

The Effect of Chlorohexidine Gel foam on the Salivary Tumor Necrosis Factor and Interleukine-6 After Extraction of Lower Third Molar.

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الخلاصة

الأهداف: الهدف من هذا البحث هو لدراسة تأثير الهلام الفموي الكلوروكسدين على وسائط الالتهاب (IL-6, TNF- α) بعد قلع الضرس السفلي الثامن (ضرس العقل) من خلال قياس (IL-6, TNF- α) للعابي قبل وبعد القلع ومعرفة الفائدة من استخدام الكلوروكسدين لتقليل الالتهاب البكتيري بعدى قلع الضرس السفلي الثامن. **المواد وطرائق العمل:** تضمنت هذه الدراسة 23 مريضاً تم تقسيمهم الى مجموعتين المجموعة الاولى (السيطرة) عددهم 12 مريضاً تم جمع عينة اللعاب لهم ثم تم قلع الضرس السفلي الثامن وعدم وضع جل فموي لهم, المجموعة الثانية 11 مريضاً تم جمع عينة اللعاب لهم ثم وضع لهم جل فموي مع الكلوروكسدين بعد قلع الضرس السفلي الثامن وتم اخذ عينة اللعاب مرة اخرى من المجموعتين بعد 7 ايام لقياس عامل نخر الورم للعابي والانتريليوكين - 6 باستخدام عدة التشخيص بالالايزا. **النتائج:** اظهرت النتائج هناك فرق معنوي لدى مستخدمين الكلوروكسدين كهلام فموي لل (IL-6) بعد اسبوع (16.20 \pm 5.22) مقارنة بخط الاساس (1.96 \pm 0.51) وكذلك في TNF (56.8 \pm 79.3) بعد اسبوع مقارنة بخط الاساس (102.9 \pm 133.3) واظهرت النتائج انه لا يوجد فرق معنوي عند (TNF- α) بعد اسبوع من القلع عند المرضى الذين لم يستخدموا اي نوع من العلاج (25.9 \pm 30.8) مقارنة بخط الاساس (95.2 \pm 131.6) واظهرت النتائج ان هناك فرق معنوي كبير في (IL-6) بعد اسبوع من القلع مقارنة بخط الاساس حيث ان النتائج على التوالي (6.20 \pm 5.22) (1.96 \pm 0.51) **الاستنتاجات:** استخدام الجل الفموي مع الكلوروكسدين يودي الى فرق معنوي لدى وسائط الالتهاب (IL-6, TNF- α) مقارنة مع المجموعة الضابطة والذي يحفز على تقليل الالم وزيادة الشفاء وتقليل الالتهاب.

ABSTRACT

Aims: This study aimed to demonstrate the effect of chlorohexidine gelfoam on the salivary Tumor Necrosis factor and Interleukin-6 after extraction of the lower third molar to compare these effects before and after extraction ' and to know the benefit of using chlorohexidine gelfoam after extraction of the lower third molar. **Materials and methods:** twenty four patients were involved, patients classified into group 1[control group], group 2 [chlorohexidine group] saliva was taken from all patients by using salivette before extraction and seven day after extraction then measure TNF and IL-6 by using [ELISA] kits' **Results:** In control group there is significance difference in (IL-6) after one week of extraction without treatment from the baseline (before extraction) and the result respectively was (1.96 \pm 0.51), (6.20 \pm 5.22), the result of (TNF- α) appeared no significance difference before and after treated the result after treatment is (25.9 \pm 30.8) and before treatment is (95.2 \pm 131.6) and the result of group used chlorohexidine gelfoam showed significance difference in both (IL-6, TNF- α) after and before treatment, the result of IL-6 after treatment is (16.99 \pm 13.31) and before treatment is (1.57 \pm 0.18) and the result of (TNF- α) after treatment is (56 \pm 79.3) and before treatment is (102.9 \pm 133.3). **Conclusion:** - the use of chlorohexidine gelfoam after extraction produce a significant effect on the salivary TNF- α and the level of IL-6 when compared with the control group which enhance the healing process and decrease the chance of infection

Key words: chlorohexidine gelfoam, patient with (third molar extraction, salivary (IL-6 and TNF- α)).

