

Evaluation of Ibuprofen, Clarithromycin and Suprax efficacy on swelling following apicectomy

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ABSTRACT

The effect of Suprax, Clarithromycin antibiotics and brufen nonsteroidal anti-inflammatory drug on the postoperative swelling after apicectomy of one upper anterior teeth was evaluated on sixty eight patients suffering from chronic periapical lesion requiring apicectomy without retrograde filling. They were divided into (5) groups according to the type of medicament administered postoperatively.

The patients were examined in the 2nd and 7th postoperative day for evaluation of postoperative swelling that may occur in the upper lip after apicectomy. The evaluation has been made by measuring the lip thickness by Sliding ruler method, face bow method and computerized photographic method. The results showed that Brufen tablets proved better control for postoperative swelling, Clarithromycin tablets, also produce significant reduction in the amount of swelling whereas Suprax capsules and paracetamol tablets produce no significant effect postoperative swelling compared to placebo.

Key Words: Ibuprofen, Clarithromycin, Suprax, swelling, apicectomy.

الخلاصة

صممت هذه الدراسة لتقييم فعالية كل من المضادين الحيويين وهما السوبراكس واكلارثرومايسين من جهة والبروفين (دواء مضاد للالتهاب اللاستيرويدي) من جهة أخرى على الورم بعد عملية قطع قمة الجذر لاجد الاسنان العلوية الأمامية. اشتملت الدراسة على (٦٨) مريضاً يعانون من آفة حول قيمة مزمنة ويحتاجون عملية قطع قمة الجذر بدون حشوة عكسية. وقد قسموا المرضى إلى خمسة مجاميع حسب نوعية العلاج المعطى لهم بعد العملية. وتم فحص المرضى في اليوم الثاني والسابع بعد العملية لتقييم درجة الورم الذي يحدث في الشفة العلوية بعد عملية قطع قمة الجذر وحسب الخطوات الآتية :

قيم الورم بعد العملية موضوعياً من خلال قياس سمك الشفة العلوية بثلاث طرق : وهي طريقة المسطرة المنزقة وطريقة القوس الوجهي وطريقة التصوير الرقمي (الحاسوبية).

بينت النتائج أن حبوب البروفين هي الأفضل في السيطرة على الورم بعد العملية. وكذلك وفرت حبوب الكلارثرومايسين تأثيراً ضد بكتيري وضد التهابي والذي أدى إلى تقليل معنوي للورم مقارنة ببقية الأدوية المستعملة ولكن أقل من البروفين. كان لكبسولات السوبراكس وكذلك حبوب الباراسيتامول تأثير غير معنوي في السيطرة على الورم بعد العملية مقارنة مع المجموعة الضابطة.

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INTRODUCTION

The two main contributing factors in the formation of post operative swelling are trauma and infection. The damage to the soft and hard tissue associated with oral surgical procedures is the usual cause of early post-operative swelling⁽¹⁾. Ibuprofen used in this study as one of Non-steroidal anti-inflammatory drugs (NSAIDs) effects by inhibiting the enzyme cyclo-oxygenase and thus prevents the conversion of arachidonic acid to prostaglandines, endoperoxidase and thromboxanes and lowering the inflammatory response⁽²⁾. However Morse⁽³⁾ proved that swelling is most likely controlled by anti-microbial action. The destruction or inhibition of the microbes would subsequently prevent the release of their inflammatory mediators and exudate, producing substances. With the inactivation of microbial irritants, the hosts own inflammatory substances would soon stop being produced, this would then allow the lymphatic system to drain the exudate, the end result would be an absence or diminution of swelling. Different approaches have been made to overcome this post operative complain. Troullos *et al*⁽⁴⁾ found that the administration of ibuprofen prior to oral surgery has been shown to significantly delay onset and severity of post operative swelling. Morse⁽³⁾ found that the antimicrobials agents cause destruction or inhibition of the bacteria which will subsequently prevent the release of their inflammatory and exudate producing substances, the end result would be an absence or diminution of swelling. The use of systemic antimicrobials to minimize post operative swelling following oral surgery has also been investigated by Bystedt *et al*.⁽⁵⁾ They reported the effect of Zidocillin, Erythromycin, Clindomycin and Doxycycline on swelling following oral surgery. Only Doxycycline displayed a significant reduction in the degree of swelling on second and fifth postoperative day. The study was designed to evaluate and compares the effect of Suprax and Clarithromycin antimicrobial agents with Ibuprofen, anti-inflammatory drugs on postoperative swelling following apicectomy.

