

C-reactive protein a better indicator of inflammation after third molar extraction

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Abstract

Purpose: The purpose of this study was to evaluate the relation between pre-operative pain and pre-operative levels of C-reactive and post-operative pain and swelling in impacted third molar surgery.

Materials and Methods: In this prospective study subjects were patients indicated for mandibular third molar extraction. Patients were assessed for certain inclusion and exclusion criteria's. A standard surgical extraction procedure was followed to reduce the bias. Hematological investigation of C-reactive protein levels were recorded pre-operatively and post-operatively. Pain, swelling and trismus in patients were assessed pre-operatively and post-operatively in an interval of 24 hours, 48 hours and 7 days. Pain and swelling were measured using verbal analogue scale and thread length measurement respectively. The mouth opening was recorded, too.

Results: Post-operative C-reactive protein levels were seen consistency raised in those cases which showed high pre-operative levels. Peak levels of C-reactive protein were seen at 48 hours post operatively. It was observed that pre-operative pain swelling and mouth opening were seen to be variable in all the cases having high C-reactive protein levels.

Conclusion: C-reactive protein was found to be a better indicator of inflammation than pre-operative pain, swelling and mouth opening for post-operative discomfort.

Key words: C-reactive protein, inflammation, third molar extraction.

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Introduction

Third molar surgery is one of the most common surgeries in dental practice. Post-operative sequelae include pain, trismus, swelling and discomfort.^[1] It has a psychological, biological and social impact on patients.^[2] These post-operative symptoms can be arbitrarily predicted by many factors associated with third-molar like pre-operative infection, pre-operative inflammation, pericoronitis, type of impaction, time required for third molar extraction, technique of extraction, intra socket medications like Zinc Oxide Eugenol packs, perioperative antibiotic use.^[3,4] But these factors are not reliable or definitive indicators for the post-operative discomfort and swelling. The knowledge of various methods to reduce the post-operative complications of third molar surgery and the reliable indicators of post-operative complications will

help the surgeon and patient to manage the post-operative discomfort faced.^[5]

C-reactive protein is an acute phase reactant of inflammation seen post-operatively or after any trauma. In a healthy individual C-reactive protein level is less than 10 mg/L which increases by two folds every 8 hours post-operatively and returns to normal in 7 days.^[6,7]

Aim of this prospective study is to show that C-reactive protein is a better indicator for the prediction of post-operative pain swelling and trismus after third molar extraction by showing the consistent relation between pre-operative C-reactive protein and post-operative discomfort symptoms.

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Materials and Methods

This study was conducted in the department of Oral and Maxillofacial Surgery in S.M.B.T. Dental College and Hospital, Sangamner; during the period from January 2011 to December 2011. The patients who had impacted third molar for extraction were included in this study. Patients who were on antibiotics and analgesics pre-operatively or allergic to the antibiotics used in the study were excluded from this study. Subjects with previous or existing cardiovascular diseases, smokers, diabetes mellitus and patients having periodontitis were excluded from this study as these patients may show the altered readings of the indicators and parameters used in this study. Patients were explained about the surgical procedure and informed written consent was taken for surgical procedure and study.

Pre-operatively presence of infection and inflammation were assessed using the pre-operative pain, swelling and presence of pus, intra-orally as well as extra orally. Swelling was recorded by measuring the distance from corner of mouth to the ear lobe on the side of indicated surgical extraction of third molar. Blood levels of C-reactive protein were checked 1 hour before the surgical procedure. Pre-operative pain was assessed by using a visual analogue scale having a readings from 0 (no pain) to 10 (extreme unbearable continuous type of pain).

The short listed cases were posted under meticulous asepsis and under local anesthesia (lignocaine 2% with adrenaline 1:2, 00,000 conc). Classical inferior alveolar nerve block along with long buccal were used to secure anesthesia. Wards incision was given in all the patients to access the third molar. Then mucoperiosteal flap was raised. Tooth was extracted by buccal and distal bone guttering. If required odontectomy (sectioning) of tooth was done. All the surgical procedures were carried out by same surgeon. Surgical extraction time varied from 18 minutes to 34 minutes with the mean of 30mins. All the patients were prescribed same post-operative Antibiotics (Penicillin 500 mg and metronidazole 400 mg tid for 5 days post-operatively), Analgesics (Diclofenac 75 mg t.i.d. for 5 days) and post-operative instructions were given.

