THE EFFECTS OF PERIODONTAL THERAPY ON BIOCHEMICAL INFLAMMATORY MARKERS ON RENAL DYSFUNCTION PATIENTS

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ABSTRACT

Introduction Recent studies have shown an association between high levels of C-Reactive Protein (CRP), Interleukin-6 (IL-6) and chronic periodontitis, association which is diminished after the periodontal treatment. Due to this association, chronic periodontitis was recently considered as a risk factor for chronic kidney disease. **The aim of the study** The purpose of this study was to demonstrate that the inflammatory chronic response observed on patients with chronic kidney disease is influenced by the chronic periodontitis that induces high levels of expression of inflammatory markers, such as IL-6 and CRP. **Materials and methods** The patients in the study were divided in two groups (a group of patients with CKD that were submitted to conservative periodontal treatment and a control group of patients without any systemic disease with moderate to severe chronic periodontitis). The periodontal therapy included root planning and debridement. After the periodontal treatment completion the patients were recalled at 15, 30, 60 and 90 days. We determined the levels of IL-6 and CRP initially and at 3 months after therapy. **Results** IL-6 and CRP levels have significantly decreased after the periodontal treatment in both groups. Additionally, significantly higher levels of haemoglobin and ferritin were observed in the control group patients, associated with the periodontal treatment. **Conclusions** Our results demonstrate that chronic periodontitis is more severe on chronic kidney disease patients, inducing a systemic inflammatory response. The periodontal therapy reduces the inflammatory component and decreases the levels of the serum markers, indicating an important interventional therapy on patients with chronic kidney disease.

Keywords: chronic kidney disease, chronic periodontitis, inflammatory markers

INTRODUCTION

The chronic kidney disease (CKD) is globally considered a public health issue mainly because of its high morbidity and mortality due to its complications.

Recent studies have demonstrated an association between high levels of C-reactive protein (CRP), Interleukin-6 (IL-6) and chronic periodontitis (CP), an association that decreases after periodontal treatment. Due to this association with the systemic inflammatory response, CP was recently considered a risk factor for CKD [1, 2, 3, 4].

The aim of the study

We considered the hypothesis that the inflammatory chronic response observed on patients with CKD is influenced by a chronic periodontitis that induces a high expression of inflammatory markers such as IL-6 and CRP.

MATERIALS AND METHODS

This study was conducted in the Speciality Ambulatory of "Sf. Apostol Andrei" Emergency Hospital Nephrology Clinic Galați in collaboration with the Periodontology Clinic of "Gr. T. Popa" University of Medicine and Pharmacy Iași. The evaluation of oral health on patients with dialysis was conducted in the hospital for the patients unfit for transport.

All the patients diagnosed with chronic periodontitis received periodontal treatment. These patients were divided in two groups. The first group included patients with CKD that were submitted to conservative periodontal therapy. The second group-the control group included patients without a systemic disease that presented moderate to severe CP, with periodontal probing depth ≥ 5 mm and attachment level ≥ 6mm and radiographic evidence of alveolar bone loss.

This study included adult patients, with the age ≥ 18 years, that didn't receive any periodontal treatment, anti-microbial and anti-inflammatory therapy during the last 6 months and that didn't use steroidal or immunosuppressive drugs [5, 6].

The patients with two laboratory diagnosis of proteinuria and/or glomerular haematuria and GFR<60mL/min/1.73m^2, measured at least 3 months in between, were diagnosed with CKD. The blood samples were collected for biochemical analysis initially and at 3 months after periodontal treatment.

The venous blood was collected in vacuumed tubes between 07:00 AM and 09:00 AM, at 12 hours after the last meal (Fig. 1).

All the patients with CP diagnosis received periodontal therapy.

Both groups received oral hygiene instructions. The periodontal therapy included root planning and debridement with Gracey curettes and ultrasound instruments (Fig. 2-4).

After the completion of the periodontal treatment, the follow-up visits were made at 15, 30, 60 and 90 days. The oral hygiene instructions and supragingival prophylaxis measures were conducted at every follow-up visit. The study was realized between March 2011 and August 2012 and it was finished after the completion of the patients' evaluation.

