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Effects of co-administered dexamethasone and diclofenac sodium on pain, swelling and trismus following third molar surgery

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Abstract

Background:The synergism between the action of non-steroidal anti-inflammatory drugs (NSAIDS) and steroids suggest that co-therapy may provide beneficial inflammatory and pain relief in the absence of side effects. The aim of the study was to compare the effect of co-administered dexamethasone and diclofenac sodium (diclofenac Na) with diclofenac Na alone on the postoperative pain, swelling and trismus after surgical removal of third molars.

Methods:A prospective randomized study was conducted at the clinic of Oral and Maxillofacial Surgery, Dentistry College/ Mustansirya University. A total of 30 patients were randomly divided into two treatment groups, the first were given dexamethasone (30 minutes preoperative 8 mg and postoperative 4 mg IV 6 hours postoperatively in two doses) and oral dose of diclofenac Na 50 mg 30 minutes before and after surgery, while the second group were given 50 mg diclofenac Na orally alone 30 minutes before and after surgery (as with first group). The overall analgesic effect of the drug was assessed postoperatively by determination of pain severity using a category rating scale. Facial swelling was measured using a tape measure placed from tragus to gonion to tragus, while interincisal mouth-opening of patients was measured using a calibrated vernier pre-operatively and post-operatively.

Results:Co-administration of dexamethasone and diclofenac Na was significantly superior to diclofenac alone for the relief of pain ($P < 0.05$), and facial swelling up to 48 hour postoperatively ($P < 0.05$). However, there was no significant difference for trismus relief between the two medication protocols ($P > 0.05$).

Conclusion:This study shows enhanced effects of co-administered dexamethasone and diclofenac Na on short-term post-operative pain and swelling, compared to diclofenac sodium alone in third molar surgery.

Introduction

Surgical removal of wisdom teeth under local anaesthesia is widely carried out in general dental practice and in many institutional surgery clinics, occupying an appreciable amount of clinical time (1,2). This procedure is usually associated with postoperative pain, swelling, and trismus (1,4) as direct and immediate

consequences of the surgical procedure(5,6), the adverse effects of the wisdom tooth surgery on the quality of life has been reported to show a three-fold increase in patients who experience pain, swelling and trismus alone or in combinations; compared to those who were asymptomatic (5,7), Many clinicians have, thus, emphasized the necessity for less pain, swelling and trismus

control in patients who undergo third molar surgery (8,9).

The introduction of non-steroidal anti-inflammatory drugs (NSAIDs, e.g. diclofenac sodium and ibuprofen) has significantly altered the management of postoperative pain in dentistry and medicine. There are 2 possible mechanisms for the efficacy of NSAIDs when administered prior to surgical trauma. The first may simply be a pharmacokinetic advantage. By administering the NSAIDs prior to pain onset, drug absorption would have begun and therapeutic blood level will be present at the time of pain onset. Second, the presence of a cyclooxygenase inhibitor at the surgical site may limit the production of prostaglandins and prostacyclins associated with hyperalgesia and edema (10,11). The use of corticosteroids (e.g. dexamethasone, betamethasone) is another preventive strategy for limiting postoperative edema and trismus following third molar extractions. Postoperative swelling and edema may be due in part to the conversion of phospholipids to arachidonic acid by phospholipase A₂, and the resultant production of leukotrienes, prostacyclins, prostaglandins and thromboxane A₂, acting as mediators of the inflammatory response. The use of steroids inhibits the initial step in this process (12). Clinical trials in oral surgery have also supported the hypothesis that preoperative NSAIDs and corticosteroids are effective in delaying and preventing many postoperative sequelae (10). The synergism between the non-steroidal anti-inflammatory drugs (NSAIDs) and steroids suggests that co-therapy may provide beneficial inflammatory and pain relief in the absence of more side effects.

The aim of the study was, thus, to compare the effect of co-administered

dexamethasone-diclofenac sodium with diclofenac sodium alone, on the postoperative management of pain, swelling and trismus following removal of impacted lower third molars.

