

## CLINICAL EVALUATION OF DEXAMETHASONE VS. METHYLPREDNISOLONE FOR REDUCING POSTOPERATIVE INFLAMMATORY SEQUELAE FOLLOWING THIRD MOLAR SURGERY

Tarek L. Al-Khateeb, BDS, MDS, PhD\*, Hussein A. Marouf, BDS, MSc, PhD\*\*,  
Mohammed A. Mahmmmod, BDS, MSc, PhD\*\*\*

أجريت هذه الدراسة لمعرفة مدى فعالية كل من دكساميثازون وميثايل برديسولون في تخفيف الألم والوذمة والتشنج العضلي للفكين وذلك بحقن احدهما ارتشاحياً في اللثة حول الرحى الثالثة السفلية قبل إزالتها جراحياً. وقد أختير ٩٠ شخصاً عشوائياً وقسموا إلى ثلاث مجموعات:

المجموعة الأولى: وتتكون من ٣٠ مريضاً حقنوا بـ ٤ ملغم دكسميثازون ٥ - ١٠ دقائق قبل الجراحة.

المجموعة الثانية: وتتكون من ٣٠ مريضاً حقنوا بـ ١٢٥ ملغم ميثايل برديسولون ٥-١٠ دقائق قبل الجراحة.

المجموعة الثالثة: وتتكون من ٣٠ مريضاً لم يحقنوا بأي دواء وكانوا بمثابة مقياس.

لقد وجد أن فترة حدوث الوذمة الوجهية بعد الجراحة قد كانت متساوية إلى حد ما في المجموعات الثلاث.

أما بالنسبة للإحساس بالألم مباشرة في نفس يوم الجراحة فقد أظهرت المجموعة الأولى التي تلقت ميثايل برديسولون أقل إحساس بالألم، وتلتها المجموعة الثانية التي تلقت دكساميثازون و ثم المجموعة الثالثة.

بالإضافة إلى ذلك وجد أن المجموعتين التي تلقت العلاج بمادة الستيرويد قبل الجراحة أظهرت تحسناً ملحوظاً في القدرة على فتح الفم.

A randomized prospective double-blind study was conducted to determine the efficacy of sub-mucosal local infiltration of dexamethasone vs. methylprednisolone in reducing postoperative pain, swelling and trismus after surgical removal of impacted mandibular third molars. Ninety patients were included in the study and were randomly divided into three groups. Each group consisted of 30 patients for which the first and second groups were given 4 mg of dexamethasone and 125 mg of methylprednisolone, respectively, at 5-10 min. preoperatively; the third group served as control. Duration of facial swelling was evaluated subjectively by the patients themselves. Severity of postoperative pain was quantified by counting the number of analgesics taken by the patients during and after surgery (six subsequent days). Trismus was determined by measuring the maximum incisal opening before surgery and on the seventh day, postoperatively. Results showed that duration of facial swelling was almost the same in the three test groups. During surgery, the methylprednisolone group showed a significantly lesser pain than the other two groups; the dexamethasone group showed less marked pain than the control group. Additionally, patients who had taken steroids had a marked increase in the incisal opening postoperatively over the control group. Trismus was significantly reduced in the methylprednisolone group as compared to the dexamethasone group. It is concluded that

Received 08/01/95; revised 22/06/95; accepted 01/10/95

•Associate Professor & Chairman, Department of Oral & Maxillofacial Surgery and Vice-Dean, Faculty of Dentistry, King Abdulaziz University

\*\*Assistant Professor, Department of Oral & Maxillofacial

Surgery, Faculty of Dentistry, King Abdulaziz University

\*\*\*Assistant Professor, Department of Oral Medicine, Faculty of Dentistry, King Abdulaziz University, P.O. Box 1540, Jeddah 21441, Saudi Arabia.

Address reprint requests to: Dr. T.L. Al-Khateeb.

preoperative local infiltration of methylprednisolone and dexamethasone significantly reduced postoperative pain and trismus after surgical removal of mandibular third molars. A 125 mg methylprednisolone is more effective in reducing postoperative inflammatory sequelae than a 4 mg dexamethasone.

