Original Article

C-reactive protein in patients with aggressive periodontitis

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KEYWORDS
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Abstract
Background/purpose: The aim of this study was to evaluate and compare the systemic levels of C-reactive protein (CRP) in peripheral blood samples of patients with aggressive periodontitis during the first twelve months of periodontal treatment, at exactly six month interval measurements, and compare them with clinical periodontal parameters.

Materials and methods: All patients (N = 45) were examined prior to the initiation of periodontal treatment. Patients were divided into two groups GAgP (Generalised form of aggressive periodontitis, N = 23) and group LAgP (Localised form of aggressive periodontitis, N = 22). Control group (CON) included 60 individuals with healthy periodontium. The levels of CRP were determined in both groups GAgP and LAgP three times in 6 month intervals during the periodontal treatment.

Results: CRP is a plasma protein that reflects the extent of the acute phase response to inflammation and is one of the markers of choice for monitoring this response. In our study, CRP levels decreased in course of periodontal treatment in both groups (GAgP and LAgP) in a similar way as bleeding on probing (BOP) and probing pocket depth (PPD) indices.

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Introduction

Periodontal disease is an inflammatory disease that affects the soft and hard structures that support the teeth.\(^1\) In gingivitis, inflammation localised to the supracrestal region of the periodontium leads to ulceration of the junctional epithelium. Although this is technically a loss of clinical attachment (because in healthy tissue the epithelium attaches to the surface of the tooth), clinical attachment loss (CAL) is used almost exclusively to refer to connective tissue attachment loss. Sites with periodontitis exhibit clinical signs of gingival inflammation and loss of connective tissue attachment. Connective tissue attachment loss refers to the pathological detachment of collagen fibres from the cemental surface with the concomitant apical migration of the junctional or pocket epithelium on the root surface.\(^2\) Diagnosis of aggressive periodontitis is made on clinical, radiographic and historical findings which show rapid attachment loss and bone destruction, and possible familial aggregation of disease. The disease often occurs in people under 35 years of age, but it may also affect older patients. Except for periodontal disease, patients are systemically healthy. Other features that may be present are periodontal tissue destruction that is greater than would be expected given the level of local factors, elevated levels of \textit{Aggregatibacter actinomycetemcomitans} or \textit{Porphyromonas gingivalis}, phagocyte abnormalities and increased production of prostaglandin \textit{E}\(_2\) and interleukin-1b.\(^3\) Early onset (aggressive) forms of periodontal diseases are detectable in all age and ethnic groups.\(^4\) This disease is divided into localised and generalised form by classification of periodontal diseases from 1999. It can be further classified on the basis of extent and severity. Aggressive periodontitis is subcategorised into localised (\(\leq 30\%\) of the teeth are affected) and generalised form (\(>30\%\) of the teeth are affected). Severity is based on the amount of clinical attachment loss (CAL) and is designated as slight (1–2 mm CAL), moderate (3–4 mm CAL) or severe (>5 mm CAL).\(^5\) Bacterial aetiology of aggressive forms of periodontitis is confirmed by the studies which have demonstrated the presence of a layer of bacterial deposits on the root surface of advanced aggressive periodontitis lesions.\(^6\) A rapid rate of destruction of the periodontium is a major criterion for the diagnosis of aggressive periodontitis.\(^6\) Diagnostic difficulty is related to the fact that periodontal destruction is often diagnosed when the attachment loss is already fairly advanced. In general, distinct alterations in the morphology of the periodontium and substantial tissue damage are necessary for establishing a clear diagnosis. CRP (C-reactive protein) is produced in response to many forms of injury other than periodontitis, such as other infections, trauma and hypoxia, and it is regulated by diverse cytokines. CRP levels have an association with smoking, obesity, triglycerides, diabetes, and periodontal disease.\(^7\) Changes in peripheral blood cellular and molecular components can be found in patients with periodontitis due to inflammatory changes of the periodontal tissues.\(^8\) Positive correlation between CRP and periodontal disease severity was proved by many studies,\(^9\) and levels of CRP decrease after nonsurgical periodontal therapy,\(^10\) but most studies have focused on CRP levels in chronic periodontitis, and very few are conducted on patients with aggressive periodontitis.\(^11\) The link between inflammation and systemic diseases, e.g. cardiovascular disease (CVD), appears to be firmly established.\(^12\) Epidemiological associations between periodontitis and CVD have been reported.\(^13,14\) Among the several biomarkers that have been proposed for cardiovascular risk stratification, high-sensitivity C-reactive protein (hs-CRP) appears to contribute to the identification of people at risk of developing CVD,\(^15\) however, the evaluation of hs-CRP has not yet been widely recommended in guidelines.\(^16\) Wohlfeil et al. compared systemic inflammatory mediators in patients with untreated aggressive and chronic periodontitis and in periodontally healthy controls. Patients with aggressive periodontitis have statistically significant elevations in serum CRP levels compared to subjects with healthy periodontium.\(^17,18\)

