PREMEDICATION WITH PIROXICAM IN PATIENTS HAVING DENTAL SURGERY UNDER GENERAL ANAESTHESIA WITH HALOTHANE OR ISOFLOURANE

M. PARSLOE, S. N. CHATER, M. BEMBRIDGE AND K. H. SIMPSON

Pain after dental surgery frequently requires analgesia [1], and patients who have undergone removal of impacted lower third molars usually experience the most severe pain during the first 12 h after operation [1, 2]. Oral opioids, including morphine [3], codeine [4] and dextropropoxyphene [5], are ineffective in relieving pain in this situation. Pain and swelling after dental surgery may be mediated by a local tissue response involving prostaglandins and leukotrienes, and thus may be treated more appropriately by non-steroidal anti-inflammatory drugs [6]. After oral surgery, aspirin provides better analgesia than paracetamol, presumably because of superior anti-inflammatory properties [1]. However, oral aspirin has a short duration of action, and repeated doses may be difficult to administer after surgery when nausea and vomiting occur commonly.

It may be useful to administer an oral non-steroidal anti-inflammatory drug before operation to provide analgesia immediately after surgery and perhaps reduce the requirement for parenteral postoperative analgesics. Ibuprofen and flurbiprofen both relieve pain after oral surgery [7–9], but their duration of action is rather short. Piroxicam is an enolic acid belonging to the oxicam group of non-steroidal anti-inflammatory drugs. It is absorbed rapidly after oral administration, produces analgesia within 2 h and has a prolonged effect, with a half-life of 38–45 h [10]. Single or multiple doses of piroxicam may be useful after oral surgery under local anaesthesia [11, 12]. The present study was designed to evaluate the use of a single dose of dispersible piroxicam 40 mg given before oral surgery under general anaesthesia. The effect of choice of volatile inhalation anaesthetic agent was assessed also by random allocation of patients to receive either halothane or isoflurane during the procedure.

SUMMARY

Pain, analgesic requirements, mouth opening and emesis were assessed in 60 patients who received either piroxicam 40 mg or placebo before dental surgery under general anaesthesia which included breathing either halothane or isoflurane. Patients went home on the day after surgery and completed a questionnaire concerning pain and emesis. There were four groups of 15 subjects: piroxicam–halothane, piroxicam–isoflurane, placebo–halothane or placebo–isoflurane. Pain increased at 2 and 4 h and had reduced by 18 h after surgery, there were no significant differences between the groups in pain scores. After operation, fewer patients in the piroxicam–isoflurane group required papaveretum compared with the piroxicam–halothane and placebo–halothane groups. Mouth opening was reduced between 2 and 4 h after surgery, but was less restricted after piroxicam–isoflurane than placebo–halothane. There was no difference between the groups in the incidence of emesis within 18 h of surgery. The postal questionnaire suggested that pain and emesis were reduced significantly during the 3 days after surgery in patients who had received piroxicam before surgery, compared with those who had received placebo.
PATIENTS AND METHODS

Local Ethics Committee approval was granted for this double-blind study which involved 60 healthy patients undergoing third molar extraction under general anesthesia (some subjects also had simple extraction of premolar teeth). Patients with no history of intolerance to non-steroidal anti-inflammatory drugs were premedicated with lorazepam 2–3 mg with either dispersible piroxicam 40 mg or placebo by mouth in a random manner, 2 h before surgery, which was always performed in the afternoon. I.v. papaveretum 5–7.5 mg was administered just before induction of anesthesia with thiopentone 3–5 mg kg⁻¹. Suxamethonium 1 mg kg⁻¹ was used to facilitate nasal intubation of the trachea and patients breathed either halothane or isoflurane and nitrous oxide in oxygen. The investigators were aware of the choice of volatile agent, which was random. Postoperative analgesia was available on request as i.m. papaveretum (< 59 kg 10 mg; 60–80 kg 15 mg; > 81 kg 20 mg), and emesis was treated with i.m. prochlorperazine 12.5 mg if necessary. All patients were nursed on the same ward, where staff checked patients' analgesic requirements regularly.

The same experienced surgeon performed all the operations using a standard technique. The number of third molars extracted and duration of surgery were recorded, and the surgeon was asked to rate the difficulty of the procedure (easy, mildly difficult, moderately difficult and very difficult). Patients were visited by the anaesthetist at 2, 4 and 18 h after surgery. Pain was assessed using a 10-cm visual analogue score and a four-point verbal rating scale (none, mild, moderate and severe). The time to request the first dose of postoperative papaveretum and the number of doses received were recorded. Maximum mouth opening was measured using calibrated calipers placed between the upper and lower incisors. The incidence of nausea and vomiting was noted. Patients were sent home on the morning after surgery and were asked to complete a postal questionnaire concerning pain and emesis during the 3 days after discharge from hospital.