We used Student's t-test to compare CKD to control group in independent samples or Mann-Whitney test. For before-and-after comparisons we used Student's t-test or Wilcoxon test.

Fig. 1. Prelevation tubes

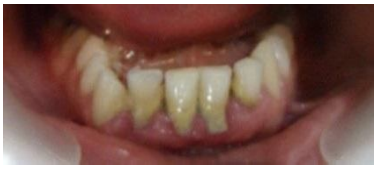

Fig. 2. Chronic periodontitis: calculus deposits and microbial plaque

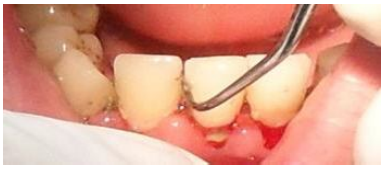

Fig. 3. Initial etiological treatment: manual calculus removal on the buccal surfaces of frontal mandibular teeth

Fig. 4. Initial etiological treatment: professional brushing on mandibular frontal teeth

For the correlations between inflammatory markers and clinical periodontal parameters we used the Pearson correlation coefficient for the variables with a normal distribution and Spearman correlation coefficient. The analysis was conducted with SPSS 13.0 V software.

RESULTS AND DISCUSSIONS

The control group and test group patients' distributions are illustrated in Figure 5 and 6.

The study group patients presented homogenous demographic characteristics and the periodontal therapy was the sole variable in both groups (Table 1).

The main cause for CKD was the hypertensive nephrosclerosis (30.6%). The most frequently identified systemic diseases in the CKD group were high blood pressure (97.2%) and diabetes mellitus (27.8%). It is important to notice that no patient used statins or iron substitution therapy during the study.

Initially, CP was more severe on patiens with CKD than in the control group, demonstrated by higher levels of IL-6 (p=0.04) and CRP (p=0.03) (Table 1) and by the patients with higher probation depth (p = 0.03) and attachement level (p = 0.003) (Table 2).

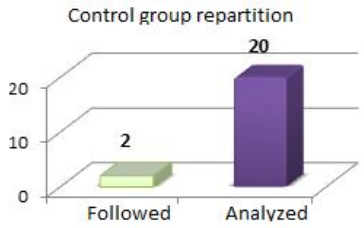

Fig. 5. Control group patients repartition

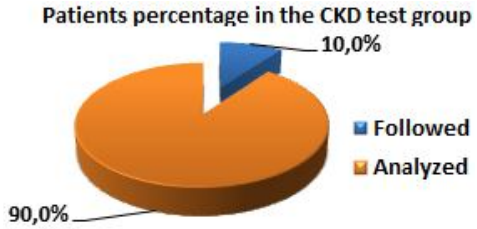

Fig. 6. Patients percentage in the CKD test group

Demographic and clinical characteristics	Study group (n=36)	Control group (n=20)	*p* Value
Age, ± SD	53.17 ± 12.00	43.4 ± 0 11.00	0.06
Male, n(%)	23 (63)	9 (45)	0.17
Diabetes mellitus, n(%)	10 (27)	--	--
BMI (kg/m^2), ± SD	26.53 ± 4.95	26.88 ± 5.10	0.8
Systolic BP (mm Hg), ± SD	143.63 ± 17.80	131.16 ± 18.20	0.01*
Diastolic BP (mm Hg), ± SD	86.11 ± 9.87	81.0 ± 11.34	0.08
Serum albumine (g/dL), ± SD	4.27 ± 0.34	4.37 ± 0.22	0.25
Serum creatinine (mg/dL), ± SD	2.39 ± 1.11	0.77 ± 0.21	0.001*
eGFR (mL/min/1.73 m^2), ± SD	34.27 ± 16.02	107.60 ± 26.73	0.001*
CKD stage			
3 n (%)	21 (58.30)	--	--
4 n (%)	12 (33.30)	--	--
5 n (%)	3 (8.30)	--	--
Biochemical characteristics			
Prohepcidin (ng/mL) ± SD	166.24 ± 55.70	147.39 ± 51.50	0.22
IL-6 (pg/mL) ± SD	4.04 ± 2.40	2.95 ± 2.20	0.04*
CRP (mg/L) ± SD	6.18 ± 5.39	3.04 ± 3.82	0.03*
Haemoglobin (g/dL) ± SD	12.72 ± 1.96	13.30 ± 1.89	0.29
Ferritin (ng/dL) ± SD	180.60 ± 129.0	184.0 ± 154.0	0.93
TSat (%)	29.30	33.90	0.01*

