient Dental Clinic of the Hospital. Periodontal status and hs-CRP were evaluated on entry to the study and 3 months after treatment. Nine age and sex-matched healthy volunteers without periodontal disease served as the control group.

Results: Periodontal clinical parameters were improved after 3 months' treatment: probing depth (PD) (mean) at baseline was 4.3 and after 3 months' treatment improved to 3.2 ($P=0.001$), clinical attachment level (CAL) (mean) was 4.6 and changed to 3.7 ($P=0.01$), bleeding on probing (BOP %) changed from 64% to 33% ($P=0.001$), and Plaque index (Pi) changed from 49% to 25% ($P=0.001$). hs-CRP level was different between the patients' group (pre treatment) and the healthy volunteers: 2.97 ± 0.58 mg/L vs. 0.25 ± 0.14 mg/L ($P=0.00002$). After completing 3 months' treatment, hs-CRP levels were decreased from 2.97 ± 0.58 mg/L to 2.3 ± 0.7 mg/L ($P=0.009$).

Conclusions: Periodontitis is an infectious condition that may be an insidious cause of chronic inflammation and may be a risk factor for future cardiovascular disease. Treating periodontitis improved inflammation, and might be used as an important prevention tool for cardiovascular disease.

Unstable Angina Pectoris and Acute Myocardial Infarction are commonly due to rupture of atheromatous plaques in the coronary arteries. Inflammation is increasingly recognized as a major component of inhibition of endothelial cells' function leading to atherosclerosis and cardiovascular disease. Periodontitis is a chronic infectious condition due to gram-negative anaerobic bacterial infection of the tooth supporting structures, including the periodontal ligament, cementum, and the supporting bones.

The purpose of this study was to determine whether periodontitis could be an infectious trigger to systemic inflammation, and whether conservative treatment (without surgery) could cure the local infection and reverse systemic inflammation.

Methods

This was a prospective case-controlled, pilot study where we were studying the correlation between periodontitis and inflammation in patients with no systemic diseases or risk factors to atherosclerosis.

None of the patients had an immunologic or an inflammatory disease, an active cancer, or a known myocardial disease.

Nine patients [out of 50 patients with periodontitis that were referred to the Outpatient Dental Clinic] (3 women and 6 men; mean age 40 ± 5 yr) were found eligible to take part in the study.

Patients were excluded who were smoking or who had any of the conventional risk factors to atherosclerosis (essential hypertension, high cholesterol or triglyceride levels, family history of premature coronary artery or vascular disease, diabetes mellitus, any immunological or known chronic inflammatory condition, or malignancy).

Medical history and physical examination were performed by a team of a Periodontist and a Cardiologist. The study was approved by the hospital's Helsinki committee and all volunteers signed a consent form before enrollment.

Each patient had at least 18 teeth and 1 interproximal area of ≥ 5 mm pocket depth. One calibrated examiner (EF) collected the following clinical data: probing depth (PD) was measured from the free gingival margin (GM) to the base of the pocket. Bleeding on probing (BOP) was considered positive if a site bled within 20 seconds after probing.¹ Clinical attachment level (CAL) was determined at all sites by measuring the distance from the cemento-enamel junction (CEJ) to the GM, adding the PD at the same site. $CAL = PD + (CEJ \text{ to } GM)$ (all measurements in millimeters). Plaque index (Pi)² was determined on each site. The data was collected and recorded using a standard manual periodontal probe. 6 sites per tooth - buccal, mesio-buccal, disto-buccal, lingual, mesio-lingual, and disto-lingual were used. Data was assessed at baseline and 3 months after active therapy.

Therapy included systemic antibiotics [Amoxicillin 500 mg + Metronidazole 250 mg T.I.D.] in the first week, an advanced oral hygiene improvement session followed by 2-4 consecutive sessions of scaling and root planing by one operator in the Outpatient Dental Clinic of the Hospital. Every patient was evaluated before the treatment and 3 months afterwards by a Periodontist. Nine healthy age and sex-matched volunteers (with no periodontitis) served as the control

group.

Statistical considerations

In order to study the difference in vascular inflammation between patients and the healthy controls a paired t-test was performed. To check the change in vascular inflammation after 3 months of treatment a paired t-test was performed.

Results

Nine patients (3 women, 6 men; 40 ± 5 yr old) with severe periodontitis were enrolled. All had severe periodontitis (without systemic disorders) and all were treated conservatively for 3 months with systemic antibiotics (for 1 week) and local periodontal treatments in the Outpatient Dental Clinic of the Hospital (as described above). 9 age and sex matched healthy volunteers without periodontal disease served as the control group. All patients came to a 2nd visit after 3 months of treatment. Periodontal clinical parameters were improved after 3 months' treatment: The PD (mean) at baseline was 4.3 and after 12 weeks of treatment improved to 3.2 ($P=0.001$), the CAL (mean) was 4.6 and changed to 3.7 ($P=0.01$), BOP % changed from 64% to 33% ($P=0.001$), and Pi changed from 49% to 25% ($P=0.001$) (Table 1).

