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Original Research

Short-Term Effectiveness of Scaling and Root Planning on Periodontal Parameters, Systemic Inflammatory, and Oxidative Stress Markers in Smokers with Chronic Periodontitis

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Abstract:

Background: Tobacco smoking is one of the main risk factor associated with periodontitis and has long-term altered inflammatory, immunological, and therapy response. This study comparatively assesses the short-term effectiveness of scaling and root planing (SRP) on clinical periodontal parameters, some systemic inflammatory and oxidative stress (OS) markers between male smokers and nonsmokers with chronic periodontitis (CP).

Materials and Methods: The study groups comprised of 131 males with severe CP (clinical attachment loss [CAL] ≥ 5 mm). They were divided into Group I (n = 51, mean age: 40.9 ± 4.6) without smoking habits (CP), and Group II (n = 80, mean age: 44.1 ± 5.81) with smoking habits (CPSM). The clinical periodontal evaluation was done by measuring gingival index (GI), plaque index, probing depth, and CAL using a UNC-15 probe. The biochemical markers estimated were interleukin (IL)-6, 10, C-reactive protein, total antioxidant capacity (TAOC), RBC - superoxide dismutase, glutathione peroxidase), vitamin C, and malondialdehyde (MDA). SRP was performed on both the study groups with a follow-up after 3 months. The periodontal status and biochemical markers were estimated at baseline and post-treatment.

Results: Smokers with CP showed significantly higher (P < 0.001 for all parameters) periodontal damage and higher systemic inflammatory and OS markers compared to non-smokers with CP (P ≤ 0.05 for TAOC, GPx, Vitamin C and MDA). Post SRP improvements in the mean values (compared to baseline values) were observed in both the groups (P < 0.001 for all parameters). Comparatively, the CPSM group showed significantly lower (P ≤ 0.05 for all parameters) relative % change post SRP in the study parameters than those of CP group.

Conclusions: Smokers with CP exhibited more periodontal damage and higher systemic inflammatory and OS burden than nonsmokers with CP. Under the study condition, SRP was effective in improving periodontal and systemic inflammatory and OS markers in both the groups, although the improvement was lower in smokers than non-smokers. SRP could be a useful supportive therapy in checking periodontitis induced inflammation and OS burden on the systemic health of smokers.

Key Words: Biochemical markers, chronic periodontitis, oxidative stress, root planing smoking

Introduction

Smoking represents a major preventable cause of many human diseases.[1] One among them is chronic destructive periodontal disease.[2] Smokers show severe sub-gingival calculus formation[2] and are more likely to have severe periodontitis compared to the non-smokers.[3] Smoking is also associated with oxidative stress (OS), in which smoke derived oxidants are the major factors in inflammatory reactions. An alteration in antioxidant defenses and upregulation of inflammation by these oxidants may lead to an extensive oxidative damage.[4-6]

With respect to periodontal tissue damage, smoking has a long term chronic effect on the local oral inflammatory and immune response.[7] It has also been implicated as a factor that reduces the effectiveness of periodontal treatment. Smokers respond to scaling and root planing (SRP) less favorably than non-smokers, especially in terms of probing level and bone level.[8] Smoking may alter the healing response through increased activity of proteolytic enzymes directed against the structural elements of periodontium, elevated levels of destructive inflammatory cytokines, and suppression of regenerative functions of periodontium.[9] The primary reason for development of periodontitis is the continued presence of periodontopathogens in the periodontium. Mechanical removal of these pathogens can reduce the inflammatory burden, but smokers show a resistance to lowering of them.[9]

Keeping in mind the above facts, this study comparatively assess the effectiveness of SRP on clinical periodontal

parameters in conjunction with systemic inflammatory and OS markers in male smokers and nonsmokers with chronic periodontitis (CP). We hypothesize that the SRP may be useful in controlling the oral inflammation derived OS in this higher risk group.

Materials and Methods

The study was approved by the Institutional Ethics Committee (registration number: 391/CPCSEA) of Grant Medical College and Sir J. J. Group of Hospitals, Mumbai. All the enrolled participants gave written consent and had the right to refuse or to withdraw consent to participate at any time without reprisal. This longitudinal study spanned a period from March 2009 to June 2011. The sample size for the study groups were calculated using the software, n-Master 2.0 (Biostatistics Department, CMC Vellore, India) keeping 5% α-error (95% CI) and 80% power.

