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Relationship between periodontal outcomes and serum biomarkers changes after non-surgical periodontal therapy

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Abstract: The systemic effect of chronic periodontitis (CP) has been suggested by several studies as an etiologic factor and modulator of diseases based on the changes in the inflammatory marker levels. This study aimed to investigate the relationship between the changes in clinical periodontal outcomes and serum biomarkers (CRP, IL-6, albumin and percentage of leukocytes) after non-surgical periodontal therapy in systemically healthy adults. An interventional study was conducted with a sample of 29 individuals without CP (control group) and 33 with CP (CP group). Periodontal clinical variables were recorded, and the serum levels of inflammatory markers were measured. Statistical analysis included the chi-square and Student's t-tests and Pearson's correlation analysis. After 90 days of non-surgical periodontal treatment, a reduction of periodontal parameters and IL-6 in both groups could be observed ($P < 0.001$). The correlation analysis revealed a directly proportional correlation between changes in the probing depth ($r = 0.349$, $P = 0.049$) and clinical attachment level ($r = 0.374$, $P = 0.034$) with CRP in the CP group. The findings suggest a reduction of IL-6 serum concentration and periodontal clinical measures 90 days after periodontal therapy in both groups.

Key words: Chronic periodontitis, Inflammation mediators, Interleukin-6, C-reactive protein, Leukocytes.

INTRODUCTION

Periodontal disease is characterized by an immuno-inflammatory process triggered by the accumulation of bacterial biofilm on the external surface of the tooth, affecting the gingival tissues, periodontal ligament, cementum, and alveolar bone in susceptible individuals (Kinane et al. 2017). The common clinical signs of periodontal disease include gingival bleeding, alveolar bone resorption, periodontal pocket formation, halitosis, dental

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mobility, and in advanced cases, spontaneous tooth loss (Kulkarni and Kinane 2014).

Epidemiological studies have suggested that chronic periodontitis (CP) may be associated as an etiologic factor and modulator of outcomes such as cardiovascular diseases (Higashi et al. 2008, Yu et al. 2015), rheumatoid arthritis (Ribeiro and Novaes 2005), chronic kidney disease (Rodrigues et al. 2014), and anemia (Pradeep et al. 2011, Carvalho et al. 2014). CP patients present increased production of systemic inflammatory cytokines (tumoral necrosis factor alpha [TNF-α], interleukin-1 beta [IL-1β], and interleukin-6 [IL-6]) (Górska et al. 2003) which can induce the acute phase plasma protein synthesis, such as the C-reactive protein (CRP), (Craig et al. 2003, Loos 2005) and reduce the serum albumin level (hypoalbuminemia) (Kolte et al. 2010, Amitha et al. 2012, Saravanan et al. 2012, Patil et al. 2015). The acute phase response is the effort made by the organism to restore the homeostasis and eliminate the cause of imbalance, resulting in systemic effects (Loos 2005, Marcaccini et al. 2009, Pradeep et al. 2011).

The primary etiologic agent is periodontopathogenic bacteria that can cause destruction of the periodontal tissues directly through the action of its components, particularly the lipopolysaccharide (LPS) present in the cell wall of gram-negative bacteria (e.g., *Porphyromonas gingivalis, Tannerella forsythia, Prevotella intermedia*), and indirectly, by stimulating the host cells to secrete inflammatory mediators that guide and regulate the destructive activity (Khattri et al. 2017). Thus, it is extremely important to stop and control the invasion of microorganisms in the subgingival environment as part of periodontal therapy, either with clinical subgingival scaling and root planning procedures or with systemic antibiotics (Van der Velden 2017, Drisko 2014).

Analyzing the impact of non-surgical periodontal therapy on inflammatory markers IL-6 and CRP in patients with CP, Marcaccini et al. (2009) noticed that the implementation of the therapy significantly reduced the concentrations of these markers after three months. The acute phase proteins have been used as a prognostic indicator of subclinical diseases or early physiological changes in the body, and these proteins are present in CP. In this context, the objective of this study was to investigate the relationship between the changes in periodontal outcomes and serum biomarkers (IL-6, CRP, albumin, percentage of leukocytes) after non-surgical periodontal therapy in systemically healthy adults with or without CP.

