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The effect of prednisolone on reduction of complaints after impacted third molar removal

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SUMMARY

Nonsteroidal anti-inflammatory drugs (NSAIDs) and steroids are able to effectively reduce postoperative sequels after impacted third molar removal. The purpose of this study was to evaluate whether a single dose of prednisolone, taken orally immediately after the operation, would increase the effects of etorikoxib (Arcoxia®) NSAID in preventing trismus and swelling after surgical removal of impacted third molars.

Patients and methods. This prospective study was conducted in a half-year period on 78 patients who had undergone third molar surgery under local anaesthesia. They were divided into two groups: prednisolone group (38 patients) and control (40 patients). In the prednisolone group 30 mg prednisolone was given to each patient immediately after surgery. Both groups had received Etorikoxib 120 mg 30 minutes before operation. They had to complete a questionnaire evaluating postoperative symptoms. Postoperative pain, facial swelling and trismus were evaluated.

Results. Postoperative administration of 30 mg prednisolone to the patients relieved trismus, swelling and pain more than non-administration of prednisolone in the control group. There was significantly less swelling on the first four postoperative days in the prednisolone group compared to control ($p<0.05$). The values of the maximal interincisal opening (MIO) and visual analogue scale (VAS) were higher for the prednisolone group than for the control group ($p<0.05$). No clinically apparent infection, disturbance of wound healing, or other corticosteroid-related complications were noted.

Conclusion. It was found that a combination of a single dose of prednisolone and Etorikoxib is well-suited for treatment of postoperative pain, trismus, and swelling after third molar surgery and should be used to diminish postoperative swelling of soft tissues.

Key words: third molar; corticosteroids, postoperative sequels.

INTRODUCTION

Surgical removal of wisdom teeth under local anesthesia is widely carried out in general dental practice and in many institutional surgery clinics, occupying an appreciable amount of clinical time. This procedure is usually associated with postoperative pain, swelling and trismus as direct and immediate consequences of the surgical procedure. Nonsteroidal anti-inflammatory drugs (NSAIDs) [1-3] and steroids [4-6] are able to effectively reduce postoperative sequels after impacted third molar removal. The activity of combined effects of these two groups of drugs has been evaluated [7-9].

By administering NSAIDs, presence of a cyclooxygenase inhibitor at the surgical site may limit the production of prostaglandins and prostacyclins associated with hyperalgesia and oedema. The apparent interactions between the mechanisms of the action of NSAIDs and steroids suggests that co-therapy may provide beneficial inflammatory and pain relief in absence of side effects [10-12].

There are two possible mechanisms for the efficacy of NSAIDs when administered prior to surgical trauma. First, through administering NSAIDs prior to pain onset, drug absorption would have begun and therapeutic blood level will be achieved at the time of pain onset. Second, presence of a cyclooxygenase inhibitor at the surgical site may limit the production of

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prostaglandins and prostacyclins associated with hyperalgesia and oedema.

Use of corticosteroids is another preventive strategy for limiting postoperative oedema and trismus following third molar extractions.

Glucocorticoids have anti-inflammatory properties, which are probably related to their actions on the microvasculature as well as to cellular effects. They also impede endothelial sticking of leucocytes and diapedesis through capillary wall. Reduced cellular adherence to the vascular endothelium is probably secondary to antagonism to the action of the migration inhibiting factor by glucocorticoids. They diminish the number of circulating eosinophils and lymphocytes. Cellular mediated immunity impairment is dosage related [13].

The plasma half-life of prednisolone is 2.1 to 3.5 hours. The biological half-life (e.g. in terms of anti-inflammatory effect) outlasts the plasma half-life, lasting from 18 to 36 hours.

Total elimination of prednisolone requires 4 biological half-lives (144 hours). It means that the maximum time that prednisolone can persist in the organism is six days.

Plasma concentrations of prednisolone vary markedly among individuals. In fact, oral contraceptives may decrease the rate of elimination of prednisolone [14].

