Comparison of controlled-release ketoprofen and diclofenac in the control of post-surgical dental pain

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Summary

Preoperative treatment with controlled-release ketoprofen or diclofenac was compared in 56 out-patients, for control of postoperative dental pain, following unilateral or bilateral surgical removal of lower third molars. Six patients were excluded due to non-compliance, leaving 50 evaluable patients.

Patients were assessed by the dental surgeon, on the day of the operation and one week later, prior to removal of sutures. Additionally, patients completed a daily diary during the postoperative week. Following surgery, scores for graded dental pain, consumption of paracetamol, incidence of dental bleeding, dysphagia, sleep disturbance and trismus were similar for the two treatment groups. However, median pain scores were consistently elevated in the diclofenac group over those seen with the ketoprofen group. The four adverse events reported were all minor and posed no problem to patient management.

Introduction

Surgical removal of impacted wisdom teeth produces moderate to severe pain which is maximal 3-6 h postoperatively and declines after 12 h[1,2]. As a result, most patients require postoperative analgesia. There is convincing evidence that non-steroidal anti-inflammatory drugs (NSAIDs) reduce the number and severity of postoperative complaints. The use of NSAIDs results in less pain and fewer side-effects than traditional opiate treatment[3,4]. Swelling and trismus are common sequelae which may persist for several days.

Placebo-controlled trials have established the efficacy of ketoprofen[5,6] and diclofenac[1] in the control of post-surgical dental pain. Patients undergoing surgery under general anaesthesia are required to starve for approximately 6 h prior to the operation, precluding the administration of oral analgesics. Prior administration of an NSAID in a controlled release formulation, ie ketoprofen (Oruvail) or diclofenac as (Voltarol Retard), should result in a reduced inflammatory response to the trauma of surgical removal and induce significant postoperative analgesia.

Materials and methods

Local ethical committee approval was obtained prior to commencement of this trial. Male or female patients, aged between 16 and 30 years, of American Society of Anaesthesiologists (ASA) grade 1 or 2 and requiring removal of impacted lower third molars under a general anaesthetic, were eligible for recruitment into the trial.

Patients with active peptic ulceration and those with a history of recurrent peptic ulceration or chronic dyspepsia were excluded. Also excluded were patients with aspirin sensitivity, those requiring concomitant treatment with a NSAID or drugs with high protein binding capacity (eg anticoagulants, hydantoins, sulphonamides), together with those patients who were either pregnant or nursing an infant.

Patients gave written, informed consent to participate at the visit prior to surgery. Demographic data were recorded and the patients issued with trial medication, which consisted of either Oruvail 200 mg or Voltarol Retard 100 mg in a double-blind, double-dummy, randomized form. Patients were instructed to take one capsule and one tablet, with a light breakfast, on the morning before operation. One further capsule and tablet were to be taken each morning for the 4 days after the operation. Patients were also issued with a supply of rescue analgesic (paracetamol 500 mg) for additional pain relief, if necessary. Any remaining medication was retrieved on day 7.

On arrival at the surgery, on the day of operation the time of consumption of the preoperative medication was noted, together with the range of movement of the temporomandibular joint. A fairly standardized technique was used for anaesthesia for unilateral or bilateral surgical removal.

Intravenous premedication consisted of diazepam (5 mg) and nalbuphine (10-20 mg). Induction of anaesthesia was by methohexitone or propofol. Patients were intubated with either suxamethonium

Table 1. Comparison of ketoprofen (n=26) and diclofenac groups (n=26)*, prior to surgery*

	Ketoprofen	*Diclofenac*
Age (years)	25.0±1.4	24.0±0.9
Sex	12, 14	12, 14
Weight (kg)	66.0±2.8	66.0±2.0
Interval between dosing and commencement of surgery (hours)	7.8±0.26	8.2±0.33
Range of movement of the temporomandibular joint (mm)	46.0±1.2	46.0±1.2
Duration of operation (min)	34.0±2.7	28.0±2.6
Unilateral/bilateral surgical removal	4U, 22B	7U, 19B

