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Periodontal Treatment Elevates Carotid Wall Shear Stress in the Medium Term

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Abstract: Periodontal disease is associated with endothelial dysfunction of the brachial artery and hemodynamic alterations of the common carotid artery. Periodontal therapy improves endothelial function. It is not known if it is able also to improve the hemodynamics of the carotid artery. The aim of the current study was to evaluate the efficacy of 2 different periodontal treatments on carotid hemodynamics: scaling and root planing (SRP) alone or together with low-level laser therapy (LLLT). Forty patients were recruited and randomly treated with SRP (n = 20) or SRP + LLLT (n = 20). Periodontal indices (plaque, gingival, and probing depth indices) were measured before and 5 months after treatment. Blood viscosity, common carotid wall shear stress, circumferential wall tension, and Peterson elastic modulus were evaluated before, soon after and 5 months after treatment. It was found that the periodontal indices improved in both groups, but significantly more so for SRP + LLLT than for SRP (decrease in gingival index 69.3% versus 45.4%, respectively, $P = 0.04$). In the SRP + LLLT group, after a transient reduction by 5% immediately after therapy, shear stress increased by 11% after 5 months. In SRP only group, however, shear stress variations were less marked. No significant changes were found for the other hemodynamic parameters in either of the groups. Periodontal disease treatment by SRP + LLLT can therefore be said to improve common carotid wall shear stress. This suggests a possible mechanism by which the treatment of periodontal disease has beneficial effects on the cardiovascular system.

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Abbreviations: η = blood viscosity, DBP = diastolic blood pressure, GI = gingival index, ID = arterial internal diameter, IDM = mean arterial internal diameter, IDR = diastolic arterial internal diameter, IDT = systolic arterial internal diameter, LLLT = low-level laser therapy, MBP = mean blood pressure, PD = pocket deep, PI = plaque index, SBP = systolic blood pressure, SRP = scaling and root planing, V1 = baseline visit, V2 = visit 2 weeks after therapy, V3 = visit 20 weeks after therapy, V_M = mean velocity, V_{SP} = systolic peak velocity.

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INTRODUCTION

The prevalence of cardiovascular events in patients with periodontal disease is higher than in the general population, probably because of some shared underlying pathophysiological mechanisms.[1] Periodontal inflammation is able to spread into systemic circulation, causing endothelial dysfunction and, finally, the development of atherosclerosis.[2–5] Furthermore, periodontal disease has been found to be associated with low arterial wall shear stress,[6,7] which is the frictional force exerted by the flowing blood on the endothelium; low values of this hemodynamic parameter alter arterial pathophysiology and cause endothelial dysfunction.[8,9] Another important hemodynamic factor influenced by periodontal disease is circumferential wall tension; very recently this has been found to be increased in large arteries, and this condition is also associated with the development of cardiovascular disease.[10]

Intervention studies have demonstrated that periodontal treatment causes improvement of endothelial function, thus highlighting the link between periodontal health and cardiovascular disease.[11]

In recent years, therapeutic options in periodontal care have been enriched by photodynamic therapy. The low-level laser therapy (LLLT) is used increasingly as an adjunctive treatment to nonsurgical periodontal treatment because it seems to improve periodontal healing, and reduce gingival inflammation and the levels of local inflammatory biomarkers.[12,13] To date, however, it is not known if an improvement in periodontal disease can influence arterial hemodynamics. Furthermore, periodontal therapy might have different effects on hemodynamics at different times from the intervention, as was recently verified for the biphasic effect of low-density lipoprotein apheresis.[14]

The aim of the current study was to evaluate the efficacy of 2 different periodontal treatments in respect to carotid hemodynamics: scaling and root planing (SRP) alone or together with LLLT. Possible differences between the effects of SRP + LLLT versus standard SRP were also explored.

METHODS

Subjects and Study Design

The study conforms to the ethical guidelines of the Declaration of Helsinki, reflected in a priori approval by the Ethic Committee of ''Azienda Ospedaliera Mater Domini'' (Catanzaro, Italy). Before the study, the authors registered the protocol to the Committee that, evaluating local regulations, did not request any further registration.

The current research was a randomized, single-blinded, single-center intervention study. Participants were consecutively recruited between February and November 2013 among outpatients referred from their general practitioners to the Dental Unit of "Magna Graecia" University in Catanzaro (Italy) for periodontal disease. Inclusion criteria were age >18 and <70 years, and periodontitis lesions needing therapy based on a dentist's opinion. Exclusion criteria were potentially childbearing women, a history of atrial fibrillation, heart failure, clinically significant oncologic, renal, hepatic, or pulmonary disease.