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INTRODUCTION

Extraction is a process that has not always been correctly measured as a consequence of the standard procedure (1) person has his or her healing ability, which is determined by his or her biotype and biological profile, consisting of cytokines and inflammation mediator. (2), Three-stage healing, inflammatory phase, proliferative phase, maturation phase, the first cycle initiated as soon as blood platelets come into contact with collagen, connective tissue when blood fills in an empty socket, this produces a platelet aggregation that forms a clot (erythrocytes and leukocytes embedded in fibrin) this clot prevents the bleeding and considers as a help for the successive stage of cicatrization (3), The platelet cycle growth factor and mediators (Cytokines) implicated in angiogenesis (4). Cytokines are soluble proteins that play a significant role in the initiation and maintenance of inflammatory and immune response as well as an intercellular cross-talking (5). Interlukine-6 is a multifunctional cytokine synthesized in response to stimuli such as infection, cell a variety trauma such as macro-phage neutrophils, keratinocytes and fibroblasts (6).

Saliva is a completely specific oral fluid formed from primary and minor salivary glands, it can be used to provide patient-related clinical statistics (7), a rapid increase in the use of saliva as a diagnostic tool in recent years, measurement of

antibodies and protein concentration, and saliva flow rate(8). Gelfoam is considered a sterile sponge as a medical tool intended for application to the bleeding surface as a hemostatic agent (9), chlorhexidine gelfoam is used as haemostatic agent, chlorhexidine is a biguanide, antiseptics, chlorhexidine is effective against both aerobic and aerobic bacteria, and leaves, chlorhexidine ransom is known to reduce the effectiveness of the oral microbe population(10), This subsequently reflects on the point of studying the impact of chlorhexidine gelfoam on the inflammatory mediator (IL-6 and TNF- α) following extraction

MATERIALS AND METHODS

Study sample: The study was approved by Research Ethics Committee board (University of Mosul, College of Dentistry, REC reference No. D.B.S./4/2432019-1). Study was carried out at the scientific committee of center of specialist dentist Nineveh Health Directorate at AL-NOOR specialist Dental Centre. The study consisted of twenty- four patient, mean aged (18-45) years need non-surgical extraction of lower third molar teeth, inclusion criteria involved healthy patient without the concomitant disease, non-smoker, nonalcoholic without known allergic history to any of our tested materials, without a history of any complication if used our mediation, patients were not currently on the prescribed drug were included'. The patient

grouped into group1[control group] twelve patients without applying gelfoam on the analgesic [500mg]paracetamol tablet on need and asked the patient to return to dentist if any sign of dry socket has appeared as[sever pain, and bleeding]' group 2 eleven patients applied gelfoam with chlorhexidine on the socket of lower third molar and asked patient to take paracetamol tablet[500]mg as a simple analgesic on need and asked the patient to return if any sign of dry socket is appeared

Saliva was collected from each patient in both groups at the beginning of the study before extraction and at the seventh(7th) day after extraction by salivette then centrifuged the saliva 10 minutes at 3000 beats then freeze then placed in eppndroff tube using (ELISA) procedure to determine the result of (IL-6 and TNF- α).

socket after extraction of lower third molar the patients received simple

Statistical analysis:

The data were expressed as a mean \pm SD difference between two experimental groups were statistically analyzed by using paired T-test of two mean and. The level of significant difference at $P \leq 0.05$.

RESULTS

The result in a mean salivary level of IL-6 and TNF- α of chlorhexidine gelfoam group after one week showed that the level of TNF- α was (56.8 \pm 79.3) compare with it at beginning of the study is (102.5 \pm 133.3) with (P-value 0.024), this mean that there is a significance difference of the level of TNF- α ,while the level of IL-6 is (16.99 \pm 13.31) after one week and (1.57 \pm 0.18) at the beginning with (P-value 0.002) , as shown in Table (1)

Table (1): changes in mean salivary levels TNF- α and IL-6 of after one week in chlorhexidine gelfoam group

Salivary Parameters	chlorhexidinegelfoam group		
	First day (before extraction) mean \pm SD	After one week of extraction mean \pm SD	P-value*
TNF- α (pg/m)	102.9 \pm 133.3	56.8 \pm 79.3	0.024
IL-6 (pg/ml)	1.57 \pm 0.18	16.99 \pm 13.31	0.002

* Significant at $P \leq 0.05$

The result in a mean salivary level of IL-6 and TNF- α of the control group after one week showed that the level of TNF- α was(25.9 \pm 30.8) after one week compared with (95.2 \pm 131.6) at the beginning of the

study with (P-value is 0.098) with no significant difference by using "paired T-test of two mean" while the result of IL-6 is(6.20 \pm 5.22) compare it with base line is (1.96 \pm 0.51) with (P-value is 0.014), it is

mean there is significance difference as shown in Table (2).

