Assessment of C-Reactive Protein Levels in Periodontal Patients Using a Standard Laboratory Procedure

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Abstract: Background: the aims of the randomized clinical trial were (i) to verify the association between periodontal disease and C-reactive protein (CRP) and (ii) to evaluate a possible reduction of serum CRP levels after non-surgical periodontal treatment.

Methods: Thirty-two subjects, 18 affected by chronic periodontitis, and 14 periodontally healthy patients, aged between 21 and 65 (41±13) were included. Clinical and radiographic examinations were used for each patient to obtain three dental indices that were used to evaluate severity of periodontal disease and changes after treatment. Periodontal patients were randomly assigned to one of two groups for different treatments: special oral hygiene instructions alone or in combination with scaling and root planing. Blood samples were taken for measurement of CRP levels and eritrosedimentation rate before and after treatment

Results: a reduction of clinical index CPSS was observed for both groups of periodontal patients after treatment but there were no statistically significant differences for CRP and ESR at baseline and between baseline and re-examination. Non statistically significant differences of CRP values between periodontal patients and healthy controls were found

Conclusions: CRP values don’t seem to change after non-surgical treatment of periodontitis, even in presence of a reduction of clinical indices.

Keywords: Periodontal disease, C-reactive protein, Inflammation, Nephelometric method.

INTRODUCTION

Several studies over the last years have shown a possible association between periodontal and cardiovascular diseases [1-6]. This can be due to common risk factors such as age, smoking, and diabetes. It can also be due to the action of Gram-negative bacteria and their products which, in the case of periodontal inflammation, may spread through the circulation and reach organs like the heart. Finally, inflammatory mediators such as TNFα, IL-1, IL-6, IFN-γ and PGE₂ can reach the bloodstream from inflamed periodontal sites [7]. Of these mediators, IL-6, released by activated macrophages, induces production of C-reactive Protein (CRP) by liver hepatocytes. CRP represents a marker of inflammation, normally present in small quantities, but it can increase dramatically within 72 hours following tissue injury. This protein can act as an opsonine, binding specific cell membrane components of microorganisms and stimulating the activation of complement fragments to enhance opsonization and elimination of bacteria. In addition, CRP can interact with natural killer cells and monocytes and may increase their tumoricidal activity [8].

In many studies CRP appears to be a risk predictor for cardiac and cerebrovascular events [1, 2, 6, 9]. When associated with smoking, hypertension or high plasma cholesterol levels, it acts as a “risk multiplier”. Concentrations >3 mg/l seem to increase the risk of myocardial infarction or stroke within 8 years by three or four times, both in medically healthy subjects and in subjects with previous episodes [10-12].

Hence, the aims of our clinical trial were (i) to verify whether levels of C-reactive protein are different between subjects affected by periodontal disease and healthy subjects using a standard laboratory procedure, and (ii) to evaluate a potential reduction of serum CRP levels after two different kinds of non-surgical periodontal therapies.

MATERIALS AND METHODS

In order to set the sample dimension, several studies were examined with the aim to detect a value of minimum difference between periodontal and healthy subjects (Table 1). On the basis of the similar
experimental design, the difference reported by Ebersole et al. (1997) of approximately 1 mg/dl between periodontal patients and controls was used, establishing an alpha error of 0.05 and a power of 0.80 for the significance test, so the number of subjects enrolled was 14 for each group.

The 42 initial subjects, 28 with chronic periodontal disease, and 14 periodontally healthy, were aged between 21 and 65 years. The subjects were enrolled by a single operator among the patients examined at the Department of Periodontology of the School of Dentistry, University of Bologna, Italy, between September 2003 and June 2004.

The exclusion criteria comprised: coronary heart disease, myocardial infarction within the last 24 months, systemic illnesses or infections, antibiotic treatment, use of aspirin or treatment with any medication known to affect the serum level of inflammatory markers in the preceding two months [4, 9, 13].

The 28 periodontal patients were randomly assigned to two treatment subgroups and the allocation sequence was made by computer. However, 10 subjects did not come back for periodontal revaluation, so the number of periodontal patients for our analyses was reduced to 10 for Group 1 and 8 for Group 2. However, no adverse effect motivated the dropouts apart an inadequate compliance to the scheduled treatment. Group I drop out rate was 29% (4/14) and 43% in Group II (6/14); the difference of 14% is slightly higher than 10%, considered the acceptable drop out selective rate. Despite this reduction in numbers at the follow-up, no significant differences were observed in demographic, dental and clinical parameters.