** p < 0.05 SD = standard deviation; n = number; BMI = body mass index; BP=blood pressure; eGFR = estimated glomerular filtration rate; CKD = chronic kidney disease; IL-6 = Interleukin-6; us-CRP = ultrasensitive C-reactive protein; TSat = transferrin saturation.*

Table 1. The initial study population characterisation

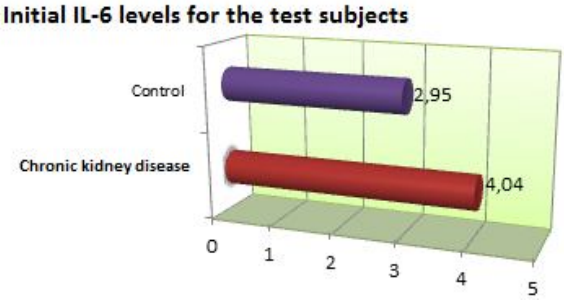

Fig. 7. Initial IL-6 levels for the test subjects

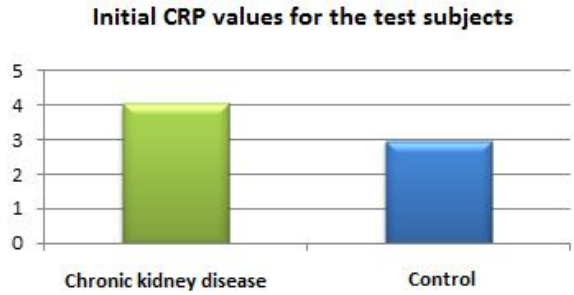

Fig. 8. Initial CRP values for the test subjects

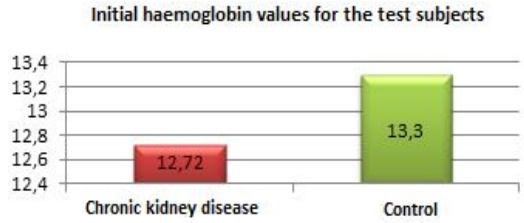

Fig. 9. Initial haemoglobin values for the test subjects

The efficiency of the periodontal therapy was demonstrated by significant dicreased inflammatory markers levels and by the clinical parameters improvements observed at 3 months after the periodontal therapy completion (Table 2).

IL-6 and CRP levels have significantly decreased after the periodontal treatment in both groups. Furthermore, significantly higher levels of haemoglobin and ferritin were observed in the control group patients, associated with the periodontal treatment (Table 3).

Parameters	CKD		Control	
	Before PT	After PT	Before PT	After PT
Number of teeth, ± SD	22.97 ± 5.20	22.33 ± 5.30	23.8 ± 5.6	23.15± 5.40
BDP %	24.08	5.97*	31.25	5.05*
PPD (mm), ± SD	**2.90 ± 1.13**	**1.99 ± 0.82***	**2.52 ± 0.41**	**1.98 ± 0.40***
CAL (mm), ± SD	**2.92 ± 0.92****	**2.20 ± 0.65***	**2.37 ± 0.40**	**2.02 ± 0.43***
GI[1], ± SD	1.36 ± 0.81	0.31 ± 0.47*	1.40 ± 0.59	0.41 ± 0.33*
PI[2], ± SD	1.18 ± 0.69	0.36 ± 0.46*	0.99 ± 0.74	0.20 ± 0.14*
Situses with PPD ≥ 5 mm, n	19.23**	4.35*	9.61	3.72*

** p<0.05 (before and after treatment in the same group).*
*** p<0.05 (comparison between the two groups before the treatment).*
PT= periodontal treatment; BDP = bleeding on probing; PPD = periodontal probing depth; CAL = clinical attachment level; GI = Gingival Inflammation: 0 = absent, 1 = mild, 2 = moderate, 3 = severe; PI = plaque index: 0 = absent, 1 = mild, 2 = moderate, 3 = severe; PPD ≥5 mm = Periodontal probing depth ≥5 mm; SD = standard deviation; n = number.