Clinical trials in oral surgery have also supported the hypothesis that preemptive NSAIDs and corticosteroids are effective in delaying and preventing many postoperative complaints.

A number of earlier studies report the effect of steroids in combination with diclofenac [10,15], ketoprofen [5] and ibuprofen [7] but not with etorikoxib.

The purpose of this study was to evaluate whether a single dose of 30 mg prednisolone, taken orally immediately after operation, would increase the effects of etorikoxib in preventing pain and swelling after surgical removal of impacted molars.

PATIENTS AND METHODS

This prospective randomized, single-dose clinical study was conducted at the Department of Maxillofacial Surgery, Tartu University Hospital, Estonia.

From January 2007 to June 2007, a total of 78 patients underwent surgical removal of third molars due to impaction or orthodontic indications. In order to obtain information about the position of the impacted third molars, radiographic examination was performed using ortopantomography (apparatus CRAEX3, Soredex Orion Corporation LTD, Finland). In our study all third molar were partially impacted according to Pell and Gregory.

All selected candidates were free of pain and other inflammatory symptoms that included swelling, hyperaemia and decreased mouth opening at the time of surgery.

The patients were divided in two groups: the prednisolone group and control.

The prednisolone group consisted of 38 patients and there were 29 women and 9 men The control group consisted of 40 patients and there were 28 women and 12 men. (Table 1).

Patient age in prednisolone group at the time of surgery ranged from 17 to 63 years (average 29.6 yrs) and each patient recieved etorikoxib 120 mg before surgery and 30 mg prednisolone immediately after surgery. Patient age in the control group ranged from 17 to 46 years (average 31.5 yrs) and these patients recieved only etorikoxib before operation.

There were 5 patients in each group in whom only an upper molar was operated. Thirty patients in the prednisolone group and 28 patients in the control group underwent operative removal of only the lower molars and 3 patients in the prednisolone group and 7 patients in the control group underwent removal of an upper molar and a lower molar during one and the same operation.

Altogether we removed 41 teeth in the prednisolone group and 47 teeth in the control group.

The symptom related factors were documented on the basis of a questionnaire. The clinical characteristics of the patients (age, operated teeth) and the medications used are presented in Table 1.

The patients were informed about the study procedure and informed consent was obtained from each patient.

Surgery

The surgical procedure was similar in all cases and was performed by the same surgeon.

Table 1. Clinical characteristics of the patients and the medications used

	Prednisolone group	Control group
Medications	Prednisolone + etorikoxib	etorikoxib
Mean age (range)	29.6+/-13 (17-63)	31.5+/-14.5 (17-46)
No of operated patients	38	40
No of operated teeth	41	47
No of patients in whom only upper molar was operated	5	5
No of patients in whom only lower molar was operated	30	28
No of patients in whom upper molar and lower molar were operated	3	7

Local anaesthesia was obtained using 1.8-3.6 mL articaine hydrochloride 4% solution with epinephrine 1/100000. The time of injection and the time of start of surgery were noted. A standard incision was used, from the anterior border of the ramus to the disto-facial corner of the second molar following the buccal gingival sulcus along the second and first molars. After periostal elevation, bone surrounding the third molar was removed with a round bur in a handpiece using a copious amount of saline irrigation. In the majority of cases, the third molar was split using a tungsten fissure bur and a straight elevator as the routine technique. The tooth was then carefully removed in several pieces. The alveolus was inspected and curetted for granualation tissue followed by irrigation with saline. After tooth extraction the mucoperiostal flaps were repositioned and partially sutured and an iodoform drain was inserted for prevent hematoma formation. The time of completion of the surgical procedure was noted.

Evaluation procedures

The patients had to complete a questionnaire evaluating postoperative symptoms: pain, temperature, cheek swelling, mouth opening (Table 2). The study was conducted over six postoperative days. Post-operative symptoms were analysed as depending on the position of the third impacted molar, duration of operation, age and postoperative treatment.