Materials & Method

Patients who attended the Oral and Maxillofacial surgery clinic of the Dentistry College of Mustansirya University, requiring surgical removal of unilateral or bilateral (at least 15 days between the two surgical procedures), impacted mandibular third molar teeth under local anaesthesia were included. The study protocol was explained to the patients in detail after which consent was obtained. Patients were randomly allocated into two groups. Criteria for exclusion of patients included: present renal or hepatic disease, blood dyscrasia, previous or present gastric ulcers, heart disease, known hypersensitivities, allergies, or reactions to any study medications, pregnancy and lactation. In addition, patients who had taken analgesics or anti-inflammatory drugs within 24 hours before surgery were excluded from the study. All selected candidates were free of pain and other inflammatory symptoms that included swelling, hyperemia and decreased mouth opening at the time of surgery.

In Group I (no=15), patients were given a combination dexamethasone (30 minutes preoperative 8 mg and postoperative 4 mg IV 6 hours postoperatively in two doses) and diclofenac sodium (50 mg orally 30 minutes preoperatively and 50 mg orally 30 minutes postoperatively). Group II patients were given diclofenac Na alone (50 mg orally 30 minutes preoperatively and 50 mg orally 30 minutes postoperatively).

The degree of surgical difficulty was assessed according to

Radiographic position (fully erupted, partially impacted or fully impacted) (13). Oral antibiotics (500 mg ampicillin-cloxacillin, and 400 mg metronidazole, were administered to all patients 30 minutes before surgery.

Operative procedure

Surgical extraction of the third molars was carried with buccal guttering technique after adequate elevation and reflection of buccal mucoperiosteal flap under local anaesthesia (2% lidocaine hydrochloride with 1:100,000 adrenaline). Tooth delivery was followed by thorough irrigation of the surgical site with normal saline (0.9%). The three-sided mucoperiosteal flap was repositioned and sutured.

Pain measurement

Preoperative pain was assessed using a four-point Category Rating Scale (14-15). Accordingly, pain was recorded as: "0-no pain" (patient experiences no discomfort), "1-mild pain" (almost unnoticeable pain), "2-moderate pain" (noticeable pain, but patient can still engage in routine daily activities), and "3-severe pain" (very noticeable pain which disturbs the patient's daily routine). For each patient, the appropriate score was recorded in the questionnaire by researcher at 48 hours and by the patient on a daily basis for 5 days. Before leaving the clinic, the researcher ensured that all patients were thoroughly instructed how to complete the pain self-assessment diary and to take medication which is 50 mg Dicofenic Na on need.

Measurement of facial width

As no published method satisfies all criteria for assessing facial swelling, it was decided to use a measuring tape to measure facial width and swelling in one-dimension only. Facial width (swelling) was measured using a measuring tape. The reference points used were the tip of tragus of left and

right ears, with the gonium in between. A single operator, repeating the procedure three times on each patient, made the measurements. The average of measurements was then taken (in cm) and recorded. The measurements were carried out just before the surgery and at post-operative days 1, 2. Postoperative swelling was expressed as a percentage increase in facial width.

Measurement of mouth-opening ability

A calibrated vernier was used to measure maximum interincisal mouth-opening ability of the patient at the commencement of the procedure. The reference point used was incisal edge of the maxillary central incisor and incisal edge of mandibular central incisor at maximum opening available.

The measurements were made in triplicate and the average was recorded in millimetres (mm). The measurement was carried out just before the surgery and at post-operative days 1, 2, and 7. Postoperative trismus was measured as a percentage decrease in mouth opening.

Medication

All patients were supplied by the required amount of medications (10 tablets 50 mg Diclofenic Na) to ensure compliance. Dexamethason was given parenterally 8 mg 30 minutes preoperatively, and then 4 mg 6 hours postoperatively in two doses. Diclofenac Na was given 50 mg, 30 minutes preoperatively; and thereafter 50 mg, 2 times daily for five days. All patients were placed on a five-day antibiotic regimen (500 mg Ampicillin-cloxacillin 4 times daily and 400 mg Metronidazole 3 times daily). All the medications were administered orally, except dexamethasone, which was administered parenterally.