### Introduction

Surgical removal of third molars causes significant pain, swelling and trismus even when teeth are removed by the gentle surgical technique. The use of synthetic glucocorticoids in reducing such postoperative sequelae has been investigated extensively<sup>12</sup> although its success is still questionable.<sup>3,4</sup> However, other studies demonstrated a statistically significant improvement in postoperative sequelae when corticosteroids were administered.<sup>5,8</sup>

Currently, various forms of corticosteroids with differing potencies and effects have been made available to choose from.<sup>1</sup> Specifically, the synthetic steroids dexamethasone and methylprednisolone have been used extensively in oral and maxillofacial surgery for their active anti-inflammatory effects.<sup>9</sup>

Most previous studies reported on administration of glucocorticosteroids through oral, intramuscular or intravenous routes, but no study has investigated the efficacy of steroids when administered by local submucosal infiltration technique around the surgical site. Further, no study has been made to compare the effect of dexamethasone and methylprednisolone in reducing postoperative sequelae.

The objective of this study was to conduct a controlled clinical investigation to evaluate and compare the effect of submucosally infiltrated dexamethasone and methylprednisolone in reducing inflammatory sequelae following surgical removal of lower third molars when administered locally at site of the surgery.

### Materials and Methods

#### Study Design

Ninety patients undergoing surgical removal of impacted mandibular third molars in the Department of Oral & Maxillofacial Surgery at King Abdulaziz University Dental School between December 1992 and 1994 were included in the present study. Age of patients were from 16 to 33 years of age, 36 of whom

were males and 54 were females. Patients who were pregnant, had a history of drug or alcohol abuse and who are suffering from renal, hepatic and hemorrhagic diseases were precluded. Other criteria for selection included no current medication specifically steroidal anti-inflammatory drugs for the last two weeks and no history of steroid medication complication. The position of impacted lower third molar was recorded from the orthopantomogram as either horizontal, mesioangular, disto-angular or vertical.

Patients included in the study were randomly selected and divided into three groups:

Group A = (n = 30: 14 males and 16 females):

Patients received no corticosteroid (control group)

Group B = (n = 30: 11 males and 19 females): 4 mg dexamethasone was infiltrated sub-mucosally around the site of surgery at approximately 5-10 min. preoperatively.

Group C = (n = 30: 13 males and 17 females): 125 mg methylprednisolone was infiltrated sub-mucosally around the site of the surgery at approximately 5-10 min. preoperatively.

#### Operative Procedure

All patients were operated on under local anesthesia (2% Lidocaine with 1:100,000 epinephrine). Before anesthesia was given, the maximum opening of the mouth was recorded as measured in millimeters from the incisal edge of the maxillary first right incisor to the edge of the right lower incisor. All surgical procedures were done by the same surgeon using a standardized technique. Impacted teeth were extracted in a routine fashion, using a bur, an air-driven handpiece and rinsing with saline to remove bone and sectioned teeth. After extraction of teeth, the patients were given postoperative instructions and prescriptions for 20 tablets of Ponstan (500 mg), one or two tablets to be taken every 3 to 4 hours as needed for pain, and Keflex (500 mg) to be taken four times a day for seven days.

#### Postoperative Evaluation

The patients were clinically examined on the

seventh day after the surgery. Maximum opening of the mouth was measured in the same manner as before surgery. The measurement was repeated twice, averaged and recorded. The difference between the preoperative and postoperative values was used as a measure of trismus. The time of onset and disappearance of postoperative swelling, as well as the time when swelling was at a maximum, were recorded by the patients themselves. The effect of steroids on pain was evaluated by having the patients report the number of analgesic pills taken on the day of surgery and the subsequent 6 days.

Data were presented as mean values and standard deviations ( $x \pm SD$ ). Analysis of variance (ANOVA) was used to compare the differences among the three groups studied. Whenever statistical analysis was performed, P values less than 5% ( $<0.05$ ) was considered statistically significant.

