Effect of periodontal treatment on serum C-reactive protein level in obese and normal-weight women affected with chronic periodontitis

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ABSTRACT

الأهداف: التحقق من تأثير علاج اللثة بالطريقة التقليدية على مستويات بروتين سي الإرتكاسي، وعلى حالة الأنسجة الداعمة للأسنان لدى النساء المصابات بالسمنة والنساء ذوات الوزن الطبيعي والمصابات بالتهاب اللثة المزمن.

الطريقة: أُجريت هذه الدراسة السريرية المقارنة في كلية الأسنان، جامعة الملك عبدالعزيز، جدة، المملكة العربية السعودية وذلك خلال الفترة من ديسمبر 2009م إلى مارس 2011م. شملت الدراسة 40 سيدة مصابة بالتهاب اللثة المتوسط إلى الحاد، وقد قُسمن إلى مجموعتين وهما: 20 سيدة مصابة بالسمنة (مجموعة الدراسة)، و20 سيدة من ذوات الوزن الطبيعي (مجموعة الشاهد). ولقد قمنا باستثناء النساء المدخنات، والحوامل، والمصابات بالأمراض الجهازية. وقد قمنا بتحليل مستويات المقاييس التالية قبل وبعد العلاج بشهرين وهي: مستويات بروتين سي الإرتكاسي، ومستوى الارتباط السريري، وعمق السبر، ودرجات النزيف من اللثة.

النتائج: لقد كان علاج اللثة فعالاً في تقليل مستويات الالتهابات اللثوية، وتقليل مستويات بروتين سي الإرتكاسي في كامل عينة الدراسة وفي كلتي المجموعتين. وأشارت النتائج إلى أن مستوى هذا البروتين قد كان قبل العلاج 0.78 (±0.51)، فيما وصلت مستوياته بعد العلاج إلى 0.55 (±0.41) ملغ/لتر في مجموع العينة (p=0.001). ولوحظ أيضاً أن مدى الاستجابة للعلاج في مجموعة الشاهد قد كان أحسن من مجموعة الدراسة، غير أن هذا الفرق لم يكن كبيراً من الناحية الإحصائية حيث بلغ متوسط التغير في مستويات بروتين سي الإرتكاسي 0.28 (±0.43) و0.19 (±0.32) ملغ/لتر.

خاتمة: أظهرت الدراسة مدى فعالية علاج اللثة في تقليل الالتهاب وتقليل مستويات بروتين سي الإرتكاسي، كما لم يكن للسمنة أي تأثير سلبي على مدى الاستجابة لهذا العلاج.

Objectives: To investigate the effect of conventional periodontal therapy on serum C-reactive protein (CRP) level and periodontal status in obese and normal-weight chronic periodontitis patients.

Methods: This is a controlled clinical trial conducted at the King Abdulaziz University Faculty of Dentistry, Jeddah, Kingdom of Saudi Arabia between December 2009 and March 2011. A total of 40 women affected with moderate to severe chronic periodontitis were selected (20 obese [test group] and 20 normal-weight [control]). Smokers, pregnant women, and subjects with any systemic disease were excluded. Serum CRP level and periodontal parameters, including clinical attachment level, probing depth, bleeding on probing and plaque scores were assessed at baseline, and 2 months after non-surgical periodontal treatment.

Results: Periodontal therapy was effective in reducing gingival inflammation, as well as serum CRP level in the total sample and within each group. The pre-treatment mean level of serum CRP was 0.78 (±0.51) and post- treatment was 0.55 (±0.41) mg/l in the total sample (p=0.001). A tendency was observed toward a better systemic response to treatment in normal-weight compared to obese women, however, it was not statistically significant (the mean changes in CRP levels after therapy were 0.28 [±0.43] and 0.19 [±0.32] mg/l).

Conclusion: Periodontal treatment is effective in reducing systemic inflammation as measured by serum CRP level, and obesity does not have a major negative impact on response to periodontal therapy.

