Effects on Serum Ceruloplasmin Levels before and After Non-Surgical Periodontal Therapy in Patients with Chronic Periodontitis

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Abstract: Background: Pro-inflammatory markers have come a long way as indicators of periodontal disease. One such marker which can be detected in the serum is the ceruloplasmin. The aim of this study was to evaluate the serum ceruloplasmin (CP) levels before and after non-surgical periodontal therapy in chronic periodontitis patients.

Methods: The study was conducted on 80 subjects. The subjects were divided into 2 groups: group 1 included chronic periodontitis patients (study group, n = 40), and group 2 included periodontally healthy subjects (control group, n = 40). Serum ceruloplasmin levels in blood sample and periodontal clinical parameters were recorded at baseline for both groups. The study group received meticulous scaling and root planing twice weekly for 2 weeks. Four weeks after treatment, the second blood sample was taken and reevaluation of clinical periodontal parameters was done.

Results: Baseline serum CP level was significantly higher in chronic periodontitis patients (study group) compared to healthy subjects (control group) (P < 0.001). Four weeks after non-surgical periodontal therapy, the mean value of serum CP concentration in study group was significantly decreased (P < 0.001).

Conclusion: Non-surgical periodontal therapy has a reducing effect on the serum CP level in chronic periodontitis patients. Serum CP level represents a potential biomarker indicator of the chronic periodontitis.

Keywords: biomarker, ceruloplasmin, non-surgical therapy, periodontitis.

I. Introduction

Periodontitis is a multifactorial inflammatory disease which generally affects the connective tissue attachment and supporting bone present around the teeth. It is generally caused by interactions between periodontal microflora and host response.¹

The most common clinical features of chronic periodontitis are the loss of clinical attachment level, alveolar bone destruction, the formation of periodontal pockets, and gingival inflammation. Additional signs and symptoms of a chronic periodontal disease are the accumulation of supra- and sub-gingival calculus, gingival enlargement or recession, bleeding, furcation involvement, the mobility of the teeth, and bad breath.²

Currently, periodontitis is diagnosed entirely on the basis of an array of clinical measurements including clinical attachment level (CAL), bleeding on probing (BOP), probing depth (PD), and radiographic findings.³ Additional information obtained by medical and family history, and specific characteristics of clinical presentation, such as quantity of local factors and location of lesions, are helpful in the differential diagnosis of specific types of periodontitis.⁴ These clinical parameters are the best currently available indicators for determining disease status; however, they only provide information about past periodontal tissue destruction and do not elucidate current disease activity nor predict future activity due to low sensitivity and positive predictive value.⁵

Therefore, advances in oral and periodontal disease diagnostic research are moving toward methods, whereby, periodontal risk can be identified and quantified by objective measures like biomarkers.⁶ One of these biomarkers that can be detected in several inflammatory conditions is ceruloplasmin (CP).⁷

Ceruloplasmin is a 122-kD multi-copper binding plasma protein containing ferroxidase activity necessary for ferric ion saturation of transferrin. Ceruloplasmin helps in transferring copper within our body and also influences the uptake of iron into the cells because of its property of conversion of ferrous form of iron to the ferric form, due to which alterations in serum iron are often accompanied by changes in serum ceruloplasmin.⁸,⁹ It thus leads to a state of hypoferremia. Ceruloplasmin is also an acute phase reactant seen to increase in inflammatory conditions.⁹,¹⁰

The aim of non-surgical periodontal treatment (NPT) is the elimination of bacterial deposits which adhere to tooth surfaces, primarily by means of dental plaque control performed by the patient, in addition to
dental scaling and root surface debridement performed by the dentist\textsuperscript{11}. Systematic reviews and meta-analysis support the effect of NPT for controlling periodontal disease by reducing inflammation\textsuperscript{12}.

This study aimed to evaluate the serum CP levels after non-surgical periodontal therapy in the chronic periodontitis patients.

II. Materials And Methods

This study was conducted on 80 systemically healthy subjects who were non-smokers selected from the patients attending outpatient department of Periodontology Department, Indira Gandhi Govt.Dental College Jammu. The subjects were divided into two groups based on periodontal health. Group 1: Study group comprised of 40 subjects (22 males and 18 females), with a mean age of 42.38 years (range 35 to 55 years); who were diagnosed with chronic periodontitis. Group 2: Control group with healthy periodontium comprised of 40 subjects (23 males and 17 females), with a mean age of 40.67 years (range 35 to 55 years).

Subjects included in our study (study group) were classified as having moderate (20 patients) or severe (20 patients) chronic periodontitis. Patients were classified according to the criteria mentioned by American Academy of Periodontology workshop in 1999 in which moderate and severe chronic periodontitis cases have clinical attachment loss of 3-4 mm, and more than 5 mm, respectively\textsuperscript{6}.