Thus, the aim of this study was to evaluate and compare the systemic levels of CRP in peripheral blood samples of 45 patients with aggressive periodontitis in course of periodontal treatment and of 60 healthy controls and their correlation with periodontal clinical parameters.

Materials and methods

Study population

All patients (N = 45) were recruited from the patient pool of the Department of Periodontology, Institute of Dental Medicine, First Faculty of Medicine and General University Hospital, Charles University, Prague, Czech Republic, from 2014 to 2016, and all patients were examined prior to the initiation of periodontal treatment. In our study, the patients were treated by conservative treatment — deep scaling and root planing, surgical techniques were not used. Deep scaling and root planing were performed three months after the first collection of CRP samples (appointment 1). We examined the periodontal parameters and measured the CRP levels in each patient every six months.

Conclusion: Our study results showed that CRP levels, as well as bleeding on probing (BOP) and probing pocket depth (PPD), indices decreased in course of periodontal treatment in patients with generalised and localised aggressive periodontitis. Therefore this marker might be exploitable as a means to evaluate periodontal health in patients with aggressive periodontitis.
Patients with aggressive periodontitis had to have at least one tooth with positive bleeding on probing (BOP) and a probing pocket depth (PPD) of >5 mm in all quadrants (excluding third molars). Probing pocket depth was assessed by WHO periodontal probe with a cut-off of 11.5 mm from six sites on every tooth present. Clinical attachment loss (CAL) is a sign of destructive periodontal disease. In our study, we measured CAL vestibulary for each tooth with a calibrated University of North Carolina probe with a cut-off of 15 mm. For the statistical evaluation, we used the highest value from the upper and lower jaw. All patients were examined at regular intervals of 6 months. The resorption process of alveolar bone was assessed in all patients radiographically at the beginning of periodontal treatment. In our study, we divided our patients into two groups — GAgP and LAgP. Group GAgP included 23 patients with generalised aggressive periodontitis (36.9 ± 6.2 years; mean age ± SD) and group LAgP included 22 patients with localised aggressive periodontitis (33.5 ± 7.7 years; mean age ± SD). Whether it is a localised or generalised aggressive periodontitis was decided based on the classification of the American Association of Periodontology from 1999.21

We used panoramic x-ray and x-ray status which included 12–14 x-ray pictures. We performed control intraoral x-rays after the third measurement of CRP, i.e. 12 months after the treatment began. We evaluated the presence or absence of lamina corticalis and the shape of the bone defects. All determined evaluation indices were assessed according to WHO oral health surveys.23

CRP determination

CRP levels (mg/L) were measured in capillary blood using QuikRead go CRP + Hb (Orion Diagnostica Oy, Finland), which works on the principle of photometry and turbidimetry. Capillary blood from the middle finger was collected from the patients before the clinical periodontal examination using a thin glass capillary. The samples were immediately processed and the established values were recorded.

Statistical analysis

For calculations descriptive statistics were used — mean, standard deviation, frequencies and standard error. This method was used to describe different groups in terms of age, CRP and other indices present in groups. For evaluation of the differences between groups, Student’s t-test and Fisher test were used. Significance level of 0.05 was used in all tests. MS Excel 2016 and Data analysis ToolPak add-in statistical software were used (Microsoft Office Professional Plus 2016, Microsoft, Redmont, WA, USA).

Results

All results are summarised in Table 1.

CRP levels in patient groups GAgP and LAgP in measurements during periodontal treatment and in control group CON (Fig. 1):

In both groups (GAgP and LAgP), CRP levels decreased during periodontal treatment, in GAgP group from 4.1 ± 4.1 mg/L to 3.1 ± 3.3 mg/L, in LAgP group from 2.6 ± 2.4 mg/L to 1.3 ± 1.7 mg/L. CRP level in control group CON was 1.9 ± 2.3 mg/L. In both groups (GAgP and LAgP), BOP index decreased during periodontal treatment, in GAgP group from 36.8 ± 32.4% to 6.8 ± 11.9%, in LAgP group from 30.4 ± 25.4% to 10.0 ± 18.2%, BOP index in control group CON was 4.6 ± 8.1% (Fig. 2). No statistically significant differences were found between all measurements during periodontal treatment in CRP levels.