Group 1 (10 periodontitis subjects) had: a baseline periodontal examination; the collection of a blood sample for evaluation of eritrosedimentation rate (ESR) and CRP; special oral hygiene instructions named hygienic therapy (see Box 1); gross scaling (full mouth); 4 sessions of scaling and root planing (one for each quadrant); periodontal revaluation and collection of a second blood sample one month after the completion of treatment.

Box 1: Special Oral Hygiene Instructions Named Hygienic Therapy

Each subject was instructed in proper oral hygiene practices:
- Bass technique for brushing lingual and buccal surfaces
- Tip for cleaning crevices and to create space (when needed) for the interdental brush
- Interdental brush in interproximal areas
- Plaque disclosing agent at least once a week.

Group 2 (8 periodontal patients) had: a baseline periodontal examination; the collection of a blood sample for evaluation of ESR and CRP; special oral hygiene instructions (hygienic therapy) as with group 1;

| Authors       | Number of Patients (N) | CRP                                      |
|---------------|------------------------|------------------------------------------|
| Ebersole et al. 1997 | 40 periodontal patients | 0.91 in periodontal patients; 0.21 in controls. |
| Beck et al. 2000       | 1550 patients with at least 10% of sites with probing depth ≥ 4 mm; 35 controls | 0.41 in patients with at least 10% of sites with probing depth ≥ 4 mm; 0.29 in patients without pockets; 0.40 in edentulous patients. |
| Slade et al. 2000      | 9145 patients without pockets; 1817 edentulous. | 0.15 in patients with generalized periodontitis; 0.09 in controls. |
| Loos et al. 2000       | 54 patients with generalized periodontitis; 43 controls. | 0.11 at baseline in periodontal patients; 0.03 of median decrease after treatment; at baseline with periodontal patients; 0.05 of median decrease after treatment. |
| Mattila et al. 2002    | 35 with adult periodontitis. | 0.40 at baseline in periodontal patients; 0.37 after treatment. |
| D’Aiuto et al. 2004    | 94 patients with severe generalized periodontitis | CRP, C-reactive protein. |
| Ide et al. 2004        | 23 patients with generalized periodontitis. | Median decrease after treatment. |
periodontal revaluation and collection of a second blood sample one month after the first. The aim of choosing different treatments was to verify if supragingival plaque control alone, obtained through hygienic therapy, could influence CRP levels.

Group 3 (14 periodontally healthy subjects) received a periodontal visit to confirm the periodontal health and the collection of a blood sample for evaluation of ESR and CRP.

Subjects of groups 1 and 2 underwent a radiological examination to obtain a radiographical status. Clinical and periodontal parameters were collected by an expert calibrated operator at baseline and at revaluation, without any blinding. The principles outlined in the Declaration Of Helsinki on clinical research involving human subjects were adhered to. All the research was conducted in accordance with Italian law.

Dental Indices

Clinical and radiographic examinations were used for each subject to obtain three dental indices that, singularly or partially associated, had already been used in previous epidemiological studies [9, 15, 16]. The indices were used to evaluate severity of periodontal disease and changes after treatment.

Panoramic Tomography Score (PTS). This was obtained by the sum of radiolucent periapical lesions, third-degree carious lesions, vertical bone pockets, furcation lesions and pericoronitis.

Clinical Periodontal Sum Score (CPSS). This represents the sum of the number of sites with probing pocket depth of 4 mm or greater, the number of gingival sites with bleeding after probing, the number of sites with visible suppuration after probing and the number of furcation lesions exceeding grade 1.

Clinical and Radiographic Sum Score (CRSS). This was calculated by the sum of the number of radiographic vertical defects, the number of furcation lesions and the CPSS.

Serum CRP Analysis

Blood samples of each patient were analyzed at the Central Laboratory of Sant’Orsola Hospital, Bologna. Serum was separated using standard laboratory techniques and C-reactive Protein was quantified by latex-enhanced nephelometry using a fully automated Behring Nephelometer Analyzer System (Dade Behring). Samples of serum were mixed with latex particles coated with anti-C-reactive protein antibodies, forming antigen-antibody complexes. Light scattering, proportional to the concentration of the analyte in the sample, was measured by nephelometric procedure. C-reactive protein concentrations in mg/dl were calculated with reference to a calibration curve. With this method the minimum detectable concentration of CRP was 0,3 mg/dl.