MATERIALS AND METHODS

STUDY DESIGN

The present interventional study was conducted in the Dental School Clinics of the Federal University of Maranhão, São Luís, Brazil, between January and October 2015. All study participants received an oral hygiene kit, attended a motivational lecture with guidance on oral hygiene (teeth brushing and flossing), were provided dental care according to their needs, and signed the informed consent form (ICF) agreeing to join the study. The study was approved by the Ethics Committee on Human Research from the Federal University of Maranhão, São Luís, Maranhão, Brazil (23115-010215/2011-16). This trial is registered with Clinicaltrials.gov (NCT02641210).

SAMPLE SELECTION CRITERIA

The sample included individuals of both sexes aged between 30 and 65 years. The exclusion criteria were individuals with diabetes, congestive heart failure, chronic kidney disease, malignant neoplasms, AIDS (acquired immunodeficiency syndrome), or arterial hypertension; pregnant women; nursing mothers; those receiving immunosuppresant medications, suffering from changes in menstrual cycle; smokers or former smokers for less than 10 years; orthodontic appliances users; history of use

of steroids or nonsteroidal anti-inflammatory drugs or antibiotics in the last 3 months predeceding the study and during the research, as well as individuals who underwent supra and subgingival scaling and periodontal surgery in the last 6 months before the investigation.

Figure 1 shows the recruitment process; initially, a convenience sample of 125 volunteers were recruited at the Dentistry School. Personal and clinical data were collected. All study participants received a urine collector and medication for worm infestation (Albendazole 400 mg single dose, Pratti-Dunaduzzi & Cia LTDA, Paraná, BRAZIL). After 15 days, individuals who met the initial criteria for selection were sent for blood collection and urine sample delivery for assessment of the serum biomarkers (total cholesterol, fasting glycemia, triglycerides, albumin, creatinine, hemoglobin, high-sensitivity CRP, leucogram, and urinary sediment examination). The risk of general disease was assessed using the parameters of the medical examination: fasting blood sugar level (categorized as <110 or ≥110 mg/dl), HDL-C level (categorized as <40mg/dl or ≥40 mg/dl), triglycerides (categorized as <150mg/dl or ≥150 mg/dl), serum albumin (between 3.5 and 5.2 g/dl), CRP (high risk – >30, medium – between 0.10 and 0.30 mg/dl and low – <0.10mg/dl), systolic blood pressure (categorized as <140 mmHg or ≥140 mmHg), creatinine (men – 0.90 to 1.30 mg/dl and women – 3.1 to 7.8 mg/dl), hemoglobin (between 12 and 16 g/dl) and total cholesterol (<170 mg/dl).

The volunteers considered to be systemically healthy after the analysis of the serum exams (67) were allocated to two groups: 33 diagnosed with CP (CP group), and 29 controls without CP (control group). The participant was considered to have CP when he/she presented at least two teeth with