For pain relief, etorikoxib was used. Postoperative pain was assessed by a 100 mm visual analogue scale(VAS) with the end points marked as „no pain“ and „worst pain ever experienced“. Absence of pain was scored as 0. If pain was present the patient was asked to select a field from 1 mm to 100 mm.

Pain was assessed using a five-point Category Rating Scale. Pain was recorded as “0-no pain”, “1-mild pain”, “2-moderate pain”, “3-strong pain”, “4-very strong pain”. An appropriate pain score was reported in the questionnaire by each patient on a daily basis for six days. Before discharge from the clinic, the operator ensured that all patients were thoroughly instructed about how to complete the diary.

Facial swelling was measured with a measuring tape in one dimension only. The reference points used were the earflap and the corner of the mouth. Patients made measurements on six postoperative days.

Trismus was evaluated by measuring the MIO with the aid of a ruler (VAS ruler) during six postoperative days. MIO measured 24 hours after procedure and in the next days also at the same time.

Table 2. Questionnaire

Patient data:						
Name						
Age						
Sex						
Complaints:						
(marked when complaint occurs)	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**
Painless						
Pain at resting						
Pain at eating						
Pain do not let sleep						
Weak pain						
Moderate pain						
Strong pain						
Very strong pain						
No swelling						
Swelling						
Nerve disorder						
Bleeding						
Fever						
Mouth opening (interincisal distance measured with a ruler)						
	mm	mm	mm	mm	mm	mm
Swelling (measured from the corner of the mouth to the earflap)						
Operated side	cm	cm	cm	cm	cm	cm
Healthy side	cm	cm	cm	cm	cm	cm
Other complaints:						

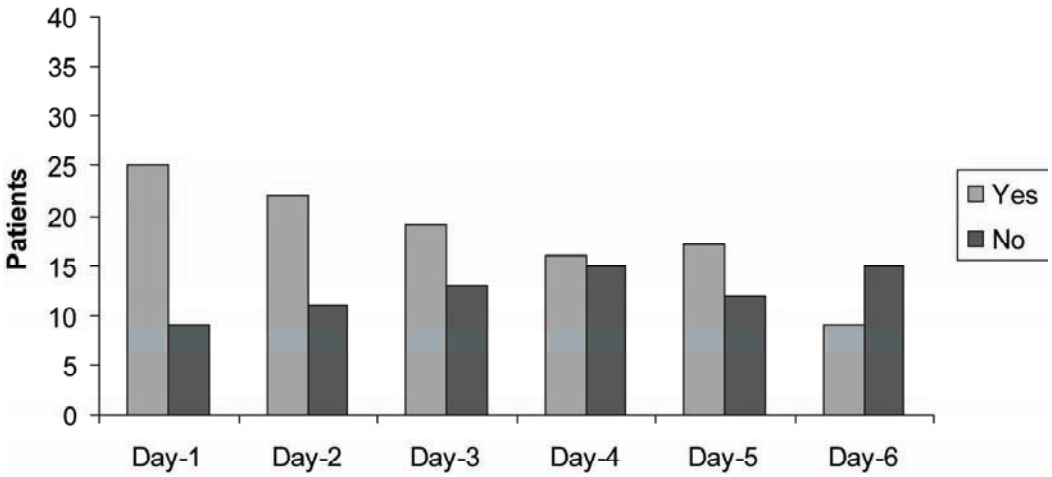

Fig. 1. Swelling in the prednisolone group

Statistical Analysis

Statistics were performed using the SPSS for Windows (v. 10.0, SPSS Inc, Chicago, IL) statistical software package. The crosstable technique was applied for assessment of the variables (pain, swelling and MIO) of two groups: prednisolone and controll. The pain VAS scores were analysed by analysis of variance (ANOVA) for repeated measures. Probability less than 0.05 was considered statistically significant.

RESULTS

A total of 78 patients who returned the properly completed questionnaire were included in the study.

Duration of procedure was 15 minutes to 60 minutes, medium time 22 minutes.

Duration of the pain was evaluated on painful days (Tables 3). Five patients in the prednisolone group had no pain on any postoperative day. Only one patient in the control group had no pain on any postoperative day.

