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EVALUATION OF EFFECT OF TREATMENT ON SERUM C - REACTIVE PROTEIN LEVELS IN PATIENTS WITH PERIAPICAL INFECTIONS. A CLINICO–BIOCHEMICAL STUDY.

Dental Science

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ABSTRACT

Purpose: The purpose of this study was to measure the serum CRP levels and its significance in monitoring prognosis of the periapical infections.
Materials and Methods: Serum samples were collected from 60 patients with periapical infections & from 30 healthy controls. Serum CRP levels were determined by using ultrasensitive turbidimetric immunoassay analyzer. After 7 days of treatment, patients were recalled to re-evaluate the serum CRP by the same procedure.
Results: In patients with periapical infections, the pre and post treatment CRP levels were statistically highly significant except Chronic Apical Periodontitis & Periapical cyst.
Conclusion: This study shows that Serum CRP levels were elevated in response to Periapical infections and also reduced significantly after treatment. The prompt treatment of these periapical infections helps to prevention of heart diseases which may result because of the elevated Serum CRP levels.

KEYWORDS

CRP, Ultrasensitive turbidimetric immunoassay analyzer, Periapical disease.

INTRODUCTION

During the recent decades, a new era of periapical research has emerged and substantial evidence is developing and showing the connection between periapical infections and systemic diseases. The concept of focal infection has re-emerged, based on new data which suggest that periapical infections contribute to the morbidity and mortality of certain systemic conditions.[1]

C-reactive protein (CRP) is one of the most dynamic acute phase protein[2] that was discovered in 1930 by William S. Tillet and Thomas Francis.[3] CRP concentrations are elevated in almost all inflammatory, infectious, and neoplastic diseases.[4] CRP levels rise in serum or plasma within 24 to 48 hours following acute tissue damage, reach a peak during the acute stage and decrease with the resolution of inflammation.[5,6,7]

CRP plays a key role in the innate immune response and is easily measured due to its long plasma half-life (12 to 18 hours).[8] In healthy individuals, CRP levels are <0.3 mg/l.[9] Serum levels of CRP could exceed 100 mg/l in the presence of overwhelming systemic infection, which provides a useful marker for tracking the course of the infection.[10] CRP is primarily synthesized in the liver parenchymal cells. The major stimuli that induce CRP synthesis include interleukin (IL-6, IL-1) and TNF-α (tumor necrosis factor α), which are inflammatory mediators.[3]

Dental caries is a relatively common infection. Untreated caries often results in pulpitis. Untreated pulpitis may progress to a localized infection at the root apex. Periapical abscesses have both local and systemic effects, because they release bacteria toxins and proinflammatory cytokines into the systemic circulation. This dissemination results in elevated serum concentrations of TH-1 type cytokines including IL-6, IL-1 and TNF-α. The presence of these cytokines stimulates the liver to produce CRP, which increases the risk for developing other systemic diseases.[11,12]

The purpose of this study is to measure the serum CRP levels and its significance in monitoring prognosis of the periapical infections and whether resolution of the periapical infection results in CRP levels reverting to the normal.

MATERIALS AND METHODS

The sample of this clinico–biochemical study consisted of 60 patients with Periapical infections. Patients with Acute & Chronic Apical Periodontitis, Acute & Chronic Periapical Abscess, Dento Alveolar Abscess, Periapical cyst, Cellulitis, Ludwig's Angina and Postoperative alveolar osteitis were included in this study. The exclusion criteria was non-odontogenic infections, immune mediated diseases, patients on immuno suppressants, neoplasms, other inflammatory conditions, those with systemic medical problems (e.g. Diabetes, Asthma, Cardiac problems, Glomerulonephritis, Chronic infectious diseases) and those who received prophylactic antibiotics.

90 subjects were selected and divided into 2 groups. Group 1: 60 patients with Periapical infections, Group 2: Control group comprising of 30 same age and sex group not suffering from any systemic disease and not under any medication. Detailed case history, complete clinical examination was recorded. When indicated Intra Oral Periapical Radiographs, Panoramic radiographs, was taken to aid the diagnosis, and a definitive diagnosis was made based on history, clinical and radiographic exams for those patients.

2ml of venous blood was collected from the Periapical infected patients and control group and it was transferred to blood collection tube containing serum separator granules and clot activator for estimation of serum CRP levels. These tubes were centrifuged (3000 rpm for 5 minutes); aliquotted and supernatants were stored in polypropylene tubes at -70C until the time of analysis.

