Intra-articular analgesia for arthroscopic meniscectomy

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Summary
Intra-articular morphine has been shown to provide prolonged analgesia after arthroscopic knee surgery; the addition of local anaesthetic agents has been reported to improve this analgesic effect. Pethidine possesses local anaesthetic properties, and therefore this study was designed to evaluate its analgesic efficacy after arthroscopic meniscectomy. Sixty patients were allocated randomly to receive intra-articular injections of pethidine 50 mg, morphine 5 mg or saline after elective arthroscopic meniscectomy. Postoperative pain was assessed using an interval visual analogue scale and measuring analgesic requirements. Both treatment groups had significantly lower pain scores compared with the control group. Patients in the pethidine group had lower pain scores than those in the morphine group at 0.5, 1 and 2 h, but significantly higher scores at 12 and 24 h. These observations suggest that the local anaesthetic effect of pethidine may be responsible for the improved early analgesia, but its duration of action appears to be less than that of morphine. (Br. J. Anaesth. 1995; 75: 552–555)

Key words

Arthroscopic surgery of the knee joint is a common day-case operation. To conduct this surgery on a day-case basis depends on the provision of adequate and prolonged analgesia [1]. Traditionally, bupivacaine has been injected into the knee joint after arthroscopy to reduce postoperative pain, but the duration of effective analgesia is usually short [2–6]. Significant synovial inflammation may activate peripheral opioid receptors [7, 8] which may account for the efficacy of intra-articular morphine in reducing post-arthroscopic pain. Morphine administered in this way provides good analgesia without systemic side effects [9–11]. The addition of bupivacaine to morphine may improve its analgesic qualities [12–13]. Pethidine has been shown to have local anaesthetic activity in vitro and in vivo [14–20], and therefore may provide improved analgesia by a combination of opioid and local anaesthetic properties.

We undertook a randomized, double-blind trial to compare the efficacy of intra-articular pethidine and morphine as analgesics after arthroscopic meniscectomy of the knee joint.

Patients and methods
After obtaining Ethics Committee approval and written informed consent, we studied 66 ASA I and II unpremedicated day-case patients undergoing general anaesthesia for arthroscopic meniscectomy of the knee joint. Patients undergoing simple diagnostic arthroscopy, biopsy or washout were not recruited.

After admission to the day ward, patients were instructed in the use of a 100-mm visual analogue scale (VAS): “0” was labelled no pain and “100” the worst pain imaginable. A standard general anaesthetic was given consisting of induction with fentanyl 1 g kg⁻¹ and propofol 2.5–5 mg kg⁻¹, and maintenance with isoflurane and nitrous oxide in oxygen. All patients were allowed to breathe spontaneously via a laryngeal mask airway. Patients were allocated randomly to receive one of three intra-articular injections: group 1 received pethidine 50 mg diluted to 25 ml with saline, group 2, morphine 5 mg in 25 ml of saline and group 3, 25 ml of saline alone. Each injection was drawn up by an anaesthetist not involved in the study. Anaesthetists involved in the study and the operating surgeon were not aware of the contents of the injectate. After injection the tourniquet remained inflated for a period of 10 min.

Patient age, sex, weight and operation time were recorded. Postoperative analgesia was provided by bolus doses of pethidine 25 mg i.v. in the recovery room or mafenamic acid 500 mg orally on request on the ward. Patients were discharged with a supply of mafenamic acid to take 6-hourly as required. VAS scores were recorded in the recovery room on awakening and at 30 min. On the day ward VAS scores were noted at 1, 2 and 4 h after operation. Before discharge home, patients were given a form containing 3 VAS to be completed at 8, 12 and 24 h.

Scores were noted at 1, 2 and 4 h after operation. Before discharge home, patients were given a form containing 3 VAS to be completed at 8, 12 and 24 h. They were also asked to record the timing and quantity of supplementary analgesia taken. A prepaid addressed envelope was provided to facilitate return of the forms.

Age, weight and duration of anaesthesia were analysed by ANOVA. The chi-square test with
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Yates’ correction factor, where appropriate, was used for categorical data. Pain scores and supplementary analgesic requirements were compared between groups using ANOVA. Significance was taken at $P < 0.05$ throughout.

Sample size was estimated using pain scores as the primary variable. Based on an SD of 20 mm, we calculated that a group size of 20 patients would be sufficient to detect a difference of 18 mm on the VAS at the 5% level of significance with 80% power.

Results

Replies were received from 90% (60/66) of patients studied (pethidine = 20; morphine = 20; saline = 20). The groups were similar in age, weight, sex and duration of operation (table 1).

VAS pain scores for the morphine group were significantly lower than the placebo group throughout ($P < 0.01$). Patients in the pethidine group also reported superior analgesia at 0–8 h ($P < 0.01$) and at 12 h ($P < 0.05$), but not at 24 h after operation compared with the control group (fig. 1). VAS pain scores were significantly less in the pethidine group than in the morphine group at 30 min and 1 and 2 h after operation ($P < 0.05$), but significantly greater at 12 and 24 h ($P < 0.05$).

Eight patients in the pethidine group, 13 patients in the morphine group and all patients in the placebo group required supplementary analgesia after operation ($P < 0.05$). The differences between the groups in mean analgesic consumption were not significant (table 2).