MATERIALS AND METHODS

Clinical study composed of (68) patients attending the department of Oral and Maxillofacial Surgery, College of Dentistry, University of Mosul, and those referred from private clinics and health centers in Mosul city from Sept (2000) till Feb (2001). They have chronic periapical lesions and require treatment by apicectomy without retrograde filling. The criteria for patient selection were, The patients having single non-vital upper anterior tooth associated with periapical lesion, confirmed by vitality tests and radiograph. The patients should also have no medications namely analgesics and antibiotics for at least (5) days before the operation and should be medically fit for surgery as well. Under local anesthesia a conventional apicectomy following raising a three sided flap was performed for each patient. The patients were classified to five groups according to medication given for each group, 1st group Suprax treated group (STG) consist of (14) patients, 2nd group consist of patients receiving Clarithromycin tab (CTG), Brofen tab Given for the third group (BTG), which consist of (13) patients, the fourth group received Paracetamol tab Consist of (14) patients the last group receive placebo consist of (12) patients. the patient were recalled at the 2nd and 7th postoperative day following surgery for evaluation of post operative swelling. Three methods were used for the measurement of swelling namely computerized photographs, sliding ruler & face bow.

Assessment of the Postoperative Complaints

In computerized photograph method each patient in the study requires (3) photographs, one preoperatively which is used as reference for subsequent measurements. The 2nd and 3rd photographs at 2nd and 7th postoperative days respectively.

With the aid of special digital camera (Kodak DC 215 Zoom digital Camera) the patient instructed to stand within the cephalometer with the head position straight and asked to look forward at a distance of 2 feet from the camera. Lateral photographs were taken and loaded into Pentium II computer. Through special programmers prepared for this purpose, these programs aided in making all the photographs in the same size to facilitate the measurements. The measurements are made by drawing certain lines on the face depending on some soft tissue cephalometric landmarks (figure 1).