Serum levels of CRP were determined by using ultrasensitive turbidimetric immunoassay analyzer (TULIP). In this procedure 400µl QUANTIA-CRP US activation buffer (R_1), 100µl QUANTIA-CRP US latex reagent (R_2) were taken in a measuring cuvette, mixed well and allowed to incubate for five minutes at 37^{0}C. Later 5 µl of sample was added to it and mixed gently. The results were recorded after four minutes on the immunoassay analyzer monitor. After 7 days of treatment, patients were recalled to re-evaluate the serum CRP by the same procedure. Data obtained were tabulated and subjected to statistical analysis by using "t" test with the help of software SPSS, 11.5 version.

FIGURE 1: Photograph showing serum samples collected for the study.

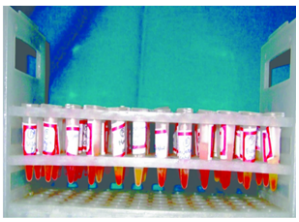

FIGURE 2: Photograph showing C-reactive protein reagents

FIGURE 3: Immunoturbidimetric analyzer

RESULTS

The Mean value of serum CRP levels in Controls group was 0.06 mg/dl. In patients with Acute Apical Periodontitis (AAP) the pre and post treatment CRP levels were statistically highly significant (p 0.002). Depend on treatment wise, when treated with antibiotics (Ab) and root canal therapy (RCT), the pre and post treatment CRP levels were statistically highly significant (p 0.00), but when treated with antibiotics and extraction(EXO) the pre and post treatment CRP levels were not statistically significant (p 0.18). In patients with Chronic Apical Periodontitis (CAP), in the pre and post treatment CRP levels were statistically not significant (p 0.08). In CAP when treated with antibiotics and RCT, pre and post treatment CRP levels were statistically significant (p 0.05), but when treated with antibiotics and extraction the pre and post treatment CRP levels were not statistically significant (p 0.89).

In patients with Acute Periapical Abscess (APA) with pre & post treatment CRP levels were statistically highly significant (p 0.002). In patients with APA when treated with antibiotics and RCT, the pre and post treatment CRP levels were statistically significant (p 0.04), but when treated with antibiotics and extraction the pre and post treatment CRP levels were not statistically significant (p 0.07). When treated with antibiotics, incision and drainage (I&D), root canal therapy the pre and post treatment CRP levels were statistically highly significant (p 0.00).

In patients with Chronic Periapical Abscess (CPA) with pre and post treatment CRP levels were statistically highly significant (p 0.002). In patients with CPA when treated with antibiotics and RCT, the pre & post treatment CRP levels were statistically not significant (p 0.07), but when treated with antibiotics and extraction the pre & post treatment CRP levels were statistically significant (p 0.02). When treated with antibiotics, incision and drainage, RCT the pre and post treatment CRP levels were statistically highly significant (p 0.01).

In patients with Dento Alveolar Abscess (DAA) with pre & post treatment CRP levels were statistically highly significant (p 0.00). In patients with DAA when treated with antibiotics, extraction, irrigation (IRR) the pre & post treatment CRP levels were statistically significant (p 0.05), but when treated with antibiotics, RCT, incision and drainage the pre & post treatment CRP levels were statistically highly significant (p 0.00). In patients with Ludwig angina (LA), with pre treatment CRP levels are reduced to normal levels, after 1weak post treatment CRP levels (mean 0.44, SD 0.28).

In patients with Periapical cyst (PC) with pre & post treatment CRP levels were statistically not significant (p 0.09). In patients with periapical cyst, when treated with antibiotics, RCT, enucleation (ENA) the pre and post treatment CRP levels were statistically not significant (p value 0.28), when treated with antibiotics, extraction, enucleation the pre and post treatment CRP levels were not statistically significant (p value 0.19). In Cellulitis (C) patients, treated with antibiotics, incision and drainage, irrigation, extraction with pre & post treatment CRP levels were statistically highly significant (p value 0.00). In patients with post operative alveolar osteitis (AO) when treated with antibiotics, zinc oxide eugenol packing (ZEP), the pre & post treatment CRP levels were statistically highly significant (p value 0.00)

Table 1: Pre and post treatment serum CRP levels (mg/dl) in periapical infections.

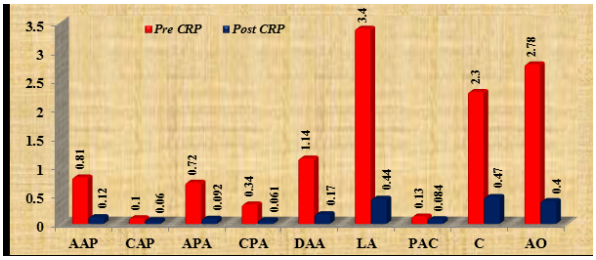

Table 2: Comparison of pre and post treatment CRP levels in different modalities of treatments

