

Preoperative Alterations of Interleukin-6 levels During Surgical Removal of Impacted Lower Third Molar

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الخلاصة

الأهداف: تحدد الدراسة الى معرفة مستوى الانترلوكين السادس (IL-6) بعد العملية الجراحية لإزالة سن العقل المظموور جراحيا في الفك السفلي **المواد وطرائق العمل:** لغرض إجراء الدراسة تم استخدام ستا وعشرين مريضا تم إجراء العملية الجراحية، لهم لإزالة سن العقل المظموور في الفك السفلي حيث تم سحب ثلاث عينات من الدم من كل مريض واحدة قبل العملية الجراحية والاخرى ساعتين بعد العملية الجراحية والاخرى بعد اربع وعشرين ساعة من اجراء العملية الجراحية وتم استخلاص مصل الدم (Serum) من العينات وفحصها باستخدام جهاز الالايذا.. **النتائج:** أظهرت النتائج ان هناك ارتفاع ملحوظ في مستوى الانترلوكين السادس واستمر هذا الارتفاع الى ٢٤ ساعة بعد العملية الجراحية مقارنة مع مستواه قبل العملية الجراحية. **الاستنتاجات:** نستنتج من الدراسة ان هناك استمرار الارتفاع في مستوى الانترلوكين بعد العملية الجراحية الى ٢٤ ساعة.

ABSTRACT

Aims: The aim of the study is to assess the blood levels of (interleukin-6) at different intervals of time after surgical removal of impacted lower third molars.. **Materials and Methods:** The study group comprised 26 patients with impacted lower third molars .All extractions were performed under local anaesthesia using the inferior alveolar nerve block together with vestibular infiltration. A buccal full thickness two sided mucoperiosteal flap was raised. Sterile low-speed straight hand pieces and sterile distilled water were used for ostectomy. After tooth removal the wound was closed with 3-0 black silk suture. Three blood samples were drawn from each patient; one before the operation, the second 2hr. post operation and the third 24hr. post operation. The blood samples were collected through venipuncture, serum separated and stored in at -20°C. Analysis was performed using the Enzyme linked Immunosorbant assay (ELISA). **Results:** The level of IL-6, in this study, showed an increase following surgery, in comparison with the level before operation. This increase in the level of Interleukin-6 remained high until 24hr after operation. **Conclusion:** Interleukin-6 (IL-6) is higher after surgical extraction of lower third molars and remained with high levels to 24hr. after operation.

Keywords: Third molar surgery, cytokines, interleukin-6.

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INTRODUCTION

The surgical removal of impacted mandibular third molars produces a significant degree of tissue trauma that causes an inflammatory reaction. The latter produces the usual postoperative signs and symptoms such as pain, facial oedema, and limited mouth opening due to muscle spasm (trismus).⁽¹⁾ Cytokines are small secreted proteins which mediate and regulate immunity, inflammation, and hematopoietic. They are produced in response to an immune stimulus. They generally, although not always, act over short distances

and short time spans and at very low concentration. (Balkwill, 2001).⁽²⁾

Interleukin-6 (IL-6) is a critical cytokine in the cascade of host response to infection which activates the acute phase response, stimulates T-lymphocytes, induces terminal differentiation of B-lymphocytes and induces C-reactive protein production.⁽³⁾

The infections cause an acute inflammatory response, which is initiated and mediated by pro-inflammatory cytokines, such as IL-6 and TNF- α .⁽⁴⁾

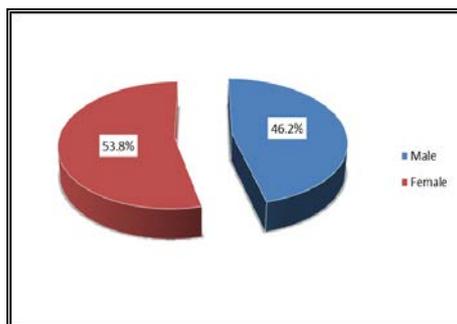
Interleukin-6 (IL-6) is a multi-

functional cytokine that exerts effects on many different types of target cell. IL-6 can be produced by a number of cell types, including monocytes, endothelial cells, and T lymphocytes. The main biological activities of IL-6 include induction of acute-phase protein synthesis in hepatocytes, induction of terminal differentiation in B cells, and activation of T cells. In mammals, IL-6 has been implicated in the development of both Th1 and Th2 responses.⁽⁵⁾

Interleukine-6 also has a role in oral cancer, Cruickshank *et al.*⁽⁶⁾ studied the response of IL-6 in patients who had undergone different types of operations (minor surgery, cholecystectomy, hip surgery, colorectal surgery and major vascular surgery), and the authors concluded that IL-6 is a sensitive and early marker of tissue damage. In the maxillofacial area, Miyawaki *et al.*⁽⁸⁾ proved that the level of IL-6 in plasma increases after different operations (cystectomy, benign tumor extirpation, etc.).