Forty participants were recruited, and gave written informed consent. These participants provided a blood sample, and completed a clinical examination in the Metabolic Disease Unit of the same university. Medical history, pharmacological treatments, and smoking habits were recorded. All patients were then scheduled for both ultrasound evaluation for common carotid hemodynamic computation, and dental inspection to measure the periodontal indices (baseline visit). Afterward, patients were randomly assigned to receive either SRP only, or together with LLLT; periodontal therapy sessions were on one or more days, depending on disease extension and severity. Patients repeated the ultrasound examination 2 weeks (V2) and 20 weeks after therapy (V3). A measurement of periodontal indices was performed again at V3. Staff members who performed the vascular measurements were blinded with respect to the periodontal therapy applied.

Biochemical and Clinical Parameters

Blood was withdrawn from an antecubital vein after 12 hours fasting. Fasting blood lipids and glucose were measured using commercially available kits. Patients having fasting glucose ≥126 mg/dL were invited to repeat the blood withdrawal. Height and weight were detected using standard methods, and body mass index was computed as weight (kg) divided by height squared (m^2). Systolic (SBP) and diastolic blood pressure (DBP) was measured with a standardized sphygmomanometer on the right arm after the participant had rested for at least 5 minutes. The average of the second and third of 3 readings was computed. Mean blood pressure (MBP) was computed according to the formula: DBP + (SBP − DBP)/3. Hypertension was defined as systolic and/or diastolic values, respectively >139 mm Hg and >89 mm Hg, or current antihypertensive treatment.[15] Diabetes was considered present if the participant was on therapy, or if fasting blood glucose determination was ≥126 mg/dL on 2 different occasions.[16] Hyperlipidemia was defined as total cholesterol ≥200 mg/dL and/or triglycerides ≥150 mg/dL, or on treatment with lipid-lowering agents.[17] Patients who smoked regularly during the previous 12 months were classified as smokers.

Blood viscosity (η) was measured at a shear rate of 225 s^{-1} in vitro on the same day of the echo-Doppler examination, using a cone/plate viscometer (Wells-Brookfield DV III, Brookfield Engineering Lab, Lorch, Germany) as previously reported.[18]

Ultrasound Study

Echo-Doppler examination for arterial diameter and blood flow velocity measurements was performed with an echocolor-Doppler Philips HD 11 XE (Royal Philips Electronics, Netherlands) equipped with a 3 to 12 MHz multifrequency linear array, and simultaneous electrocardiogram recording. For arterial diameter and blood flow velocity measurement, the examination was performed as previously described and calculations were made accordingly.[10,19,20] Briefly, parameters were measured 1 cm proximally to the left and right carotid bulb, obtaining 2 sets of measurements for each patient. Therefore, 40 hemodynamic measurements were considered for each group. Internal diameter (ID) was defined as the distance between the leading edge of the echo produced by the intima–lumen interface of the near wall, and the leading edge of the echo produced by the lumen–intima interface of the far wall. Internal diameter was measured offline at the T and R wave of the electrocardiogram as, respectively, maximum and minimum diameter during the cardiac cycle; mean ID (ID_M) was calculated as $ID_R + ((ID_T - ID_R)/3)$. Blood flow velocity was detected with the sample volume reduced to the smallest possible size (1 mm) and placed in the center of the vessel. The angle between the ultrasound beam and the longitudinal vessel axis was kept between 44° and 56°. Systolic peak velocity (V_{SP}) and mean velocity (V_M) during the cardiac cycle were automatically measured with auto-tracking as the mean of 3 cardiac cycles.

Common carotid peak and mean wall shear stresses (dynes/cm^2) were as follows:

Peak wall shear stress = $4\ \eta\ V_{SP}/ID_T$

Mean wall shear stress = $4\ \eta\ V_M/ID_R$

where blood velocities are expressed in cm/s, IDs in cm, and η in poise.

Common carotid peak and mean parietal tensions (dynes/cm) were as follows:

Peak parietal tension = SBP ($ID_T/2$)

Mean parietal tension = MBP ($ID_R/2$)

where blood pressures are expressed in dynes/cm^2 and IDs in cm.

Common carotid Peterson elastic modulus (dynes/cm^2) was as follows:

Peterson elastic modulus = $(SBP - DBP)\ ID_M/(ID_T - ID_R)$

where blood pressures are in dynes/cm^2 and IDs in cm.