## Results

### Basic Data

The mean age for the 30 patients in each of the three groups was 24.2, 23.7 and 25.3, respectively. No statistically significant differences existed among the three groups in relation to age or sex as shown in Table 1.

Data on the position and impaction of the mandibular third molars in the three groups are presented in Tables 2 and 3. The mesioangular position and partial bony impaction status were the most common in all groups. Mean surgery times for Groups A, B and C were 11.9, 13.2 and 12.7 minutes,

Table 1. Basic data of patients evaluated.

Group	Sex		Mean age (years)
	Females	Males	
A (Control)	16	14	24.2
B (Dexamethasone)	19	11	23.7
C (Methylprednisolone)	17	13	25.3

Table 2. Preoperative position of the third molars.

Group	Tooth Position			Vertical
	Hori- zontal	Mesio- angular	Disto- angular	
A (Control)	5	15	2	8
B (Dexamethasone)	4	13	3	10
C (Methylprednisolone)	7	12	2	9

Table 3. Impaction status of the third molars.

Group	Bony Impaction		
	None	Partial	Total
A (Control)	7	17	6
B (Dexamethasone)	5	16	9
C (Methylprednisolone)	3	19	8

Table 4. Operation time for the three groups.

Group	Operation time (min) $x \pm SD$
A (Control)	11.9 $\pm$ 3.7
B (Dexamethasone)	13.2 $\pm$ 4.1
C (Methylprednisolone)	12.7 $\pm$ 5.2

respectively. The differences among the three groups were not statistically significant (Table 4).

### Evaluation of Swelling, Pain and Trismus

The duration of facial swelling was almost the same in the three groups for which it was at a maximum during the second postoperative day and lasted an average of 4-5 days. Group C (methylprednisolone) used a significantly lesser medication during surgery than Group B (dexamethasone) and Group A ( $P < 0.001$ ). However, the three groups showed no significant differences in the total number of analgesics taken after surgery (Table 5).

Maximum opening of the mouth was significantly improved on the seventh postoperative day in Groups B and C as compared to Group A ( $P < 0.05$ ,  $P < 0.001$ , respectively). The differences in incisal opening, as calculated from the measurements made and after surgery, were  $5.6 \pm 3.1$  mm in Group C,  $8.5 \pm 5.9$  mm Group B, and  $12.3 \pm 7.4$  mm in Group A as shown in Table 6. As is apparent, Group C showed statistically significant increase in the incisal opening on the seventh postoperative day compared to Group B ( $P < 0.02$ ).

Table 5. Pain medications taken after surgery in the three groups. (Values represent mean  $\pm$  standard deviation of number of pills per patient).

Time	Group A (Control)	Group B (Dexame thasone)	Group C (Methypre dnisolone)
Day of surgery	5.9 $\pm$ 1.8	3.7 $\pm$ 1.1	2.2 $\pm$ 0.4*
Total postoper- ative period	11.3 $\pm$ 7.2	10.8 $\pm$ 5.9	11.1 $\pm$ 6.3

\*Significance level,  $P < 0.001$ .

Table 6. Differences in incisal opening in the three groups. (Values represent mean  $\pm$  standard deviation of differences in millimeters between operative and postoperative measurements).

Time after surgery	Differences in incisal opening (mm)		
	Group A (Control)	Group B (Dexamethasone)	Group C (Methylprednisolone)
Seventh day	12.317.4	8.5 $\pm$ 5.9*	5.6 $\pm$ 3.1**

\* Significance level,  $P < 0.001$ .

\*\* Significance level,  $P < 0.001$ .

### Discussion

The anti-inflammatory effects of glucocorticosteroids are well-documented although their exact mechanism of action is yet to be clearly defined. It is claimed that corticosteroids reduce edema and inflammation by decreasing permeability of capillary endothelium and therefore reducing the amount of fluid, protein, macrophages and other inflammatory cells entering areas of tissue injury.<sup>10</sup>

For more than 30 years, glucocorticosteroids have been used in an attempt to minimize or prevent postoperative sequelae after surgical removal of impacted third molars. Several studies have been published in the literature on this subject.<sup>12</sup> Most studies have reported that steroids significantly reduce the pain, swelling and trismus<sup>34</sup> while a few has not shown any benefit from the administration of steroids.<sup>58</sup> These studies are difficult to compare because a variety of steroids was evaluated using dissimilar study designs and methods of evaluating pain and swelling.

