

ADAM JAKIMIAK<sup>1, B-F</sup>, MARTYNA KOCHAŃSKA<sup>2, B-D</sup>, MONIKA MICHALSKA<sup>2, B-D</sup>,  
MATEUSZ CELEJ<sup>2, B-D</sup>, ANDRZEJ WOJTOWICZ<sup>1, E, F</sup>, WOJCIECH POPOWSKI<sup>1, A-F</sup>

## Serum Concentration of C-Reactive Protein in Patients Treated for Acute and Chronic Odontogenic Infections

### Stężenie białka C-reaktywnego w surowicy krwi pacjentów leczonych z powodu ostrych i przewlekłych zębopochodnych stanów zapalnych

<sup>1</sup> Dental Surgery Department, Medical University of Warsaw, Warsaw, Poland

<sup>2</sup> Medical University of Warsaw, Warsaw, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;  
D – writing the article; E – critical revision of the article; F – final approval of article

#### Abstract

**Background.** C-reactive protein (CRP) performs many important functions in the body, among which the binding, detoxification and elimination of tissue breakdown products seem to be the most important ones. CRP measurement is a fast and simple method for detecting inflammatory processes.

**Objectives.** The aim of the study was to determine the serum CRP level in peripheral blood during acute and chronic odontogenic infections before and after surgical treatment.

**Material and methods.** Serum CRP levels were determined by immunochromatography. Blood samples were collected from the fingertip of study participants, and Actim CRP dipstick tests were performed prior to, 24 hours after and 7 days after surgical treatment.

**Results.** There were no significant differences ( $p = 0.132$ ) between the baseline CRP level and after 24 hours in the entire group with chronic infections. In patients with non-elevated baseline CRP, surgical intervention caused a CRP increase after 24 hours in 8 out of 11 of the subjects. In chronic periapical periodontitis, CRP was significantly lower after 7 days in 19 out of 20 subjects ( $p = 0.005$ ). In acute infections, CRP was markedly elevated. After 7 days of therapy, a statistically significant ( $p = 0.0002$ ) reduction of CRP by 40 mg/L was recorded in 16 subjects, however, CRP remained elevated compared to the normal range in 13 cases.

**Conclusions.** Our study revealed significant CRP level variations depending on the type of odontogenic infection, treatment time and treatment itself. Although acute inflammation induced higher CRP values, chronic inflammation was still noticeable in the collected data (**Dent. Med. Probl. 2016, 53, 3, 332–337**).

**Key words:** C-reactive protein, acute odontogenic infections, chronic odontogenic infections, acute phase reaction.

**Słowa kluczowe:** białko C-reaktywne, ostry zębopochodny stan zapalny, przewlekły zębopochodny stan zapalny, reakcja ostrej fazy.

C-reactive protein (CRP) was first described in 1930 by Tillett and Francis [1], and its name is associated with its ability to bind the main cell membrane protein of Streptococci. At first, CRP was believed to be excreted only under pathogenic conditions, during inflammatory reactions, but discovery of its synthesis in the liver showed that this protein is also present under physiologic

conditions [2, 3]. CRP performs many important functions in the body, among which binding and detoxification of tissue breakdown products and their elimination seem to be the most important ones. It attaches to bacteria, which activates the complement system. This initiates opsonization of the bacterial cell, which is followed by the phagocytosis and lysis of the foreign cells.

CRP levels under normal conditions are low and do not exceed 5 mg/L. CRP synthesis and excretion increases considerably under acute inflammatory conditions and malignancies, achieving values above 100 mg/L [4]. CRP could be a differentiating marker for viral and bacterial infections. A study by Nakayama et al. [5] shows that the mean CRP level in bacterial infections is 81 mg/L, and 19 mg/L in infections caused by adenoviruses. Serum CRP fluctuations can also be associated with smoking, obesity and diabetes [6].

A CRP molecule is comprised of 5 identical peptide subunits connected by non-covalent bonds in a ring structure [7, 8]. It forms a defensive complex together with the complement system. During an ongoing infection, bacteria produce substances which stimulate a gene for transcription of a nuclear regulator, kappa B factor, which in turn stimulates interleukin-6, which finally promotes CRP synthesis. CRP activates the complement system, which causes CRP accumulation. This is a strong and effective mechanism which yields a rapid and effective response to inflammatory factors. When bacterial infection begins, CRP sends a pro-inflammatory signal that activates the immune system and leads to monocyte infiltration, which is necessary for antigen presentation and antibody-dependent destruction of bacterial cells [9].