Study groups

Individuals visiting the Department of Dentistry, Grant Medical College, Mumbai, constituted the study population, who were clinically evaluated for CP according to the criteria of the American Academy of Periodontology (1999),[10] and the periodontal examination was performed as documented by Armitage.[11] They were further grouped into the study groups based on their smoking status.

Group I (CP): Never smoker with severe CP (clinical attachment loss [CAL] ≥ 5 mm); *n* = 51 (mean age 40.9 ± 4.6)

Group II (CPSM): Current smoker with severe CP (CAL ≥ 5 mm); *n* = 80 (mean age 44.1 ± 5.81)

The enrolled participants were otherwise healthy, without any major illness and consumption of antioxidants, antibiotics, anti-inflammatory, or any other drugs, and had not received any periodontal therapy for at least 6 months prior to the inception of the study. Those excluded were diabetics, alcoholics, having a past illness and receiving any treatment (including periodontal treatment).The patients in the smoker group were current smokers (predominantly cigarette smokers) with smoking habit for over 3 years and frequency of smoking ≥ 5 cigarettes/day (as reported during interview and clinical evaluation). They have also reported the absence of any major illness and medication. Smokers with any systemic illness, other oral diseases, and who had received periodontal therapy in the last 6 month before the inception of the study were excluded.

Clinical measurements

The periodontal status of all individuals was evaluated by measurement of gingival index (GI) as developed by Loe and Silness (1963),[12] plaque index (PI) as described by Silness and Loe (1964).[13] The probing depth (PD) and the CAL measurements were recorded at six sites around each tooth (i.e., mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual).[11] All clinical measurements were evaluated by a single investigator using University of North Carolina (UNC-15) probe (Hu-Friedy, Chicago).

Sample collection

Venous blood (4 ml) from all the participants was collected following standard precautionary measures. Of this, 1 ml blood was subjected for plasma preparation which was used for analysis of total antioxidant capacity (TAOC), RBC-SOD, and GPx. The remaining 3 ml of blood was used to obtain serum, which was stored at −4°C until further analysis. The serum was analyzed for IL-6, 10, CRP, vitamin C, and malondialdehyde (MDA). All the biochemical markers (except IL-6 and -10) were measured on calibrated semi auto analyzer BIOTRON BTR-830 (Ranbaxy Laboratories, India). IL-6 and -10 were analyzed using quantitative chemiluminescence assay (IMMULITE 1000, SIEMENS, Germany). The blood samples were collected twice once at baseline and 3 months post SRP therapy.

Biochemical studies

Inflammatory markers

IL-6/-10 were analyzed using the quantitative chemiluminescence assay (IMMULITE 1000), following the instruction of the manufacturer. Briefly, 100 μl of serum was loaded in the respective test units and was allowed to react with respective IL assay reagents, which contains alkaline phosphatase conjugated to murine monoclonal anti IL-6/-10 antibodies, respectively, in the buffer. The standard calibration was done using IL adjusters provided with a kit that contains low and high lyophilized ILs in a nonhuman serum matrix. Serum CRP was measured by the quantitative latex turbidity method using the CRP-TURBI kit from Spinreact (Spain) [14] according to the manufacturer's instructions.

OS markers

Plasma TAOC was measured by the Ferric Reducing Ability of Plasma assay according to the method of Benzie and Strain.[15] The RBC-SOD and GPx were measured using the RANSOD kit[16] and RANSEL kit[17] respectively (Randox Laboratories, UK). Serum vitamin C content was measured using the dinitrophenylhydrazine method.[18] Serum MDA was estimated according to the method of Satoh.[19]

Periodontal therapy

Group I and Group II patients received periodontal therapy, which included SRP and oral hygiene instructions. The instructions included a demonstration of Bass technique of brushing[20] and information to brush twice daily after meals. The SRP was performed by qualified periodontologists using an ultrasonic instrument (Electro Medical System, Switzerland) and manual Gracey curettes (Hu-Friedy, Avco). The patients were followed up after 3 months for periodontal and biochemical evaluation.

Statistical analysis

The measured clinical parameters and biochemical markers were subjected to statistical analysis using Statistical Package for Social Sciences (IBM-SPSS statistics, version 20). The values were expressed as mean ± standard deviation across the study groups. The normality assumption for the study parameters was tested using criteria recommended by George and Malery 2003.[21] Independent sample *t*-test was employed to find statistical significance for baseline mean values of the study parameters and paired sample *t*-test was used for comparing the baseline and post-treatment mean values. Relative percentage change for each study parameters is calculated using the following formula; (pretreatment value - post-treatment value/ pretreatment value * 100) and the statistical significance was checked by independent sample *t*-test. $P < 0.05$ is considered to be statistically significant for all the statistical tests employed.

