Clinical evaluation of the efficacy of orthal-forte (prolytic enzymes, trypsin and chymotrypsin) on postoperative sequel following the removal of lower impacted third molar

Dr. Tahani Abdul-Aziz Al-Sandook[1], Dr. Nahla Othman Mohammad Tawfik[2], Dirar Ahmed Qassim[3]

[123]College of dentistry, University of Mosul, IRAQ

ABSTRACT

Back ground: Surgical removal of impacted lower third molars is still the most common routine surgical procedure done by oral and maxillofacial surgeons. It is usually associated with postoperative sequelae (swelling, pain and trismus).

Objectives: A study was made to assess the efficacy of prroteolytic enzyme orthtal-forte on the post operative sequelae of impacted mandibular third molar extraction.

Patients and Methods: A total of 30 patients were scheduled to undergo third molar surgery and were divided randomly into 2 groups, 15 patients received Orthtal-Forte tablets and conventional treatment while the control group (15 patients) received conventional treatment only. Facial swelling, pain and the degree of mouth opening were measured for each patient on the 1st, 2nd, 3rd and 7th days postoperatively.

Results: T he use of orthal-forte a proteolytic enzyme resulted in better analgesic activity which was statistically significant on day one after third molar removal. It has anti-inflammatory activity, it reduce swelling and increase mouth opening more than conventional therapy.

Conclusion: This study demonstrated that Orthal- forte is an effective and superior analgesic in the treatment of moderate to severe acute pain resulting from third molar surgery with good anti-inflammatory activity.

Key words: Proteolytic enzyme, pain, third molar, trismus, swelling.

Introduction

The removal of lower third molars is still the most common routine surgical procedure done by oral and maxillofacial surgeons[1] which is not risk free because it involves trauma to soft and bony tissue, resulting in pain, which has a significant effect on the patient's quality of life.[2,3] This pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.[4,5] In addition trismus and swelling are a common postoperative sequelea which is related to local inflammatory reaction, with cycloxygenase (COX) and prostaglandins playing an important crucial role in these complications.[6,7] To increase patient satisfaction after third molar surgery and to reduce the side effects, it is important to facilities planning of proper management and to prescribe medication such as corticosteroids,[8] nonsteroidal anti- inflammatory drugs,[9] a combination of corticosteroids paracetamol and nonsteroidal anti-inflammatory drugs,[10,11] or enzyme preparations such as serratiopeptidase.[12,13]

Proteolytic enzymes (or proteases) refer to the various enzymes that digest (break down into smaller units) protein. These enzymes include the pancreatic proteases chymotrypsin and trypsin, bromelain (pineapple enzyme), papain (papaya enzyme), fungal proteases, and Serratia peptidase (the "silk worm" enzyme).[14] Orthal forte (trypsin and chymotrypsin) are given as enteric coated tablets.[15] Proteolytic enzymes are administered to hasten the healing of damaged tissue and thus promote a complication free recovery[13, 16.] The present study was undertaken to evaluate the analgesic, anti-inflammatory efficacy of orthtal-forte on swelling, pain and trismus after surgical extraction of impacted mandibular third molars.

Materials and Methods

Thirty healthy patients of both sexes randomly selected among patients who require surgical removal of impacted surgical third molar extraction with local anesthesia (2% lidocaine with epinephrine 1:80.000) in the outpatient oral surgery clinic- at maxillofacial department in college of dentistry, university of Mosul, Iraq. Informed consent was obtained from participating patients. The study was approved by the local ethical committee. Patient selection patients selected had no preexisting medical conditions or medications that would influence their ability to undergo surgery or alter their wound healing after surgery; they had symmetrical bilateral lower third molar impaction; they had no discernable active pathology associated with the third molars and the impactions were such that surgical time and trauma would not be excessive and mask the possible influence of flap design after surgery.

Clinical information retrieved included patients' biodata, number of impaction. Others are type/angulation of impaction was classified as mesioangular, vertical, horizontal, distal. Position of impaction was classified as I, II and III depending on the amount of space available between the second molar and ramus. The depth of impaction was categorized as A,B and C depending on (Winter's line). Times taken to extract in minute as well as the complications were documented.