The MIO was measured on different postoperative days in mm/+-deviation.

The patients of the prednisolone group were able to open their mouth postoperatively more than the patients of the control group (Table 4). There was a significant increase ($p<0.05$) in the MIO during 6 postoperative days in the prednisolone group compared to control. The patients of the prednisolone group opened their mouth an average of 2.48mm more than the patients of the control group on each postoperative day.

There was less swelling on the first five postoperative days in the prednisolone group than in control (Figures 1 and 2). There was significantly less swelling on the first four postoperative days. An average of 10.2 more patients in the prednisolone group compared to control had no swelling on the first four days.

On the 6th postoperative day, all symptoms had returned to preoperative level in both groups. Neither group demonstrated any side effects or other complications during the follow-up period.

DISCUSSION

In this study we evaluated the efficacy of a single dose of prednisolone in the control of facial swelling, pain and trismus associated with the surgical removal of impacted third molars. This randomized, single-dose clinical study revealed that postoperative administration of 30 mg prednisolone is effective in modulating the intensity of both clinical parameters, pain and swelling, elicited by the surgical removal of

Table 3. Duration of pain in the study groups

	Prednisolone group	**Control group**
Duration of pain (days)	No of patients	No of patients
0	**5**	**1**
1	2	2
2	4	7
3	5	9
4	6	4
5	6	8
6	10	8

Table 4. Maximal interincisal opening (MIO) in the study groups (mm)

Postoperative	**Day-1**	**Day-2**	**Day-3**	**Day-4**	**Day-5**	**Day-6**
Prednisolone group	[illegible]	31.8±10	35±10.9	39.2±11	40.2±10.5	40.7±11
Control group	27.3±9.6	29.5±10.3	32.4±10.6	34.8±10.4	37.3±9.1	39.4±8.9

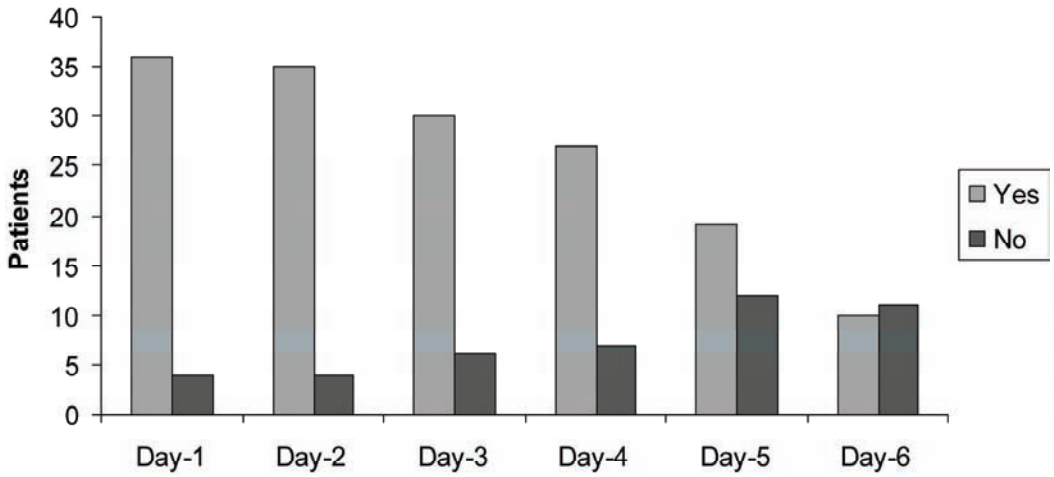

Fig. 2. Swelling in the control group

impacted third molars. To the best of the authors' knowledge, this is the only published study to evaluate coadministration of prednisolone and etoricoxib after osteotomy.