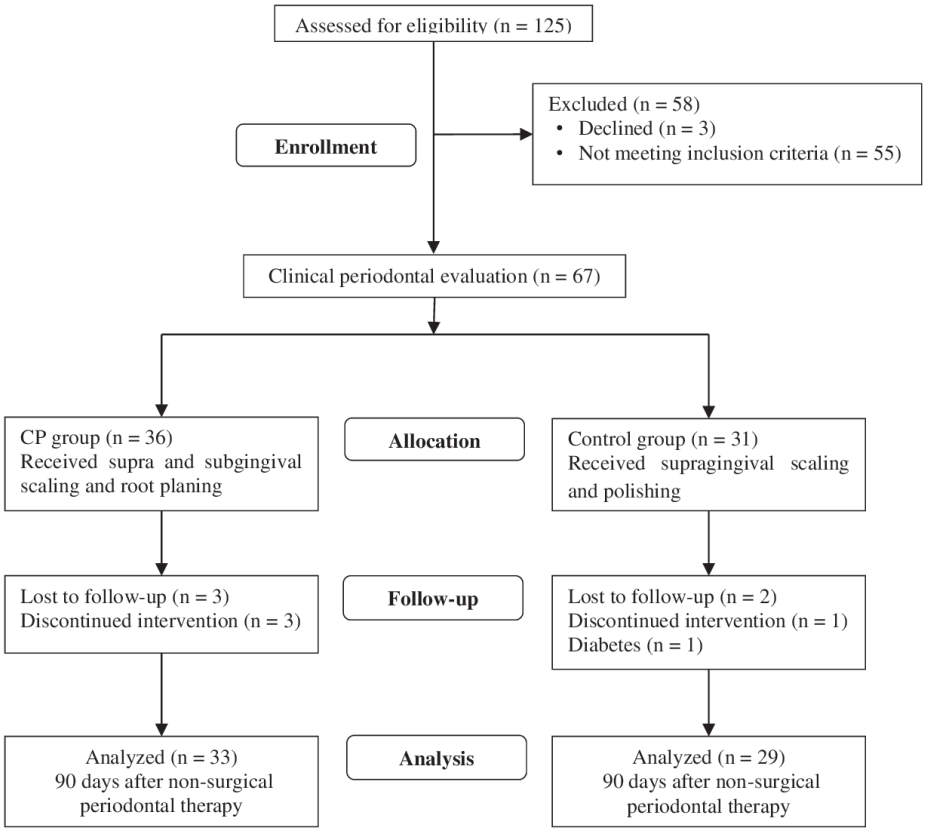

Figure 1 - Flowchart of study recruitment.

clinical attachment level ≥ 6 mm and probing depth ≥ 5 mm in one or more sites (Machtei et al. 1992).

GENERAL AND PERIODONTAL EVALUATION

In the clinical evaluation, anamnesis was performed for obtaining the demographic data, current and previous medical history, medications being taken, in addition to physical examination (checking of blood pressure, weight, height, and body mass index).

A single examiner performed the oral and periodontal examination using a Williams' millimetric periodontal probe and dental mirror. The periodontal examination included the probing of six sites on each tooth (mesiobuccal, buccal, distobuccal, mesiopalatal, palatal, distopalatal), performed by a trained periodontist examiner (Kappa test 0.81 for the probing depth and 0.77 for the clinical attachment level). We evaluated the clinical parameters of probing depth (PD), gingival recession (GR), clinical attachment level (CAL), visible plaque index (VPI), and bleeding on probing index (Ainamo and Bay 1975).

SERUM BIOMARKERS ANALYSIS

Venous blood samples were collected from the upper limbs of the participants (20 ml). Part of the collected blood was analyzed within 2 h after the blood collection using the automatic hematology analyzer ADVIA® 120 (Siemens Healthcare Diagnostics, Erlangen, Germany) by standard laboratory methods. The remaining blood anticoagulated in EDTA was centrifuged at 3,000 rpm for 10 min. The serum was aliquoted in Eppendorf tubes and stored at −80 °C. The IL-6 level was assessed in serum by an immunoassay technique using the ELISA commercial kit (IBL International), according to manufacturer's instructions. The readings were done by an automatic microplate reader, and the absorbance was read at a wavelength of 450 nm in a MULTISKAN EX-LAbsystem spectrophotometer (Spectramax 190, Modular device).

PERIODONTAL THERAPY

A single periodontist conducted the non-surgical periodontal therapy, according to the study group. The supragingival and subgingival scaling and root planing under local anesthesia were performed using ultrasound and Gracey and mini Gracey's curettes from the main collection (5-6, 7-8, 11-12, and 13-14), polishing with Robson's brush and fine-grained prophylactic paste. This therapy was performed in two sessions during a period of 7 days, with no time limit, according to necessity. In each session, the individuals received oral hygiene instruction (OHI) for the use of toothbrush by the modified Bass' technique, dental flossing and other complementary means (interdental brush, single-tuft brush, tongue brushing, and chemical plaque control), according to individual need.

The patients in the control group received basic periodontal therapy according to Protocol 1; the ones in the CP group were treated according to Protocol 2.

PROTOCOL 1:

Consultation timetable for dental prophylaxis and supragingival scaling:

Visit 1 - Screening, ICF signing, clinical and periodontal evaluation, receiving of the urine collector and vermifuges.

Visit 2 - 15 days later: Delivery of urine, 1st blood collection, and guidance on oral hygiene.

Visit 3 - 7 days later: Supragingival scaling, polishing with Robson's brush, and topical application of fluoride.

Baseline 0 - 1 day after therapy, day 0 for the beginning of the 3-month space counting; one day after visit 3.

Visit 4 - 90 days after baseline (2nd blood collection and periodontal evaluation).