Efficacy of the treatments was assessed by measuring the following parameters. Swelling was recorded using scale from 0= none, 1= Intra-oral swelling, 2= Intra- and extra-oral swelling and 3= Obstruction of the angle of mandible. Truisms: maximal interincisal opening was measured in mm. Pain assessment was measured by counting the number of the acetaminophen table (paracetamol 500mg, SDI) taken by the patients.

Surgical procedure

All the patients were treated by the same surgical operator and dental assistant under standard clinical conditions. Lidocaine 2% HCl with 1:80,000 epinephrine (Xylocaine; Dentsply Pharmaceutical, York, PA) was used for local anesthetic in all study patients. All lower third molar surgery in the study patients was performed in 1 visit. The flap designs used were the envelope flap and standard modified flap. The envelope flap involved a sulcular incision from the first to the second mandibular molar and a distal relieving incision along the external oblique ridge to the mandibular ramus .A lingual flap distal to the second molar was also raised to protect the lingual neurovascular bundle. The standard flap involved an incision from the distobuccal edge of the second molar dropping at a slight oblique angle curving forward into the mandibular vestibule. The second part of the incision was relieving incision from the mandibular ramus to the distobuccal aspect of the second molar . As with a the envelope flap a lingual mucoperiosteal flap was also used. Once the flap was reflected, the surgical site was inspected. Any bone overlying the crown of the impacted third molar was removed with a round surgical bur. If the tooth required sectioning a fissure bur was used. Copious irrigation with sterile saline was used throughout rotary instrumentation. Following delivery of the tooth, any dental follicular soft tissue was removed and the socket thoroughly irrigated with saline. No dressing or hemostatic material was placed in any of the sites. The surgical site was closed with interrupted sutures using 4-0(SILK BRAIDED,China).

Post-operative follows up:

The patients were divided into two groups containing 15 patients in each group. All the patient were put on the following regime: Amoxil 500mg+Claviulanic acid 125mg (Klamoks 625mg,1x2, Bilim, Turkey) and Metronidazol 500mg (1x3, SDI). Treated group (15 patient) received Orthal-forte tablet, (1x3, Syria) while control group(15patient) were treated in similar manner with regard to operative and the post-operative follow up except orthal-forte was not prescribed to them. All the drugs were used for 3days.

Postoperative assessment

Patients attended on days 1, 2, 3and 7 after surgeries for the data to be recorded. Adverse drug reactions observed during the study were also recorded. The surgical sites were reviewed for any signs of swelling, infections.

Statistical analysis All the data are presented as mean ± standered deviation (SD). Independent students t test and ANOVA were used to compare the measurements of swelling, pain, mouth opening ability, in and between groups.. $P < 0.05$ was considered statistically significant. The statistical analysis was performed with the SPSS 7.5software package.

RESULTS

30 patients who required prophylactic removal of impacted lower third molars were randomly distributed to one of the two study groups. The treatment groups had similar demographic and baseline clinical characteristics (Table 1, 2).

Table 1: Demographic characteristic of the study patients (n=30)

Parameters		Control	Orthal Forte
Total No. Of patient		15	15
Age (years) Mean ± SD		20.87 ± 3.18	23.93 ± 3.54
Gender	Male	7	5
	Female	8	10
Occupations	Student	7	7
	House Wife	1	0
	Officer	5	8

Table 2: Bony impaction characteristics of the study patients (n=30)

Parameters		Control (n=15)	Orthal Forte (n=15)
Class	I	–	–
	II	11	8
	III	4	
Level	A	5	7
	B	10	11
	C	–	–
Angulations	M	2	5
	D	4	4
	H	7	4
	V	2	2

All the enrolled patients completed the study. The mean time taken for surgery was statistically similar among all the groups (Table 3).