The patients were assessed at the intervals of 24 hours, 48 hours, and 7th days after the surgery. Patients were assessed for pain, swelling and C-reactive protein by exactly the same method as used pre-operatively. The data collected was tabulated and analyzed using the statistics software named SPSS latest version number 14 and chi-square test was used to measure the correlation between the pre-operative blood level of CRP (pre-operative indicator of post-operative discomfort) with the post-operative measures of pain and swelling measured post-operatively at regular intervals of 24 hours, 48 hrs and 7 days. The association between the pre-operative pain measurement

(pre-operative indicator) with post-operative pain and swelling was also measured using same chi-square test method. And lastly the similar association was measured using same chi-square test between pre-operative swelling which was also set as one of the pre-operative indicator of post-operative discomfort, and post-operative pain and swelling (parameters of post-operative discomfort).

To check the C-reactive protein levels pre and post-operatively, 5 ml of patient's blood was drawn each time and was centrifuged at 3000 rpm for 10 minutes to obtain serum separately which was used for further test of CRP levels. The test kit used was of latex slide agglutination test kit. It contains a slide, a reagent and a control agent. The reagent and patient's serum is mixed on a slide and is checked for agglutination. Also the control agent's agglutination is checked simultaneously. The maximum dilutions of serum are to be checked for agglutination and then the number of dilutions is multiplied by 0.6. this give the value and amount of CRP level present in patient's serum. The high sensitivity CRP (hs-CRP) test is a latex particle enhanced immunoturbidimetric assay.

Results

In this study the sample size includes 102 patients (36 females and 66 males) with the age ranging from 20 years to 54 years (mean 28years). The post-operative CRP levels were seen to be consistently high in those with higher values of CRP pre-operatively. The association between the preoperative CRP and post-operative symptoms of discomfort (post-operative pain and swelling) showed to be significant using the chi square test. The chi-square test values for correlation between pre-operative CRP and post-operative pain using SPSS 14 software were 125.273, 126.976 and 129.034 at 24 hours 48 hours and 7 days respectively with difference of freedom of 101 and the *P*-value < 0.05 and >0.025. And that between Pre-operative CRP (pre-operative indicator) and post-operative swelling were 128.132, 130.847 and 135.769 at 24 hrs, 48 hrs and 7 days post-operatively, with *P*-value derived from the reference table to lie between 0.05 and 0.025 which shows the association between pre-operative indicator i.e. pre-operative CRP level in blood and readings of post-operative pain and swelling is statistically significant [Figures 1, 2, 3]. Also the chi-square test results for association of pre-operative pain with post-operative pain showed the results to be 115.374, 112.435 and 113.572 at 24 hours, 48 hours and 7th day respectively with the *P*-value between 0.4 and 0.1 according to the corresponding value of chi-square test for the sample of our study in the *P*-value value reference table. Also the association between pre-operative pain (pre-operative indicator) and post-operative swelling by chi-square test were 6.24, 3.18 and 5.12 at 24 hrs, 48 hrs and 7 days post-operatively with the *P*-value derived from

the reference table with above values to be *P*-value between 0.4 and 0.1. This shows the association in between the pre-operative pain (pre-operative indicator) and post symptoms of discomfort is statistically not significant [Figures 4, 5, 6]. And lastly the association of pre-operative swelling (pre-operative indicator) and post-operative pain were measured by chi-square test with the values to be 110.528, 113.229 and 114.375 at 24 hours, 48 hours and 7th day respectively and that with post-operative swelling the Chi-square test values were 107.623, 98.541 and 93.56 with a *P*-value to be between 0.6 and 0.2 as referred from the table of chi-square test values with *P*-value. This shows that the association between pre-operative swelling (pre-operative

indicator) and post-operative symptoms of discomfort (post-operative pain and swelling) is statistically not significant [Figures 7, 8, 9].