PROTOCOL 2:

Consultation schedule for supra and subgingival scaling and root planing:

Visit 1 - Screening, ICF signing, clinical and periodontal examination, receiving of the urine collector and vermifuges.

Visit 2 - 15 days later: Delivery of urine, 1st blood collection, and guidance on oral hygiene.

Visit 3 - 7 days later: periodontal therapy by supra and subgingival scaling and root planing.

Visit 4 - 7 days later: periodontal therapy by supra and subgingival scaling and root planing.

Baseline 0 - 1 day after therapy, day 0 for the beginning of the 3-month space counting; one day after visit 4.

Visit 5 - periodontal maintenance interconsultation after 30, 60 (where there was no data collection), and 90 days (2nd blood collection and periodontal examination).

STATISTICAL ANALYSIS

Statistical analysis was performed using STATA statistical software, version 12.0 (Stata Corp 2011. Stata Statistical Software: Release 12. College Station, TX: Stata Corp LP). The descriptive data were expressed as frequencies, mean, and standard deviation.

Initially, the normality of the distribution of the continuous variables was measured through the Shapiro-Wilk test. The inferential analysis consisted of the following methods: to assess the effect of the periodontal therapy in the variables albumin, IL-6, CRP, leukocytes percentage, and periodontal parameters, the paired Student's t-test was used; for the comparison of the corresponding absolute delta (final value – initial value) between the groups, the Student's t-test was used for independent samples; for the categorical variable, the chi-square test was used. The deltas were analyzed by the Spearman's correlation coefficient to show the relationship between the changes in the variables after non-surgical periodontal therapy. The significance level adopted was 5%.

RESULTS

Table I shows female gender was predominant in both groups (60.6% in the CP group and 62.1% in the control group). In the CP group, the average age and BMI were 41.1 ± 7.8 years and 26.1 ± 3.7, respectively, whereas, in the control group, the average age and BMI were 39.6 ± 9.0 years and 25.4 ± 3.3, respectively. The data showed no statistically significant differences in gender (P = 0.886), age (P = 0.488), and body mass index (P

TABLE I
General characteristics and periodontal markers in baseline between study groups.

Variables	CP Group		Control Group		P value
Gender [n (%)]					0.886
Male	13	(39.4)	11	(37.9)	
Female	20	(60.6)	18	(62.1)	
Age in years [means (±SD)]	41.1	(7.8)	39.6	(9.0)	0.488
BMI [means (±SD)]	26.1	(3.7)	25.4	(3.3)	0.444
VPI [means (±SD)]	8.60	(8.32)	2.13	(2.63)	<0.001
GBI [means (±SD)]	11.61	(9.90)	1.17	(1.22)	<0.001
CAL [means (±SD)]	2.95	(0.54)	2.04	(0.33)	<0.001
PD [means (±SD)]	2.43	(0.47)	1.82	(0.23)	<0.001

BMI = Body mass index. VPI = Visible plaque index. GBI = Gingival Bleeding Index. CAL = Clinical Attachment Level. PD = Probing depth. ±SD = standard deviation.

= 0.444) between the study groups. The CP group presented worse levels of the basal periodontal markers compared to the control group (P < 0.001).

Table II shows the periodontal and serum biomarker changes after non-surgical periodontal therapy. A reduction of all the periodontal parameters was observed after 90 days in the CP group, and there was a reduction in the average PD and CAL in the control group. A reduction in the IL-6 level in both groups after 90 days (P < 0.001) was also seen. In the comparative analysis of changes (Δ) between the groups, a statistically greater reduction of the periodontal parameters and eosinophils in the CP group was observed. Also, a statistically significant difference in the changes in the number of lymphocytes between the two groups was noticed, but in the CP group, an increase was observed after periodontal therapy.

The correlation between the changes in the periodontal parameters and serum markers after

TABLE II
Comparison of variables changes after non-surgical periodontal therapy between the study groups.