Dental Evaluation

A dentist performed a complete examination of oral health, evaluating 3 different periodontal indices as previously reported.[10] Briefly, inflammation of gingiva was evaluated by the gingival index (GI): 24 gingival margins were scored 0 to 3 upon inspective signs of inflamed mucosa and bleeding.[21] The plaque index (PI) is an indicator of gingival plaque burden. Its determination includes visual clinical evaluation of each tooth on the mesial, distal, buccal, and lingual aspect.[22] Finally, the pocket deep (PD) index was used to give an indication of deep inflammation involving the periodontal ligament, dental cementum, and alveolar bone. A periodontal probe (PCP/15 AIR, Henry Schein, Milan), with millimeter markings 1 to 15, measured the distance from the gingival margin to the base of the sulcus, or periodontal pocket, along the main axis of the tooth. The examiner calibrated his probing pressure between 10 and 20 g before each patient's examination. The depth of dental pockets was detected at 6 sites in each tooth (distofacial, facial, mesiofacial, distolingual, lingual, and mesiolingual).[23] Pocket depth was scored as: 0 to 2 mm = 0; 2.1 to 4 mm = 1; 4.1 to 6 mm = 2; and >6 mm = 3. A mean of all measurements for each tooth was considered.

As known, periodontal indices are usually a sum of mean scores by each dental element divided for the number of evaluated teeth, that is, a mean value for the patient indicating the severity of the disease. As in previous works, here, the sum value was also considered, indicating the spread of the disease in each patient.[6]

Dental Therapy

Patients underwent an SRP periodontal treatment that entailed some degree of invasiveness. In detail, scaling consists in removing mucobacterial plaque and tartar from supragingival and subgingival teeth surfaces; root planing consists of the removal of deposits of subgingival calculus, granulation tissue, and infected or necrotic cementum, by manual tools such as curettes.[24,25] Randomized patients then received adjuvant LLLT, through a 940-nm diode laser (Ezlase™ soft-tissue diode laser—Biolase Technology Inc. 4 Cromwell, Irvine, CA) with 3 cycles of irradiation for each pocket, each lasting 30 seconds. Dosimetric values were power 3 W, pulse frequency 15 Hz, pulsed emission mode of laser light, on time (pulse duration) 10 milliseconds, time-off (relaxation time) 20 milliseconds, average power 1 W, optical fiber, and tips 300 to 400 μm.

Statistical Analysis

All variables had normal distribution, except triglycerides. The Student *t* test or Mann–Whitney *U* test were used to compare baseline values of continuous variables between the 2 groups, and the χ^2 test was used for categorical variables. The Student *t* test was also used to compare percentage variations after therapy between the 2 groups. The Student *t* test for paired data was used to compare periodontal indices before and after therapy within the same group.

The general linear model for repeated measures, the Huynh-Feldt test, was used to verify the within-subjects effect of the treatments on hemodynamic parameters (shear and tensile forces) at the 3 time points (V1–V3) into the same treatment group; in the same model, tests of within-subjects contrasts were performed to compare V1 to each of the other 2 time points. A P value <0.05 was considered statistically significant. Statistical analyses were performed by PASW 18.0 for Windows.

TABLE 1. Baseline Characteristics of Periodontal Patients Divided According to the Treatment

	Scaling and Root Planing + Laser Therapy	Scaling and Root Planing	*P*
Age, y	57.2 ± 10.3	56.6 ± 8.7	0.84
Male, %	45	25	0.19
Systolic blood pressure, mm Hg	127 ± 14	133 ± 18	0.22
Diastolic blood pressure, mm Hg	77 ± 8	83 ± 11	0.06
Body mass index, kg/m^2	27.5 ± 5.7	29.4 ± 4.0	0.24
Blood glucose, mg/dL	97.7 ± 9.1	93.1 ± 8.8	0.13
Total cholesterol, mg/dL	213 ± 47	200 ± 33	0.33
HDL cholesterol, mg/dL	49 ± 11	55 ± 11	0.08
Triglycerides, mg/dL	157 ± 75	116 ± 42	<0.01
Smoking, %	40	40	0.50
Arterial hypertension, %	45	55	0.51
Dyslipidemia, %	60	35	0.49
Obesity, %	20	35	0.49
Diabetes mellitus, %	5	10	0.31

Student *t* test for all continuous variables, except Mann–Whitney *U* for triglycerides. χ^2 test for all categorical variables. HDL = high-density lipoprotein.

