Evaluation of the Variations in the Levels of Perioperative Inflammatory Markers After Open Reduction and Internal Fixation of Maxillofacial Fractures

Parveen Sharma 1 · Rishi Kumar Bali 1 · Avneet Kaur 2 · Shivani Gaba 1 · Guneet Dhillon 3

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Abstract

Introduction Postoperative infectious complications are commonly encountered in open reduction and internal fixation (ORIF) of maxillofacial fractures. An early diagnosis of infectious processes is the key in preventing morbidity/mortality which could be in the form of loss of hardware and sepsis. To prevent these, various markers of inflammation have been studied in different disciplines of surgery but are found scarce in maxillofacial practice.

Material and method The present study was designed to evaluate the perioperative variations in the levels of inflammatory markers. We analysed temperature, TLC, DLC, ALT, AST and CRP in 50 patients of ORIF. Their values were recorded preoperatively as well as at 24 h, 48 h, third day and seventh day postoperatively. The correlation of inflammatory markers with the type of anaesthesia and length of surgery were also analysed.

Results The ranges of various markers in the perioperative phase were: temperature (97.6 °F–99.2 °F), TLC (5100/mm3–18200/mm3), neutrophils (51–91%), AST (12–86 IU/L), ALT (12–96 IU/L) and CRP (1.2–150 mg/L). Mean values of all the inflammatory markers achieved their peak values within 24 h postoperatively. These values showed a decline thereafter, with the day 3 and day 7 values being even lower than their preoperative values. This fall in the values was highly significant (p < 0.001) except ALT where the fall was significant (p < 0.05). The data obtained could be used as a reference range by the surgeons for monitoring the recovery of the patient. It could also help in timely interception and expeditious management of an infectious episode in the postoperative phase.

Keywords Trauma · Inflammatory markers · Infectious complications

Introduction

Patients undergoing surgery often develop systemic inflammatory response syndrome (SIRS) in response to trauma. Early detection of infection can be difficult as many signs and symptoms may actually mimic a postoperative SIRS.

There is a wealth of literature supporting the use of various inflammatory markers in diagnosis and monitoring of treatment of infectious complications in postoperative patients [1–4]. Various authors have studied markers including total leucocyte count (TLC), C-reactive protein (CRP), aspartate transaminase (AST) and alanine transaminase (ALT) in patients with SIRS and sepsis [5].

Behaviour of inflammatory markers and their correlation with infection in the postoperative phase have been evaluated in various disciplines of surgery. However, similar studies in maxillofacial surgery have been found to be very scarce. We therefore designed a study to evaluate perioperative variations in the levels inflammatory markers in open reduction and internal fixation (ORIF) of maxillofacial fractures.
An attempt was made to establish an acceptable range of variations in the values of inflammatory markers in ORIF and co-relate these variations to the length of surgery, type of anaesthesia used and occurrence of postoperative infection.

**Patients and Methods**

This prospective study was carried out in the period October 2012–October 2014. It included 50 patients undergoing ORIF of maxillofacial fractures. Patients with significant medical compromise, pathological fractures, concomitant injuries and pregnancy were excluded.

Information regarding history of present illness along with detailed local examination to assess the fracture site and type was obtained from all the patients. Standard radiographs were taken to establish the site and displacement of fracture. Appropriate anaesthesia was decided in consultation with the anaesthetist. Duration of the procedure from the time of incision and closure was recorded.

**Collection of Data**

Patients’ age, sex and fracture site involved were recorded. We measured clinical variables including temperature, TLC, Differential leucocyte count (DLC), CRP, AST and ALT.

Measurements were taken preoperatively and immediately after surgery (within 30 min), at 24 h, 48 h, 3rd and 7th postoperative day to assess their variation in perioperative period.

**Analysis of Data**

A database was constructed using Microsoft Excel (Microsoft, Redmond, WA). The statistical analysis was performed with the help of SPSS software (version 15.0, SPSS Inc, Chicago). Results are expressed as number (%) or mean (SD). The changes in values of the markers at different intervals were compared to the preoperative values (which were considered as baseline). The significance of differences was assessed using Student’s paired “t” test and ANOVA “F” test, as appropriate. Probabilities of less than 0.05 were accepted as significant.

**Results**

**Clinical Results**

Age of patients ranged from 18 to 50 years. Prevalence of maxillofacial fractures was high in age group of 21–30 years (42.0%) followed by 31–40 years (30.0%). In age group ≤ 20 years and 41–50 years, the prevalence of maxillofacial fractures was found to be 14% in each age group. Seventy per cent of the tested patients were male, and 30% were female.