The aim of the study was to determine the serum CRP level in peripheral blood during acute and chronic odontogenic infections before and after surgical treatment.

## Material and Methods

The study included 2 groups of patients, female and male, aged 25–40, 20 persons each. The subjects included did not take any long-term medications and were not being treated for any general diseases. Patients with periodontitis were excluded from the study. The first group included patients with chronic odontogenic infections requiring multiple extractions. The second group was composed of patients with acute odontogenic infections (apical) and diagnosed intraoral abscesses. In both groups, surgical procedures were performed under local anesthesia with 2% lignocaine and noradrenalin. In patients with multiple retained roots with necrotic pulp, multiple extractions were performed during one session, periapical lesions were curetted and, in the case of extensive wounds, sutures were applied. In patients treated for intraoral abscesses, apart from the incision and pus drainage, an antibiotic

(amoxicillin + clavulanic acid 1 g) was prescribed (1 tablet every 12 hours for 7 days, starting 1 hour after surgery). Patients presented every day during the treatment period for check-ups, during which rubber drains were replaced and the abscess cavity was rinsed with 0.5% metronidazole. Each study participant had an Actim CRP® (Medix Biochemica, Espoo, Finland) (Fig. 1) blood dipstick test performed three times. Blood samples were collected from the fingertip. Tests were performed prior to the surgical intervention, 24 hours later and 7 days later. The Wilcoxon test was performed for statistical analysis of the results.



Fig. 1. Actim CRP dipstick test

The Actim CRP dipstick test is based on the immunochromatography technique. It contains monoclonal antibodies to human CRP, which are bound to blue latex particles. The carrier membrane of the dipstick is divided into three CRP-specific zones that bind the latex particles, if the study sample contains CRP. The dipstick absorbs solution from a probe. If the solution contains CRP, binding to the antibodies attached to latex particles occurs. The latex particles flow up with the sample solution along the dipstick, and if they are bound with CRP, they are caught by specific antibodies in the test zones. The number of blue lines on the dipstick corresponds to CRP level in the tested solution (Fig. 2). A red, control line confirms that the test was correctly performed. The Medical University of Warsaw Ethics Committee approved the study (protocol number KB61/2013).

The Wilcoxon test was used in the statistical analysis. P-values of  $\leq 0.05$  were considered statistically significant.

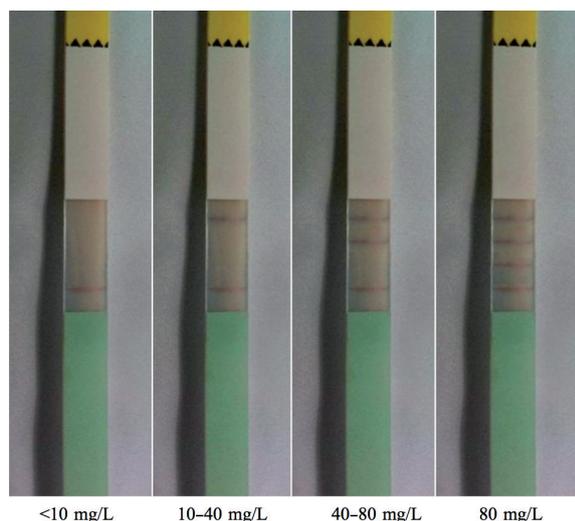


Fig. 2. Examples of results of Actim CRP dipstick test according to CRP concentration

## Results

The results from the tests revealed variations of the serum CRP level in both chronic and acute odontogenic infections.

In chronic local odontogenic infections, the CRP level prior to surgical intervention varied from 10 to 40 mg/L. In the next test, which was performed 24 hours after tooth extraction, a CRP level increase by approximately 30 mg/L from the < 10 mg/L range to the 10–40 mg/L range was observed in 8 out of 20 subjects. In 9 out of 20 subjects, in which CRP level was elevated prior to surgery, its values remained unchanged after 24 hours. CRP level decreased below 10 mg/L in 3 subjects (Table 1). There were no statistically significant differences ( $p = 0.132$ ) between the baseline values and CRP level after 24 hours in the entire group. However, a tendency was observed in patients with local chronic infections and non-elevated baseline CRP, that surgical intervention caused a CRP increase after 24 hours in 8 out of 11 of these subjects (Table 1) [10–12].