	CP group		P value	Control group		P value
	Baseline means (±SD)	**90 days means (±SD)**		**Baseline means (±SD)**	**90 days means (±SD)**	
VPI (%)	8.60(8.32)	1.80 (1.58)	**<0.001**	2.13 (2.63)	1.61 (2.00)	0.624
	Δ = -6.8 (7.6)[a]			**Δ = -0.3 (3.1)[b]**		
GBI (%)	11.61 (9.90)	1.60 (1.91)	**<0.001**	1.17 (1.22)	0.88 (0.98)	0.302
	Δ = -10.0 (9.7)[a]			**Δ = -0.3 (1.4)[b]**		
CAL (mm)	2.95 (0.54)	1.82(0.30)	**<0.001**	2.04 (0.33)	1.43 (0.25)	**<0.001**
	Δ = -1.1 (0.4)[a]			**Δ = -0.6 (0.3)[b]**		
PD (mm)	2.43 (0.47)	1.49 (0.21)	**<0.001**	1.82 (0.23)	1.29 (0.17)	**<0.001**
	Δ = -0.9 (0.4)[a]			**Δ = -0.5 (0.2)[b]**		
ALB (g/dL)	4.48 (0.22)	4.42(0.23)	0.238	4.50 (0.23)	4.45 (0.30)	0.421
	Δ = -0.06 (0.18)[a]			Δ = -0.05 (0.24)[a]		
IL-6 (pg/mL)	15.97 (8.58)	3.94 (3.33)	**<0.001**	14.58 (5.18)	2.89 (1.13)	**<0.001**
	Δ = -12.02 (6.30)[a]			Δ = -11.68 (5.47)[a]		
CRP (mg/L)	0.27 (0.33)	0.24 (0.34)	0.674	0.24 (0.39)	0.22 (0.34)	0.855
	Δ = -0.03 (0.40)[a]			Δ = -0.01 (0.48)[a]		
NEU (%)	54.88 (8.37)	53.4 (9.68)	0.509	53.23 (7.65)	54.0 (7.73)	0.698
	Δ = -1.47 (5.03)[a]			Δ = 0.78 (3.69)[a]		
EOS (%)	4.11 (3.76)	3.61 (3.03)	0.554	3.44 (2.81)	3.77 (2.96)	0.593
	Δ = -0.50 (1.67)[a]			**Δ = 0.41 (1.75)[b]**		
BAS (%)	0.71 (0.27)	0.62 (0.30)	0.209	0.83 (0.42)	0.64 (0.27)	0.091
	Δ = -0.09 (0.32)[a]			Δ = -0.15 (0.34)[a]		
LYM (%)	34.06 (8.32)	36.98 (9.78)	0.195	36.21 (7.29)	35.94 (7.41)	0.786
	Δ = 2.92 (6.05)[a]			**Δ = -0.52 (3.19)[b]**		
MON (%)	6.22 (1.93)	5.73 (1.51)	0.260	6.27 (1.71)	5.70 (1.34)	0.211
	Δ = -0.48 (1.24)[a]			Δ = 0.78 (3.69)[a]		

Δ = Difference between final and initial value. Different lowercase letters mean significant differences (P < 0.05) between groups (Student's t test for independent samples). VPI = Visible plaque index. GBI = Gingival Bleeding Index. CAL = Clinical Attachment Level. PD = Probing depth. ALB = Albumin. IL-6 = Interleukin 6. CRP = C-Reactive Protein. NEU = Neutrophils. EOS = Eosinophils. BAS = basophils. LYM = Lymphocytes. MON = Monocytes. P value = probability value of comparative analysis between the baseline and 90 days in the same group.

non-surgical periodontal therapy was analyzed in the present study. In the control group, only a significant direct correlation was found between the changes in the PD and percentage of EOS (Table III). In the CP group, direct correlations were observed in the changes between PD and CRP, CAL and CRP, and PD and BAS. Also, an inverse correlation between CAL and BAS was detected (Table IV).

DISCUSSION

The study hypothesis was based on the biological plausibility that CP is the product of the inflammatory response to bacteria constituting the dental biofilm; however, it is a patient's inherent susceptibility that determines the final result of the disease process through the release of mediators (IL-6, TNF-α, MMPs, and PGE2) producing acute phase proteins (CRP) (Craig et al. 2003, Loos 2005, Marcaccini et al. 2009, Rodrigues et al. 2014) and alterations in vascular permeability that result in reduction of serum albumin levels (Kolte et al. 2010, Amitha et al. 2012, Saravanan et al. 2012, Patil et al. 2015).

Vidal et al. (2009) observed that non-surgical periodontal therapy was effective in reducing the

TABLE III
Correlation of variables changes (Δ) between periodontal outcomes and serum biomarkers after periodontal therapy in the control group.