Table 3: Duration of surgery of the study group (mean ± SD)

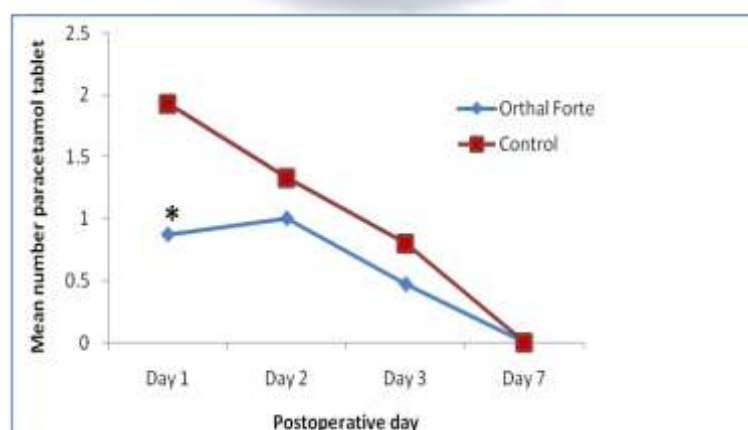| Parameters	Control (n=15)	Orthal Forte (n=15)	p=
Duration of surgery (min)	15.33 ± 7.5	15.2 ± 9.41	0.966

Figure 1: Comparsion between the mean number of Paracetamol tablet, day 1 through day 7 [22,23].
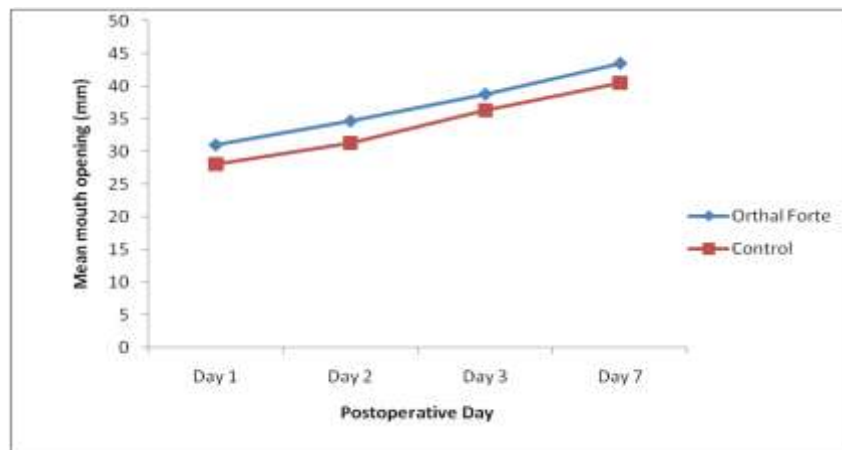
Figure 2: Comparison between the mean Mouth opening (mm), day 1 through day 7

Figure 3 show that there was swelling in both the groups on day 1 and day 3, which reduced to on day 7. In comparison, in the orthal forte group, the swelling was on day 5 as well, but reduced suddenly to insignificant swelling on day 7. This suggests that orthal forte has good anti-inflammatory effect.
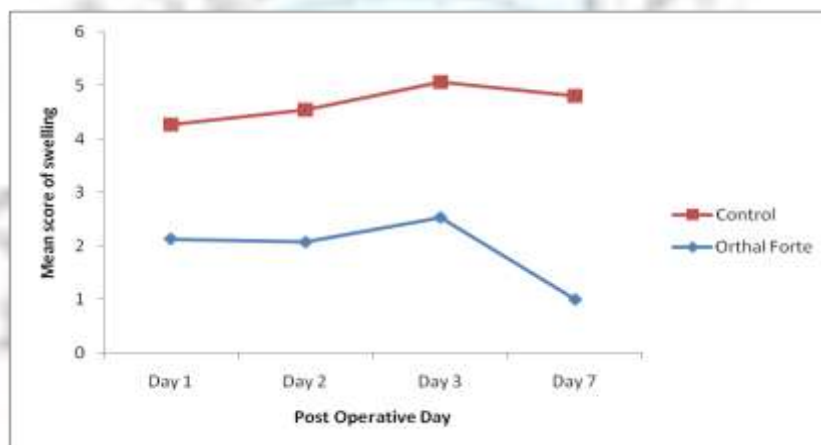