However, it is clear that the type and the dose of steroids, as well as the duration and route of administration, can have a significant impact on the efficacy of the agent. The decision as to route of administration depends on the clinician's expertise and preference. Orally administered glucocorticosteroids are rapidly and almost completely absorbed; however, repeated dose is required to maintain adequate blood concentration throughout the immediate postoperative period.<sup>11</sup> The intravenous route offers instantaneous blood levels but requires expertise and additional armamentarium.<sup>3,7,12</sup> Studies of intramuscular doses suggest that this route of administration can be effective in a single dose given either preoperatively or postoperatively.<sup>6,13</sup> These results imply that with high doses, the repository is significant throughout

the first seven operative days and that additional doses may not be necessary. However, the clinician's experience, the patient's discomfort and the added armamentarium may be a hindrance.

In the present study, local infiltration of the steroid submucosally around the site of surgery was chosen as it is expected to provide a repository effect in a way similar to the intramuscular route (i.e. slow absorption and prolonged duration of action). In addition, submucosal infiltration technique does not require clinician's expertise or additional armamentarium. This is considered an advantage of this technique over the intravenous and intramuscular routes of administration.

Various corticosteroids have been used in the previous studies.<sup>12</sup> However in the present study, dexamethasone and methylprednisolone were selected since they are potent, cause minimal sodium retention and have interminable biological potency.

Evaluation of facial swelling from surgical procedures is most enigmatic since the swelling involves a three-dimensional volumetric change at the tissue and cellular levels. Various methods have been developed for assessing the degree of postoperative swelling.<sup>7,14,16</sup> However, these methods lack the sensitivity required to detect significant differences in swelling and seem not to be more accurate than estimations made by the patients themselves.<sup>17</sup>

In this study, we deliberately decided to have the patients evaluate themselves since we were mainly concerned with the postoperative duration of the swelling. The decision was due to the fact that there was no objective way to assess the degree of intraoral swelling as perceived by the patients themselves. This investigation indicates that the two steroids tested were more effective in reducing the duration of swelling as compared to the control. Swelling was at a maximum on the second postoperative day and lasted for 4-5 days in all groups.

Assessment of trismus and pain were not that troublesome since it relies heavily on the patient's cooperation. The two variables are inter-related and are results of surgical trauma. Trismus has been considered as a one single variable demonstrating the most complete assessment of postoperative inflammatory response.<sup>17</sup> Since complete recovery does not occur early, the clinical evaluation of trismus was conducted on the seventh postoperative day. Trismus was significantly reduced in Groups B

and C patients as compared to the control group. However, the two tested steroids differed in their effect on the decrease of maximum mouth opening as calculated from the preoperative and postoperative measurements. Group C showed less reduction in the incisal mouth opening on the seventh postoperative day as compared to Group B.

Experimental group patients demonstrated lesser pain than the control group on the day of surgery but not on any other day after surgery. This may probably be due to the fact that single dose steroids does not have a continuous effect because it is rapidly metabolized after surgery. Also, on the day of surgery, pain was less significant in Group C as compared to Group B.

Results of this study indicated that pain and trismus were less in patients who received methylprednisolone compared to those who received dexamethasone. This difference can be attributed to the fact that methylprednisolone (125 mg) is five times more potent than dexamethasone (4 mg). A 125 mg-dose of methylprednisolone is equivalent to 625 mg of hydrocortisone, whereas 4 mg of dexamethasone is equivalent to 106 mg of hydrocortisone.<sup>2</sup> These findings suggest that potency and dosage of steroids can have a significant impact on the efficacy of the agent.