Mandible fracture was the most common type of fracture which was present in 78.0% patients, followed by zygomaticomaxillary complex fracture (10.0%), LeFort I/II fracture (6.0%) and other types of fracture (6.0%).

To reconstruct the fracture, local anaesthesia was used in majority of the cases (68.0%), while general anaesthesia was used in rest of the cases (32.0%).

Duration of procedure ranged between 60 and 180 min with a mean duration of 101.20 ± 23.36 min. Fifty-two per cent of the procedures were completed in less than 90 min; only 12% cases took more than 120 min to complete.

Table 1 shows the change in temperature at different postoperative intervals as compared to baseline value. The change in body temperature from its baseline value (preoperative) was found to be statistically significant at all the studied intervals except immediately after procedure.

**Laboratory Results**

Variation in the laboratory parameters at different postoperative intervals as compared to baseline value is given in Tables 2, 3, 4 and 5.

The time period for various ORIF procedures was statistically correlated with various postoperative values of inflammatory markers. The association was not found to be statistically significant at any point of time.

The range of various inflammatory markers in the perioperative phase is given in Table 6.

**Discussion**

In the postsurgical phase, the signs of inflammation may often mask an infectious process. This may lead to a delay in diagnosis of infections with resultant loss of hardware and an increase in morbidity and mortality. Therefore, it is important for the surgeon to diagnose the condition early by looking at the clinical signs and correlating them with the markers of inflammation. The ideal marker should be able to distinguish between the inflammatory response and infection allowing earlier identification of patients with a specific disease process [6].

Knowledge about the natural behaviour of inflammatory markers may be helpful in the diagnosis of postoperative complications following ORIF. Although it would not be practical to set numeric limits for the inflammatory markers, it is useful to be aware of their natural response after surgery [7, 8].
| Table 1 | Change in temperature (°F) at different postoperative intervals |
|--------|---------------------------------------------------------------|
| Time interval | Mean | SD | Mean change | SD of change | Mean % change | SD % change | “t” | “p” |
| Preoperative | 98.52 | 0.29 | | | | | | |
| Immediate post-op. | 98.55 | 0.24 | 0.03 | 0.04 | 0.03 | 0.28 | −0.73 | 0.469 |
| 24 h | 98.42 | 0.21 | −0.10 | 0.04 | −0.11 | 0.26 | 2.83 | 0.007 |
| 48 h | 98.37 | 0.18 | −0.15 | 0.03 | −0.15 | 0.24 | 4.39 | < 0.001 |
| Day 3 | 98.36 | 0.22 | −0.16 | 0.04 | −0.17 | 0.28 | 4.20 | < 0.001 |
| Day 7 | 98.29 | 0.19 | −0.23 | 0.04 | −0.23 | 0.31 | 5.31 | < 0.001 |

| Table 2 | Change in TLC (× 10⁹/L) at different postoperative intervals |
|--------|---------------------------------------------------------------|
| Time interval | Mean | SD | Mean change | SD of change | Mean % change | SD % change | “t” | “p” |
| Preoperative | 10.7 | 2.2 | | | | | | |
| Immediate post-op. | 11.2 | 2.3 | 0.49 | 0.34 | 6.44 | 18.26 | −1.45 | 0.154 |
| 24 h | 11.3 | 2.3 | 0.64 | 0.40 | 8.73 | 23.46 | −1.61 | 0.113 |
| 48 h | 10.3 | 1.5 | −0.40 | 0.32 | −1.06 | 18.12 | 1.23 | < 0.001 |
| Day 3 | 9.5 | 1.2 | −1.25 | 0.32 | −8.85 | 17.77 | 3.93 | < 0.001 |
| Day 7 | 8.7 | 1.1 | −2.04 | 0.32 | −16.41 | 16.33 | 6.42 | < 0.001 |

