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PREOPERATIVE PIROXICAM FOR POSTOPERATIVE ANALGESIA IN DENTAL SURGERY

G. L. HUTCHISON, S. L. CROFTS AND I. G. GRAY

SUMMARY
Fifty patients were allocated randomly to receive placebo or piroxicam 40 mg, 2.5 h before surgical removal of lower third molars under general anaesthesia. A significantly greater number of patients in the piroxicam group did not require opioid analgesia after operation (P < 0.05). The piroxicam group also required fewer doses of paracetamol in the first 24 h after recovery from anaesthesia (P < 0.05), and the time from recovery to first postoperative analgesia was longer in those patients who had received piroxicam (P < 0.05). Piroxicam did not significantly prolong the duration of recovery from anaesthesia.

KEY WORDS

Piroxicam is an oxicam non-steroidal anti-inflammatory drug (NSAID). Its plasma half-life has been estimated at 45 h (allowing once-daily dosage), with the peak plasma concentration occurring 2-4 h after oral administration [1]. Several studies have demonstrated its efficacy as an analgesic following dental extractions or minor dental surgery such as removal of impacted third molars. Piroxicam in single doses of 20 or 40 mg has been shown to produce analgesia equivalent to or better than that produced by aspirin 648 mg (single dose) [2-5], mefenamic acid 500 mg (single dose) [6] or acetaminophen 500 mg (8-hourly, three doses) [7]. Three studies have demonstrated that, compared with aspirin, piroxicam produces peak analgesia more slowly [2-4], although Ohnishi, Kawai and Ogawa detected no difference in the time of onset of analgesia when comparing piroxicam with mefenamic acid [6]. Several investigators have noted the prolonged analgesia resulting from a single dose of piroxicam [2-4, 7-9]. Parsloe and colleagues demonstrated that the analgesic effects of a single dose of piroxicam 40 mg persisted into the 3rd day after operation [9]. None of the above studies reported any symptoms of peptic ulceration, bronchospasm or generalized allergy associated with the use of piroxicam.

One disadvantage of piroxicam as a postoperative analgesic is its slower onset of action compared with other oral agents and alternative routes of administration. This difficulty may be overcome by preoperative administration of the drug. Piironen, Sjöblad and Oikarinen [10] studied the effects of piroxicam 20 mg administered either before or 3 h after surgery, in patients undergoing extraction of an impacted lower third molar under local anaesthesia. Postoperative pain scores at 2, 3 and 4 h were significantly lower in the group who had received preoperative medication.

The present study was designed to investigate the preoperative use of piroxicam in patients undergoing the surgical removal of lower third molars under general anaesthesia.

PATIENTS AND METHODS
The study was approved by the local Ethics Committee. All patients gave informed consent before participation in the trial.

We studied 50 patients undergoing surgical removal of lower third molars under general anaesthesia (some patients were also undergoing additional extractions). Exclusion criteria were: history of asthma or peptic ulceration, or other upper GI pathology; pregnancy or breast feeding;...
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Allergy to aspirin or other NSAID and any contraindication to the standard anaesthetic technique used.

Premedication was administered 2.5 h before the estimated time of surgery: patients received either two capsules of piroxicam 20 mg or two placebo capsules, prepared and allocated randomly by the hospital pharmacy. Placebo and active capsules were identical in appearance. The timing of this premedication was chosen to ensure that as many patients as possible recovered from anaesthesia between 2 and 4 h after drug administration, during the peak effect of the piroxicam. The investigators were unaware of the nature of the capsules received by the patients until the study ended. No other premedication was given.

All patients were anaesthetized in a standard manner. Anaesthesia was induced with thiopentone 4-5 mg kg⁻¹. Suxamethonium 1 mg kg⁻¹ was then administered, a nasotracheal tube passed, and the throat packed. Anaesthesia was maintained with 2% isoflurane in nitrous oxide (6 litre min⁻¹) and oxygen (3 litre min⁻¹) via a Bain circuit, with the patient breathing spontaneously.

When surgery was completed, the inhalation agents were discontinued and a stop-clock started. This clock was taken with the patient to the recovery area, and was switched off when the patient first responded to command. In this way, the duration of recovery was measured. The time at which the patient received the premedicant drug, the time at which anaesthesia was induced and the time at which the anaesthetic was stopped were also recorded and, at a postoperative visit, the time at which analgesia was first received was noted, together with the total number of analgesic doses required in the first 24 h after operation.

Nausea and vomiting were treated with i.m. prochlorperazine 12.5 mg, if necessary.

Statistical analyses

Normally-distributed data (age, anaesthetic time, recovery time and dose—recovery time) were analysed using Student's t test. Sex distributions were compared using a chi-square test.

The number of paracetamol doses required in the first 24 h was analysed using the Mann—Whitney U test, and a chi-square test was performed to compare the number of patients in each group who did not require opioid analgesia.

Recovery—analgesia times were treated as being analogous to survival data. “Survival” curves were plotted to indicate the proportion of patients in each group who had received no analgesia by a given time after operation, and the recovery—analgesia times for the two groups were compared using the log rank test (this compares the observed rate at which patients requested analgesia with the rate which might be expected if piroxicam and placebo were equally effective [11]).

RESULTS

Of the patients who were otherwise suitable for inclusion in the study, three were excluded because of a history of asthma, and four because of documented peptic ulceration. Two other patients refused to participate.