Results

Clinical measurements

The comparison of baseline clinical measurements between the CP and CPSM groups indicate a significant difference ($P < 0.001$ for all) in clinical parameters (Table 1).

Following SRP therapy, the paired t-test showed significantly lowered ($P < 0.001$ for all) clinical parameters compared to their corresponding baseline values in both the Groups (Table 2). The relative % change in clinical parameters with respect to baseline values in CPSM and CP Groups ranged between 3.31-36.6% and 14.58-43.21%, respectively, and was significantly lower ($P < 0.001$ for all except GI, $P = 0.098$) in CPSM than CP Group (Graph 1).

Biochemical studies

The baseline comparison of biochemical markers evaluated between the two study groups revealed significantly higher ($P = 0.012$) MDA and significantly lowered ($P < 0.05$) TAOC, GPx, and Vitamin C in CPSM group than CP Group. IL-6, CRP, and RBC-SOD were relatively higher, and IL-10 was relatively lower in CPSM Group, but could not reach statistical significance ($P > 0.05$) compared to those of CP Group (Table 1).

After SRP therapy, the average post-treatment values got significantly changed ($P < 0.001$) compared to their corresponding baseline values in both the Groups (Table 2). The relative % change in biochemical parameters with respect to baseline values in CPSM and CP Groups ranged between −13.28% to 14.56% and −22.31% to 33.53%, respectively, and was significantly lower ($P < 0.001$ for all) in CPSM compared to those of CP Group (Graph 1).

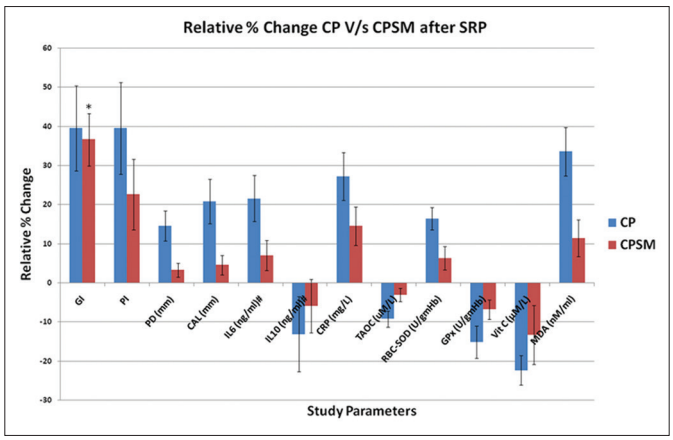
Discussion

Tobacco smoking shifts the balance between destructive cytokines and protective cytokines such that a destructive profile is more prevalent in smokers, which may have a negative periodontal effect.[22] Smoking may have negative periodontal effects through vascular alterations, altered neutrophil function,[2,3,7,23] decreased IgG production,[24] decreased lymphocyte proliferation,[25] increased prevalence of periodontopathogens,[7] bone resorption,[26] and altered fibroblast attachment and functions.[22,27] These in turn pose difficulty in eliminating pathogens by mechanical therapy showing a negative local effect on the periodontium.

Table 1: Comparison of baseline clinical parameters and biochemical markers between CP and CPSM groups.

Clinical parameters	Mean±SD		*P** value
	Group CP (*n*=51)	Group CPSM (*n*=80)	
GI	2.40±0.47	1.83±0.45	<0.001
PI	2.35±0.55	2.98±0.51	<0.001
PD (mm)	5.41±0.45	5.82±0.48	<0.001
CAL (mm)	7.63±0.90	8.45±0.96	<0.001
Biochemical markers			
Inflammatory			
IL6 (ng/ml)#	18.59±4.71	20.05±3.85	0.194
IL10 (ng/ml)#	6.41±1.12	5.75±2.48	0.190
CRP (mg/L)	3.39±0.35	3.48±0.49	0.242
Oxidative stress			
TAOC (uM/L)	860.69±74.41	810.00±78.07	<0.001
RBC-SOD (U/gHb)	534.86±81.06	549.63±68.70	0.266
GPX (U/gHb)	8.76±1.34	8.09±0.97	0.003
Vitamin C (μM/L)	27.06±2.65	21.84±2.78	<0.001
MDA (nM/ml)	4.31±0.37	4.51±0.49	0.012