	ALB	IL-6	CRP	NEU	EOS	BAS	LYM	MON
VPI	r= -0.132 p= 0.492	r= -0.093 p= 0.629	r= 0.124 p= 0.519	r= -0.010 p= 0.955	r= 0.126 p= 0.513	r= -0.153 p= 0.427	r= -0.010 p= 0.956	r= -0.077 p= 0.689
GBI	r= 0.082 p= 0.669	r= -0.140 p= 0.467	r= 0.046 p= 0.809	r= 0.226 p= 0.237	r= -0.081 p= 0.672	r= -0.209 p= 0.276	r= -0.213 p= 0.265	r= 0.052 p= 0.787
CAL	r= 0.103 p= 0.594	r= 0.183 p= 0.340	r= 0.280 p= 0.140	r= 0.032 p= 0.865	r= 0.364 p= 0.051	r= -0.206 p= 0.281	r= -0.176 p= 0.359	r= -0.102 p= 0.595
PD	r= 0.141 p= 0.465	r= -0.146 p= 0.447	r= 0.311 p= 0.100	r= 0.086 p= 0.656	**r= 0.383** **p= 0.040**	r= -0.191 p= 0.320	r= -0.241 p= 0.206	r= -0.125 p= 0.518

VPI = Visible plaque index. GBI = Gingival Bleeding Index. CAL = Clinical Attachment Level. PD = Probing depth. ALB = Albumin. IL-6 = Interleukin 6. CRP = C-Reactive Protein. NEU = Neutrophils. EOS = Eosinophils. BAS = basophils. LYM = Lymphocytes. MON = Monocytes. r = Spearman's correlation coefficient. p = probability value.

TABLE IV
Correlation of variables changes (Δ) between periodontal outcomes and serum biomarkers after periodontal therapy in the CP group.

	ALB	IL-6	CRP	NEU	EOS	BAS	LYM	MON
VPI	r= 0.062 p= 0.733	r= -0.046 p= 0.799	r= -0.022 p= 0.904	r= -0.015 p= 0.931	r= 0.034 p= 0.850	r= -0.030 p= 0.867	r= 0.049 p= 0.786	r= -0.011 p= 0.948
GBI	r= 0.267 p= 0.139	r= -0.123 p= 0.501	r= 0.195 p= 0.284	r= -0.006 p= 0.997	r= -0.077 p= 0.673	r= -0.049 p= 0.788	r= 0.084 p= 0.647	r= -0.233 p= 0.198
CAL	r= -0.175 p= 0.337	r= -0.116 p= 0.526	**r= 0.374** **p= 0.034**	r= 0.007 p= 0.969	r= 0.077 p= 0.672	**r= -0.391** **p= 0.026**	r= -0.012 p= 0.947	r= 0.134 p= 0.462
PD	r=-0.139 p=0.447	r= -0.135 p= 0.459	**r= 0.349** **p= 0.049**	r= 0.094 p= 0.606	r= 0.042 p= 0.817	**r= -0.391** **p= 0.026**	r= -0.069 p= 0.706	r= -0.064 p= 0.726

VPI = Visible plaque index. GBI = Gingival Bleeding Index. CAL = Clinical Attachment Level. PD = Probing depth. ALB = Albumin. IL-6 = Interleukin 6. CRP = C-Reactive Protein. NEU = Neutrophils. EOS = Eosinophils. BAS = basophils. LYM = Lymphocytes. MON = Monocytes. r = Spearman's correlation coefficient. p = probability value.

periodontal parameters (VPI, gingival bleeding index, PD, and CAL) even 6 months after the therapy, corroborating the results of the study by Higashi et al. (2008) wherein the therapy was effective in systemically healthy patients and the ones with CP within the space of 90 days after the non-surgical periodontal therapy.

The findings related to the reduction in the IL-6 level after non-surgical periodontal therapy in individuals with CP support the previous studies performed (Marcaccini et al. 2009, Vidal et al. 2009, Graziani et al. 2010). Previous studies that did not observe a decrease in the IL-6 level after non-surgical periodontal therapy were not found.