Figure 3: Comparison between the mean Swelling score, day 1 through day

Cheek swelling

The considerable increase in cheek thickness in both groups in the postoperative period appeared when comparison of preoperative and postoperative measurement. The maximum cheek thickness observed in 3rd postoperative day in two groups (Fig.3).the statistical significant reduction in extent cheek swelling in orthal-forte group at 2nd, 3rd and 7th postoperative days as compared to control group
.
The cheek swelling in orthal-forte group was less than in the control group.

Pain intensity scores

There was a significant reduction in mean pain intensity scores at the 1st, 2nd,3rd and 7th postoperative days in orthal-forte group as compared to the control group (Fig.1).

The patients in the orthal-forte group reported lower mean pain scores at 7th day than those in control group, but no significant differentce between two groups.

Interincisal difference

Analysis of the data showed a significant reduction in interincisal distance for both groups postoperatively compared to preoperative values. The control froup showed more truisms than orthal-forte, but no significant difference between them in the mean maximal interincisal distance throughout the follow-up period (Fig.2).

Discussion

The surgical removal of an impacted third molar tooth can result in considerable pain, swelling, and dysfunction. Swelling usually reaches its maximum within 48-72 hours of the surgical procedure.[1-3] Minimizing tissue damage can control the amount of postsurgical edema.[9] Some believe that ice applied to the operated area decreases vascularity and thereby diminishes transudation. However, no controlled study has verified this practice. [7],[8] The vasoactive amines cause vasodilation, thereby increasing blood flow to the inflamed area. The inflammatory process is necessary if healing is to occur but inflammation also causes edema, pain, and trismus. Mechanism of action : On being absorbed, the enzymes are taken up by the circulating enzyme inhibitors i.e. alpha antitrypsin and alpha 2 macroglobuline, level which rise steeply following injury and tissue destruction. This rise in inhibitor levels is responsible for the period of operative fibrinolytic shut down and maintenance of inflammatory edema which delay healing. These also facilitate the action of plasmin which is necessary to open up the blocked microcirculation, resolve oedema and initiate healing.

References

[1]. Kim JC, Choi SS, Wang SJ, Kim SG. Minor complications after mandibular third molar surgery: type, incidence, and possible prevention. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006: 102: e4–e11.

[2]. Sato F., Ricardo L., sprino L., de Araújo D., Emanuel S., de Moraes M., Short-Term Outcome of Postoperative Patient Recovery Perception After Surgical Removal of Third Molars. J Oral Maxillofac Surg2009; 67:1090-1091

[3]. White RP, Shugars DA, Shafer DM, Laskin DM, Buckley MJ, PhillipsG: Recovery after third molar surgery: Clinical and health-related quality of life outcomes.J Oral Maxillofac Surg 2003; 61:535-544.

[4]. Yuasa H, Sugiura M. Clinical postoperative findings after removal of impacted mandibular third molars: prediction of postoperative facial swelling and pain based on preoperative variables. Br J Oral Maxillofac Surg 2004: 42: 209–214.

[5]. Grossi GB, Maiorana C, Garramone RA, Borgonovo A, Creminelli L, Santoro F. Assessing Postoperative Discomfort after Third Molar Surgery: A Prospective Study. J Oral Maxillofac Surg 2007: 65: 901–917.

[6]. Ehrich EW, Dallob A, De Lepeleire I, et al: Characterization of rofecoxib as a cyclooxygenase-2 isoform inhibitor and demonstration of analgesia in the dental pain model. Clin Pharmacol Ther 1999: 65:336–347.

[7]. Bonnefont J, Courade JP, Alloui A, Eschalier A. Antinociceptive mechanism of action of paracetamol. Drugs 2003: 63: 1–4.