Values for mean±SD, *P values are obtained using independent sample *t*-test, *P* values<0.05 is considered to be statistically significant #*n*=30, CRP: C-reactive protein, TAOC: Total antioxidant capacity, SOD: Superoxide dismutase, GPX: Glutathione peroxidase, MDA: Malondialdehyde, GI: Gingival index, CAL: Clinical attachment loss, IL: Interleukin, PI: Plaque index, PD: Probing depth, SD: Standard deviation, CP: Chronic periodontitis



Graph 1: Relative % change in clinical parameters and biochemical markers after scaling and root planing between chronic periodontitis and CPSM groups, Values are mean ± standard deviation, relative % change is calculated using the formula ([Pre-treatment value–Post-treatment value]/ Pre-treatment value *100), Negative value indicates post-treatment higher value and vice versa. *P* values are obtained using independent sample *t*-test, *P* values < 0.05 is considered to be statistically significant # *n*=30, *$P = 0.098$ for GI, $P < 0.001$ for all parameters

Table 2: Comparison of baseline and post-treatment values of clinical parameters and biochemical markers in CP and CPSM Groups.

Clinical parameters	Mean±SD				*P** value
	CP (*n*=51)		CPSM (*n*=80)		
	Baseline	Post-treatment	Baseline	Post-treatment	
GI	2.40±0.47	1.47±0.48	1.83±0.45	1.15±0.30	<0.001
PI	2.35±0.55	1.39±0.49	2.98±0.51	2.32±0.53	<0.001
PD (mm)	5.41±0.45	4.65±0.51	5.82±0.48	5.63±0.47	<0.001
CAL (mm)	7.63±±0.90	6.10±1.02	8.45±0.96	8.06±0.94	<0.001
Biochemical markers					
Inflammatory					
IL6 (ng/ml)#	18.59±4.71	14.65±4.12	20.05±3.85	18.60±3.57	<0.001
IL10 (ng/ml)#	6.41±1.12	7.19±1.08	5.75±2.48	6.00±2.43	<0.001
CRP (mg/L)	3.39±0.35	2.39±0.38	3.48±0.49	2.98±0.52	<0.001
Oxidative stress					
TAOC (μM/L)	860.69±74.41	910.0±68.01	810.0±78.07	834.88±83.9	<0.001
RBC-SOD (U/gHb)	534.86±81.06	442.8±71.46	549.63±68.7	515.88±73.4	<0.001
GPX (U/gHb)	8.76±1.34	9.63±1.09	8.09±0.97	8.65±1.07	<0.001
Vitamin C (μM/L)	27.06±2.65	30.99±3.73	21.84±2.78	24.69±3.11	<0.001
MDA (nM/ml)	4.31±0.37	2.70±0.45	4.51±0.49	4.00±0.52	<0.001

Values for mean±SD, * *P* values are obtained using paired sample *t*-test, *P* values<0.05 is considered to be statistically significant. *P* value is<0.0001 for both the study groups. #*n*=30, SD: Standard deviation, CRP: C-reactive protein, TAOC: Total antioxidant capacity, SOD: Superoxide dismutase, GPX: Glutathione peroxidase, MDA: Malondialdehyde, GI: Gingival index, CAL: Clinical attachment loss, IL: Interleukin, PI: Plaque index, PD: Probing depth, SD: Standard deviation, CP: Chronic periodontitis

Furthermore, the inflammatory cytokines alter the ratio of RANKL/OPG (important factors for bone resorption and modeling) and lead to greater bone loss in smokers.[22,27] Similarly, significantly elevated proinflammatory cytokines and chemokines[25,28] and decreased levels of regulator T-cells and NK-cells reflects the immunosuppressant effects of smoking which leads to an enhanced susceptibility to periodontitis.[25] With all the above alterations a tainted clinical observation with respect to periodontal parameters may be expected in smokers. The present study has observed that CPSM group showed significantly ($P < 0.001$) lower GI and higher PI, PD, and CAL as compared to CP group. The obtained results are in accordance to the studies.[27-29] Post SRP improvement in clinical parameters was observed in both the groups. However, the smokers showed lower therapy response compared to non-smokers. The PD and CAL measurements are the best way to assess the presence or absence of additional periodontal damage,[11] post SRP improvement in these parameters are significantly lower in CPSM than CP group (Graph 1), which shows that periodontal tissue healing and gain in attachment level is much lower in smokers than in non-smokers. This could be attributed to the negative effect of smoking on therapy outcome with respect to clinical parameters as also documented by Shiloah *et al.* 2014.[30]