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Periodontitis, a common chronic disease caused primarily by bacterial infection, destroys the soft tissues and bone that support the teeth and ultimately may lead to tooth loss if not treated.[1] Periodontitis affects the majority of adult population worldwide, and in Saudi Arabia it was reported to affect 72%.[2,3] Recent evidences suggest that periodontal infection might also influence individuals' overall health by acting as an aggravating factor to systemic inflammation where serum levels of several inflammatory markers in periodontitis patients were significantly elevated compared to healthy controls.[4-8] Periodontal infection is implicated as a possible risk factor for cardiovascular diseases, adverse pregnancy outcome, and poor glycemic control in diabetics.[9-16] It has been shown that individuals with periodontitis are more prone to cardiovascular diseases than periodontally healthy individuals.[10,11] Pregnant women who were affected with periodontitis were found to be more likely to deliver preterm low birth weight babies when compared to periodontally healthy pregnant women.[12] Severe periodontal infection was also found to aggravate the risk of poor glycemic control in patients with type 2 diabetes.[13] Furthermore, treatment of periodontitis with scaling and root planing was suggested to reduce level of inflammatory markers such as serum C-reactive protein (CRP) level.[14-16] C-reactive protein is implicated in the pathogenesis of several chronic conditions including cardiovascular diseases.[17]

Individuals are not alike in their susceptibility to periodontitis as certain environmental and systemic factors (such as smoking and diabetes) increase the risk for developing periodontitis.[2] Obesity has recently been suggested as a possible risk factor for periodontitis.[18-22] In one study, it was considered to be the second strongest risk factor for periodontitis preceded only by smoking.[22] The biological mechanism by which obesity may predispose to periodontitis is not totally understood. A probable mechanism is through increasing secretion of certain proinflammatory cytokines that are known to be associated with destruction of periodontal tissues, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α).[19] Several proinflammatory molecules, including TNF-α and IL-6, have been shown to be synthesized and secreted by adipose tissue.[23-25] Both TNF-α and IL-6 induce acute-phase hepatic protein production such as CRP.[26] They might also impair intracellular insulin signaling, and subsequently may lead to insulin resistance.[23,27] Elevated plasma levels of TNF-α, IL-6, and CRP are associated with obesity and insulin resistance.[24,27] Insulin resistance has recently been suggested to explain the association between obesity and periodontitis.[28] Although obesity might contribute to the development of periodontitis, little is known about the effect of obesity on the outcome of periodontal treatment.[29] The objectives of this study were to examine the effect of periodontal treatment on serum level of CRP in patients affected with moderate /severe periodontitis and to determine if the response to periodontal therapy differs between obese and normal-weight chronic periodontitis patients.

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Methods.

Study population and design. The sample for the present study was recruited from an adult patient population who attended the Faculty of Dentistry clinics at King Abdulaziz University (KAU), Jeddah, Kingdom of Saudi Arabia between December 2009 and March 2011. Since the prevalence of smoking among male patients affected with periodontitis is high, only female patients were recruited. The study was conducted in full accordance with the principles of Helsinki Declaration and was reviewed and approved by Deanship of Scientific Research at KAU. An informed consent was obtained from each participant prior to their enrollment in the study.

Female patients, 35 years of age or older who suffer from generalized moderate/severe chronic periodontitis, and have at least 20 teeth were asked to participate. Classification of periodontitis was made according to the criteria of the American Academy of Periodontology International Workshop for Classification of Periodontal Diseases.[30] Specifically, individuals were considered to have generalized moderate/severe chronic periodontitis if they had ≥3mm of clinical attachment loss at ≥30 of the sites. Those with any of the following criteria were excluded: (1) presence of systemic diseases or infection, (2) periodontal therapy in the previous 12 months (3) systemic antibiotic use in the previous 3 months, (4) pregnancy or lactation, (5) smokers, and (6) those who require antibiotic prophylaxis before periodontal treatment. A total of 40 consecutive female patients, 20 obese and 20 normal-weights were included. A full mouth periodontal examination, excluding third molars and partially erupted teeth, was performed for