[8]. Micó-Llorens JM, Satorres-Nieto M, Gargallo-Albiol J, Arnabat- Domínguez J, Berini-Aytés L, Gay-Escoda C. Efficacy of methylprednisolone in controlling complications after impacted lower third molar surgical extraction. Eur J Clin Pharmacol. 2006; 62:693-8.

[9]. Benetello V, Sakamoto FC, Giglio FP, et al: The selective and non-selective cyclooxygenase inhibitors valdecoxib and piroxicam induce the same postoperative analgesia and control of trismus and swelling after lower third molar removal. Braz J Med Biol Res 2007: 40:1133.

[10]. Buyukkurt MC, Gungormus M, Kaya O. The effect of a single dose prednisolone with and without diclofenac on pain, trismus, and swelling after removal of mandibular third molars. J Oral Maxillo fac Surg. 2006; 64: 1761- 6.

[11]. López-Carriches C, Martínez-González JM, Donado-Rodríguez M. Analgesic efficacy of diclofenac versus methylprednisolone in the control of postoperative pain after surgical removal of lower third molars. Med Oral Patol Oral Cir Bucal. 2005;10:432-9.

[12]. Al-Khateeb TH, Nusair Y. Effect of the proteolytic enzyme serrapeptase on swelling, pain and trismus after surgical extraction of mandibular third molars. Int J Oral Maxillofac Surg 2008: 37:264-268.

[13]. Chopra D, Rehan HS, Mehra P, Kakkar AK. A randomized, double blind, placebo-controlled study comparing the efficacy and safety of paracetamol, serratiopeptidase, ibuprofen and betamethasone using the dental impaction pain model. Int J Oral Maxillofac Surg. 2009;38: 350-5.

[14]. Gruenwald J, Brendler Th, Jaenicke C. Physicians' desk reference® for herbal medicines.2007:Pp593, 847.

[15]. Orthal forte from cipla chymotrypsin. http://WWW.Drug update .com.

[16]. Martin Levine. Topics in dental biochemistry. Springer-Verlag Berlin Heidelberg, London New York. 2011: Pp 12, 27.

[17]. Viswanatha Swamy AHM, Patil PA. Effect of some clinically used proteolytic enzymes on inflammation in rats. Indian J Pharm Sci. 2008; 70(1): 114–117.

[18]. Mazzone A, Catalani M, Costanzo M, Drusian A, Mandoli A, Russo S, et al. Evaluation of Serratia peptidase in acute or chronic inflammation of otorhinolaryngology pathology: A multicentre, double-blind, randomized trial versus placebo. J Int Med Res. 1990;18: 379–88.

[19]. Trevani AS, Andonegui G, Giordano M, Nociari M, Fontan P, Dran G, et al. Neutrophil apoptosis induced by proteolytic enzymes. Lab Invest. 1996; 74 :711–21. [PubMed].

[20]. Jutila MA, Kishimoto TK, Finken M. Low-dose chymotrypsin treatment inhibits neutrophil migration into sites of inflammation in vivo: Effects on Mac-1 and MEL-14 adhesion protein expression and function. Cell Immunol. 1991; 132: 201–14. [PubMed].

[21]. Jadav S P, Patel N H, Shah TG, Gajera M V, Trivedi H R, Shah B K. Comparison of anti-inflammatory activity of serratiopeptidase and diclofenac in albino rats. J Pharmacol Pharmacotherp, 2010; 1(2): 116-117.

[22]. Grossi GB, Maiorana C, Garramone RA, Borgonovo A, Beretta M, Farronato D, Santoro F. effect of submucosal injection of Dexomethasone on Postoperatve Discomfort after Third Molar Surgery: A prospective study. J Oral Maxillofac Surg, 2007a;65:2218-2226.

[23]. Grossi GB, Maiorana C, Garramone RA, Borgonovo A, Beretta M, Farronato D, Santoro F. Assessing Postoperative Discomfort after Third Molar Surgery: A prospective study. J Oral Maxillofac Surg. 2007b; 65:901-917.