Periodontitis was improved in all 9 patients that completed 3 months of treatment.

Inflammation was expressed by measuring hs-CRP. There was a difference between hs-CRP levels before treatment (2.97 ± 0.58 mg/L) compared with the control group (0.25 ± 0.14 mg/L) ($P=0.00002$), as well as between post treatment (2.33 ± 0.7 mg/L) and the control group (0.25 ± 0.14 mg/L) ($P=0.00009$).

There was a reduction of hs-CRP level after treatment ($P=0.009$) but the reduction was mild compared with levels of hs-CRP in the healthy group.

Discussion

Patients with periodontitis had high levels of hs-CRP, a marker of systemic inflammation, that was improved

TABLE 1. Periodontal studies

	Before	After	P
PD (cm)	4.3	3.2	0.001
BOP (%)	64.0	32.0	0.01
PP (%)	49.0	25.0	0.01

after 3 months of conservative local periodontal treatment without surgery.

Intravenous infusion of *S. sanguis* into rabbits has been shown previously to cause changes in the ECG, heart rate, blood pressure, and cardiac contractility consistent with the occurrence of myocardial infarction. The ECG changes began 30 seconds after infusion of *S.sanguis*, followed by alterations in blood pressure and respiratory rate. These changes occurred intermittently over a 30-minute period and changed within one heartbeat to a normal pattern and suddenly back to abnormal.^{2,3}

Five longitudinal studies have shown that oral conditions were associated with the onset of coronary heart disease while controlling for a variety of established coronary heart disease risk factors. In addition to published evidence, preliminary findings from the Dental Atherosclerosis Risk in Communities study also indicated that periodontal disease could be associated with carotid intima-medial wall thickness, a measure of subclinical atherosclerosis, after adjusting for factors known to be associated with both conditions.⁴ A survey in the early 1970s found that adults with severe periodontitis had a 25% increased risk of coronary heart disease relative to those with minimal periodontal disease. More than that, periodontal disease and poor oral hygiene were strongly associated with total mortality.⁵

Mean bone loss scores and probing pocket depth scores per tooth were measured in 1147 men during 1971-1986 in the Normative Aging Study and in the Dental Longitudinal Study. Information gathered during follow-up examinations showed that 207 men developed coronary heart disease (CHD), 59 died of CHD, and 40 had cerebral strokes. Incidence odds ratios adjusted for established cardiovascular risk fac-

TABLE 2. Comparing vascular inflammation before and after 3 months of periodontal treatment

	hs-CRP before treatment	hs-CRP after treatment	hs-CRP volunteers
Mean(mg/L)	2.97	2.33	0.25
SD (mg/L)	0.58	0.7	0.14
t-test	0.009		0.00009

tors were 1.5, 1.9, and 2.8 for bone loss and total CHD, fatal CHD, and stroke, respectively. Levels of bone loss and cumulative incidence of total CHD and fatal CHD indicated a biologic gradient between severity of the periodontal disease and the occurrence of cardiovascular disease.⁶⁻⁸

Creactive protein (CRP)

CRP is an independent risk factor for coronary heart disease,⁹⁻¹¹ and recent evidence suggests that lowering CRP levels reduces the rate of atherosclerosis progression,¹² and decreases the risk of recurrent cardiovascular events.¹³ Given its growing importance in potentially predicting and/or preventing cardiovascular events, it is important to find endogenous and infectious causes of CRP elevation, and to find out ways of reducing high levels of CRP.

Summary

We have demonstrated in this study that periodontitis may cause inflammation, and that inflammation could be reversible if periodontitis was treated appropriately.

Conclusions

Periodontitis might be an insidious infectious cause of systemic inflammation and future cardiovascular events. Treating periodontitis may inhibit systemic inflammation and could be used as an important prevention tool. Larger studies as well as longer periods of time and using different treatment attitudes (maybe more aggressive) are needed to verify our findings before we could consolidate our recommendations. Still, we are enlightening a possible insidious cause of cardiovascular disease that could be prevent-

able and treatable. This approach could be used (if proved beneficial) as a preventive tool to decrease cardiovascular mortality and morbidity.

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Correspondence to:

Arnon Blum, MD
 Department of Internal Medicine A
 Baruch-Padeh Poriya Medical Center
 Lower Galile 15208
 Israel
 navablum@hotmail.com
 bluma@mail.nih.gov