In the group treated for chronic periapical periodontitis, CRP prior to and during treatment did not exceed 40 mg/mL. In the subsequent test, performed 7 days after surgical intervention and following initial wound healing, CRP was significantly lower ( $p = 0.005$ ) in 19 out of 20 subjects and returned to the normal range.

In acute local odontogenic infections, the baseline CRP level was markedly elevated, varying from 40 to 80 mg/L, and exceeded 80 mg/L in 4 subjects. 24 hours after abscess incision, the values did not change significantly and remained elevated in 11 persons, a further CRP increase was

Table 1. CRP alterations during treatment of chronic odontogenic infections

	Baseline CRP level – mg/L	24 h after surgery		7 days after surgery	
		CRP level – mg/L	tendency	CRP level – mg/L	tendency
1	< 10	< 10	=	< 10	=
2	10–40	10–40	=	< 10	↓
3	10–40	< 10	↓	< 10	↓
4	< 10	10–40	↑	< 10	=
5	10–40	10–40	=	10–40	=
6	< 10	10–40	↑	< 10	=
7	< 10	< 10	=	< 10	=
8	10–40	10–40	=	< 10	↓
9	< 10	10–40	↑	< 10	=
10	10–40	10–40	=	< 10	↓
11	< 10	10–40	↑	< 10	=
12	10–40	10–40	=	< 10	↓
13	10–40	< 10	↓	< 10	↓
14	< 10	10–40	↑	< 10	=
15	10–40	10–40	=	< 10	↓
16	< 10	10–40	↑	< 10	=
17	< 10	< 10	=	< 10	=
18	< 10	10–40	↑	< 10	=
19	< 10	10–40	↑	< 10	=
20	10–40	< 10	↓	< 10	↓

observed in 2 subjects, and a decrease was noted in 4 patients ( $p = 0.414$ ) (Table 2).

After abscess incision and 7 days of therapy, a pronounced reduction of CRP by 40 mg/L was recorded in 16 subjects, which was highly statistically significant ( $p = 0.0002$ ). In 4 subjects, the serum CRP concentration did not change versus the baseline level and remained elevated. Among patients with a CRP reduction, its level returned to the normal range in 3 patients, and remained elevated within the range of 10–40 mg/L in the remaining subjects.

Local clinical improvement was observed in all patients with uneventful healing. All symptoms of acute inflammation subsided.

## Discussion

Inflammatory conditions induce many changes in the body, manifested by typical clinical signs. Bacteria, being an infectious factor, activate the immune system, leading to changes in blood bio-

**Table 2.** CRP alterations during treatment of acute odontogenic infections

	Baseline CRP level – mg/L	24 h after surgery		7 days after surgery	
		CRP level – mg/L	tendency	CRP level – mg/L	tendency
1	40–80	40–80	=	10–40	↓
2	40–80	40–80	=	< 10	↓
3	10–40	40–80	↑	10–40	=
4	10–40	10–40	=	< 10	↓
5	40–80	40–80	=	10–40	↓
6	40–80	40–80	=	< 10	↓
7	40–80	40–80	=	10–40	↓
8	40–80	40–80	=	10–40	↓
9	40–80	40–80	=	40–80	=
10	10–40	40–80	↑	10–40	=
11	40–80	10–40	↓	10–40	↓
12	10–40	10–40	=	< 10	↓
13	40–80	40–80	=	40–80	=
14	40–80	10–40	↓	< 10	↓
15	40–80	40–80	=	10–40	↓
16	40–80	10–40	↓	< 10	↓
17	40–80	40–80	=	10–40	↓
18	40–80	10–40	↓	10–40	↓
19	10–40	10–40	=	< 10	↓
20	40–80	40–80	=	10–40	↓

chemical profile, which are typical of the acute inflammatory phase [13].

CRP is a gamma-globulin synthesized by hepatocytes and is one significant factor in inducing the defensive mechanisms of the body that have an effect on immune cells. Serum CRP concentration is an inflammatory marker, and its levels rise under active inflammatory conditions [14, 15].