One patient agreed to take part in the study, but was unable to swallow the capsules. She was later found to have been assigned to the placebo group. Twenty-four patients therefore remained in the placebo group, and 25 received active medication.

There were no significant differences in age and sex distribution, anaesthetic time, recovery time or dose—recovery time between active and placebo groups (table I). The measured dose—recovery times occurred between 2 and 4 h for all but one of the patients who received piroxicam (this patient recovered 263 min after her dose had been

| TABLE I. Demographic and anaesthetic data for the active and placebo groups (mean (SD)) |
|---------------------------------|------------|----------------|
| Piroxicam | Placebo | | |
| Sex (M/F) | 10/15 | 7/17 |
| Age (yr) | 24.2 (5.1) | 24.1 (5.0) |
| Anaesthetic time (min) | 28.3 (10.7) | 29.1 (8.2) |
| Recovery time (min) | 9.4 (2.4) | 9.8 (2.6) |
| Dose—recovery time (min) | 194.5 (27.0) | 194.9 (35.2) |
administered). Three patients in the placebo group had dose–recovery times which exceeded the target range (up to 272 min).

Recovery–analgesia times were longer in the piroxicam group (median 393 min, range 18 min to >24 h) than in the placebo group (median 199.5 min, range 6 min to >24 h) (log rank test, \( P < 0.05 \)). Recovery–analgesia times are displayed in the form of “survival” curves in figure 1. The curves indicate the proportion of patients in each group who had received no analgesia by a given elapsed time since recovery from anaesthesia. (Those patients who had not requested analgesia by 15 h after recovery continued without needing analgesia for the full 24 h of the study.)

Significantly fewer patients in the piroxicam group required opioid analgesia (chi-square test, \( P < 0.05 \)), and the piroxicam group also received fewer doses of paracetamol than the placebo group (one-tailed Mann–Whitney \( U \) test, \( P < 0.05 \)) (table II).

![Figure 1. "Survival" curves for the active and placebo groups, representing the proportion of patients in each group who had not required any analgesia since recovery from anaesthesia.](https://academic.oup.com/bja/article-abstract/65/4/500/341402)

The data for the patients who required opioids after surgery were examined separately, in an effort to identify possible causes of additional analgesic needs. In both the piroxicam and the placebo group there was no significant difference, in terms of duration of anaesthesia or dose–recovery time, between patients who required opioids and those who did not.

<table>
<thead>
<tr>
<th>Number of doses</th>
<th>Piroxicam</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papaveretum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>19</td>
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</tr>
<tr>
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<td>11</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Paracetamol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
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</table>

**DISCUSSION**

Premedication was timed successfully to allow patients to recover from anaesthesia during the peak effects of piroxicam, or shortly thereafter. Patients who received piroxicam and also required postoperative opioids had dose–recovery times similar to other patients in their group. The need for opioid analgesia was unrelated to the timing of premedication or the duration of anaesthesia and surgery. This bears out the results of Parsloe and colleagues [9], who found no relationship between postoperative pain and the duration or difficulty of surgery.

Piroxicam was shown to have no significant effect on the duration of recovery from anaesthesia, as might be expected from its non-sedative nature.

Parsloe and others have conducted a similar study [9], allocating patients randomly to receive preoperative piroxicam or placebo, combined with halothane or isoflurane anaesthesia (four groups in all). Opioid analgesia was prescribed in an "on request" manner, and visual analogue pain scores were recorded at 2, 4 and 18 h after surgery. A significant difference in analgesic requirement was detected between two of the groups, but pain scores were not significantly different.

In our study, analgesia was also prescribed on request. A comparison of pain scores would have been valid only during the period immediately after recovery, before any of the patients had received analgesia. During this time, a patient...
who is obviously in pain may be unable to record a visual analogue pain score. Under these circumstances, the patients' requirements for analgesia appear to give a better indication of the severity of their pain, therefore pain scores were not assessed.

Parsloe's group [9] did not demonstrate any reduction in postoperative requirement for opioid which could be ascribed to piroxicam alone. In the first 18 h after operation, patients who had received piroxicam and isoflurane required significantly less analgesia than those who had received piroxicam and halothane or placebo and halothane. A synergistic effect between piroxicam and isoflurane was postulated to explain this observation. However, no significant differences in analgesic requirements could be detected between the piroxicam with isoflurane and placebo with isoflurane groups, or between the piroxicam with halothane and placebo with halothane groups. Lack of significance may have been because of the small number of patients in each group (15).

By examining larger numbers of patients in each group, we were able to detect a significant effect of piroxicam on postoperative opioid requirement. The proportion of patients in each group who required opioids was similar to the corresponding proportions found by Parsloe and colleagues in their isoflurane groups. In the current study, 24% of the patients who received piroxicam and 54% of those who received placebo required opioids after operation. Corresponding figures from Parsloe's study were 27% and 60%, respectively. This similarity is striking, as Parsloe used an anaesthetic technique similar to that used here, apart from the addition of papaveretum 5–7.5 mg, given just before induction of anaesthesia. Their use of opioids during operation appeared to have had little effect on postoperative requirements for analgesia.

While significant differences in paracetamol requirements and recovery–analgesia times were detected, the most important finding of the present study was the opioid-sparing effect of piroxicam premedication.

ACKNOWLEDGEMENTS

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REFERENCES