| Table 3 | Change in neutrophil count at different postoperative intervals |
|--------|---------------------------------------------------------------|
| Time interval | Mean | SD | Mean change | SD of change | Mean % change | SD % change | “t” | “p” |
| Preoperative | 75.28 | 8.72 | | | | | | |
| Immediate post-op. | 79.60 | 6.97 | 4.32 | 0.80 | 6.37 | 18.26 | −5.37 | < 0.001 |
| 24 h | 78.18 | 7.73 | 2.90 | 1.18 | 4.71 | 11.91 | −2.46 | 0.017 |
| 48 h | 73.28 | 5.54 | −2.00 | 1.21 | −1.56 | 11.93 | 1.66 | 0.001 |
| Day 3 | 69.84 | 5.83 | −5.44 | 1.32 | −6.10 | 12.56 | 4.11 | < 0.001 |
| Day 7 | 64.16 | 4.71 | −11.12 | 1.07 | −13.93 | 9.26 | 10.41 | < 0.001 |

| Table 4 | Change in AST and ALT (IU/L) at different postoperative intervals |
|--------|---------------------------------------------------------------|
| Time interval | Mean | SD | Mean change | SD of change | Mean % change | SD % change | “t” | “p” |
| Preoperative (AST) | 36.94 | 12.63 | | | | | | |
| ALT | 39.82 | 13.78 | | | | | | |
| Immediate post-op. (AST) | 46.24 | 25.03 | 9.30 | 3.34 | 33.24 | 81.55 | 2.79 | 0.008 |
| ALT | 43.84 | 20.31 | 4.02 | 17.39 | 13.52 | 42.97 | 1.635 | 0.109 |
| 24 h (AST) | 45.16 | 17.44 | 8.22 | 2.24 | 30.62 | 60.08 | 3.67 | 0.001 |
| ALT | 42.84 | 15.30 | 3.00 | 14.11 | 13.03 | 33.66 | 1.504 | 0.139 |
| 48 h (AST) | 38.48 | 12.98 | 1.54 | 1.90 | 13.16 | 51.15 | 0.81 | 0.421 |
| ALT | 36.28 | 11.05 | −3.54 | 12.18 | −3.06 | 29.96 | −2.054 | 0.045 |
| Day 3 (AST) | 32.98 | 13.11 | −3.96 | 1.84 | −4.33 | 43.02 | −2.15 | 0.037 |
| ALT | 30.40 | 9.83 | −9.42 | 11.91 | −18.93 | 26.76 | −5.595 | < 0.001 |
| Day 7 (AST) | 27.34 | 14.16 | −9.60 | 2.18 | −21.15 | 41.90 | −4.40 | 0.000 |
| ALT | 24.46 | 11.83 | −15.35 | 2.17 | −34.58 | 32.47 | −7.076 | < 0.001 |
Levels of temperature, TLC, CRP, AST and ALT, were measured preoperatively, immediately after surgery, after 24 h, 48 h, 3rd day and 7th day postoperatively.

Leucocyte count increases in response to acute infection, trauma or inflammation [9]. This is caused by a normal response of the immune system triggering the bone marrow to release additional stored white blood cells into the blood. While the TLC has discriminatory capability for serious injury, it could not, in isolation, reliably rule in or out serious injury [10].

In our study, the minimum value of TLC was found to be 5100 mm$^3$ and 18,200 mm$^3$ was the maximum value postoperatively. Maximum rise in TLC was seen 24 h postoperatively and began to decline subsequently. All patients showed normal counts by the end of 7th day postoperatively.

The range of neutrophils was found to be 51–91%. Highest values were seen in the immediate postoperative period and declined subsequently.

Durila et al. [5] evaluated 43 patients and concluded that sequential measurements of ALT and AST can be used for early differentiation of sepsis and postoperative SIRS. These investigations are cheap, are routinely available and can be helpful in screening of patients in sepsis.

CRP is an acute-phase protein produced by the liver in response to inflammation and infection [12–14] and is a valuable marker of infection [15]. It rises within 4–6 h of injury, peaks at 24–48 h and then falls rapidly once the inflammation resolves. This rapid rise and fall of CRP makes it a more sensitive marker to follow than WBC [16].

In our study, the range of CRP was found to be 1.2–150 mg/L. The CRP values were highest at 24-h postoperative period and showed a decline from 24 to 48 h. The higher postoperative levels could be due to body’s response to surgical insult. The values of CRP 24 h postoperatively were significantly higher as compared to baseline preoperative values, whereas the values for the 3rd and 7th day were significantly lower. This was in accordance with the study of Kiran and Rajendra [17], wherein they evaluated CRP levels perioperatively in ORIF of mandibular fractures and correlated the prognosis with the convalescent period.