Table (2): mean salivary levels of TNF- α and IL-6 after one week in control group (n=12).

Salivary Parameters	control	control	P-value
	First day (before extraction) mean \pm SD	After one week mean \pm SD	
TNF- α	95.2 \pm 131.6	25.9 \pm 30.8	0.098
IL-6	1.96 \pm 0.51	6.20 \pm 5.22	0.014*

* Significant at $P \leq 0.05$

Comparison in salivary levels of TNF- α and Interlukine-6 among the two groups on the first day of the study are seen in the table (3) There were no significant differences of both salivary biomarkers between groups.

Table (3): Comparison in salivary levels of TNF- α and Interlukine-6 among the two groups at the first day of the study.

Parameters	Group I Mean \pm SD	Group II Mean \pm SD	P-value*
TNF- α (Pg/ml)	95.2 \pm 131.6 A	102.9 \pm 133.3 A	0.930
IL-6 (Pg/ml)	1.96 \pm 0.51 A	1.57 \pm 0.18 A	0.161

* Independent t- test was used. Means that do not share a letter are significantly different.

While table(4) showed the comparison in salivary levels of TNF- α and Interlukine-6 among the two groups after one week There was a significant difference in IL-6 and TNF- α between group I and group II, with $p < 0.05$.

Table (4): Comparison in salivary levels of TNF- α and Interlukine-6 among the two groups after one week.

Parameters	Group I Mean \pm SD	Group II Mean \pm SD	P-value*
TNF- α (Pg/ml)	25.9 \pm 30.8 A	56.8 \pm 79.3 A	0.028
IL-6 (Pg/ml)	6.20 \pm 5.22 B	16.99 \pm 13.31 A	0.018

** Independent t- test was used. Means that do not share a letter are significantly different.

DISCUSSION

The effects of extraction have not always been evaluated, several complications of mucosal and osseous may occur after extraction, bone resorption with alveolar process collapse, aging cleft, or gingival recession in the area surrounding the extraction site(11), according to the result of this study the level of TNF- α in group I and group II (chlorhexidine gel foam group) show a decrease in value from the beginning study and the seventh day after extraction with significant difference in group I and no significance difference in group II.

TNF- α is expressed on activated macrophages and lymphocytes as well as other types of cells, this a potent pro inflammatory cytokines exerting pleiotropic effects on various types of cells and playing a critical role in chronic inflammatory disease pathogenesis such as rheumatoid arthritis(12).

Every person has his or her healing ability, which is determined by his or her biotype and biological profile consisting of cytokines and inflammation mediator(2) TNF can function independently or in combination with another mediator, it exists in the form of TNF- α and TNF- β .(12)

TNF- α is released by activated macrophages but much less by other cell types, TNF- α and TNF- β binding to the same receptors, both of which have a half-life of 15-18 minutes but which indicate

metabolic and hemodynamic changes, the presence of endogenous transmembrane soluble TNF-receptors-(STNFRS) inhibiting possible uncontrolled TNF activity:- TNF- α has a cytotoxic effect on endothelial cells, which increases the adhesion molecule and improves vascular permeability directly and indirectly by stimulating neutrophils, helping to release prostaglandins, PGE₂, stimulating PAF (thrombocyte activating factor) and coagulation,

TNF and IL-1 are the most significant inducements of acute phase response (13) which is why, at the beginning of our research, it is high above the seventh day after extraction

According to the findings of this research, the amount of TNF in the control group and chlorhexidine showed an increase in value from the start of the test with substantial differences in both groups. Among numerous different antimicrobials used for anti-inflammatory response is chlorhexidine, which most practitioners have embraced because of its proven antimicrobial activity as well as availability and low cost. As most freshly isolated bacteria are inhibited in vitro by the extremely low chlorhexidine concentration. It could be hypothesized that an antiseptic agent might arrest periodontitis. Serra et al (2009) using a blunted needle syringe to apply 2 % chlorhexidine gel three times in 10 minutes to the bottom of single- rooted teeth and

recorded a 99.4% decrease in total colony-forming units and black-pigmented bacteroid, a decrease is compared to the effect of scaling and root planning:

In his research, Baber et al (2019) recommended the use of chlorhexidine in antiseptic surgery to prevent inflammatory reaction induction(7).

CONCLUSION

Chlorhexidine gelfoam produces a significant effect on salivary IL-6 and TNF- α when compared it with the level in control and treatment group which may enhance healing of socket after extraction of lower third molar and decrease susceptibility of infection.

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