STATISTICAL ANALYSIS

Statistical analysis was performed using a computer statistical package (SPSS 11.0, SPSS Inc. 2001, Chicago IL). Levene statistic was used to verify the homoschedasticity of variance. The significance of differences of CRP and ESR between Groups 1, 2 (periodontal subjects) and 3 (controls) was calculated using analysis of covariance, by taking age as a covariate because of the different mean age between periodontal and healthy subjects, or Kruskal – Wallis analysis. The significance of differences between periodontal subjects (Groups 1+2) and controls (Group 3) was calculated with the Mann Whitney test or with the Student t-test. Subgroup analyses were carried out in order to verify internal comparability of each subgroup (pre-specified analyses). Finally, 95% confidence intervals were calculated.

RESULTS

Four patients of Group 1 and 6 patients of Group 2 did not come back for periodontal revaluation, so the number of periodontal patients for our analyses was reduced to 10 for Group 1 and 8 for Group 2.

Thirty-two subjects (53% males) completed the study. Participants were mostly non-smokers (75%). The two groups of periodontal subjects (groups 1 and 2) displayed a similar median age of 44-48 years. Control subjects had a median age of 33±15 years (Table 2). No significant differences were observed in demographic, dental and clinical parameters after the loss of subjects at follow-up.

Table 3 describes the subject population considering dental and clinical parameters. A reduction of clinical index CPSS at reevaluation for periodontal patients was observed: the reduction was 34% for group 1 patients and 38% for group 2 patients. Non statistically significant differences between Groups 1 and 2 (periodontal patients) were observed for clinical
index CPSS, radiographic index PTS, clinical and radiographic sum score CRSS and number of sites with probing pocket depth ≥ 4 mm.

Table 4 shows the mean values of CRP and ESR among the three groups of subjects examined at baseline and at second examination. At baseline p was equal to 0.007 for ESR with a significant interaction group-age. All the other differences were not statistically significant. Even by grouping periodontal subjects (group1 + group2), no statistically significant differences were observed with the healthy control group (group3). No significant difference of CRP values between smokers and non-smokers was observed.

Table 2: Description of the Subject Population using Age (mean ± SD), Gender and Smoking Habits

|                | Group 1 (n=10) | Group 2 (n=8) | Group 3 (n=14) |
|----------------|---------------|---------------|---------------|
| Age            | 44±12         | 48±8          | 33±15         |
| Gender         |               |               |               |
| males          | 4 (40%)       | 5 (63%)       | 8 (57%)       |
| females        | 6 (60%)       | 3 (38%)       | 6 (43%)       |
| Smoker         |               |               |               |
| No             | 7 (70%)       | 7 (87%)       | 10 (71%)      |
| ≤10/day        | 3 (30%)       | -             | 2 (14%)       |
| >10/day        | -             | 1 (13%)       | 2 (14%)       |

Table 3: Description of Subject Population Considering Dental and Clinical Parameters (mean value ± SD)

|                                             | Group 1 (n=10) | Group 2 (n=8) | Group 3 (n=14) |
|---------------------------------------------|---------------|---------------|---------------|
| Number of natural teeth                     | 25±5          | 28±2          | 30±2          |
| Number of sites with probing pocket depth ≥ 4 mm | 62±34        | 84±27         | -            |
| Panoramic Tomography Score                  | 10±6          | 9±2           | -            |
| Clinical Periodontal Sum Score              |               |               |               |
| baseline                                    | 70±36 (47-83) | 97±53 (59-135) | -            |
| revaluation                                 | 46±33 (25-67) | 60±33 (36-84) | -            |
| Clinical and Radiographic Sum Score         | 77±35         | 100±52        | -            |

DISCUSSION

Several studies in the last years have shown a possible association between periodontal disease and ischaemic heart disease (IHD) [3, 10, 11, 16, 18-20]. This association may partially be explained considering common risk factors like high levels of serum lipids, inflammatory and haemostatic factors. However, this hypothesis has not been supported by all authors. Hujoel et al. (2001) [21] argued that while periodontitis may coexist with IHD, it does not necessarily imply an

Table 4: C-reactive Protein (mg/dl) and Eritro-Sedimentation Rate (mm/h) Values Among the Subject Population (mean ± SD)

|        | Group 1 (n=10) | Group 2 (n=8) | Group 3 (n=14) |
|--------|---------------|---------------|---------------|
| CRP    |               |               |               |
| baseline | 0.34±0.13 (0.25-0.42) | 0.32±0.01 (0.30-0.34) | 0.32±0.01 (0.12-0.52) |
| revaluation | 0.42±0.28 (0.24-0.60) | 0.32±0.01 (0.30-0.34) | - |
| ESR    |               |               |               |
| baseline | 13.0±9.5 (7.0-19.0) | 9.4±7.0 (4.4-14.4) | 6.0±3.4 (4.2-7.8) |
| revaluation | 10.9±10.0 (4.7-17.1) | 5.9±3.9 (3.1-8.7) | - |