According to Gwak et al. [18], the CRP diminishes significantly 2 days after surgical intervention and achieves its normal range 5–7 days after surgery. Persistent rise in CRP level beyond third day or any subsequent rise in CRP level was consistent with a septic complication in the patient [19]. This correlates with the mean CRP levels in the present study which was observed (9.00 mg/L) 7th day postoperatively. The fall in CRP concentration may be delayed when postoperative complications are present [20, 21]. Most cases of fever immediately following surgery are self-limiting, but it is critical not to miss more serious aetiology like development of sepsis. The maximum temperature was found to be 99.2 °F, while the maximum mean temperature was 98.5 °F in the immediate postoperative period. There was no sharp rise in temperature in our study.

### Table 5 Change in CRP (mg/L) at different postoperative intervals

| Time interval     | Mean   | SD     | Mean change | SD of change | Mean % change | SD % change | "t"       | "p"       |
|-------------------|--------|--------|-------------|--------------|---------------|-------------|-----------|-----------|
| Preoperative      | 35.34  | 30.97  |             |              |               |             |           |           |
| Immediate post-op.| 45.72  | 34.70  | 10.38       | 1.65         | 46.67         | 58.99       | − 6.29    | < 0.001   |
| 24 h              | 48.23  | 32.46  | 12.89       | 3.33         | 77.11         | 103.50      | − 3.87    | < 0.001   |
| 48 h              | 34.17  | 25.34  | − 1.17      | 3.50         | − 27.05       | 90.96       | 0.33      | 0.739     |
| Day 3             | 18.32  | 15.91  | − 17.02     | 3.52         | − 29.27       | 62.27       | 4.84      | < 0.001   |
| Day 7             | 9.00   | 10.57  | − 26.34     | 3.78         | − 68.42       | 30.16       | 6.96      | < 0.001   |

### Table 6 Perioperative range of inflammatory markers

| Variable | Minimum | Maximum |
|----------|---------|---------|
| Temperature | 97.6 °F | 99.2 °F |
| TLC | 5.1 ($\times 10^9$/L) | 18.2 ($\times 10^9$/L) |
| Neutrophils | 51% | 91% |
| AST | 12 IU/L | 86 IU/L |
| ALT | 12 IU/L | 96 IU/L |
| CRP | 1.2 mg/L | 150 mg/L |

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No case of local or systemic infection was seen in the study. All the inflammatory markers showed a rise in the immediate postoperative period as compared to their preoperative levels. The mean levels of all these markers peaked within 24 h showing a downward trend thereafter. However, the CRP levels continued to rise till 48 h in three cases; these three cases involved midfacial fractures which required submental intubation. This in addition to the manipulation required to disimpact them could have led to increased surgical insult resulting in a delay in fall of CRP.

It is safe, therefore, to assume that, in general, the levels of inflammatory markers should show a downward trend after 48 h of an uncomplicated ORIF surgery. Most of the levels decline to their respective normal range by the end of 7th postoperative day. The mean values fell below preoperative values at day 3 and day 7. This fall in the values was highly significant \( p < 0.001 \) except ALT where the fall was significant \( p < 0.05 \).

The correlation between length of surgery and variation in the levels of inflammatory markers was not found to be significant in our study. However, the value of TLC and neutrophils was constantly higher when the time period of surgery was more than 120 min.

Also, the type of anaesthesia employed did not have any significant impact on the inflammatory markers, during the perioperative period.

The study has been able to compile the levels of perioperative inflammatory markers after ORIF in a series of 50 patients of maxillofacial fractures. Variation of these markers during postoperative phase could depend on the individual’s response towards the surgical insult, the nature of surgical procedure, types of drugs used and presence or absence of infection.

The data obtained could be beneficially employed to diagnose complications very early and thus improve the prognosis. Such data could also be used to benefit the patient by helping to judge early switch from intravenous to oral route and termination of antibiotic therapy. This could further prevent the development of resistant microorganisms. A consolidated database of perioperative inflammatory markers after ORIF of maxillofacial fractures could be created, if further multicentric studies are initiated.

Conclusion

The levels of inflammatory markers showed a downward trend 48 h after an uncomplicated surgery. Most of the values declined to their respective normal range by the end of 7th postoperative day. An acceptable range of various perioperative inflammatory markers in uncomplicated ORIF procedures has been established. Such consolidated data of easy-to-use inflammatory markers could be used by surgeons to diagnose and intervene early in cases of postoperative infectious sequelae.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no competing interests.

Ethics Statement The study design was approved by the Board of Studies of the University. An informed consent was obtained from all the patients.

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