*Includes available data on non-compliant patients
Results expressed as mean±standard error

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Table 2. Comparison of symptomology during the postoperative period

Symptom		Postoperative time interval 2 h	4 h	6 h	1 day	2 days	3 days	4 days	5 days	6 days	7 days
Dental pain	K	20	19	20	18	16	14	14	17	12	8
	D	21	22	22	16	14	14	14	20	15	9
Paracetamol consumption	K		7	7	12	13	11	7	13	12	
	D		12	7	4	6	7	6	10	10	
Dental bleeding	K	14	21	19	13	10	4	2	1	2	
	D	14	20	13	7	3	2	1	1	0	
Dysphagia	K				17	17	12	11	6	6	
	D				16	13	9	7	8	6	
Sleep disturbance	K				7	10	2	2	1	0	
	D				5	3	3	2	3	1	

K, ketoprofen group (n=25); D, diclofenac group (n=25)
Figures indicate numbers of patients experiencing a particular symptom in that time period. Note that one patient in each group was excluded due to protocol violation

or atracurium. Anaesthesia was maintained on oxygen/nitrous oxide and halothane supplements, from a McKesson 882 RA/GA continuous flow machine. Patients were allowed to breathe spontaneously, after suxamethonium, or maintained on intermittent positive pressure ventilation (IPPV), after atracurium, using an East-Freeman Autovent.

Severity of perioperative bleeding and duration of operation were recorded. Two hours after surgery, on recovery from the anaesthetic and prior to discharge home, pain scores, incidence of bleeding and range of movement of the temporo-mandibular joint were noted. A patient diary was used to record pain scores, consumption of paracetamol, dental bleeding, dysphagia and sleep disturbance. On return to the surgery for removal of the sutures (day 7), dental pain scores were recorded, together with the range of movement of the temporomandibular joint and any side effects to treatment.

Severity of postoperative pain was recorded using both a horizontal 10 cm visual analogue scale (VAS) and a graded category scale, from none (1) to very severe (5). Dental bleeding was recorded as none (1), slight (2), moderate (3) or heavy (4). Mouth opening was measured as the distance (in mm) between the upper and lower edges of the central incisors. Dysphagia was recorded as none (1), slight (2), moderate (3) or severe (4). Any sleep disturbance, experienced by the patient, was also recorded.

Comparisons were made between the ketoprofen and diclofenac sub-groups, using the Student t-test and the Wilcoxon rank sum test as appropriate.

Results

Fifty-six patients were recruited into this study. Two patients were allocated trial numbers and medication but withdrew before surgery. Three further patients were excluded from efficacy estimations due to non-compliance. Finally, one patient number was not allocated, leaving 50 evaluable patients.

The ketoprofen and diclofenac sub-groups were comparable with respect to age, sex, weight, duration of preoperative treatment, range of movement of the temporomandibular joint, preoperative premedication and duration of operation (Table 1). Additionally, approximately equal proportions of each treatment group were subjected to unilateral or bilateral surgical removal of lower third molars.

Analysis of responses to graded assessments (pain, dental bleeding and dysphagia) was invalidated by the small numbers reporting in each category. Accordingly data is presented indicating presence or absence of the complaint. This technique was also applied to analysis of paracetamol consumption. The experiences of the two treatment groups were similar in the immediate postoperative period and during the postoperative week (Table 2). There was no significant difference in requirement for paracetamol, dental bleeding, dysphagia or sleep disturbance, for the two treatment groups. Postoperative trismus was present on assessment at day 7 (Table 3). However, there was a trend that median pain scores, as assessed by visual analogue scale, were consistently elevated in the diclofenac group over the ketoprofen group (P=0.086) postoperatively (Figure 1). When treatment with the two active medications was concluded on the 5th postoperative day, median pain scores rose, but not significantly (Figure 1).