RESULTS

All 40 recruited patients randomly underwent SRP (n = 20) or SRP + LLLT (n = 20). Visit 2 weeks after therapy and V3 were 2.0 ± 1.5 and 20.8 ± 6.3 weeks after periodontal treatment in the whole sample, without differentiating between groups (data not shown). Table 1 shows baseline clinical and biochemical characteristics, and the prevalence of cardiovascular risk factors in the participants. No significant differences between treatment groups were observed at the time of recruitment, except for triglycerides that were slightly higher in the laser therapy group. Moreover, no significant differences in baseline periodontal indices or hemodynamic parameters were detected between the groups.

Figure 1 shows the periodontal characteristics of the patients at baseline and V3. Both groups showed a substantial improvement in the periodontal indices, although additional laser treatment improved clinical response with respect to SRP only. In detail, in the group undergoing SRP + LLLT (Fig. 1A), reductions by 69.3 % for GI, 67% for PD, and 59.7% for PI were observed. In the group without laser (Fig. 1B), a reduction of mean periodontal indexes by 45.4 % for GI, 50.2% for PD, and 52.8% for PI was observed. The between groups differences in terms of the percentage variations of GI only were statistically significant ($P = 0.04$). Sum indexes showed similar reductions (data not shown).

Figure 2 shows the trend in hemodynamic parameters. In the SRP + LLLT group (Fig. 2A), mean shear stress decreased by 5% briefly after therapy, and increased by 11% compared with

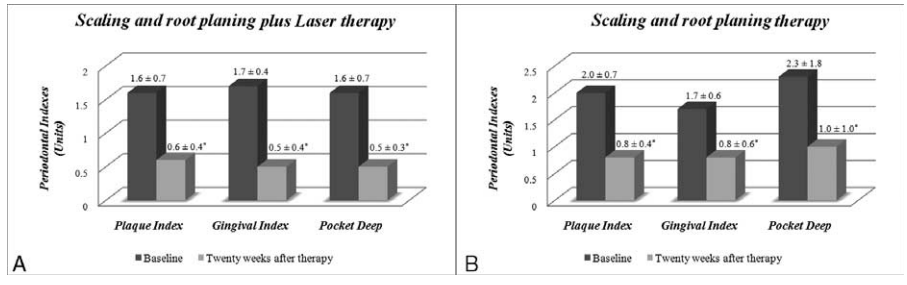

FIGURE 1. Therapeutic efficacy on periodontal indices into the two patient groups. Student *t* test for paired data. $^*P < 0.001$ versus baseline within groups.

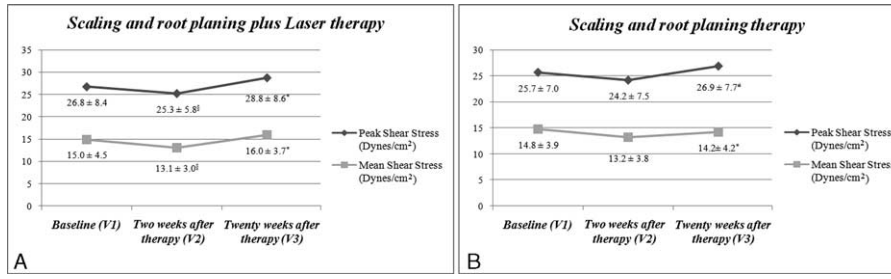

FIGURE 2. Common carotid hemodynamic behavior after periodontal therapy in the two treatment groups. A, General linear model. Mean shear stress: F = 10 and $P < 0.001$ for trend. Peak shear stress: F = 8.5 and $P < 0.001$; P for within-subjects contrasts test = V1 versus V2: $^{\S}P < 0.05$ and *V1 versus V3: $P < 0.001$. B, General linear model. Mean shear stress: F = 6.2 and $P < 0.01$ for trend. P for within-subjects contrasts test = V1 versus V2: $^{\S}P$ = ns and V1 versus V3: $^{\#}P < 0.05$. General linear model for peak shear stress: F = 4.3 and $P < 0.05$; P for within-subjects contrasts test = V1 versus V2: $^{\S}P$ = ns and V1 versus V3: $^{*}P < 0.01$. V1, baseline visit; V2, visit 2 weeks after therapy; V3, visit 20 weeks after therapy.

baseline after 20 weeks; both differences were statistically significant compared with the baseline. Similar results were obtained for peak shear stress. In the SRP group (Figure 2B), results were conflicting: mean shear stress decreased after therapy at the 2 time points, whereas peak shear stress showed a trend similar to the SRP + LLLT group, although the increase further after therapy (5%) was less evident.