CRP levels and PPD index in patient groups GAgP and LAgP in measurements during periodontal treatment and in control group CON (Fig. 3):

In both groups (GAgP and LAgP), PPD index decreased during periodontal treatment, in GAgP group from 6.9 ± 2.4 mms to 4.2 ± 2.7 mms, in LAgP group from 7.5 ± 3.1 mms to 4.4 ± 2.1 mms, PPD index in control group CON was 1.5 ± 0.7 mms. CRP levels and CAL index in patient groups GAgP and LAgP in measurements during periodontal treatment and in control group CON (Fig. 4):

CAL index increased during periodontal treatment in GAgP group from 8.9 ± 2.3 mms to 9.7 ± 2.7 mms, in LAgP group this index decreased during periodontal treatment...
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Table 1  Levels of CRP and clinical periodontal parameters in all tested groups.

| AGE   | CRP I. (mg/L) | CRP II. (mg/L) | CRP III. (mg/L) | BOP I. (%) | BOP II. (%) | BOP III. (%) | PPD I. (mms) | PPD II. (mms) | PPD III. (mms) | CAL I. (mms) | CAL II. (mms) | CAL III. (mms) |
|-------|---------------|----------------|-----------------|------------|-------------|--------------|--------------|---------------|----------------|--------------|---------------|----------------|
| GAgP  | Mean 36.9     | 4.1            | 4.2             | 3.1        | 36.8        | 19.8         | 6.8          | 6.9           | 5.1           | 4.2          | 8.9           | 9.0            |
|       | SD 6.2        | 4.1            | 4.6             | 3.3        | 32.4        | 26.4         | 11.9         | 2.4           | 3.1           | 2.7          | 2.3           | 2.4            |
| LAgP  | Mean 33.5     | 2.6            | 1.7             | 1.3        | 30.4        | 16.5         | 10.0         | 7.5           | 5.4           | 4.4          | 8.4           | 7.4            |
|       | SD 7.7        | 2.4            | 1.4             | 1.7        | 25.4        | 17.0         | 18.2         | 3.1           | 2.1           | 2.1          | 3.4           | 3.6            |
| CON   | Mean 23.4     | 1.9            | 4.6             | 1.5        | 4.6         | 1.5          | 2.0          | 2.0           | 2.0           | 2.0          | 2.0           | 2.0            |
|       | SD 1.3        | 2.3            | 0.7             | 1.2        | 1.3         | 2.3          | 1.2          | 1.2           | 1.2           | 1.2          | 1.2           | 1.2            |

BOP: bleeding on probing, CAL: clinical attachment loss, CON: control group, CRP: C-reactive protein, GAgP: group of patients with generalised aggressive periodontitis, LAgP: group of patients with localised aggressive periodontitis, PPD: probing pocket depth, SD: standard deviation.

Figure 1  Levels of CRP (mean ± SE, mg/L). CRP levels in patient groups GAgP and LAgP in stages of periodontal treatment and in control group CON (*statistically significant differences).

Figure 2  CRP levels and BOP index in stages of periodontal treatment (mean ± SE, mg/L). CRP levels and BOP index in patient groups GAgP and LAgP in stages of periodontal treatment and in control group CON (*statistically significant differences).
from $8.4 \pm 3.4$ mms to $7.7 \pm 3.9$ mms, CAL index in control group CON was $2.0 \pm 1.2$ mms.

Statistical comparisons of CRP levels and clinical periodontal parameters in patient group GAgP between measurements during periodontal treatment (Table 2):

Statistically significant differences ($p \leq 0.05$) were found between all measurements during periodontal treatment in BOP and PPD indices and I. vs. II. in CRP levels. This corresponds to the healing of periodontium with severe process of destruction of periodontium.