Adrenal glucocorticoids are used in higher doses as anti-inflammatory agents. The mechanism of the anti-inflammatory action of glucocorticoids is unclear. It is probably related to their actions on the microvasculature as well as to cellular effects. Glucocorticoids impede endothelial sticking of leucocytes and diapedesis through capillary wall. Lysosomal stabilization, inhibition of polymorphonuclear leucocyte migration, reversal of increased capillary permeability, and suppression of fibroblast function are some proposed mechanisms for anti-inflammatory activity [13]. Prednisone, or its active form prednisolone, is five or six times more potent than endogenous hydrocortisone, respectively [16]. Clinically significant improvement with these drugs is measurable 3 hours after administration, and peak effectiveness is reached at 6 to 12 hours.

It was found by us that a combination of a single dose of prednisolone and NSAID is well-suited for treatment of postoperative pain, trismus and swelling after dental surgical procedures. Several studies have highlighted the combination therapy of steroids with diclophenac, ketoprofen and ibuprofen, but not with etorikoxib.

In this study the prednisolone dosage was set at 30mg proceeding from the fact that the average treatment dosage used by internists for acute conditions orally is 20-30 mg/day [17].

We chose Etoricoxib because of its many positive aspects. Onset of action occurs as early as 24 minutes after dosing. Time until maximum plasma concentration is about one hour. Bioavailability is nearly one hundred percent. Half-life is approximately 22 hours. Dosing once a day is convenient for patients [2,3,18].

Mostly steroids have been administered already pre- [19-21] or perioperatively [22] to achieve a better effect. Corticosteroid therapy may not be required in all wisdom tooth removals but should be indicated only in cases of some technical difficulty, depending on the molar degree of impaction, need to remove bone tissue and patient age and gender.

As steroids have many systemic side effects, it is not recommended to use these drugs unreasonably. They have a propensity to induce side reactions, as evidenced by endocrine toxicity as well as behavioural and ocular adverse effects. The increased incidence of hypertension, chronic infection, osteoporosis and impaired glucose tolerance as metabolic complaints of large doses of corticosteroids must be carefully considered [13,14,23]. In every clinical situation where systemic glucocorticoid use is considered, the benefit-to-risk ratio is important. Therefore, it is not advisable to use these drugs routinely before any wisdom tooth operation. One of the aims of this study was to provide additional information about the possibility to use steroid treatment postoperatively in case the surgeon evaluates the operation as too traumatic or longer than expected.

Concurrent use of NSAIDs and corticosteroids should be avoided when possible because of the risk of producing gastrointestinal tract haemorrhage. In this study we preferred etoricoxib to other NSAIDs because of its better cyclooxygenase 1(COX-1) selectivity and protection of the gastric mucosa [3]. Cyclo-oxygenase is responsible for generation of prostaglandins. Two isoforms, COX-1 and COX-2, have been identified. The COX-2 is an isoform of the enzyme that has been shown to be induced by pro-inflammatory stimuli and has been postulated to be primarily responsible for synthesis of prostanoid mediators of pain, inflammation, and fever. Etoricoxib is an oral selective cyclo-oxygenase 2 (COX 2) inhibitor within the clinical dose range.

According to studies of clinical pharmacology, etoricoxib produces dose-dependent inhibition of COX-2 without inhibition of COX-1 at doses of up to 120 mg daily [2,3,18]. Etoricoxib does not inhibit synthesis of gastric prostaglandins and has no effect on platelet function [2].

Different administration routes have been used for steroids in oral surgery.

Previous studies have suggested parenteral administration for better efficacy [5,19,24]. This study demonstrated that the oral route is effective and more convenient to use; besides, it ensures rapid and almost complete absorption. It should be used when extensive postoperative swelling of the soft tissue is anticipated.

Combination therapy is indicated for young healthy adults after a careful anamnesis.

CONCLUSION

In absence of contraindications for corticosteroid administration, the use of single-dose prednisolone appears to be a safe and effective method to reduce postoperative clinical symptoms in third molar surgery. It appeared that a combination of a single dose of prednisolone and etoricoxib is well suited for treatment of postoperative pain, trismus, and swelling after dental surgical procedures and should be used when extensive postoperative swelling of the soft tissue is anticipated.

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