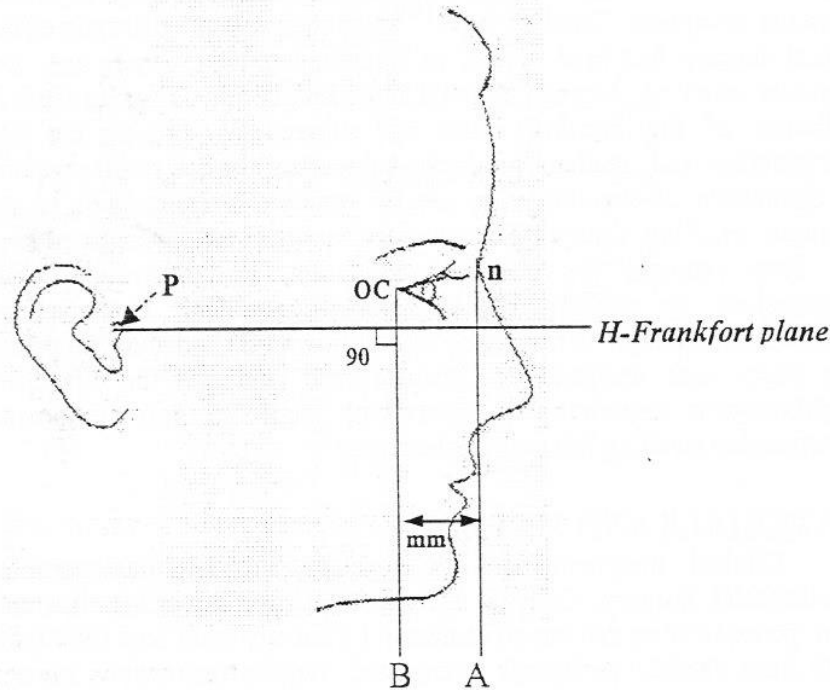


Figure (1): Profile analysis

The distance between A and B line is measured to the nearest (0.05) mm for the (3) photographs from the computer (figure 2). The degree of edema of upper lip calculated by subtracting of preoperative A-B distance from postoperative A-B distance. The derived data multiplied by minimizing factor of the photograph from the natural size of patient's head to give a natural amount of swelling of the lip. These data used later for comparison with data obtained from other two methods of measurements. In the sliding ruler method Measurements of the lip thickness by ruler were made preoperatively in order to calculate the swelling at 2nd and 7th days postoperatively (figure 3).

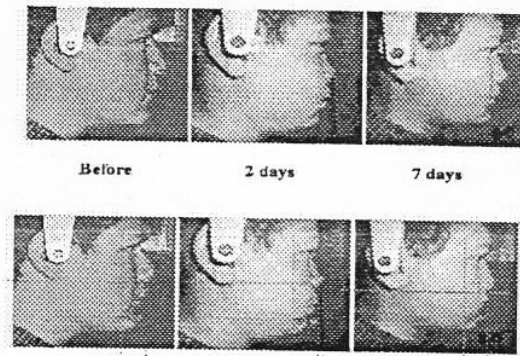


Figure (2): Measuring swelling of the lip from computerized photograph

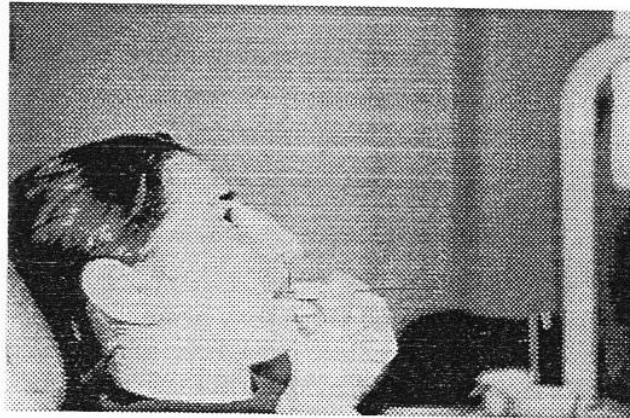


Figure (3): Measuring the swelling of lip by sliding ruler method

The readings were made by two examiners to avoid inter examiner variability. This method has the advantage that the anterior part of the ruler was a fixed point as it rested on hard tissues. The amount of swelling obtained by subtracting the preoperative lip thickness from the postoperative lip thickness and the data were recorded for the 2nd and 7th days follow up period.

The face bow method used in this study to evaluate the postoperative swelling, is similar to that used in prosthetic dentistry Hanau face bow, that consists of frame with two sliding pointers and bite fork, but the incisal pin was replaced by a metal ruler (figure 4).

After setting the patient in comfortable position on the dental chair the sliding pointer positioned inside the external auditory meatus of both ears and adjusted to be at the same millimeter scale for left and right side to be used as a reference for subsequent measurements during follow up period. The bite fork inserted into a patient mouth and the patient asked to bite on it with its slot positioned between the (2) upper central incisors, then locked in the position. After that the metal ruler adjusted to just touch the upper lip over the corresponding tooth (figure 4). The amount of edema obtained by subtracting the postoperative measurements from the preoperative readings. The data obtained from the three methods were recorded and analyzed.



Figure (4): Measuring swelling of the lip by face bow method

Statistical Analysis

1. Analysis of variance (ANOVA), significant test at $\alpha < 0.05$.
2. Duncan's multiple range test, significant differences considered at $\alpha = 0.05$.
3. Chi square test, significant at $p > 0.05$.