Parametric data were analysed using analysis of variance. Visual analogue pain scores were arcsine root transformed before two-way analysis of variance [13]. Non-parametric data were analysed using Kruskall–Wallis analysis of variance, Mann–Whitney U, Fisher's exact and Chi-square tests.

RESULTS

Demography (table I), type, duration and difficulty of surgery (table II) were not significantly different in the four groups of 15 patients.

There were no significant differences between the groups in pain scores during the first 18 h after surgery. In addition, males and females did not have significantly different pain scores at any time. Pain increased at the 2- and 4-h assessment ($P < 0.01$) and had reduced by 18 h ($P < 0.01$) in all four groups. Postoperative pain was not related to the duration or difficulty of surgery. Fewer patients received postoperative papaveretum after piroxicam–isoflurane compared with piroxicam–halothane ($P < 0.005$) or placebo–halothane ($P < 0.025$) (table III). The time to receive the first dose and the number of doses of postoperative opioid did not differ significantly between the groups (table III), and were not related to the duration or difficulty of surgery. Eighteen percent of all patients received two doses of opioid within

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**Table I. Mean (SD) age, weight and sex distribution (n = 15 in each group)**

<table>
<thead>
<tr>
<th></th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Sex (M:F)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piroxicam–halothane</td>
<td>21.5 (2.9)</td>
<td>61.3 (8.0)</td>
<td>5:10</td>
</tr>
<tr>
<td>Piroxicam–isoflurane</td>
<td>23.3 (3.2)</td>
<td>66.4 (9.5)</td>
<td>8:7</td>
</tr>
<tr>
<td>Placebo–halothane</td>
<td>23.6 (3.3)</td>
<td>58.0 (8.7)</td>
<td>4:11</td>
</tr>
<tr>
<td>Placebo–isoflurane</td>
<td>22.6 (4.4)</td>
<td>61.4 (7.4)</td>
<td>5:10</td>
</tr>
</tbody>
</table>

**Table II. Mean (SD) number of third molars extracted, duration of surgery and difficulty of surgery (n = 15 in each group)**

<table>
<thead>
<tr>
<th></th>
<th>No. 3rd molars extracted</th>
<th>Duration (min)</th>
<th>Moderate/very difficult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piroxicam–halothane</td>
<td>3.2 (1.1)</td>
<td>28.7 (13.3)</td>
<td>7</td>
</tr>
<tr>
<td>Piroxicam–isoflurane</td>
<td>3.1 (0.9)</td>
<td>24.4 (11.8)</td>
<td>8</td>
</tr>
<tr>
<td>Placebo–halothane</td>
<td>3.5 (0.7)</td>
<td>28.9 (14.2)</td>
<td>6</td>
</tr>
<tr>
<td>Placebo–isoflurane</td>
<td>3.3 (1.1)</td>
<td>24.9 (15.2)</td>
<td>9</td>
</tr>
</tbody>
</table>
TABLE III. Percent of patients requiring postoperative analgesia, mean (SD) time to receive first dose of analgesia and number of patients requiring two doses of analgesia within 18 h of surgery. *Significantly fewer patients required analgesia after piroxicam—isoflurane than after piroxicam—halothane or placebo—halothane (P < 0.05: Fisher's exact test)

<table>
<thead>
<tr>
<th></th>
<th>Requiring analgesia (%)</th>
<th>Time to analgesia (h)</th>
<th>Two doses analgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piroxicam—halothane</td>
<td>87</td>
<td>2.7 (1.9)</td>
<td>3</td>
</tr>
<tr>
<td>Piroxicam—isoflurane</td>
<td>27*</td>
<td>5.8 (2.7)</td>
<td>0</td>
</tr>
<tr>
<td>Placebo—halothane</td>
<td>73</td>
<td>3.5 (2.6)</td>
<td>4</td>
</tr>
<tr>
<td>Placebo—isoflurane</td>
<td>60</td>
<td>3.7 (2.6)</td>
<td>4</td>
</tr>
</tbody>
</table>

Fig. 1. Mean (SEM) restriction in mouth opening in each group at each postoperative assessment. Mouth opening reduced significantly between 2 and 4 h after surgery (F = 2.90, P < 0.05), mouth opening more restricted after placebo—halothane than after piroxicam—isoflurane (F = 3.02 P < 0.05) (two-way analysis of variance with repeated measures on one factor).