each participant by a single calibrated examiner who achieved a 93% intra-examiner reliability in detecting probing depth within 1mm. Intra-examiner reliability was calculated by comparing 2 measurements performed on 5 chronic periodontitis patients not related to the study. Blood samples were obtained and stored for measurement of CRP. Then, periodontal treatment consisting of oral hygiene instruction and scaling and root planing were performed by one operator. Another full mouth periodontal examination and blood sample collection was performed to all participants after 2 months.

Study variables. Weight in kilograms and height in meters were measured. Body mass index (BMI), was then computed from weight in kilograms divided by the square height in meters. Obese subjects were those with BMI of ≥30 kg/m^2 and normal-weight with 18.50 to <25 kg/m^2. Socio-demographics and periodontitis risk factors were obtained from all participants. Periodontal assessment was undertaken by recording the following clinical parameters at 6 sites per each tooth: probing depth (PD), gingival recession (GR), clinical attachment level (CAL), bleeding on probing (BOP), and plaque scores (PS). Probing depth was recorded in mm using a manual periodontal probe as the distance from the free gingival margin (FGM) to the bottom of the sulcus/pocket. Whereas, the distance from the cemento-enamel junction to the FGM represented GR. Clinical attachment level was calculated from the measurements of GR and PD. Bleeding on probing was recorded by visual observation of the presence of bleeding (yes or no) after a site has been probed for a pocket depth measurement and then the percentage of sites with BOP for each patient was calculated. Presence of plaque deposits was recorded as yes or no prior to the assessment of probing depth and then the percentage of sites with plaque deposits for each patient was calculated.

To assess serum CRP level, blood samples were drawn at baseline and at 2 months after treatment. The samples were then coded so that the technician conducting laboratory assay was blinded to subjects' identity and study sequence. Blood samples were immediately stored at -80°C. Samples were processed by an experienced technician using the Enzyme Linked-Immuno- Sorbent Assay (ELISA) for quantification of serum CRP levels.

Statistical analysis. Descriptive statistics and distribution of the continuous variables were conducted to explore the data. Socio-demographics, periodontal parameters, and CRP were compared between the test and control group at baseline using independent sample t-test. The difference in the mean values of periodontal parameters and serum CRP, between baseline and 2 months post-treatment, were compared between the test and control group using independent sample t-test. Within each group the mean values at baseline and at 2 months were compared using paired t-test. All the statistical tests were 2 tailed and *p*-value <0.05 was considered statistically significant. Sample size calculation was conducted using standalone power analysis statistical program (G*Power 3.1.3, Kiel, Germany). A sample size of 17 subjects per group was needed in order to detect an effect size (delta) of one in the study parameters at an alpha level of 0.05 with 80% power.

Results. The mean age of study sample was 43.7 (±8) years. The mean age was not significantly different between obese (mean age, 44 [±8.4]) and normal-weight group (mean age, 43.4 [±7.8]), (*p*=0.80). Periodontal parameters were not significantly different between the

Table 1 - Clinical periodontal parameters and C-reactive protein at baseline in obese and normal-weight women included in this study at the Faculty of Dentistry clinics at King Abdulaziz University (KAU), Jeddah, Kingdom of Saudi Arabia.

Parameters	Obese (n=20)	Normal-weight (n=20)	*P*-value
Clinical attachment level (mm)	3.37±0.80	2.95±0.76	0.093
Probing depth (mm)	2.70±0.48	2.60±0.46	0.527
Probing depth ≥5 mm (%)	6.90±8.49	6.40±8.09	0.850
Plaque score (%)	70.44±24.49	57.37±23.33	0.097
Bleeding on probing (%)	81.29±18.95	74.83±23.16	0.346
C-reactive protein (mg/l)	0.96±0.41	0.60±0.56	0.025

Data are expressed as mean±standard deviation

Table 2 - The effect of periodontal treatment on the clinical periodontal parameters and C-reactive protein in the total sample (n=40) of women in a study at the Faculty of Dentistry clinics at King Abdulaziz University (KAU), Jeddah, Kingdom of Saudi Arabia.