RESULTS

This study designed to evaluate the efficacy of Suprax (cefixime as trihydrate), Clarithromycin antibiotics and Ibuprofen anti-inflammatory on the postoperative swelling following apicectomy of one upper anterior teeth. A total of (68) patients were included in this study (33 male and 35 female), age range from (10-49 year). Five patients were excluded due to the failure of follow up. Therefore, only the data of (PATG) that the mean amount of swelling in BTG and (CTG) significantly differs that, less swelling was observed. Also the (BTG) produces significantly less swelling from that of (CTG) ($p < 0.05$) in the 2nd follow up day. While in the 7th follow up day, patients of STG of (63) patients were analysed. Table (1) shows details of the cases.

Table (1): Details of the cases

		STG	CTG	BTG	PATG	PLTG	Total
No. of Patients		13	13	12	13	12	63
Mean Age (years)		22.46	28.77	24.41	27.00	23.00	Range
Sex	No.	8	5	4	6	6	29
	No.	5	8	8	6	7	34
Operation Time(min)	Mean	34.07	32.84	32.41	44.5	38.84	
	Range	(15-90)	(15-50)	(20-45)	(20-70)	(25-50)	
Surgical Trauma	Mild	2	1	3	1	0	7
	Moderat	11	10	8	12	12	53
	Severe	0	2	1	0	0	3

In the sliding ruler method, analysis of variance (ANOVA) was done on (5) treated groups and showed that there was a significant difference in the swelling between groups ($p < 0.0001$). When Duncan's Multiple Range test was followed, the analysis of results showed from that and (PLTG) in, (CTG) and (BTG) show significantly less amount of swelling from that of (PATG) and (PLTG) patients as shown in table (2) and figure (5). While in facebow method the (BTG) patients produce significantly less amount of swelling ($p < 0.05$) than other groups in the 2nd follow up day. While in the 7th day, in general the Suprax, Clarithromycin and Brufen groups showed nearly no swelling in comparison with the (PATG) and (PLTG) as shown in table (3) and figure (6). In computerized photographic method the patients in (BTG) and (CTG), produce significantly very little amount of swelling ($p < 0.05$) comparing to that of (PATG) and (PLTG) patients in the 2nd postoperative day.

Table (2): Mean amount of swelling (mm) by sliding ruler method of all treated groups

P.O*	Statistics	STG	CTG	BTG	PATG	PLTG
2 nd Day	$\bar{X} \pm SE$	3.230 ± 0.22	2.730 ± 0.24	1.708 ± 0.16	3.307 ± 0.12	3.541 ± 0.17
	Duncan's	(AB)	(B)	(C)	(A)	(A)
7 th Day	$\bar{X} \pm SE$	0.384 ± 0.15	0.115 ± 0.06	0.250 ± 0.06	1.000 ± 0.23	1.208 ± 0.30
	Duncan's	(B)	(B)	(B)	(A)	(A)

* Post operative day, \bar{X} : mean, SE: standard error

Means with same letters horizontally was non-significant at 0.05, using Duncan multiple range test.

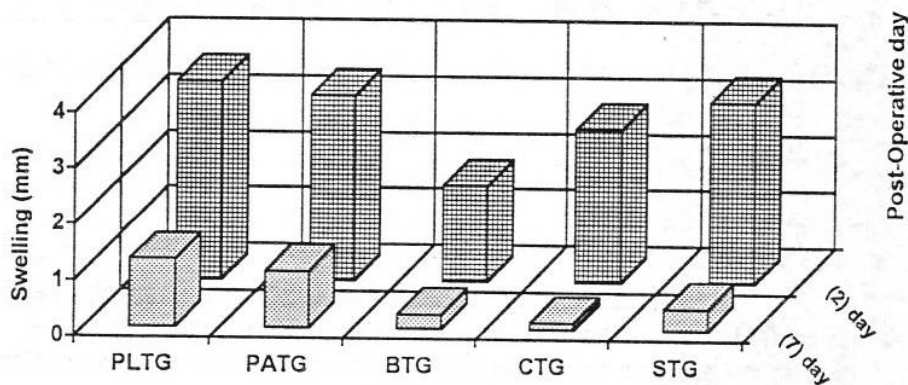


Figure (5): Mean amount of swelling of all treated groups (sliding rule method)

Table (3): Mean amount of swelling in (mm) by face bow method of all treated groups