Fig. 2. Percent of subjects with moderate or severe pain on a four-point scale during the 3 days after surgery. Overall pain was significantly worse after placebo than after piroxicam (Z = 2.06, P < 0.05) (Mann–Whitney U test).

18 h of surgery, but none of these was in the isoflurane—piroxicam group.

Mouth opening was reduced significantly between 2 and 4 h after surgery (P < 0.05), and was more restricted in the placebo—halothane group compared with the piroxicam—isoflurane group (P < 0.05) (fig. 1). There was no significant correlation between mouth opening and difficulty of surgery, postoperative pain or analgesic requirements.

There was no significant difference between the groups in the overall incidence of emesis during the first 18 h after surgery, with 20% nausea and 17% vomiting.

Ninety-two percent of patients returned the questionnaire documenting pain and emesis during the first 3 days after surgery. These were analysed comparing the placebo and piroxicam groups and disregarding the effect of the volatile anaesthetics. During the first 3 days after discharge from hospital the placebo group complained of significantly more pain than the piroxicam group (P < 0.05); on the 3rd day after surgery, 36% of the placebo group experienced moderate to severe pain compared with 16% of the piroxicam group (fig. 2). More patients reported severe pain after placebo (29%) than after piroxicam (8%) (P < 0.05). After discharge from hospital, the incidence of emesis was significantly greater in the placebo group (39%) than the piroxicam group (15%) (P < 0.05).

DISCUSSION

The pattern of pain in this study was similar to that noted in previous studies [1,2]. Pain scores during the first 18 h after surgery were not influenced by the use of piroxicam or the choice of
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volatile anaesthetic agent. However, the pain scores may have been modified by the administration of postoperative parenteral analgesia. Patients who had received piroxicam–isoflurane required less postoperative papaveretum, and therefore presumably had less pain, than those who had been given piroxicam–halothane or placebo–halothane.

Some inhalation anaesthetics, for example trichlorethylene, methoxyflurane, enfurane [14] and isoflurane [15] are analgesic when inhaled in low concentrations. Isoflurane may therefore have contributed to analgesia in the early postoperative period. It has been suggested that halothane has poor analgesic properties and may even cause increased sensitivity to pain in volunteers [16]. Although this finding has since been questioned [17], the halothane groups did seem to fare worse than the isoflurane groups immediately after surgery.

Mouth opening was restricted in all four groups, especially between 2 and 4 h after surgery. Duration and difficulty of surgery were not predictive of pain or restriction of mouth opening. Therefore prescription of postoperative analgesia should not be based on these criteria. Reduced mouth opening did not correlate with pain, suggesting that restriction of mouth opening may result from swelling and oedema. The piroxicam–isoflurane patients had better mouth opening than the placebo–halothane patients, suggesting that there may be an interaction between piroxicam and isoflurane. A synergistic effect is postulated, as the isoflurane–piroxicam patients were consistently better than the other groups during the first 18 h after surgery.

Opioids were given after surgery in the present study, as is the standard practice in our unit. However, the use of opioids after oral surgery is of questionable value and may lead to increased emetic sequelae. In the present study, nausea and vomiting were seen in 33% of the patients within 18 h of surgery, but emesis was not increased by the use of piroxicam. If postoperative emesis is a problem when analgesia is required, parenteral non-steroidal anti-inflammatory drugs may be of value.

The results of the postal questionnaire showed that pain and emesis after discharge from hospital following dental surgery may be more common than is appreciated. Approximately 33% of patients who had placebo experienced moderate to severe pain and nausea or vomiting during the 3 days after surgery. Patients who had received piroxicam had significantly less pain and emesis during this time. The pharmacokinetics of piroxicam would explain the prolonged analgesia, but the lower incidence of nausea and vomiting were surprising. The results of the questionnaire should be interpreted with caution, as it did not include questions concerning the use of analgesics after discharge from hospital, and the placebo group may have required more supplementary analgesia, which resulted in emesis.

It may be an advantage to give piroxicam for a longer period before surgery as it is necessary to administer it for at least 3 days to achieve maximum anti-inflammatory effect [18]. Pain relief is poor if patients are allowed to self-prescribe analgesics after oral surgery [1], therefore it may be valuable to prescribe piroxicam for a few days after surgery, when the dispensible form is particularly useful, as it is easy to swallow.

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