MATERIALS AND METHODS

This prospective, controlled, randomised study comprised 26 patients of both genders (46.2 % male and 53.8 % female); age was between 17-29 years with a mean of (24.9 years), who required surgical removal of impacted lower third molar Figure (1).



Figure(1): Percentage of both genders; male and female

Radiographs were taken to assess third molar eruption and angulations in relation to the adjacent second molar.

The inclusion *criteria* for selection were medically fit patients with partially or completely impacted lower third molars.

The exclusion criteria were:

- 1-Any drug taken before blood sample.
- 2- Pregnancy or lactating mother.
- 3- Compromised systemic disease.
- 4- Alcohol or drug addiction.
- 5- Acute pericoronitis or severe periodontal disease and pathological lesion locally at the time of operation.

Surgical Protocol

The surgical extraction of impacted molars as followed: Under local anaesthesia using the inferior alveolar nerve block together with vestibular infiltration using 2% lidocaine hydrochloride and 1:80,000 adrenalin, a buccal two sided full thickness mucoperiosteal flap was raised. Sterile low-speed straight hand piece and sterile distilled water were used for ostectomy or tooth sectioning when required. The tooth was removed and the socket was irrigated. The wound was closed with 3-0 black silk suture. The patient was given amoxillin capsules 500 mg (1*3) for five days and paracetamol tablets 500 mg as needed for pain. All patients were given written instructions regarding post-operative care.

Measurement of IL-6

Three blood samples were drawn from each patient; one immediately before the operation, the second 2hrs. post operation. and the third 24hrs. post operation. The samples allowed to clot at room temperature for 30 minutes. Sera were separated by centrifugation at 1500 round per minute for 10 min. Sera were separated as soon as possible from the clot of red cells after centrifugation to avoid IL-6 production by blood cells that falsely could increase its values. The blood samples were drawn by venipuncture, serum was separated⁽⁷⁾ and stored in aliquots at -20°C until measured of interleukine-6 by the ELISA. Commercially available ELISA kits (Boster immunoleader, U.S.A.) were used to determine the serum concentrations of IL- 6, using the procedures provided by the manufacturers. The statistical paired sample T-test was used in this study which provided by Statistical Package for Social Sciences (SPSS) software (version 19.0, SPSS Inc., USA) for comparing the levels of IL-6 at different intervals of time.

RESULTS

In the present study, it an attempt was made to determine the presence and level of IL-6 after surgical extraction of lower third molars. The predominant position of impacted third molar according to the Pell and Gregory classification was class I (42.3%), followed by class II (46.2%) and

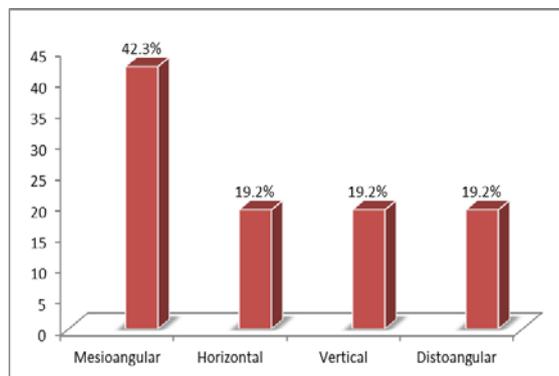
class III (11.5%). Level A (34.6 %) Level B (50%) and Level C (15.4%).The most common tooth angulation was the mesioangular (42.3%), distoangular (19.2)%, horizontal (19.2)% and vertical (19.2%) angulations (Table 1,2) and (Figure 2,3, 4).

Table (1): Percentage of impacted lower third molar angulations in patients under study.