PQ*	Statistics	STG	CTG	BTG	PATG	PLTG
2 nd Day	$\bar{X} \pm SE$	3.307 \pm 0.24	2.77 \pm 0.20	1.75 \pm 0.20	3.307 \pm 0.13	3.67 \pm 0.18
	Duncan's	(AB)	(B)	(C)	(AB)	(A)
7 th Day	$\bar{X} \pm SE$	0.423 \pm 0.18	0.230 \pm 0.12	0.291 \pm 0.11	0.961 \pm 0.20	1.291 \pm 0.18
	Duncan's	(B)	(B)	(B)	(A)	(A)

*Post operative day, \bar{X} : mean, SE : standard error.

Means with same letters horizontally was non-significant at 0.05, using Duncan multiple range test.

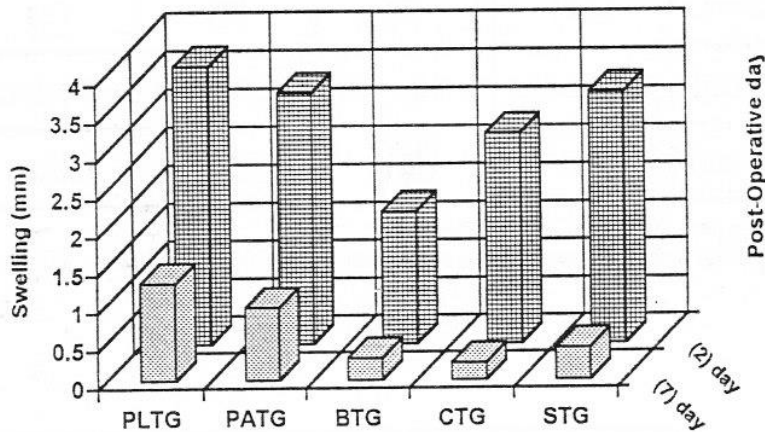


Figure (6): Mean amount of swelling in all treated groups (face bow method)

At 7th day post operatively resolution of swelling in all groups occurred and there was no significant difference among them (table 4 and figure 7).

Statistical analysis has been made for the three methods of evaluation of post operative swelling, proved no significant difference between them using unpaired t-test ($p \leq 0.05$).

Table (4): Mean amount of swelling in (mm) by computerized photographic method of all treated groups

P.O*	Statistics	STG	CTG	BTG	PATG	PLTG
2 nd Day	$\bar{X} \pm SE$	3.680 \pm 0.47	2.686 \pm 0.25	1.620 \pm 0.03	4.86 \pm 0.08	5.65 \pm 0.27
	Duncan's	(BC)	(CD)	(D)	(AB)	(A)
7 th Day	$\bar{X} \pm SE$	0.15 \pm 0.005	0.21 \pm 0.01	0.04 \pm 0.03	0.53 \pm 0.005	0.77 \pm 0.25
	Duncan's	(A)	(A)	(A)	(A)	(A)

* Post operative day. \bar{X} : mean, SE: standard error

Means with same letters horizontally was non-significant at 0.05, using Duncan multiple range test.