Discussion

The results of this investigation concur with previous studies in that intra-articular opioids were found to improve postoperative pain scores after arthroscopic surgery of the knee joint [9–11]. The local anaesthetic effect of pethidine is well recognized. It has been used for central block as the sole intrathecal agent for Caesarean section [15, 16], prostatic and perineal operations [17, 18], and peripherally for i.v. regional anaesthesia (IVRA), both in conjunction with prilocaine [19] and alone in volunteers [20]. The study by Oldroyd, Tham and Power [20] indicated that a solution of 0.2% pethidine had significant local anaesthetic action; this concentration was used in the present study. The first pain scores in both the pethidine and morphine groups were comparable, and significantly lower than those in the control group ($P < 0.01$).

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Table 1 Patient characteristics and operative details (mean (SD or range) or number)

<table>
<thead>
<tr>
<th></th>
<th>Pethidine (n = 20)</th>
<th>Morphine (n = 20)</th>
<th>Saline (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>32.1 (18–57)</td>
<td>29.5 (18–48)</td>
<td>32.1 (18–57)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.5 (7.4)</td>
<td>75.8 (14.5)</td>
<td>75.8 (13.4)</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>15:5</td>
<td>17:3</td>
<td>15:5</td>
</tr>
<tr>
<td>Duration (min)</td>
<td>44.2 (16.1)</td>
<td>38.5 (13.6)</td>
<td>36.7 (10.8)</td>
</tr>
</tbody>
</table>

Table 2 Mean (SD) analgesic consumption and number of patients in each group requiring supplementary analgesia in the first 24 h after surgery. *P < 0.05 compared with saline group

<table>
<thead>
<tr>
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<th>Morphine (n = 20)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Pethidine (mg)</td>
<td>7.5 (14.3)</td>
<td>16.25 (14.7)</td>
<td>26.5 (19.3)</td>
</tr>
<tr>
<td>Mefenamic acid (mg)</td>
<td>375 (553.1)</td>
<td>475 (450.9)</td>
<td>850 (558.4)</td>
</tr>
<tr>
<td>No. patients requiring supplementary analgesia</td>
<td>8*</td>
<td>13*</td>
<td>20</td>
</tr>
</tbody>
</table>
sole anaesthetic agent for arthroscopy and found that it was possible to operate on the pethidine group by 19 min [21]. Analysis of our VAS pain scores indicated that the duration of local anaesthesia was 2–4 h. The duration of analgesia achieved in both groups in this study was greatly in excess of that which would have been expected after systemic absorption. The reason for such protracted antinociception remains unclear, but active metabolites such as morphine-6-glucuronide may be responsible, as pethidine lacks an active metabolite and has approximately one-third of the effective duration of analgesia as morphine.

There are several mechanisms whereby intra-articular opioids may mediate analgesia. Peripheral opioid receptors exist in inflamed tissue [8], and agonists acting here induce antinociception by attenuating the excitability of the input terminal. There may also be prevention of release of substance P and other excitatory transmitters from the peripheral endings of afferent nerve fibres. There is recent evidence of the existence of opioid receptors in synovial tissue, innervated by peptidergic neurones, susceptible to substance P [22, 23].

However, some recent studies have not demonstrated such effective analgesia from intra-articular opioids [4, 5]. The reasons for these differences may be reflected in the technique used in these studies. We have demonstrated that more effective analgesia is obtained if the tourniquet is left inflated for a minimum of 10 min after injection of the drugs [11]. This period probably represents the time required for interaction between the drug and the opioid receptor within the joint. Another important factor is the volume and dose of analgesic administered, as a higher concentration of opioid in a lower volume appears to increase the speed of onset [10, 11]. Although there were no significant differences in mean supplementary analgesic requirements between the three groups, more patients in the control group needed additional analgesia during the 24 h after surgery. The sample size was determined using difference in pain scores as the primary variable. Had the size of the groups been larger, a significant reduction in analgesic consumption may have been seen. However, the trend towards lower analgesic requirements in the study groups was associated with significantly improved pain scores.

There are several possible mechanisms, other than a local anaesthetic effect, which may explain the difference in analgesic effect between morphine and pethidine when administered intra-articularly. Although a 10:1 potency ratio between the two drugs is commonly accepted for systemic analgesic effects, this ratio may not accurately reflect the situation of intra-articular injection. Ideally a dose-response curve for each drug should be constructed, and the optimal doses compared. Similarly, pharmacodynamic differences may exist at peripheral opioid receptors. Although it has been demonstrated that absorption of morphine after intra-articular injection results in inadequate plasma concentrations to provide systemically mediated analgesia [11], significant absorption of pethidine may occur because of its higher lipid solubility.

Ekbloom’s group reported intraoperative dizziness in approximately one-third of patients after intra-articular injection of pethidine 200 mg [21]. Plasma concentration were not recorded in that study, but it is plausible that substantial plasma and CNS concentrations may have been reached. However, as local anaesthetic agents are effective analgesics intra-articularly, and pethidine does exert a local anaesthetic effect, it seems likely that this mechanism is at least partly responsible for analgesia. It is possible that pethidine’s early analgesic effect may be due to a combination of systemic absorption, peripheral opioid receptor occupancy and local anaesthesia. A further study comparing groups receiving intra-articular pethidine, bupivacaine or parenteral pethidine may help to resolve these questions.

In conclusion, this paper has demonstrated the efficacy of intra-articular morphine and pethidine. It seems likely that pethidine does exert a local anaesthetic effect at joint level, but because of its ephemeral nature it is unlikely to supersede morphine for clinical use.

Acknowledgement

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References

14. Power I, Brown DT, Wildsmith JAW. The effect of fentanyl,