Results

A total of 30 patients (equally distributed into groups I and II) who completed the study were included in the analysis. The mean age of the participants was 27.9 years (range, 19–45 years; group I: 29.8 years and group II: 26.1). The male-to-female ratio was 1:1.1. The radiographic analysis of the type of impactions showed that mesio-angular impaction constituted 50.0% of cases, followed by disto-angular impaction (20.0%, Table 1).

For group I, the mean pain score on days 1 and 2 was significantly lower than that for group II ($p < .05$, Table 2). Co-administration of Dexamethasone-diclofenac led to a significant reduction in both postoperative pain and swelling on Days 1 and 2 when compared with diclofenac Na alone ($P < 0.05$).

Although there was no significant difference between the two groups with regard to reduction in mouth opening, the "trismus" scores of group I (2.1 mm) were lower than those of group II (3.1 mm) between 24 h and 48 h.

By the post-operative 7th day, all symptoms had restored to the preoperative level in both groups. Neither groups demonstrated any adverse reaction, side effect or other complications (e.g., tendency for bleeding) during the follow-up period.

Discussion

By pharmacologically controlling the extent of the inflammatory process, the intensity or severity of postoperative sequelae such as pain, swelling and trismus, may be reduced (16-17). One technique that has been proposed for reduction of postoperative inflammation is the administration of corticosteroids (16). Cortisol and the synthetic analogue of cortisol have the capacity to interfere with the physiologic processes of inflammation

and, thus, suppress the development of local fever, redness, swelling and tenderness by which inflammation is recognized (16). Another technique is to control the synthesis of prostaglandins. Prostaglandins play a major role in the induction of pain, inflammation, and fever (3-11). The reduction of biosynthesis of prostaglandins by inhibition of the cyclo-oxygenase enzyme system is considered an important mechanism of action of NSAIDs. When administered preoperatively, NSAIDs have been shown to be particularly effective in combating postoperative pain (3-11).

Preventive strategies for postoperative management of pain and inflammation are based on the known ability of NSAIDs to block the arachidonic acid cascade. When NSAIDs are administered preoperatively, absorption of the medication may start before the initiation of tissue trauma, so synthesis of prostaglandins and the subsequent inflammatory response will be reduced. Prevention of the inflammatory response may decrease the sequelae of tissue trauma; especially the accompanying pain (11). Diclofenac Na has been shown to be useful in controlling postoperative pain after removal of third molars (18). Diclofenac Na is known to possess both analgesic and anti-inflammatory effect. Due to its anti-inflammatory effects (18). The administration of dexamethasone may synergize the anti-inflammatory effect of NSAID and contribute to the reduction of inflammatory exudates as well as edema and pain. Therefore the co-administration of diclofenac Na and dexamethasone may be expected to reduce post-operative pain more than that achieved with diclofenac Na alone (18).

Regardless of the drug combination used, the pattern of postoperative pain

has been reported to increase between the post-operative days 1 and 3, after which the symptoms subside gradually within one week [19-22]. Our results confirm this observation. The comparison of pain intensity between the dexamethasone-diclofenac Na group and diclofenac Na group showed significant difference between the two groups ($P < 0.05$), indicating an enhanced analgesic effect of diclofenac Na when administered in combination with dexamethasone. This finding corroborates with those of previous reports [3,23-26]. Schultze-Mosgau et al [25] investigated the combined use of ibuprofen and methylprednisolone for pain relief, concluding that this combination has good analgesic and anti-inflammatory action. It has also been reported that a single dose administration of a glucocorticoid reduces tissue levels of bradykinin and suppresses circulating levels of cortisol and beta-endorphin [25]. As known, bradykinin and kallidin are the two kinins that act independently as well as synergistically with products of the arachidonic acid cascade to produce both hyperalgesia as well as increased vascular permeability [26].