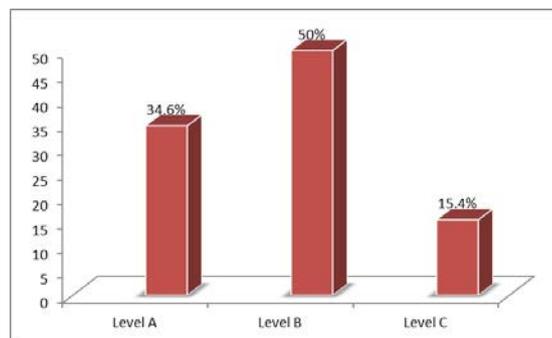
Mesioangular	Horizontal	Vertical	Distoangular
42.3%	19.2%	19.2%	19.2%

Table (2): Positions of impacted lower third molar according to Pell and Gregory classification

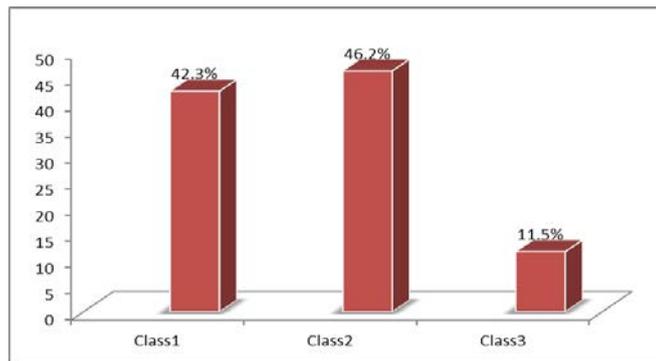
Class I	Class II	Class III
42.3%	46.2%	11.5%
level A	level B	level C
34.6%	50%	15.4%



Figure(2): Number and percentage of impacted lower third molar angulations in patients under study.



Figure(3): Percentage of impacted lower third molar positions in patients under study.



Figure(4): Percentage of impacted lower third molar positions in patients under study.

The results showed that IL-6 increased after surgical removal of impacted lower third molar (Table.3). The increase of IL-6 was 2hr post-operative compared with that before operation , but was not statistically

significant at P - value ≤ 0.05 (Table. 4) Figure (5). However there was a high significant increase in the level of IL-6 pre-operative and 24hrs.post operative at p -value ≤ 0.05 (Table.4).

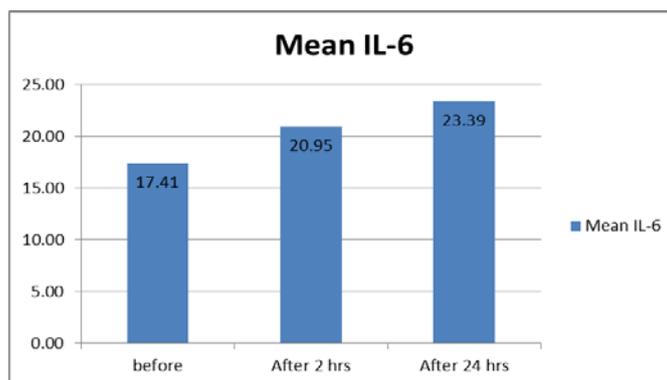
Table (3): Descriptive statistics of IL-6 (pg/ml).

Duration	Mean	N	S.D.
Before operation	17.4	26	9.84
2 hours after operation	20.95	26	13.6
24hours after operation	23.38	26	10.26

Table (4): Paired sample T-test results comparing between same group at different time.

Pairs	df	p- value ≤ 0.05
0 hr – 2 hr	25	0.327
0 hr – 24 hr	25	0.019*
2 hr -24hr	25	0.034*

(* Significant)



Figure(5): Showed the mean IL-6 in relation to different interval of time.

DISCUSSION

Several authors have found a correlation between the increase in IL-6 and postoperative complications, such as in-

fections. ^(10,11)

Di Padova *et al*⁽¹²⁾ detected IL-6 one hour after starting the operation (cholecystectomy), remaining significantly high 72

hours later. In this study, IL-6 was detected after surgical extraction of lower third molars and there was a high level of IL-6 at 24hrs. after surgery. Other authors have found the same result in burn lesions or after elective surgery.^(7,13, 14) Given that IL-6 is a mediator of the acute stage reaction in human beings; Bellón *et al* stated that it is reasonable to believe that an increase in IL-6 levels in serum after surgery is related to the degree of tissue damage. This has been demonstrated in several studies on operated patients, IL-6 being an early and sensitive marker of surgical damage. In general, the greater the surgical damage, the stronger the IL-6 response in serum and the higher the concentration.⁽¹⁵⁾

Since this cytokine is one of the most important cytokines involved in the physiological response to trauma, inflammation and infection also found to be increased after surgical removal of impacted lower third molar.⁽¹⁶⁾ research remains to be carried out in order to determine whether IL-6 concentration in serum simply reflects the level of tissue damage or plays a more active role in the host defense mechanism or in the induction of postoperative complications.

CONCLUSION

After surgical extraction of lower third molars, there was a significant increase in IL-6 levels, which was evident 2 hours after surgery, remaining high till 24hrs

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