Table 2. Initially and at 3 months after periodontal therapy periodontal parameters

	CKD ± SD		Control ± SD	
	Before periodontal therapy	After periodontal therapy	Before periodontal therapy	After periodontal therapy
Prohepcidin (ng/mL)	166.24 ± 55.70	153.29 ± 56.90*	147.39 ± 51.50	131.72 ± 47.10**
IL-6 (pg/mL)	**4.04 ± 2.40**	**3.28 ± 2.10****	**2.95 ± 2.20**	**2.09 ± 1.40***
Us-CRP (mg/L)	**6.18 ± 5.30**	**4.08 ± 3****	**3.04 ± 3.80**	**2.20 ± 2.30***
Serum Fe (µg/dL)	81.60 ± 25.50	91.10 ± 24.90	99 ± 24.20	100.90 ± 18.30
Tsat (%)	29.30	30.40	33.90	30.90*
Ferritin (ng/dL)	180.60 ± 129	171.70 ± 125	184 ± 154	222 ± 205*
Haemoglobin (g/dL)	12.70 ± 5.30	12.20 ± 6.20	13.30 ± 7.90	14.10 ± 6.80*

** p<0,05, ** p< 0.01. CKD = chronic kidney disease; IL-6 = Interleukin-6; us-CRP = ultrasensitive C-reactive protein; Fe = iron; TSat = transferrin saturation*

Tabel 3. Biochemical and inflammatory markers before and at 3 months after treatment

A significant association was observed between CRP and serum IL-6 in the CKD group after periodontal therapy (Table 3).

According to the statistical analysis, none of the independent variables was significantly and independently associated to the dependent variable on CKD patients, while in the control group only IL-6 (95% CI -45.40 la -4.49; p=0,02) was being significant.

This study evaluated the impact of the periodontal therapy on the inflammatory response and determined for the first time a causal association between the CP activity and high levels of inflammatory markers.

The inflammation has a key-role in the atherosclerosis pathogenicity; systemic chronic inflammation was associated with cardiovascular unwanted results on patients with CKD, although the nature and the source of inflammation aren't always very clear. Chronic periodontitis is an infectious chronic disease determined by Gram-negative bacteria that induce the systemic inflammatory response [7, 8, 9].

The local tissue destruction influences a systemic dissemination of periodontal pathogenic agents and their products (e.g., lipopolysaccharides) and local inflammatory mediators, like IL-1, IL-6 THF-α and PG E2, among others. This has shown that CP induces an inflammatory acute phase as a response which can be measured by the serum level of CRP.

We observed that CP was more severe on patients with CKD than in the group of patients without systemic diseases. Furthermore, at 3 months after periodontal therapy, we observed a significant reduction of the clinical parameters CAL and PPD, both being markers of CP severity, confirming the treatment success.

Next to a clinical improvement of CP, we observed diminished levels of IL-6 and CRP, both markers of systemic inflammatory response, confirming the results of other publications [10, 11, 12].

CONCLUSIONS

Our conclusions suggest that CP is more severe on patients with chronic kidney disease and that it induces a systemic inflammatory response.

The periodontal therapy reduces the inflammatory component and decreases the markers' serum levels, indicating an important interventional therapy on patients with CKD. Considering the chronic inflammation a risk factor for atherosclerotic cardiovascular diseases on patients with high blood pressure and diabetes mellitus, the main causes for CKD, the immediate CP diagnosis, followed by periodontal therapy, is plausible to represent an important preventing measure for CKD in clinical daily practice.

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