Discussion

Many studies demonstrate that baseline levels of CRP in apparently healthy men and women are highly predictive of future risk of heart attack, stroke, sudden cardiac death, and the development of peripheral arterial disease.^[7-9] C-reactive protein is an acute reactant of an inflammation produced by liver and may be a good indicator of general status of inflammatory condition of body.^[9] It is secreted

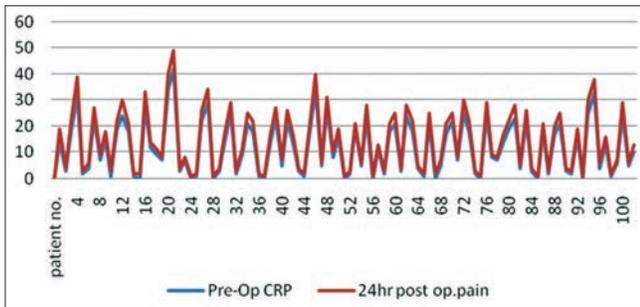


Figure 1: Correlation between pre-operative CRP levels and post-operative pain which shows that the rise and fall in pre-operative CRP corresponds to the rise and fall in post-operative pain at 24 hrs

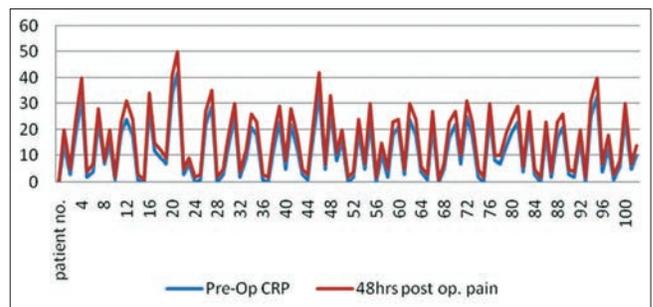


Figure 2: Correlation between pre-operative CRP levels and post-operative pain which shows that the rise and fall in pre-operative CRP corresponds to the rise and fall in post-operative pain at 48 hrs

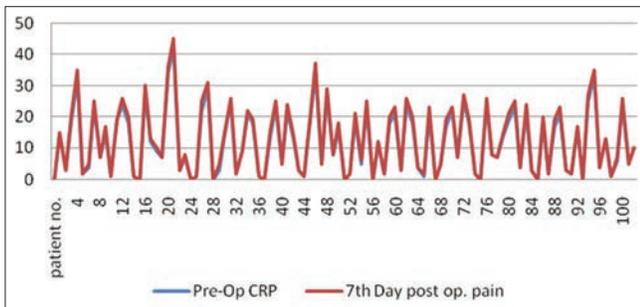


Figure 3: Correlation between pre-operative CRP levels and post-operative pain which shows that the rise and fall in pre-operative CRP corresponds to the rise and fall in post-operative pain at 7 days

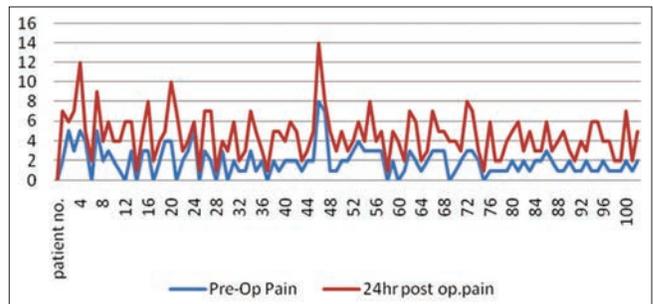


Figure 4: Correlation between pre-operative pain and post-operative pain measured by verbal analogue scale which shows that the rise and fall in pre-operative pain does not corresponds to the rise and fall in post-operative pain at 24 hrs