AAP	no	Treatment	CRP (mg/dl)			
			Preoperative	Postoperative	t	p
	7	Ab + RCT	0.58 ± 0.19	0.09 ± 0.01	6.68	0.00
	2	Ab + EXO	1.65 ± 0.43	0.22 ± 0.14	3.50	0.18
CAP	6	Ab + RCT	0.12 ± 0.06	0.07 ± 0.01	2.51	0.05
	3	Ab + EXO	0.07 ± 0.01	0.060.05	0.15	0.89
APA	3	Ab + RCT	0.68 ± 0.25	0.10 ± 0.05	4.91	0.04
	2	Ab + EXO	0.77 ± 0.10	0.05 ± 0.01	9.67	0.07
	4	Ab + I&D + RCT	0.73 ± 0.15	0.11 ± 0.05	10.02	0.00
CPA	2	Ab + RCT	0.37 ± 0.04	0.06 ± 0.04	9.67	0.07
	3	Ab + EXO	0.42 ± 0.11	0.04 ± 0.02	7.32	0.02
	4	Ab + I&D + RCT	0.27 ± 0.04	0.08 ± 0.02	6.36	0.01
DAA	2	Ab + EXO + RCT	0.99 ± 0.05	0.18 ± 0.07	1.00	0.05
	7	Ab + I&D + RCT	1.19 ± 0.33	0.17 ± 0.06	8.87	0.00
LA	2	Ab + I&D + IRR	3.40 ± 0.28	0.44 ± 0.28		
PC	3	Ab + RCT +ENA	0.14 ± 0.05	0.08 ± 0.01	1.46	0.28
	2	Ab + EXO+ENA	0.12 ± 0.02	0.09 ± 0.01	3.29	0.19
C	3	Ab + I&D + IRR	2.30 ± 0.26	0.47 ± 0.21	20.67	0.00
AO	5	Ab + IRR + ZEP	2.78 ± 0.65	0.40 ± 0.18	8.10	0.00

DISCUSSION

Odontogenic infections are common, but many patients with these infections may be asymptomatic. Inflammatory mediator's IL-1 and Prostaglandin E (PG E) were found to be increased in patients with asymptomatic odontogenic infections indicating the presence of occult infections. These occult infections constitute a risk for the development of postoperative complications but are difficult to detect through clinical examinations.[15]

The findings of previous studies indicated that serum CRP levels are often elevated in patients with odontogenic infections and postoperative complications following tooth extraction. Because CRP is a sensitive maker for infection, preoperative CRP testing may have the potential to identify such patients with increased risks of postoperative infections and provide guidance for the use of preventive therapeutics.[16,17,18]

In previous study approximately 75% of the dental emergency patients had serum CRP levels greater than 5 mg/L. Following dental treatment and/or antibiotic therapy, CRP concentration rapidly returned to a level below 5 mg/L in approximately 50% of the patients who had elevated CRP levels, but remained at the elevated level (5 mg/L) in the other 50% of the patients 1 week after treatment.[15]

In this present study approximately 67 % of the patients with periapical infections including acute and chronic infections had serum CRP levels greater than 0.5 mg/dl. In acute Odontogenic infections, most of the patient's serum CRP levels were highly elevated (0.72 to 3.4 mg/dl), but in chronic Odontogenic infections, low but elevated (0.13 to 0.34 mg/dl) than normal serum CRP levels which ranges between 0 to 0.1mg/dl. One week following dental treatment and antibiotic therapy, CRP concentration returned to a level below 0.5 mg/dl in 100% of all periapical infection patients.

Serum CRP levels may be a sensitive indicator of Odontogenic infections and tissue injuries commonly seen in an outpatient dental emergency clinic. Such elevation in CRP levels may be transient in some patients but more persistent in others. [19,20]

It is evident that the dental literature concerning the acute phase response is sparse; references to CRP per se are even more meager. Boucher et al. found 90% of patients with acute alveolar abscesses to have CRP in their sera whereas only 31% of those diagnosed with chronic alveolar abscesses had positive tests.[18] It is interesting to note that in much of the early dental research involving CRP the protein was not detected in the serum of normal control patients. This unfortunate oversight was due only to the limitations inherent in the immunological methods used at the time. The aforementioned studies used such immunological methods as capillary precipitation, slide latex agglutination, flocculation, and radial immunodiffusion in the attempt to identify and measure CRP levels.[12] Today the enzyme-linked immunosorbent assay (ELISA) combines the utmost in sensitivity (detecting picograms of CRP in a 50 µl sample) with speed and low cost.[21,22]

CONCLUSION

To conclude this study shows Serum CRP levels are elevated in response to Periapical infections and are reduced significantly after appropriate treatment of these infections is instituted. Lowering of Serum CRP levels helps in reducing risk of other diseases especially the Atherosclerotic Cardiovascular Diseases. Appropriate and prompt treatment of the Periapical infections will thus go a long way towards prevention of cardiovascular diseases and other complications which may result because of the elevated Serum CRP levels.

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