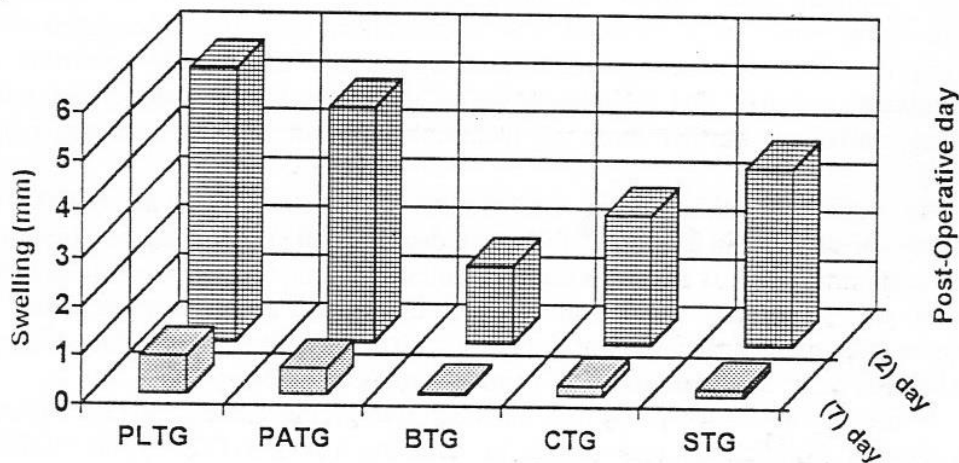


Figure (7): Mean amount of swelling of all treatment groups (computerized photographic method)

Discussion:

At the 2nd postoperative day, the group that medicated by Brufen (BTG) demonstrated little degree of swelling which is statistically highly significant comparing with other groups ($p < 0.01$). As Brufen (Ibuprofen) is one of the NSAIDs, its mechanism of action, is mediated chiefly through inhibition of biosynthesis of prostaglandins. These drugs are reversible inhibitors of cyclooxygenase (COXI, COXII). COXI, which is non-inducible and present in many tissues, includes platelets, stomach and kidney. COXII is induced by cytokines and endotoxins at the site of inflammation. Brufen inhibited the (2) isozymes about equally. Therefore, during Brufen therapy, inflammation is reduced by decreasing the release of mediators from granulocytes, basophils and mast cells. Also Brufen decreases the sensitivity of vessels to bradykinin and histamines affect lymphokine production from T-

lymphocyte and reverse vasodilation all these events contribute to lowering the postoperative swelling. ^(6,7) The CTG showed less degree of swelling in the 2nd day from the PATG and PLTG which is significant statistically ($p < 0.05$). This effect of Clarithromycin antimicrobes on limiting the postoperative swelling can possibly be explained by the fact that Clarithromycin acts on the different arms of immune systems. With the knowledge that macrolids can augment the monocyte-macrophage differentiation and improve the phagocytic function of macrophage⁽⁸⁾. The augmented macrophages will be more efficient in clearing up the debris and haematoma around the operative site, which result in shortening the period of local tissue damage, decreasing the amount of wound discharge and reducing the chance of infection. On the other hand, the suppression of systemic inflammatory response is possibly mediated by modulating cytokine production or function, as it was demonstrated that macrolides affect the levels of both pro-inflammatory and anti-inflammatory cytokines⁽⁹⁾.

Similar results have been demonstrated by Woo *et al.*⁽¹⁰⁾ in their experiment on a Guinea pig model. They found that Clarithromycin attenuates local and systemic inflammatory response induced by surgical trauma.

Clarithromycin was chosen in present study because it has a relatively long half-life as it may be given at a dose of (250) mg tablet every (12) hrs for (5-7) days with or without meal which is more convenient to patients. In addition, Clarithromycin, which is a macrolid like erythromycin with some advantages over erythromycin, it causes less gastrointestinal upsets and has a wide spectrum of antimicrobials activity that includes some of anaerobic bacteria associated with endodontic infection. Further more no undesirable side effects have been noticed in this study.

No significant difference has been found between the (PATG) and (PLTG) in the degree of swelling in 2nd and 7th follow up days ($p > 0.05$). This may be explained as that acetaminophen is a weak prostaglandin inhibitors in the peripheral tissue and possesses no significant anti-inflammatory effect. So acetaminophen alone is inadequate therapy for inflammatory condition such as postoperative swelling, though it may be used as an analgesic adjunct to anti-inflammatory therapy⁽⁶⁾.

While at the 7th follow up day, the medicated groups namely (STG, CTG and BTG) showed significantly less degree of swelling from the (PATG) and (PLTG). Such results may be attributed to the fact that swelling at the 7th day nearly disappeared completely either by the effect of Brufen if it is due to the inflammatory process or by antibiotics namely Suprax and Clarithromycin if it is due to the bacterial infection.