This study has also tried to assess the systemic inflammatory and OS markers and effect of SRP on them in smokers with periodontitis. Nicotine or its metabolite can modulate pro and anti-inflammatory cytokine profile like; IL-1, IL-6, TNF-α, IL-10, etc., and may lead to immunosuppression and/or reduction in inflammatory response.[31] Macrophages from smokers release greater amounts of matrix metallo proteiases-9 and tissue inhibitor of metallo proteiases-1 and produce more TNF-α and IL-10.[32] Elevated IL-6 and CRP was reported in chronic obstructive pulmonary diseases associated current smokers than respective controls.[33] Cesar-Neto *et al.* 2007[34] showed significantly higher levels of some inflammatory cytokines like IL-1β, IL-8 in periodontal tissues of CP than healthy individuals, furthermore, depressed IL-10 level was reported in smokers with periodontitis than in non-smokers.[34] In the present study also it was found that IL-10 in CPSM group was relatively lower than CP and IL-6 was relatively higher, but the values did not reach statistical significance ($P = 0.190$ and 0.194 respectively) (Table 1). SRP resulted in significantly improving IL-10 and decreasing IL-6 ($P < 0.001$) in both the groups (Table 2), which is similar to the findings of the studies.[35,36] Furthermore, CRP, an acute phase systemic inflammatory marker was reported to be significantly higher[37] and non-significant slightly higher[38] in smokers than non-smokers with periodontitis. Shimada and Komatsu 2010,[39] showed that SRP was effective in decreasing CRP levels in both smokers and non-smokers with CP. The present study has observed relatively higher, but non-significant ($P = 0.242$) levels of CRP in CPSM compared to CP group (Table 1). Further, the SRP therapy was helpful in improving CRP in both the groups ($P < 0.001$) (Table 2). Overall, the inflammatory markers were higher in smokers than non-smokers and SRP was effective in lowering IL-6, CRP, and improving IL-10 in both the groups. However, the improvement in these markers was lower in smokers than non-smokers (Graph 1) that could be again attributed to the negative effect of smoking on cytokine and inflammatory balance.

An imbalanced cytokines and inflammatory status are associated with a disturbed oxidant: Antioxidant balance. Various studies[4,5,40] in literature have associated cigarette smoking and OS, and most of them have observed higher incidences of OS in smokers. Smoking may directly be the

source of OS and when it is associated with periodontitis may contribute additionally to the OS burden in the host.[4,5,40] In our previous study,[41] we have demonstrated higher OS in smokers than non-smokers with periodontitis and also discussed the effect of SRP in CP group.[42] The present study emphasizes the effect of SRP on OS markers in CPSM Group and the comparison of relative % change between CPSM and CP groups.

Buduneli *et al.* 2006[40] reported insignificant difference in TAOC levels post therapy in smokers with gingivitis and Akpinar *et al.* 2013[43] reported the insignificant difference in serum total AO status after 6 weeks of SRP therapy. However, serum TOS were significantly reduced after SRP.[43] The insignificant change in above studies could be due to recruitment of patients with gingivitis and follow-up after 6 weeks, respectively. However, Guentsch *et al.* 2008[44] reported improved TAOC following SRP therapy in smokers with periodontitis which is in accordance with the results of the present study. Smoking is associated with altered expression and activity of AO enzymes specially SOD[38,43-45] and GPx.[46-49] The present study has observed a relatively higher but non-significant ($P = 0.266$) RBC-SOD activity and significantly lower ($P = 0.003$) GPx activity in CPSM than CP (Table 1). The SRP was effective in significantly ($P < 0.001$) lowering SOD activity and improving GPx activity in both the groups (Table 2). Yoshie H et al 2007[50] have evaluated salivary aspartate aminotransferase, alanine aminotransferase, and low-density lipoprotein levels which reflected inflammation and destruction of periodontal tissue and reported that SRP was effective in reducing the inflammatory enzymes in CP patients. On a similar paradigm, the AO enzymes may change after SRP in smokers. However, their smoking habit may hamper the effectiveness of therapy outcome in improving these markers up to the levels of non-smokers.