Written informed consent was obtained from all subjects at the baseline. Ethical clearance was taken from the ethical committee of the institution prior to the study. The subjects who had any systemic diseases that could influence the outcome of therapy, patients who had received surgical periodontal treatment in the last six months, those having acute inflammatory conditions that might affect serum CP level, pregnant, smokers, and those who were on immunosuppressive chemotherapy were excluded from the study.

A careful clinical examination, a documented case history, a panoramic radiograph, and the first blood sample were performed for all study populations at the baseline.

Following this, the chronic periodontitis patients received full-mouth scaling and root planing under local anesthesia. Scaling was done using piezoelectric ultrasonic scalers, and root planing was performed using specific Gracey curettes. No antibiotics were prescribed following this treatment. Oral hygiene instructions were given. Scaling and root planing therapy was repeated twice weekly for two weeks. After four weeks of treatment, the second serum samples were taken.

The bleeding on probing index (BOP), probing pocket depth (PPD) and clinical attachment level (CAL) were measured at the beginning of the study in both groups and four weeks after treatment in the study group. These clinical parameters were recorded using a Williams’ periodontal probe (Hu-Friedy, Chicago, IL, USA).

Blood samples were withdrawn from the antecubital vein under aseptic condition. The samples were centrifuged at 2000 rpm for 10 min. Serum samples were collected and stored in Eppendorf tube at -20 °C until the time of assay.

Serum CP level was analyzed by using Human CP ELISA Kit (Assaypro LLC, USA) which is designed for detection of human CP in plasma and serum samples.

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of the distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. The significance of the results was judged at the 5% level.

III. Results

The age of the subjects in the control group ranged from 35 to 55 years with mean and standard deviation (SD) of 40.67 ± 3.08 years. Twenty-three (57.5%) were males and 17 (42.5%) were females.

The age of the patients in the study group also ranged from 35 to 55 years with mean and SD of 42.38 ± 6.13 years. Twenty-two (55%) were males and 18 (45%) were females [Table 1]. Demographic data of all study populations are illustrated in Table 1. There was no significant difference between the two groups regarding age and gender.

<table>
<thead>
<tr>
<th>Table 1- Demographic data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender (n%)</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Age (Years)</td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td>Mean±SD</td>
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Regarding clinical parameters (PPD, CAL, and BOP), the values of the mean and SD were 5.02 ± 0.67, 4.56 ± 1.54 and 4.58 ± 0.58 respectively. There was a significant difference between the chronic periodontitis group and the healthy control group at the baseline and after non-surgical periodontal therapy (P < 0.001). Furthermore, the mean and SD of the clinical parameters (PPD, CAL, and BOP) in the chronic periodontitis group after treatment were 4.11 ± 0.39, 3.62 ± 1.37 and 0.29 ± 0.53 respectively. These values showed a significant reduction after the treatment compared to its values at the baseline [Table 2].

The mean values of serum CP level in the study group and the control group at the baseline were 44.50 ± 10.46 and 18.21 ± 3.20 respectively. These values showed a significant difference between the two groups (P < 0.001). In chronic periodontitis patients (study group), the mean value of serum CP level after treatment was recorded at the baseline for all subjects, and after non-surgical therapy in chronic periodontitis patients. Serum samples were used to investigate the level of CP because it is mainly synthesized by the liver and then secreted into the blood.

**Table 2- Comparison of different parameters**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Study group (n=40)</th>
<th>Control group (n=40)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceruloplasmin</td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td></td>
<td>44.50±10.46</td>
<td>18.21±3.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>28.28±5.37</td>
<td>18.21±3.20</td>
<td>0.001</td>
</tr>
<tr>
<td>PPD</td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.02±0.67</td>
<td>0.92±0.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>4.11±0.39</td>
<td>0.92±0.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAL</td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.56±1.54</td>
<td>0.0±0.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>3.62±1.37</td>
<td>0.0±0.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BOP</td>
<td>Before</td>
<td>After</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.58±0.58</td>
<td>0.07±0.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>0.29±0.53</td>
<td>0.07±0.20</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Statistically significant at P ≤ 0.05. PPD: probing pocket depth; CAL: clinical attachment level; BOP: bleeding on probing index

The mean values of serum CP level in the study group and the control group at the baseline were 44.50 ± 10.46 and 18.21 ± 3.20 respectively. These results showed that there was a significant difference between the two groups (P < 0.001).

In chronic periodontitis patients (study group), the mean value of serum CP level after treatment was significantly reduced compared to its value at the baseline [Table 3].

