Pilot study on the association of chronic periodontitis in patients with chronic kidney disease

ABSTRACT

Introduction: Chronic periodontitis (CP) is a bacterial infection of the supporting soft tissue in the subgingival dental plaque that can trigger systemic inflammation. Objective: The objective of this study was to evaluate the incidence of CP in patients with predialytic and chronic kidney disease. Material and Methods: The definition of ESRD was based on the Kidney Disease Outcome Quality Initiative proposed by the National Kidney Foundation. The Modification of Diet in Renal Disease equation [P2] was used to estimate the glomerular filtration rate (GFR) from the plasma creatinine level. C-reactive protein (CRP) was used to determine the inflammatory response in 30 patients divided in three groups: group 1 (G1) was composed of six patients without CKD and with CP; group 2 (G2) comprised 19 patients with CKD and localized CP; and group 3 (G3) was composed of five patients with CKD and generalized CP. The severity of CP was based on the probing depth (PD). Bacteria were identified by polymerase chain reaction. Results: C-reactive protein in G1 (2.4 ± 2.5 mg/L) did not differ from that in G2 (4.6 ± 4.5 mg/L, p = 0.1), but a tendency to differ compared to G3 (7.6 ± 3.8 mg/L, p = 0.05) was observed. Probing depth in G1 (2.1 ± 0.6 mm) was less severe than in G2 (PD = 2.9 ± 1.2 mm, p = 0.05) and G3 (PD = 4.3 ± 0.8 mm, p = 0.04). Statistical differences in the frequency of the bacteria isolated in all three groups were not observed. Conclusion: Despite the limited number of patients, our results suggest that generalized CP is more frequent in patients with ESRD.

Keywords: C-reactive protein, inflammation, periodontal disease, periodontal pathogens, end-stage renal disease.

INTRODUCTION

Chronic inflammatory overload has been suggested as a risk factor for end-stage renal disease (ESRD),1 and it also contributes for the risk of cardiovascular disease (CVD), especially atherosclerotic.2

Chronic periodontitis (CP) is a bacterial infection of supporting soft tissues in the subgingival dental plaque that can lead to a chronic systemic inflammatory response. Chronic periodontitis is associated with elevated serum levels of C-reactive protein (CRP), which decrease after treatment.3,4 The objective of this study was to evaluate the incidence of CP in patients with predialytic chronic kidney disease (CKD).

MATERIAL AND METHODS

This is a transversal study with 30 patients with CP and without predialytic CKD group 1 (G1) included patients without ESRD (n = 6); group 2 (G2) included patients with CKD and localized CP; and group 3 (G3) patients with CKD and generalized CP (n = 5).

Patients in G1 had hypertension and CP but not CKD. Smokers, patients on non-steroidal anti-inflammatory medication, those who used antibiotics within the past three months, pregnant women, patients with HIV, decompensated diabetics, patients with other infections or fever of unknown origin, those who were treated for periodontitis within the last six months, those with less than 14 teeth, and those who refused to sign the informed consent were excluded.

The diagnosis of CKD was based on the Kidney Disease Outcomes Quality Initiative (KDOQI) proposal of the National Kidney Foundation. Serum level of CRP, measured by high sensitivity nephelometry, was expressed in milligrams per liter (mg/L) and used to evaluate the inflammatory response.
One investigator was responsible for the periodontal exam at the Oral and Maxillofacial Surgery Outpatient Clinic of the UFJF. Clinical parameters such as probing depth (PD), clinical insertion level (CIL), plaque index (PI), and gingival index (GI) were evaluated. Clinical parameters were determined on six sites in all teeth. Chronic periodontitis was classified as generalized when more than 30% of the sites had PD > 4 mm and as localized when less than 30% of the sites presented PD ≤ 4 mm.

The subgingival calculus and the biofilm were removed from the most apical inflamed site (PD > 3 mm) with sterilized Gracey curettes and transferred, immediately, to Eppendorf tubes containing 200 µL of bacterial lytic solution. The material was stored in a freezer at -20°C, and extraction of the bacterial DNA genome, performed according to a methodology established previously, to be used as a mold in polymerase chain reactions.