Based on earlier clinical studies that postoperative pain can be reduced by combining long-acting anesthetics with non-steroidal anti-inflammatory agents,<sup>18</sup> it can be concluded that further clinical trials are needed to compare the effect of steroids, non-steroidal anti-inflammatory drugs and long-acting local anesthetics in reducing postoperative sequelae. Additional studies are also necessary to further define the benefits of postoperative administration of dexamethasone and prednisolone. Finally, more sensitive measuring techniques to quantify the decrease of postsurgical swelling need to be developed.

#### References

1. Montgomery MT, Hogg JP, Roberts DL, Redding SW. The use of glucocorticosteroids to lessen the inflammatory sequelae following third molar surgery. *J Oral Maxillofac Surg* 1990;48(2): 179-87.
2. Gersema L, Baker K. Use of corticosteroids in oral surgery. *J Oral Maxillofac Surg* 1992;50(3):270-77.
3. Sisk AL, Bonnington GJ. Evaluation of methylprednisolone and flurbiprofen for inhibition of the postoperative inflammatory response. *Oral Surg Oral Med Oral Pathol* 1985;60(2): 137-45.
4. Troullos ES, Hargreaves KM, Butler DP, Dionne RA. Comparison of nonsteroidal anti-inflammatory drugs, ibuprofen and flurbiprofen with methylprednisolone and placebo for acute pain, swelling and trismus. *J Oral Maxillofac Surg* 1990;48:945-52.
5. Schaberg SJ, Stuller CB, Edwards SM. Effect of methylprednisolone on swelling after orthognathic surgery. *J Oral Maxillofac Surg* 1984;41(6): 356-61.
6. Pedersen A. Decadronphosphate in the relief of complaints after third molar surgery. A double-blind, controlled trial with bilateral oral surgery. *Int J Oral Surg* 1985; 14 (3):235-40.
7. Beirne OR, Hollander B. The effect of methylprednisolone on pain, trismus and swelling after removal of third molars. *Oral Surg Oral Med Oral Pathol* 1986;61(2): 134-38.
8. Weber CR, Griffin JM. Evaluation of dexamethasone for reducing postoperative edema and inflammatory response after orthognathic surgery. *J Oral Maxillofac Surg* 1994;52 (1):35-39.
9. Gilman AF, Rail TW, Nies AS eds. The pharmacological basis of therapeutics. 8th ed. New York: Pergamon Press, 1990:1442-454.
10. Brooks PM, Kean WF, Buchanan WW. The clinical pharmacology of anti-inflammatory agents. Philadelphia: Taylor and Francis, 1986:125.
11. Ware WH, Campbell JC, Taylor RC. Effect of a steroid on postoperative swelling and trismus. *Dent Prog* 1963;3:116-17.
12. Huggman GG. Use of methylprednisolone sodium succinate to reduce postoperative edema after removal of impacted third molars. *J Oral Surg* 1977;35:198-99.
13. ElHag M, Coghlan K, Christmas P, Harvey W, Harris M. The anti-inflammatory effects of dexamethasone and therapeutic ultrasound in oral surgery. *Br J Oral Maxillofac Surg* 1985;23:17-23.
14. Holland CS. The development of a method of assessing swelling after third molar surgery. *Br J Oral Surg* 1979;17:104-14.
15. van Gool AV, Ten Bosch JJ, Boering G. A photographic method of assessing swelling following third molar removal. *Int J Oral Surg* 1975;4(3): 121-29.
16. Neupert EA, Lee JW, Philput CB, Gordon JR. Evaluation of dexamethasone for reduction of postsurgical sequelae of third molar removal. *J Oral Maxillofac Surg* 1992;50:1177-183.
17. BergeTI. Visual analogue scale assessment of postoperative swelling. A study of clinical inflammatory variables subsequent to third molar surgery. *Acta Odontol Scand* 1988;46:233-40.
18. Dionne RA, Wirdzek PR, Fox PC, Dubner R. Suppression of postoperative pain by the combination of a nonsteroidal anti-inflammatory drug, flurbiprofen and a long-acting local anesthetic, etidocaine. *J Am Dent Assoc* 1984;108:598-601.