Parameters	Pre-treatment	8 weeks post-treatment	*P*-value
Clinical attachment level (mm)	3.16±0.80	2.88±0.67	0.002
Probing depth (mm)	2.65±0.47	2.44±0.41	0.001
Probing depth ≥5 mm (%)	6.65±8.19	3.08±3.58	0.002
Plaque score (%)	74.25±4.86	45.11±5.01	0.001
Bleeding on probing (%)	66.39±22.69	34.45±15.70	0.001
C-reactive protein (mg/l)	0.78±0.51	0.55±0.41	0.001

Data are expressed as mean±standard deviation

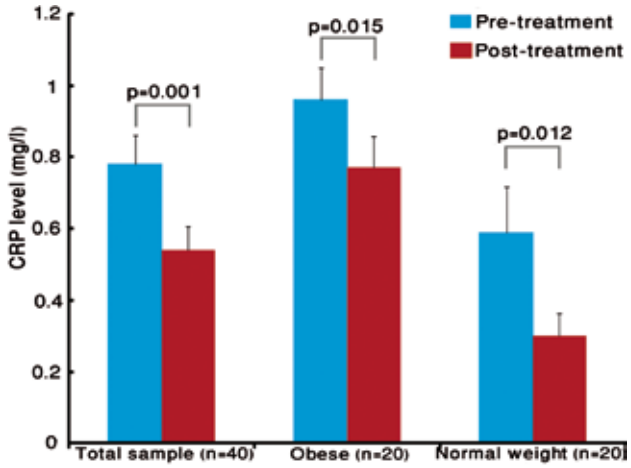

Figure 1 - The mean C-reactive protein level (CRP) (mg/l) before and after periodontal treatment in obese and normal-weight women included in this study at the Faculty of Dentistry clinics at King Abdulaziz University (KAU), Jeddah, Kingdom of Saudi Arabia.

Table 3 - Mean differences in periodontal parameters and C-reactive protein between pre- and post-periodontal therapy in obese and normal-weight women included in this study at the Faculty of Dentistry clinics at King Abdulaziz University (KAU), Jeddah, Kingdom of Saudi Arabia.

Parameters	Obese (n=20)	Normal-weight (n=20)	Between groups *p*-value
Clinical attachment level (mm)	0.29 ±0.53	0.27±0.57	0.938
Probing depth (mm)	0.23±0.33	0.19±0.27	0.663
Probing depth ≥5 mm (%)	3.85±6.89	3.30±6.94	0.803
Plaque score (%)	32.97±18.42	13.83±4.64	0.105
Bleeding on probing (%)	34.88±18.47	20.20±5.52	0.207
C-reactive protein (mg/l)	0.19±0.32	0.28±0.43	0.480
Data are expressed as mean ±SD			

2 groups at baseline; whereas, CRP was significantly higher in the obese group (**Table 1**). The mean CRP was 0.96 (±0.41) mg/l in the obese versus 0.60 (±0.56) mg/l in the normal-weight group, (p=0.025). There was also a trend toward a better periodontal health among normal-weight as compared to the obese women. The mean clinical attachment loss was 3.4 (±0.8) mm among the obese versus 2.95 (±0.76) mm among the normal-weight (p=0.09). After periodontal treatment, there was a significant decrease in all clinical periodontal parameters as well as CRP level in the total sample and within each group as shown in **Table 2** and **Figure 1**. Although the decrease in CRP level in normal-weight group was greater than that in the obese group; the difference between groups was no statistically significant (p=0.48) as shown in **Table 3**.