Specific oligoinitiators for the following species were used in the polymerase chain reactions: Fusobacterium nucleatum, Aggregatibacter actinomycetemcomitans, Prevotella nigrescens, Eikenella corrodens, Porphyromonas gingivalis, and Treponema denticola.

The Mann-Whitney test was used to compare the clinical and demographic characteristics of the study groups and periodontal clinical parameters. The Chi-square test was used to correlate pathogenic bacteria and mean CRP, using the software SPSS version 13.0. A level of p < 0.05 was considered as statistically significant.

**RESULTS**

Thirty out of 49 patients evaluated fulfilled preestablished inclusion criteria. Among patients with CKD, the disease was caused by hypertension in 30%, diabetic renal disease in 13%, glomerulonephritis 10%, and by other causes in 47%.

Table 1 shows patient data. The age of the patients was similar in all three groups: G1, 49 ± 9 years; G2, 57 ± 11 years; and G3, 54 ± 10 years. As a rule, a preponderance of male gender was observed. Although it did not reach statistical significance, higher blood pressure levels were observed in patients with CKD and CP, both in G2 (153 ± 16 mmHg vs. 133 ± 17 mmHg in the control group, p < 0.4), and in G3 (170 ± 12 mmHg vs. 133 ± 17 mmHg, p < 0.09). Glomerular filtration rate was higher in G1 (mean 90 mL/min/1.73 m²) but it did not differ between G2 (mean 33 ± 22 mL/min/1.73 m²) and G3 (mean 30 ± 19 mL/min/1.73 m²) (p > 0.05).

**Table 1**

<table>
<thead>
<tr>
<th>Clinical-laboratorial parameter</th>
<th>Control group</th>
<th>Localized CP</th>
<th>p</th>
<th>Generalized CP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>49 ± 9</td>
<td>57 ± 11</td>
<td>0.1</td>
<td>54 ± 10</td>
<td>0.6</td>
</tr>
<tr>
<td>Male (%)</td>
<td>100%</td>
<td>80%</td>
<td>0.1</td>
<td>50%</td>
<td>0.1</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>133 ± 17</td>
<td>153 ± 16</td>
<td>0.4</td>
<td>170 ± 12</td>
<td>0.09</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>83 ± 10</td>
<td>90 ± 11</td>
<td>0.1</td>
<td>90 ± 14</td>
<td>0.4</td>
</tr>
<tr>
<td>GFR (mL/min/1.73 m²)</td>
<td>90 ± 5</td>
<td>33 ± 22</td>
<td>0.00</td>
<td>30 ± 19</td>
<td>0.04</td>
</tr>
<tr>
<td>Number of teeth</td>
<td>20 ± 4</td>
<td>23 ± 4</td>
<td>0.3</td>
<td>23 ± 7</td>
<td>0.5</td>
</tr>
<tr>
<td>PI</td>
<td>0.7 ± 0.4</td>
<td>1 ± 0.6</td>
<td>0.2</td>
<td>1.5 ± 0.8</td>
<td>0.1</td>
</tr>
<tr>
<td>GI</td>
<td>0.9 ± 0.4</td>
<td>1.2 ± 0.7</td>
<td>0.2</td>
<td>2.7 ± 0.1</td>
<td>0.04</td>
</tr>
<tr>
<td>PD (mm)</td>
<td>2.1 ± 0.6</td>
<td>2.9 ± 1.2</td>
<td>0.05</td>
<td>4.3 ± 0.8</td>
<td>0.04</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>2.4 ± 2.5</td>
<td>4.6 ± 4.5</td>
<td>0.1</td>
<td>7.6 ± 3.8</td>
<td>0.05</td>
</tr>
<tr>
<td>F. nucleatum (%)</td>
<td>0%</td>
<td>5.5%</td>
<td>0.7</td>
<td>50%</td>
<td>0.1</td>
</tr>
<tr>
<td>E. corrodens (%)</td>
<td>83.3%</td>
<td>100%</td>
<td>0.2</td>
<td>75%</td>
<td>0.6</td>
</tr>
<tr>
<td>P. gingivalis (%)</td>
<td>83.3%</td>
<td>71.4%</td>
<td>0.5</td>
<td>50%</td>
<td>0.4</td>
</tr>
<tr>
<td>P. nigrescens (%)</td>
<td>33.3%</td>
<td>47%</td>
<td>0.4</td>
<td>33.3%</td>
<td>0.7</td>
</tr>
<tr>
<td>A. actinomycetemcomitans (%)</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T. denticola (%)</td>
<td>50%</td>
<td>47%</td>
<td>0.6</td>
<td>66.6%</td>
<td>0.5</td>
</tr>
</tbody>
</table>