CRP, C-reactive protein; ESR, eritrosedimentation rate (95% confidence interval).
increased risk of myocardial infarction or stroke. In this case, periodontitis treatment would remove the risk of inducing coronary disease and completely edentulous subjects would have a reduced risk of IHD. Hujoel et al. found edentulous patients to have no lesser risk of developing coronary heart disease than periodontal patients [21].

Chong et al. (2000) [22] and Armitage (2000) [23], in a review of studies published in the last years, concluded that the association between periodontitis and IHD is not evident and that they could simply be parallel phenomena [24-28]. Seymour [29] and Beck et al. [27] concluded that, while many studies indicate a relationship between this two multifactorial disorders, a cause-effect relationship has not been demonstrated in any of them. However, several studies in the last years have shown that increased serum C-reactive Protein levels seem to be a risk predictor for coronary heart disease [1, 2, 5, 6, 9].

As shown in Table 1, in the National Health and Nutrition Estimates Survey III (NHANES III) reported by Slade et al. [30] and Beck et al. [31] the median value of CRP was 0.41 mg/dl for patients with more than 10% of sites with probing pocket depth ≥ 4 mm, and 0.28 mg/dl for healthy patients. Ebersole et al. [17] reported an even more evident difference between periodontal patients and controls: 0.91 mg/dl vs. 0.22 mg/dl. Instead, Loos et al. [21], Mattila et al. [9] and D’Aiuto et al. [32] observed much smaller values for both periodontal patients and controls.

In the present study, at the baseline, median CRP values among periodontal patients were not as high as those reported by Ebersole et al. [17], but similar to those reported by Ide et al. [33] and to those of the NHANES III reported by Slade et al. [30] and Beck et al. [31], where the same nephelometric method was used. With this method, the minimum detectable concentration of CRP was 0.3 mg/dl. The same nephelometric method was used in the NHANES III. The nephelometric method was also used in the studies of Ide et al. [33] and Loos et al. [21], but with a different ratio of reagent to serum in the samples, obtaining smaller minimum detectable concentrations of CRP: 0.02 mg/dl and 0.03 mg/dl respectively. Different methods were used in the studies of Montebugnoli et al. [16] and D’Aiuto et al. [32], with CRP minimum detectable values of 0.02 mg/dl. At the second examination group 1 showed an increase in the mean CRP value, in spite of a statistically significant reduction of clinical periodontal sum score. Even if this result is not statistically significant, it seems to indicate a trend completely opposite to the expected one. This could be explained by the presence of a single subject with a CRP value much bigger than the others (1.21 mg/dl). The cause of this higher value is not clear, but it was probably due to non-periodontal unrecognized reasons. The absence of statistically significant differences among periodontal and healthy groups before and after the treatment could be explained by the use of the standard nephelometric method that does not appear sensitive enough for periodontal purposes.

Smokers were included in our study, like in the studies of Ebersole et al. [17], Beck et al. [31] and Mattila et al. [9]. Smoke is considered a factor able to alter CRP levels [10, 34, 35]. However in our study, as in the studies of Friedriksson et al. [36] and Loos et al. [3], there was no statistical difference of CRP values between smokers and non-smokers.

In a recent study of D’Aiuto et al. (2004) [32] on 94 sistemically healthy subjects with severe generalized periodontitis, there was a median decrease of 0.05 mg/dl of CRP 6 months after non-surgical therapy. This decrease was observed in subjects that presented less than 30% of residual pockets and less than 30% of residual bleeding sites.

Mattila et al. [9] obtained a median decrease of 0.03 mg/dl after mechanical therapy and, when indicated, the use of metronidazole (Table 4). On the contrary no statistically significant difference for CRP values is reported before and after mechanical treatment in the study of Ebersole et al. [17].

One month after completion of mechanical treatment we observed a reduction of sites with pd ≥ 4 mm, bleeding after probing and visible suppuration in both group 1 and 2, with a consequent decrease of CPSS clinical index of 34% for patients of group 1 and 38% for patients of group 2. The greater reduction in Group 2 patients, that were not treated with scaling and root planning, was unexpected but it could be explained by the small number of patients.