Statistical comparisons of CRP levels and clinical periodontal parameters in all patients (groups GAgP and LAgP together) between measurements during periodontal treatment (Table 2):

Statistically significant differences ($p \leq 0.05$) were found between all measurements during periodontal treatment in BOP and PPD indices and II. vs. III. in CAL index and II. vs. III. and I. vs. III. in CRP levels.
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Table 2  Statistical comparison of CRP levels and clinical periodontal parameters in patient groups GAgP, LAgP and GAgP + LAgP between stages of periodontal treatment.

| Group          | I vs. II (p) | II vs. III (p) | I vs. III (p) |
|----------------|--------------|----------------|---------------|
| CRP GAgP       | 0.922        | 0.071          | 0.216         |
| LAgP           | 0.043*       | 0.140          | 0.024*        |
| GAgP + LAgP    | 0.389        | 0.023*         | 0.022*        |
| BOP GAgP       | 0.017*       | 0.005*         | 0.000*        |
| LAgP           | 0.0002       | 0.030*         | 0.001*        |
| GAgP + LAgP    | 0.000*       | 0.000*         | 0.000*        |
| PPD GAgP       | 0.000*       | 0.018*         | 0.000*        |
| LAgP           | 0.001*       | 0.035*         | 0.000*        |
| GAgP + LAgP    | 0.000*       | 0.001*         | 0.000*        |
| CAL GAgP       | 0.840        | 0.002*         | 0.022*        |
| LAgP           | 0.090        | 0.248          | 0.287         |
| GAgP + LAgP    | 0.130        | 0.002*         | 0.862         |

*Statistically significant differences (p ≤ 0.05).

BOP: bleeding on probing, CAL: clinical attachment loss, CRP: C-reactive protein, PPD: probing pocket depth.

Statistical comparisons of CRP levels and clinical periodontal parameters between patient group GAgP and control group CON in measurements during periodontal treatment (Table 3):

Statistically significant differences (p ≤ 0.05) were found between values in all measurements during periodontal treatment in GAgP and CON groups in values of PPD and CAL indices, between values of BOP index I. vs. II. during periodontal treatment in LAgP and CON groups and between CRP levels in measurement II. in LAgP and CON groups.

Statistical comparisons of CRP levels and clinical periodontal parameters between a group of all patients (groups GAgP and LAgP together) and control group CON in measurements during periodontal treatment (Table 3): Statistically significant differences (p ≤ 0.05) were found between values in all measurements during periodontal treatment in the group of all patients (groups GAgP and LAgP together) and CON group in values of PPD and CAL indices, between values of BOP index in measurements I. vs. II. during periodontal treatment in the group of all patients (groups GAgP and LAgP together) and CON group and between CRP levels I. vs. II. during periodontal treatment in the group of all patients (groups GAgP and LAgP together) and CON group.

Discussion

The treatment of aggressive periodontitis should be timely, with absolute compliance to the treatment plan, and with perfect cooperation between patient, dentist and dental hygienist. CRP as an inflammatory protein could contribute to more complete understanding of the condition of periodontal tissues during periodontal therapy and after its completion, i.e. during the recall. CRP could indicate exacerbation of inflammatory process before the onset of its own clinical features — increase in bleeding on probing24 and deepening of periodontal pockets. In our study, we found BOP and PPD indices significantly decreased after precise execution of deep scaling and root planing in the initial phase of periodontal treatment.

Bleeding on probing is a sign of inflammation and indicates some sort of destruction and erosion to the lining of the sulcus or the ulceration of sulcular epithelium. The blood comes from the lamina propria after the ulceration of the lining.2

Bokhari et al. confirmed that the BOP index is the only periodontal parameter which shows significant relationship to systemic parameters such as CRP and fibrinogen levels, and white blood cell count.25 In our study in patients with aggressive periodontitis we demonstrated statistically significant differences in BOP development between measurement I. vs. CON and between measurement II. (i.e. after subgingival treatment) vs. CON.

Patients with aggressive periodontitis have statistically significant elevations in serum CRP levels compared to subjects with healthy periodontium. Elevated CRP in these subjects might represent a contribution of periodontal infection to systemic inflammation in relatively young individuals.21 In patients with aggressive periodontitis increased levels of CRP could be a united indicator of both the condition of periodontal tissues and the risk of systemic
diseases, such as cardiovascular diseases. In the study of Goyal et al., significantly higher levels of CRP were demonstrated in patients with generalised aggressive periodontitis. In our study statistically significant differences in CRP levels were found between I. vs. II. and I. vs. III. measurements in group LAgP. On the contrary, in group GAgP, no statistically significant differences were found in CRP levels between all three measurements during the initial phase of periodontal treatment. This could show that conservative (non-surgical) therapy might have been insufficient in patients with generalised aggressive periodontitis for the reduction of inflammatory process in periodontal tissues. Nevertheless, the results in our study could also indicate that using BOP index in the clinical examination might be more pertinent than measuring CRP levels to evaluate healing of periodontal tissues.

Conflict of interest

The authors declare that they have no conflict of interests associated with this work.

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