Another important element involved in maintaining the antioxidant defense is vitamin C. Studies[4,51] have documented lower vitamin C levels in smokers than in non-smokers, which is in accordance with our study, where it is significantly ($P < 0.001$) lowered in CPSM than in CP group (Table 1). Furthermore, SRP was helpful in improving vitamin C level significantly ($P < 0.001$) in both the groups (Table 2). Effect of SRP with respect to vitamin C levels in smokers with periodontitis is contradictory. Buduneli *et al.* 2006[40] reported statistically insignificant change in salivary vitamin C concentration in smokers with gingivitis after 1 month of SRP, while Mathias *et al.* 2014[52] showed increased levels of vitamin C in 38% of smokers with periodontitis. The present study has demonstrated significant ($P < 0.001$) improvement in vitamin C post SRP in both the groups (Table 2). Tobacco smoke can be the cause of a gingival damage by decreasing vitamin C, operating through a vasoconstriction, and a reduction of AO properties.[51] Vitamin C might play a critical role in the etiology and/or progression of periodontitis in smokers. Smoking contributes to oxidative tissue damage and given the AO properties of vitamin C, it might act as a potential moderator in smoking-periodontitis relationship.[53]

The degree of oxidant: antioxidant imbalance is also evaluated by measuring the levels of MDA, which is one of the customarily used indicators of lipid peroxidation (LPO) and may be a potential biomarker indicating OS.[54] The effect of ROS in periodontitis is enhanced due to smoking which may increase the tissue destruction resulting from OS and leads to higher LPO. Increased circulating products of LPO (F_2- isoprostanes) in smokers have been documented[55]. Similar observations of higher MDA among the smokers are also reported by studies.[4,44,45,47,56] which is in accordance to our finding (Table 1). Futhermore, SRP showed significant ($P < 0.001$) improvement in MDA levels in both the groups (Table 2). Similar to our finding, studies in the literature have reported that SRP therapy significantly decreases TBARs[29] and MDA[44] in smokers with periodontitis. Since SRP is involved in the removal of periodontopathogens; a source of local and systemic inflammation and OS, induced through LPO. The net effect of the therapy has been observed in lowering LPO products like MDA.

Smoking has been implicated as a factor that reduces the effectiveness of periodontal treatment. Smokers may respond to non-surgical periodontal therapy less favorably than non-smokers.[8] The effect of smoking on non-surgical therapy includes decreased clinical response, decreased the reduction in pocket depth, and decreased gain in clinical attachment.[26] Smoking also increases the risk of having clusters of periodontopathogens after periodontal treatment.[57] In sync with the above theories, the present study showed significantly ($P < 0.001$) lowered SRP response in CPSM group compared to CP (Graph 1) which could be attributed to smoking habits of individuals in CPSM group. Erdemir *et al.* 2007[58] reported that the clinical response to nonsurgical intervention is impaired in smoking and it seems to negatively influence the serum markers like folic acid following a non-surgical intervention. In light of this, our study also shows that clinical response to SRP was compromised in smokers, which seems to negatively influence the serum regulators of inflammation, antioxidant defense, and tissue repair as evident from the obtained results. Taken together, the present study has observed that smokers with CP exhibit more clinical periodontal damage and relatively higher inflammatory and OS compared to non-smokers with CP. Further, the SRP was effective in improving clinical and biochemical markers with respect to their baseline values in both the groups, although the therapy response is lower in smokers than non-smokers (Graph 1).

In sync with urban Indian social customs with respect to smoking habits, only male individuals could be enrolled in this study. Furthermore, their smoking status was based on the oral information obtained during enrollment for the study.

Furthermore, a better inter- and intra-group comparison could not be feasible as healthy smokers (smokers without periodontitis) could not be recruited. We recommend further longitudinal studies with longer duration of follow-up and inclusion of individuals with different mode of tobacco consumption to investigate and monitor the therapy response with respect to the causality role of smoking/tobacco use on inflammatory damages to periodontium and its effect on systemic biochemical inflammatory and OS markers to support our findings.

Conclusions

Smokers with CP exhibited more periodontal damage and higher systemic inflammatory and OS burden than non-smokers with CP. Under the study condition, SRP was effective in improving periodontal and systemic inflammatory and OS markers, despite the improvement was lower in smokers than non-smokers and the relative % change could be a way of quantifying and representing the therapy response. This study may be a foot forward to have a holistic approach to deal with the negative effects of smoking on periodontium and the overall well-being of an individual with the smoking habit.

Clinical Impact

SRP therapy could be a useful support in checking and/or hindering periodontitis-induced inflammation and OS burden on the systemic health of smokers.

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