CP: chronic periodontitis; SD: standard-deviation; SBP: systolic blood pressure; DBP: diastolic blood pressure; GFR: glomerular filtration rate; PI: plaque index; GI: gingival index; PD: probing depth; CRP: C-reactive protein.
Groups did not differ in the mean number of teeth: G1 = 20 ± 4 vs. G2 = 23 ± 4 (p = 0.3), and G3 = 23 ± 7 (p = 0.5). Plaque index (0.7 ± 0.4 in G1; 1.0 ± 0.6 in G2; and 1.5 ± 0.8 in G3), GI (0.9 ± 0.4 in G1; 1.2 ± 0.7 in G2; and 2.7 ± 0.1 in G3), and PD (2.1 ± 0.6 mm in G1; 2.9 ± 1.2 mm in G2; and 4.3 ± 0.8 mm in G3) indicated more severe CP in patients in G3 compared to G1.

Mean (± SD) CRP tended to be more elevated in patients with CKD and generalized CP (7.6 ± 3.8 mg/L) when compared to the control group (2.4 ± 2.5 mg/L, p = 0.05), and it did not differ between G1 and G2 (4.6 ± 4.5 mg/L). Statistically significant differences in the frequency of the bacteria isolated in all three groups were not observed.

**DISCUSSION**

Our study demonstrated that Fusobacterium nucleatum, Prevotella nigrescens, Eikenella corrodens, Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Treponema denticola are frequently found in CP, being associated with a more pronounced systemic inflammatory response in patients with generalized CP and predialytic CKD.

The mechanism of the inflammatory response to periodontal pathogens seems to involve the systemic dissemination of bacteria, antigen, endotoxins, and inflammatory cytokines. Since it is a site of chronic systemic inflammation, it is biologically plausible to accept CP as a risk factor for ESRD. For example, Kshirsagar et al. observed that a GFR < 60 mL/min/1.73 m², after adjusting for risk factors for cardiovascular disease and ESRD, was associated with mild (Odds Ratio, 2.00; 95% CI, 1.23 to 3.24) and severe (Odds Ratio 2.14; 95% CI, 1.19 to 3.85) periodontal disease.

Davidovich et al. also observed the association of a higher degree of gingival inflammation and probing depth through the entire spectrum of CKD when compared with healthy individuals. Shultis et al. observed an association between diabetic kidney disease and periodontal disease. In our study, higher serum levels of CRP in patients with CKD and more generalized periodontal disease are consistent with those results; however, the nature of our study, based in a single evaluation of CP, does not allow the establishment of a definitive positive cause-effect relationship.

Chronic periodontitis is associated with altered endothelial function that improves after treatment. Chronic periodontitis leads to lower bioavailability of nitrous oxide and dysfunctional endothelium and, therefore, could explain the increase in systolic blood pressure in our patients with CKD and generalized periodontal disease.

**CONCLUSION**

To conclude, patients with CKD have CP caused by Gram-negative anaerobic bacteria, which leads to a systemic inflammatory response, especially in the generalized form of periodontitis. Patients with CKD should be evaluated regularly for CP which, if diagnosed, should be treated vigorously when identified.

**REFERENCES**