An analysis of the effect of acute and chronic odontogenic infections within the alveolar region of the jaw on serum CRP level revealed variations of its value in both groups. A marked increase in serum CRP, up to a range of 40–80 mg/L, is observed in alveolar abscesses as a reaction to ongoing acute inflammatory conditions. A similar tendency can be noticed in the study by Dražić et al. [16], where the mean values in acute, purulent odontogenic infections were: 27 mg/L in patients with good drainage, 34 mg/L in those with poor drainage, and 82 mg/L in patients with poor drainage and elevated body temperature. In the last group, there were single cases with approximately 100 mg/L. In chronic infections, the results

were less consistent. Serum CRP was not always elevated, and when it was, it did not exceed 40 mg/L. To sum up this issue, odontogenic infections within the alveolar region of the jaw induce a serum CRP increase up to 100 mg/L. This is characteristic of infections with the Gram-positive bacteria that are responsible for most odontogenic infections. Serum CRP level under inflammatory conditions within the alveolar process indicates the extent and intensity of the inflammation [14, 15]. When serum CRP exceeds 100 mg/L, a different cause of CRP elevation should be considered. Such a result could suggest an underlying general inflammatory condition or malignancy [17].

By measuring CRP levels during the treatment of odontogenic infections, the effect of surgery on serum CRP variations was also assessed. In the case of acute inflammatory conditions in generally healthy people, no clear effect of the surgery itself on CRP level could be observed. The trauma caused by surgery did not intensify the immunological response. The results in the group treated for chronic odontogenic infection were different. Surgical intervention activated the immune response in those patients in whom chronic infection had not increased serum CRP. In this group, an increase from < 10 mg/L to the range of 10–40 mg/L was observed. These observations could indicate that the immune capacity of local tissues in chronic periapical periodontitis prevented the initiation of the acute phase reaction. It was only after the tissues were disturbed during surgery that the general reaction was initiated, which involves, among others, elevation of serum CRP. Such results confirm the assumption that odontogenic infection can become a source of focal infection under favorable conditions. For this reason, it is justified to administer short-term antibiotic coverage in patients with an impaired immune system, who are susceptible to the propagation of inflammatory conditions.

The CRP levels measured 7 days after surgery in the chronic odontogenic infection group decreased to < 10 mg/L, which is considered to be the threshold value for the initiation of inflammation in the body. In the acute odontogenic infection group, a marked reduction of serum CRP was observed 7 days after surgery, leading to a substantial decrease, but in most cases it still remained elevated despite a subsidence of clinical signs of acute inflammation. Similar results were obtained by Dražić et al. [16], where CRP dropped to 10 mg/L or less 7 days after surgery. To sum up, the measurements of serum CRP reflected increased values, especially in acute odontogenic infections. A drop in CRP level is clearly visible after 7 days, when treatment is completed.

## Conclusions

Clinicians can evaluate the intensity of inflammatory conditions by using a simple serum CRP dipstick test. This makes it possible to rapidly decide how to manage the patient, including whether antibiotic therapy is necessary. This has special significance with regard to patients with general comorbidities, who present for exclusion of infection foci or treatment of acute and chronic odontogenic infections [18]. This study, performed on 40 patients, showed elevated serum CRP concentrations in subjects with chronic odontogenic infections which did not exceed 10–40 mg/L. In acute odontogenic infections, the baseline CRP level was relatively high as compared to chronic infections, but did not exceed 80 mg/L, which corresponds to the so-called acute phase reaction of the immune system. In this study group, no increase in immunological response due to surgical

procedures (multiple tooth extractions) was observed. Serum CRP level returned to the normal range 7 days after multiple extractions of teeth causing chronic periapical periodontitis, which, in connection with clinical image, indicates a subsidence of inflammatory conditions. The CRP level decreased significantly 7 days after incision of intraoral abscesses, but in most cases, the values remained above the normal range despite a clinical subsidence of acute inflammation signs. CRP levels did not exceed 80 mg/L in odontogenic infections regardless of the type of inflammation. Therefore, it can be assumed that when CRP highly exceeds 100 mg/L at the beginning of the treatment process and maintains high values 7 days after the surgical procedure despite a subsidence of clinical signs of acute inflammation, other causes than odontogenic infections should be considered and such situations require further examination [18].

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**Address for correspondence:**

Wojciech Popowski  
Dental Surgery Department  
Medical University of Warsaw  
Nowogrodzka 59  
02-006 Warszawa  
Poland  
tel.: +48 22 502 12 42  
e-mail: wojtepop@op.pl

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