Even though it is necessary to take into consideration the limited number of the subjects examined, the present study shows that (i) non-surgical therapy induces an improvement of clinical periodontal indices, even in subjects that were only instructed to correct plaque control. Moreover it appears evident that (ii) a standard nephelometric method is not sensitive...
enough to detect difference in CRP values between periodontal and non-periodontal subjects.

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REFERENCES

[1] Berk BC, Weintraub W, Alexander RW. (1990) Elevation of C-reactive protein in “active” coronary artery disease. Am J Cardiol 65: 168-172. https://doi.org/10.1016/0002-9149(90)90079-G

[2] Liuzzo G, Biasucci LM, Gallimore JR et al. (1994) The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. N Engl J Med 331: 417-424 https://doi.org/10.1056/NEJM199408183310701

[3] Loos BG, Craandijk J, Hoek FJ, Paulien ME, van Dillen V, van der Velden U. (2000) Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. J Periodontol 71: 1528-1534. https://doi.org/10.1902/jop.2000.71.10.1528

[4] Mercado FB, Marshall RL, Kielstov AC, Bartold PM. (2001) Relationship between rheumatoid arthritis and periodontitis. J Periodontol 72(6): 779-787. https://doi.org/10.1902/jop.2001.72.6.779

[5] Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. (1998) Plasma concentrations of C-reactive protein and risk of developing peripheral vascular disease. Circulation 97: 425-428. https://doi.org/10.1161/01.CIR.97.5.425

[6] Toss H, Lindhal B, Siegbahn A, Wallentin L. (1997) Prognostic value of increased fibrinogen and C-reactive protein levels in unstable coronary artery disease. FRISC study group. Fragmin during instability in coronary artery disease. Circulation 96: 4204-4210. https://doi.org/10.1161/01.CIR.96.12.4204

[7] Page, RC. (1998) The pathobiology of periodontal diseases may affect systemic diseases:inversion of a paradigm. Ann Periodontol 3, 108-120. https://doi.org/10.1902/annals.1998.3.1.108

[8] Ebersole JL, Cappelli D. (2000) Acute phase reactants in infections and inflammatory diseases. Periodontol 2000 23: 19-49. https://doi.org/10.1034/j.1600-0757.2000.230103.x

[9] Mattila K, Vesanen M, Valtonen V. et al. (2002) Effect of treating periodontitis on C-reactive Protein levels: a pilot study. BMC Infect Dis 2(1): 30. https://doi.org/10.1186/1471-2334-2-30

[10] Ridker PM, Cushman M, Stampfer MJ, Tracy PR, Hennekens CH. (1997) Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 336(14): 973-979. https://doi.org/10.1056/NEJM199704033361401

[11] Ridker PM, Hennekens CH, Buring JE, Rifai N. (2000) C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med 342(12): 836-843. https://doi.org/10.1056/NEJM2000033233421202

[12] Blake GJ, Rifai N, Buring JE, Ridker PM. (2003) Blood pressure, C-reactive protein and risk of future cardiovascular events. Circulation 108(24): 2993-2999.

[13] Noack B, Genc RJ, Trevisan M, Grossi S, Zambon JJ, De Nardin E. (2001) Periodontal infections contribute to elevated systemic C-reactive protein levels. J Periodontol 72(9): 1221-1227. https://doi.org/10.1902/jop.2000.72.9.1221

[14] Mattila KJ, Asikainen S, Wolf J, Jousimies-Somer H, Valtonen V. Nieminen M. (2000) Age, dental infections and coronary heart disease. J Dent Res 79(2): 756-760. https://doi.org/10.1177/00220345000790020901

[15] Montebugnoli L, Servidio D, Miaton RA, Prati C. (2002) Relazione tra patologia odontoiatrica e aterosclerosi. Dental Cadmos 9: 19-40.

[16] Montebugnoli L, Servidio D, Miaton RA, Prati C, Tricoci P, Melloni C. (2004) Poor oral health is associated with coronary heart disease and elevated systemic inflammatory and haemostatic factors. J Clin Periodontol 31: 25-29. https://doi.org/10.1111/j.0303-6979.2004.00432.x

[17] Ebersole JL, Machen RI, Steffen MJ, Willmann DE. (1997) Systemic acute phase reactants, C-reactive protein and haptoglobin, in adult periodontitis. Clin Exp Immunol 107(2): 347-352. https://doi.org/10.1111/j.1365-2249.1997.207-1162.x