Post-surgical facial edema is difficult to quantify accurately, since it requires a three-dimensional measurement with an irregular, convex surface and can manifest itself internally as well as externally. Over the years, numerous researchers have tried various techniques in an effort to objectively measure edema [23,26], most of which are indirect assessments of the altered contours of skin surface. Measurement tools mentioned in the literature have included visual analog scales, trismus recordings, standardized stereo-radiographic or photographic measurements, computerized tomography, modified face bow devices, ultrasonography, facial plethysmographs, or various

other means of taking direct facial measurements [23,26]. In the present study, a single measurement from the tip of tragus to gonion to the tip of contralateral tragus was taken. The recordings were made in triplicate and the average was recorded. It is noteworthy to mention herein that the cheek swelling following third molar surgery is diffuse in different planes and is very difficult to measure accurately. The co-administration of dexamethasone diclofenac Na preoperatively and postoperatively, produced a clear reduction in postoperative pain and cheek swelling. The mean increase in facial swelling in days 1 and 2 in Group I (dexamethasone- diclofenac Na combination) was significantly less than that of Group II (diclofenac Na only). This result shows that co-administration of dexamethasone diclofenac Na also enhances the control of postoperative facial swelling [24,27-29].

Independent T-test did not show any significant difference in reduction of mouth opening (trismus) between the study groups ($P > 0.05$). While this observation does not corroborate with those of previous reports [21,22,25], the enhanced effect of steroids on mouth-opening may be observed clinically. In the present study, the mean reduction in mouth-opening between the post-operative days 1 and 2 were 2.1 mm and 3.1 mm, for groups I (dexamethasone and diclofenac Na) and II (diclofenac Na only), respectively. This shows a "clinically significant" difference in the interincisal distance. These results indicate a positive clinical association between the adjunct use of dexamethasone and postoperative recovery of trismus in third molar surgery.

The time course for pain and facial swelling findings described in the

present study are in agreement with others indicating similar symptoms that reached a maximum at Days 1 or 2 postoperatively and generally resolved at Day 7 [30,31].

The potency and dosage of dexamethasone within the first 24 h (total of 16 mg, including pre-operative dose) was adequate to enhance the efficacy of diclofenac Na. It appears that steroids are preferably administered pre-operatively, extending the coverage up to 24–48 hours after surgery. Intravenous administration of dexamethasone, as done in the present study, enhances earlier bioavailability in comparison to oral administration [9]. Such treatment with high dosage does not impair adrenal function. Additionally, intravenous administration of dexamethasone prior to third molar surgery bears no detrimental impact on wound healing, even in patients predicted to be at high risk for delayed clinical recovery [9].

Conclusion

This study shows enhanced effects of co-administered dexamethasone and diclofenac Na on short-term post-operative pain and swelling, compared to diclofenac Na alone in third molar surgery.

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Table (1) Types of impactions

Types	Frequency (%)
Mesioangular	15 (50.0)
Distoangular	6 (20.0)
Horizontal	6(16.0)
Vertical	3(12.0)
Total	30 (100)

Table (2) Mean value of Pain intensity, facial swelling and mouth opening at Days 1 and 2 (D1, D2) in group I (Dexamethasone-diclofecac Na) and group II (Diclofenac only). ± SD(statistical difference)

Group	N	Pain intensity		Facial Swelling		Mouth Opening	
		D1	D2	D1	D2	D1	D2

Group I	15	0.62 ± 0.6	0.5 ± 0.51	30.9 ± 1.6	31.0 ± 1.58	36.0 ± 11.2	38.1 ± 10.05
Group II	15	1.64 ± 0.9	1.3 ± 0.62	31.7 ± 1.6	32.04 ± 1.5	39.2 ± 11.3	36.0 ± 10.02

* $p < 0.05$