Only 4 of the 52 patients (8%) reported experiencing any side effect to treatment. Adverse events were limited to drowsiness (ketoprofen, one patient), mild stomach ache (ketoprofen, one patient), self-induced mouth ulceration (ketoprofen, one patient), and sleepiness (diclofenac, one patient).

Discussion

It is widely accepted that NSAIDs have a major role in the control of pain following surgery[7-10]. However, these are usually given either intra- or postoperatively[1]. If these drugs are given preoperatively, then this tends to be in the form of an intramuscular injection, with premedication.

The objective of this trial was to evaluate the analgesic effects of preoperative treatment with controlled-release ketoprofen and diclofenac prior

Table 3. Comparison of the range of movement (mm) of the temporomandibular joint

	Ketoprofen (n=25)	Diclofenac (n=25)
Before operation (day 0)	46±1.2	46±1.2
Suture removal (day 8)	36±1.7	38±1.7

Result expressed as mean±standard error

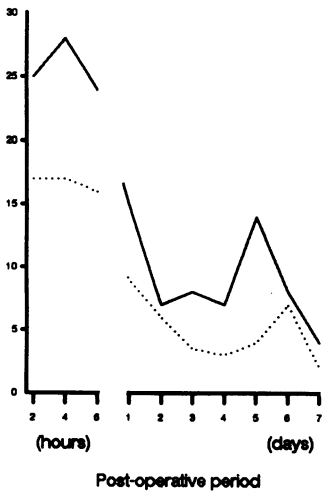

Figure 1. Median pain scores for patients receiving controlled-release ketoprofen (· · ·) were lower than those for diclofenac (—) during the postoperative period (P=0.086)

to surgical removal of impacted lower third molars. It was hypothesized that suppression of prostaglandin synthesis prior to surgical insult would result in reduced tissue oedema and pain production. The delivery systems used in these pharmaceutical products result in sustained blood levels of the active components: the t_{max} for Oruvail[11,12] is of the order of 4.9-7.5 h, compared with 4 h for Voltarol Retard[13]. In patient terms, this meant that the trial medication could be consumed with a light breakfast prior to surgery, thus enabling treatment while maintaining 'Nil by Mouth' for the 6 h preoperative period.

Acute postoperative pain is inadequately controlled by paracetamol alone[1,14], whereas NSAIDs have been proved to be effective[1,5,6]. Previous studies have shown that both ketoprofen[9] and diclofenac[1] are superior to paracetamol in the control of early postoperative pain. Ketoprofen and diclofenac effectively and markedly controlled the pain and swelling of dental surgery, both during the early postoperative period and during the subsequent week. It was particularly noticeable that the patients experienced excellent pain relief during the postoperative period. A dramatic lack of distress on awakening from anaesthesia was observed, which greatly facilitated patient management. Additionally, there was a trend that pain control in the postoperative week was superior with ketoprofen. Similar benefit of use of drugs with a prolonged duration of action, for postoperative analgesia has been noted previously[1]. The persistence of post-operative trismus for 7 days after surgery, despite NSAID treatment, has also been reported previously[15].

In retrospect, it was felt that NSAID active treatment, which concluded on 4th postoperative day should have been extended until the time of suture removal on the 7th postoperative day. Indeed, a number of patients contacted the dental surgery, following completion of active treatment, reporting symptoms typically associated with this type of surgery, but which had been absent, hitherto. The few side effects to treatment seen in this study were all minor and posed no problems in patient management. In particular, the case of mouth ulceration was probably unrelated, being noted by the dental surgeon as localized ulceration, commonly associated with nervous trauma or cheek-biting.

Day-case surgery, in general, is now being advocated on medical, social and economic grounds[16]. It can be concluded therefore that oral NSAIDs in controlled-release formulation, given preoperatively, would have a useful place in the control of postoperative pain after outpatient dental procedures.

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