Hypoalbuminemia has been associated with the presence of CP in several studies, and the inverse relationship between serum albumin concentration and periodontal disease is well reported in the literature on elderly people, as in the studies by Kolte et al. (2010) and Saravanan et al. (2012). Amitha et al. (2012) conducted a study in 60 individuals aged between 30 and 40 years, dividing them into periodontally healthy groups and groups with CP, demonstrating the same findings, as well as Patil et al. (2015) in the clinical trial composed of adults and elderly people. However, none of the previous studies assessed the impact of CP non-surgical periodontal therapy on the concentrations of serum albumin, and in the present study, there were no statistically significant changes in serum albumin levels after non-surgical periodontal therapy in both groups.

In this study, CRP, an acute phase protein analyzed by some researchers (Górska et al. 2003, Craig et al. 2003, Loos 2005, Marcaccini et al. 2009), was not sensitive enough to detect the control of periodontal inflammatory process since there was no significant alteration 90 days after the non-surgical periodontal therapy. The criterion used to select the individuals diagnosed with periodontitis (Machtei et al. 1992) may have identified those with levels of extension and severity of CP with low systemic effects so that CRP was not able to detect the periodontal inflammation at levels outside the normal range. Almaghlouth et al. (2014) also did not detect a change in the serum CRP after 90 days of periodontal therapy, although, another study indicated that patients undergoing periodontal therapy experience short-term perturbations in the serum CRP levels (Graziani et al. 2010), 24 hours after periodontal instrumentation.

Cytokines are potent local mediators of inflammation that are produced by various cells and found in CP as potential markers for the diagnosis and include TNF-α, IL-1α, IL-1β, and IL-6. The leukocyte recruitment according to the severity of the disease (Nussbaum and Shapira 2011) may lead to an increase in the correlations between the inflammatory markers and its progression. In the present study, a significant alteration in the marker levels after therapy (Δ) could be seen between the groups with CP and without CP in the ratio of 4:1, respectively, presenting itself as an important indicator of the systemic inflammatory process caused by CP.

No studies could be found in the literature concerning the selection of systematically healthy individuals, through strict eligibility criteria, being confirmed by complete blood count markers and serum albumin level, as well as by the demographic characteristics of the individuals. Marcaccini et al. (2009) included systemically healthy individuals but did not eliminate the possibility of worm infestation, which is also responsible for increasing the serum inflammation markers, unlike this study.

The present study attempted to show a plausible association between serum albumin, CRP, IL-6, leukocytes, and CP in systematically healthy adults. Nevertheless, there were limitations: lack of analysis in another substrate, such as the gingival crevicular fluid, and for ethical reasons, the impossibility of comparison with a group composed of individuals diagnosed with periodontitis not having received periodontal therapy for 90 days.

This latter limitation has outlined the type of the study as interventional, and at the end, it was expected that between the groups, a statistically significant difference would occur 90 days after the therapy, a finding which was observed for the periodontal parameters and IL-6, proving that the parameters mentioned did not evolve in a similar way and that the impact of the periodontal therapy was associated with the management of CP.

Although the association of CP with the systemic markers has not been statistically proven, the results suggest that low concentrations of albumin and high levels of other markers are associated with the presence of CP in such a way that these data should be taken into account once they serve as parameters for the detection of systemic alterations (Kolte et al. 2010, Amitha et al. 2012, Saravanan et al. 2012, Patil et al. 2015).

Besides that, a significant reduction in the IL-6 level was observed in both groups after non-surgical periodontal therapy, and there was no change in albumin, CRP, and leucocytes after therapy. However, the analysis of the correlation between the biomarkers showed that there was a positive proportional relationship between neutrophils and lymphocytes in both groups and a positive correlation between the probing indicators and eosinophils in the group without periodontitis. In the CP group, direct correlations between some serum markers and periodontal probing measurements, and inverse correlations between basophils and probing measurements were detected.

Some procedures adopted to guarantee the study quality should be highlighted. Strict eligibility criteria were used for selecting the sample. The initial evaluation included blood tests, urine analysis, and all participants were given a vermifuge. This fact reduced the inclusion of patients with systemic impairment or presence of worm infestation, which can cause systematic errors in the evaluation of the hypothesis of the study.

In conclusion, the findings of this study suggest that non-surgical periodontal therapy improves periodontal outcomes and reduces the serum IL-6 levels in systemically healthy adults. Also, changes in the periodontal oucomes may show an effect on the CRP level and basophils percentage.

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AUTHOR CONTRIBUTIONS

All the authors participated equally in the paper, collecting and analysing the data, as well as writing the paper.

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