Discussion. In the present study, the effect of periodontal therapy on serum CRP level and periodontal status in obese and normal-weight women affected with chronic periodontitis was studied. The results showed that periodontal therapy is effective in reducing gingival inflammation as well as serum CRP level in the total sample and within each group. These results are consistent with previous studies that showed a decrease in CRP level after treatment of periodontitis with scaling and root planing.[14,15,31-33] In contrast, other studies did not show a change in CRP level after periodontal therapy.[34,35] The variability in the results among different studies could be attributed to differences in baseline values of inflammatory markers, characteristics and susceptibility of the studied population, and periodontitis severity. The time interval between periodontal treatment and blood collection for CRP level assessment varies among different studies. Ide et al[34] found no reduction in CRP level 6 weeks after periodontal treatment whereas Mattila et al[33] observed a reduction in CRP levels at 6-week post-treatment. Iwamoto et al[15] collected blood 4 weeks post-periodontal therapy and reported a significant reduction in CRP, whereas Elter et al[36] reported a trend but no significant reduction in serum levels of CRP during the 4-week interval. In other studies, a significant reduction in CRP was only found 6 months after periodontal treatment.[31,32] In the present study, evaluation of response to periodontal therapy and the assessment of CRP level post-treatment were undertaken 2 months post-treatment. The choice of the 2 months follow up is based on the conclusion from a previous critical review of the literature.[37]

The observed decrease in the CRP level after periodontal therapy in the present study is probably due to the marked reduction in the infection burden. Periodontitis is primarily caused by Gram-negative bacteria that are part of the plaque biofilm deposited on the teeth.[1] These periodontal pathogens are involved in aggravating systemic inflammation and immune response in addition to their role in increasing gingival inflammation and destruction of periodontal tissue. Periodontal therapy is effective in reducing local inflammation and improving the periodontal clinical parameters by reducing bacterial load in periodontal pockets and improving the antibody titers and avidity to periodontal pathogens. This in turn may decrease the infection burden and systemic inflammation.

The findings of the present study showed a trend toward a better systemic response to periodontal therapy in normal-weight compared to obese women; the difference however, was not statistically significant. These findings support the results of a recent study in which obesity was not found to negatively interfere with the improvement in the periodontal clinical parameters or the decrease in the circulating proinflammatory cytokine levels after periodontal treatment.[29] In the present study, the definition of obesity was based on the body mass index (BMI) which is highly associated with fat mass and morbidity and mortality.[38] Although BMI adequately predicts obesity-related disease risk in most populations, it has some limitations. For example, the BMI does not consider body fat distribution and therefore does not differentiate between abdominal and general obesity. Abdominal obesity is associated with a higher morbidity than general obesity.[39] Future studies that include other measures of obesity such as waist circumference are warranted. The periodontal therapy in the present study consisted of the common initial treatment of periodontitis in clinical practice, namely, oral hygiene instructions and removal of bacterial plaque and calculus deposits from the tooth surfaces. Although this therapy has resulted in a marked improvement in periodontal status, periodontal inflammation was not completely eliminated. Response to other forms of periodontal treatment such as surgical periodontal therapy might show different results from the one observed in the present study.

Study limitation. It has to be noted that this study included only women; therefore, it does not provide evidence on the effect of non-surgical periodontal therapy in obese men.

In conclusion, the results of the present study confirm the effect of periodontal therapy on reducing systemic inflammation in both obese and normal-weight women. Further studies need to assess the effect of surgical periodontal therapy on CRP and other systemic inflammatory markers such as TNF-α and IL-6 in obese individuals. As periodontitis is a common infectious disease in Saudi Arabia, prevention and management of periodontal infection might have a substantial health implication. Furthermore, health care providers need to consider periodontal infection as a potential reason for increasing level of serum CRP.

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Ethical Consent

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.