No significant changes were found in either of the groups for peak and mean circumferential wall tension and Peterson elastic modulus (data not shown).

DISCUSSION

The current results demonstrate that periodontal disease therapy can improve shear stress in the medium term, if successful, despite a transient worsening of the common carotid hemodynamic profile. It was still not clear if wall shear stress is a modifiable risk factor for atherosclerosis, although the current data partially address this point by demonstrating that wall shear stress can be modified by periodontal therapy in an antiatherogenic way.

In fact, the medium-term direction of shear stress change by therapy is favorable, because in regions where low shear stress occurs, the atheroprotective genes are suppressed and the pro-atherogenic genes are upregulated, promoting the atherosclerotic process.[8] The entity of shear stress variation following periodontal healing is relevant, compared with the variations of the same parameter in diabetics, or those caused by aging. The percentage increase of mean shear stress observed in the current study, for example, is more than half of the difference that is observed between diabetics and healthy patients, and corresponds to a hemodynamic profile of approximately 9 years younger.[20,26]

Any arterial wall shear stress increase should imply important and positive consequences in terms of a possible reversion of the known association between periodontal disease and cardiovascular diseases. Probably, also, the previously described improvement in endothelial function after treatment of periodontal disease might, at least partially, rely on the hemodynamic improvement demonstrated in the current study.[11] Indeed, in a previous study, a strong relationship between baseline brachial artery wall shear stress and flow-mediated dilation has been reported.[27]

The worsening of common carotid hemodynamic features observed V2 is another original finding that needs to be discussed. It is about half of the long-term improvement, in absolute values; furthermore, it is transient. This result is in line with carotid shear stress reduction previously found in patients shortly after an extracorporeal circulation.[14] Similar to those previous findings, the current results might be because of a brief increase of the systemic release of inflammation molecules during treatment of periodontal disease.[28,29]

Apart from shear stress variations, the current study did not find any significant effect of the therapies on circumferential wall tension but, previously, it has been shown that periodontal inflammation is associated with increased parietal tension of the common carotid.[10] Probably, changes in the arterial features inherent to the vessel wall structure and mass are not pronounced enough to allow any perceivable positive effect to be recorded as far as 5 months after a periodontal intervention. Nonrecoverable damage to arterial walls because of periodontal diseases cannot be excluded, however.

There is currently no clear picture in respect to alterations in common carotid arterial stiffness because of periodontal disease, with one previous study reporting no such alterations but another demonstrating an elevated central arterial stiffness.[10,30] Looking at the current results, an effect on carotid stiffness because of treatment for periodontal disease can be ruled out, at least in the medium term.

The findings demonstrate that the increase in wall shear stress is much more pronounced in the SRP + LLLT group compared with the SRP only group. Because the SRP + LLLT group also shows a greater improvement in periodontal indices, it is not possible to determine, however, whether the increase in shear stress is induced by the most effective therapy or by use of the laser itself. Furthermore, specifically designed studies comparing SRP versus SRP + LLLT are needed, selecting patients with the same treatment responses.

The pathophysiological explanation of these findings is beyond the scope of the current study, although it might rely on the systemic low-grade inflammation characterizing periodontal disease. In fact, periodontal inflammation might reduce wall shear stress by an enlargement of the internal diameter of large arteries, as in rheumatoid arthritis.[7,31] Conversely, low shear stress might in turn also locally enhance vascular inflammation.[32] Furthermore, it has been demonstrated that oral pathogens as *Porphyromonas gingivalis* can infect endothelial cells.[33]

LIMITATIONS

The current study has some limitations. First, the small number of enrolled patients, because of the complexity of vascular examinations. Second, the fact that inflammatory

markers were not determined, which means that it is only possible to speculate about the mechanisms underlying the current results. Third, the arterial site chosen does not allow endothelial function studies to be performed locally. Finally, as in other studies using the present wall shear stress measurement method,[6,10,14,20] a parabolic blood flow profile has been assumed for the common carotid; other measurement methods using computational flow dynamic reconstruction based upon magnetic resonance data,[34] overcome this assumption. In a clinical context, however, requiring repeated measurement of hemodynamic parameters through echo-Doppler use is probably advantageous compared with the expensive, time consuming, and complex magnetic resonance imaging techniques.

CONCLUSIONS

The current study demonstrates a medium-term improvement in some carotid hemodynamic factors in patients undergoing a successful treatment for periodontal disease. This effect might be a mechanism by which the management of periodontal disease is beneficial for vascular function. Furthermore, larger studies are needed, also to confirm the mechanisms underlying these results and their pathophysiological implications.

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