These findings are in agreement with other study⁽³⁾ who found that antibiotics effectively controlled much of pain, while simultaneously prevent the swelling by destruction or inhibition of the microbes and prevent release of their inflammatory mediators and exudate. So the host own inflammatory substances would soon stop production, allow the lymphatic system to drain, result in diminution of swelling. No significant difference ($p > 0.05$) has been found among the three methods used for evaluation of postoperative swelling after apicectomy. Since any method for evaluation the postoperative facial swelling should satisfy the following criteria, firstly the accuracy should be assessed. Secondly the measurement should be in volume units and thirdly the method should be both practical and ethical in clinical situation and not be limited by static apparatus⁽¹¹⁾. No method used in this study satisfies all of these criteria. In an attempt to develop a satisfactory method, a direct physical measurement using sliding ruler, face bow and computerized photograph

were investigated. The sliding ruler and face bow methods proved to be more satisfactory and convenient for both patient and operator, less time consuming, acceptable clinically and ethically by the patient. In addition, the computerized photographic technique offered no additional advantage since the photographs are one-dimensional image and the swelling measured only in one plane (anterio-posterior). Furthermore, such method is much more sophisticated, time consuming and expensive, considerable posing error are possible, and not all patients agreed to take three photographs. For these reasons this procedure was applied only on (10) patients and the remaining study completed by the classical ruler and face bow methods.

Observation from this study demonstrated that, the classical methods for measuring a facial swelling must not be refuted as it confirmed its validity in clinical and research workers.

REFERENCES

1. Pöllman L. Long terms follow-up of postoperative swelling. *Int J Oral Surg.* 1983; 12: 90-94.
2. O'Brien TP, Roszkowski M T, Wolff L F, Hinrichs J E, Hargreaves M. The effect of a non-steroidal anti-inflammatory drugs on tissue levels of immunoreactive prostaglandin E2 immunoreactive leukotriene, and pain after periodontal surgery. *J Periodontol.* 1996; 67(12): 1037-1316.
3. Morse DR. Asymptomatic tooth with necrotic pulp and associated periapical radiolucencies: Relationship of flare-up endodontic instrumentation, antibiotic usage and stress in three separate practices of three different time period. *Int J Psychosom.* 1986; 13(1): 3.
4. Troullos ES, Hargreaves KM, Butler DP. Comparison of non-steroidal anti-inflammatory drugs, Ibuprofen and flurbiprofen to methylprednisolone and placebo for acute pain, swelling and Trismus. *J Oral Maxillofac Surg.* 1990; 48: 945-954.
5. Bystedt H, Nord CE, Nordenram A. Azidocillin, Erythromycin, Clindamycin and Doxycycline on postoperative complication after surgical removal of impacted mandibular third molars. *Int J Oral Surg.* 1980; 9: 157-165.
6. Laurence DR, Bennett PN, Brown MJ. Inflammation, arthritis and non-steroidal anti-inflammatory drugs (NSAIDs). In: Laurance DR, Bennett PN, Brown MJ. *Clinical Pharmacology.* 8th Edn. Churchill Livingstone, New York. 1997; Ch 5, Pp: 249-256.
7. Katzung BG, Furst DE. Non steroidal anti-inflammatory drugs; Disease Modifying Antirheumatic Drugs, Non-opioid Analgesic; Drug used in Goat. In: Katzung BG. *Basic and Clinical Pharmacology* 7th Edn. Appleton & Lange USA. 1998; Ch 36, Pp: 578-602
8. Keicho N, Kudoh S, Yotsumoto H, Akagawa S. Erythromycin promotes monocyte to macrophage differentiation. *J Antibiotic.* 1994; 47, 80-89.
9. Kita E, Sawaki M, Mikasa K, Hamda K, Takeuchi S, Maeda K, Narita N. Alteration of host response by along term treatment of Roxithromycin. *J Antimicrob Chemother.* 1993; 32: 285-294
10. Woo PC, Chow LW, Ma ES, Yuen KY. Clarithromycin attenuate inflammatory response induced by surgical trauma in guinea pig model. *Pharmacol Res.* 1999; 39(1): 49-54.
11. Holland CS. The development of a method of assessing swelling following third molar surgery. *Br J Oral Surg.* 1980; 17: 104-114.