**Table 3 - Correlation between ceruloplasmin and periodontal parameters in study group**

<table>
<thead>
<tr>
<th>Periodontal parameters</th>
<th>Ceruloplasmin in study group before</th>
<th>Ceruloplasmin in study group after</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPD</td>
<td>r 0.350</td>
<td>0.121</td>
</tr>
<tr>
<td></td>
<td>p 0.032</td>
<td>0.421</td>
</tr>
<tr>
<td>CAL</td>
<td>r 0.380</td>
<td>0.104</td>
</tr>
<tr>
<td></td>
<td>p 0.014</td>
<td>0.473</td>
</tr>
<tr>
<td>BOP</td>
<td>r 0.007</td>
<td>0.312</td>
</tr>
<tr>
<td></td>
<td>p 0.964</td>
<td>0.052</td>
</tr>
</tbody>
</table>

*Statistically significant at P ≤ 0.05. PPD: probing pocket depth; CAL: clinical attachment level; BOP: bleeding on probing index

**IV. Discussion**

It has long been established that simple and non-invasive diagnostic tools that allows rapid screening, provides accurate predictive information and enables reliable evaluation of periodontal disease status would be of great value to both dentists and patients. Potential diagnostic biomarkers for diagnosis of periodontal disease is the latest modality and mainly includes locally produced proteins of host and bacterial origin such as enzymes, immunoglobulins, cytokines and also includes genetic/genomic biomarkers such as deoxyribonucleic acid and messenger ribonucleic acid of host origin, bacteria and bacterial products, ions, steroid hormones and volatile compounds. One such potential marker recognized is the ceruloplasmin.

Ceruloplasmin is a 132-kDa pro-inflammatory marker protein with multiple copper-binding domains seen to increase in systemic infections. Ceruloplasmin has the ability to create a state of hypoferraemia, which increases the natural resistance of the body to fight the disease. Ceruloplasmin also acts as a downstream target for hypoxia inducible factor (HIF-1α) which is created in an area of local inflammation during the infections. It is also seen to play a central role in excessive superoxide generation in phenotypically hyperactive and primed peripheral blood polymorphonuclear neutrophils (PMNs). Ceruloplasmin functions an anti-inflammatory agent and it can also work as a proinflammatory molecule.

This study was conducted on 80 subjects, divided into 2 groups. Forty patients suffering from chronic periodontitis served as a study group while the control group was represented by 40 periodontally healthy subjects. The aim was to evaluate the serum CP levels after non-surgical periodontal therapy in the chronic periodontitis patients. The clinical periodontal parameters (PPD, CAL, BOP) were recorded at the baseline for all subjects, and after non-surgical therapy in chronic periodontitis patients. Serum samples were used to investigate the level of CP because it is mainly synthesized by the liver and then secreted into the blood.

The present study revealed that there was a significant elevation in PPD, CAL and BOP values in chronic periodontitis patients as compared to healthy subjects at the baseline. In chronic periodontitis patients, the mean values of periodontal parameters after scaling and root planing (SRP) were found to be significantly reduced compared to its value at the baseline [Table 2].
decreased when compared to their baseline values. The improvement in clinical parameters after SRP may be attributed to the resolution of inflammatory response and the cessation of periodontal disease destruction. These outcomes result in a relative gain of clinical attachment and a reduction of the probing depth\textsuperscript{18,19}.

These results are in agreement to the studies conducted by Mohammed et al.,\textsuperscript{20} Chan and La\textsuperscript{21} and De Micheli et al.,\textsuperscript{22} who found significant reduction in probing pocket depth and bleeding on probing following nonsurgical therapy. Also, Darby et al.\textsuperscript{23} showed that SRP resulted in improvement in the clinical attachment loss measurements mean values.

At the baseline, the serum CP levels of the study group was statistically significantly higher than that of control subjects. The higher level of the serum CP in chronic periodontitis patients may be because of the role of CP as a proinflammatory mediator, acute phase protein and an anti-inflammatory function which is carried by an antioxidant, bactericidal, and ferroxidase activities\textsuperscript{24}. Moreover, the higher level of CP during inflammation could be attributed to its role as a protease inhibitor\textsuperscript{18}.

In the present study, the results revealed that SRP significantly reduced the level of serum CP in chronic periodontitis when compared to its value at the baseline. This reduction in the CP level can be attributed to the effect of SRP on removal of local factors; thus, it can decrease the inflammatory response and consequently decrease the mediators that stimulate acute phase protein production\textsuperscript{22}. The results of the present study about the effect of SRP on serum levels of CP in the chronic periodontitis subjects are in accordance to the study conducted by Mohammed AA et al.\textsuperscript{20}

V. Conclusion
Non-surgical periodontal therapy has a reducing effect on the serum CP level in chronic periodontitis patients. Serum CP level represents a potential biomarker indicator of the chronic periodontitis.

References

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