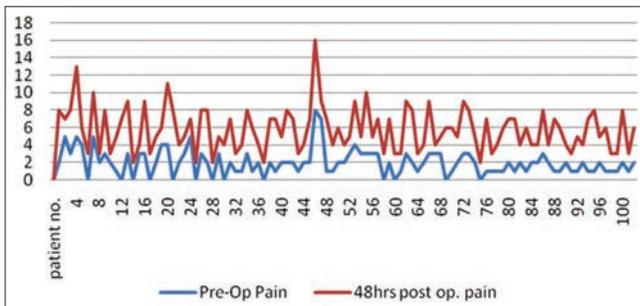


Figure 5: Correlation between pre-operative pain and post-operative pain measured by verbal analogue scale which shows that the rise and fall in pre-operative pain does not corresponds to the rise and fall in post-operative pain at 48 hrs

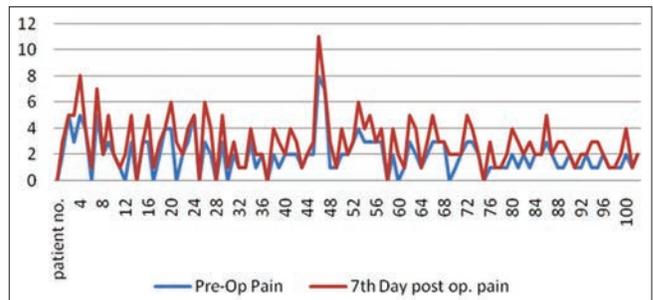


Figure 6: Correlation between pre-operative pain and post-operative pain measured by verbal analogue scale which shows that the rise and fall in pre-operative pain does not corresponds to the rise and fall in post-operative pain at 7days

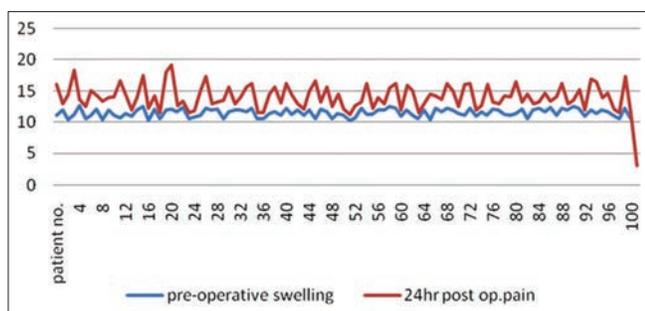


Figure 7: Correlation between pre-operative pain and post-operative swelling measured by thread which shows that the rise and fall in pre-operative swelling does not corresponds to the rise and fall in post-operative pain at 24 hrs

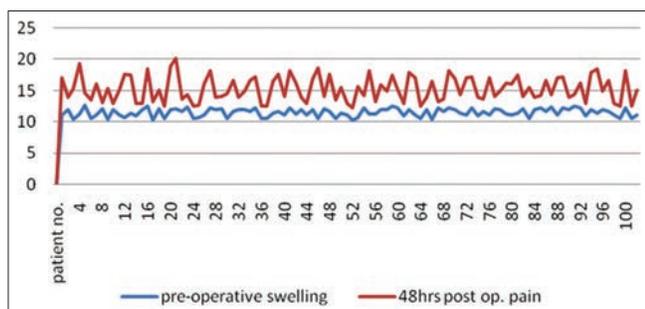


Figure 8: Correlation between pre-operative pain and post-operative swelling measured by thread which shows that the rise and fall in pre-operative swelling does not corresponds to the rise and fall in post-operative pain at 48 hrs

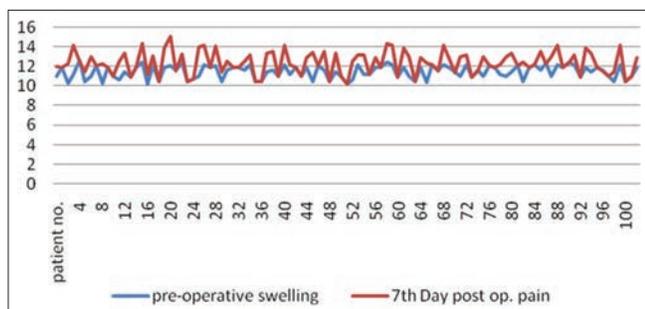


Figure 9: Correlation between pre-operative pain and post-operative swelling measured by thread which shows that the rise and fall in pre-operative swelling does not corresponds to the rise and fall in post-operative pain at 7 days

by hepatocytes in response to interleukin-6 (cytokines) secreted from the inflammatory sites. There are other cytokines such as tumor necrosis factor (TNF), IL-1, and transforming growth factor- α are also involved. C-reactive protein is seen to be elevated in many inflammatory disorders and is used to predict the outcomes of those conditions after treatment.^[10,11]