[18] Joshipura KJ, Rimm EB, Douglass CW, Trichopoulos D Ascherio A, Willett WC. (1996) Poor oral health and coronary heart disease. J Dent Res 75(6): 1631-1636. https://doi.org/10.1177/00220345007506090301

[19] Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. (2002) Comparison of C-Reactive Protein and Low Density Lipoprotein Cholesterol Levels in the Prediction of First Cardiovascular Events. N Engl J Med 347(20), 1557-1565. https://doi.org/10.1056/NEJMoa021993

[20] Jansson L, Lavststed S, Frithiow L, Theobald H. (2001) Relationship between oral health and mortality in cardiovascular diseases. J Clin Periodontol 28: 762-768. https://doi.org/10.1034/j.1600-065X.2001.2280807.x

[21] Hujoo MP, Drangsholt M, Spierkerman C, Derouen TA. (2001) Examining the link between coronary heart disease and the elimination of chronic dental infections. JADA 132: 883-889. https://doi.org/10.14219/jada.archive.2001.0300

[22] Chong PH, Kezele B. (2000) Periodontal disease and atherosclerotic cardiovascular disease: confounding effects or epiphenomenon? Pharmacotherapy 20: 805-818. https://doi.org/10.1592/phco.20.9.805.35189

[23] Armitage GC. (2000) Periodontal infections and cardiovascular disease-how strong is this association? Oral disease 6, 335-350. https://doi.org/10.1111/j.1601-0852.2000.tb00126.x

[24] Mattila KJ, Nieminen MS, Valtonen VV. et al. (1989) Association between dental health and acute myocardial infarction. Br Med J 298: 779-781. https://doi.org/10.1136/bmj.298.6676.779

[25] Mattila KJ, Nieminen MS, Valtonen VV, Huttunen JK. (1995) Dental infection and the risk of new coronary events: prospective study of patients with documented coronary artery disease, Clin Infect Dis 20, 558-592. https://doi.org/10.1093/clinids/20.3.588

[26] Beck JD, Garcia R, Offenbacher S. (1996) Periodontal disease and cardiovascular disease. J Periodontol 67: 1123-1137. https://doi.org/10.1902/jop.1996.67.10s.1123

[27] Beck JD, Offenbacher S, Williams R, Gibbs P, Garcia R. (1998) Periodontitis: a risk factor for coronary heart disease? Ann Periodontol 3: 127-141. https://doi.org/10.1902/annals.1998.3.1.127

[28] Louis-Delgado O, Echeverria-Garcia JJ, Berini-Aytes L, Gay-Escoda C. (2004) Periodontitis as a risk factor in patients with ischemic heart disease. Med Oral 9(2): 125-137.
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[29] Seymour R.A. (2001) Heart of the matter. Br Dent J 190: 106. https://doi.org/10.1038/sj.bdj.4800896a

[30] Slade GD, Offenbacher S, Beck JD, Heiss G, Pankow GS. (2000) Acute-phase inflammatory response to periodontal disease in the U.S. population. J Dent Res 79: 49-57. https://doi.org/10.1177/00220345000790010701

[31] Beck JD, Offenbacher S. (2000) Oral disease, cardiovascular disease and systemic inflammation. Periodontol 2000; 23: 110-120. https://doi.org/10.1034/j.1600-0757.2000.230111.x

[32] D’Aiuto F, Pakar M, Andreou G. et al. (2004) Periodontitis and systemic inflammation: control of the local infection is associated with a reduction in serum inflammatory markers. J Dent Res 83(2): 156-160. https://doi.org/10.1177/154405910408300214

[33] Ide M, Jagdev D, Coward PY, Crook M, Barklay GR, Wilson RF. (2004) The short-term effects of treatment of chronic periodontitis on circulating levels of endotoxin, C-reactive protein, tumor necrosis factor- alpha, and interleukin- 6. J Periodontol 75(3): 420-428. https://doi.org/10.1902/jop.2004.75.3.420

[34] Das I. (1985) Raised C-reactive Protein levels in serum from smokers. Clin Chim Acta 153(1): 9-13. https://doi.org/10.1016/0009-8981(85)90133-0

[35] Tsiara S, Eliaf M, Mikhailidis DP. (2003) Influence of smoking on predictors of vascular disease. Angiology 54(5), 507-530. https://doi.org/10.1177/000331970305400501

[36] Fredriksson MI, Figueredo CM, Gustafsson KG, Årman BE. (1999) Effects of periodontitis and smoking on blood leucocytes and acute-phase proteins. J Periodontol 70(11): 1355-1360. https://doi.org/10.1902/jop.1999.70.11.1355

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