C-reactive protein reflects the measure of inflammation and immune injury of tissues. It is been also implicated that increased levels of C-reactive protein could directly participate in amplifying the immune response leading

to increased tissue damage. C-reactive protein acts synergistically with lipopolysaccharides to induce tissue factor production by monocytes. According to Edward T.H. Yeh^[12] C-reactive protein is not only a marker but also an amplifier of inflammation. Since inflammation is believed to have a role in the pathogenesis of post-operative events, measurement of inflammatory markers has been proposed as a method to improve the prediction of the risk of these events. However, the most important current use of CRP is in primary prevention, that is, in the detection of high risk among individuals not yet known to have a problem.^[13]

A healthy lifestyle decreases serum CRP levels, while obesity, physical inactivity, and smoking increase them.^[14,15] C-reactive protein is considered as a marker which can predict the future cardiovascular diseases. It was also found that the smokers have the high levels of the basal C-reactive protein. Due to this reason, the patients with previous cardiovascular diseases and smokers were not included in this study as it may alter the readings of the C-reactive protein levels pre and post-operatively. As shown by Amir Ur Rehman^[16] in his study patients having periodontitis are been showed to have raised levels of C-reactive proteins either. For this reason in this study all the patients were screened for periodontitis and were excluded from this study.

Third molar surgery is one of the most common minor surgical procedure in which transalveolar surgical extraction becomes a choice of procedure for oral surgeon by raising the mucoperiosteal flap and by using surgical bone cutting burs and sometimes chisel and mallet. This produces post-operative pain and swelling which may get aggravated by pre-existing inflammation and infection.^[8] Pre-operative analgesics and antibiotics are not always recommended but are prescribed in cases which showed pre-operative pain, swelling and inflammation. But these are not so reliable indicators for post-operative pain, swelling and trismus. This has been seen in cases of this study also that pre-operative pain, swelling and trismus are not reliable indicators of post-operative discomfort. Rather pre-operative level of C-reactive protein is consistently seen to be raised in cases in which post-operative pain, swelling and trismus was found to be more.

C-reactive protein levels in circulation are attenuated by NSAIDs, corticosteroids and antibiotics. Pre-operative combinations of Opioids and NSAIDs are more efficacious for reducing the post-operative pain, swelling and trismus.^[17] Also pre and post-operative levels of C-reactive protein are reduced by use of pre-operative analgesics and antibiotics.^[18] Also these days` studies are being published to show the effective methods of decreasing the levels of C-reactive protein in circulation by use of statins.^[19] The limitations of this study are the sample size should be more and should be done in various geographic regions all over the world to see the racial and ethenic changes.

Conclusion

Post-operative discomfort symptoms like pain, swelling and trismus were consistently more in those patients who were seen to have high levels of C-reactive protein pre-operatively and less post-operative discomfort in those who had lower pre-operative CRP levels. Although these patients; with high levels of post-operative discomfort; does not necessarily show pre-operative pain, swelling, infection or higher inflammation. C-reactive protein levels were reached higher on post-operative period till 48 hours and were comparatively less on the 7th day post-operatively.

Thus pre-operative levels of C-reactive protein were seen to be a reliable indicator than other indicators like pre-operative pain swelling and inflammation for prediction of post-operative discomfort symptoms like post-operative pain, swelling and trismus. Thus evaluation C-reactive protein levels will help pre-operatively for taking pre-operative medications to keep the C-reactive levels and post-operative discomfort to the minimal.

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