Alkalinization of local anaesthetic for intra-articular instillation during arthroscopy

C. E. Richmond

SUMMARY

Intra-articular instillation of a local anaesthetic agent for pain relief after arthroscopy has not been shown consistently to be beneficial. Alkalinization of a local anaesthetic agent may be expected to improve onset time, quality and duration of the block. In a prospective, double-blind, randomized, placebo-controlled study, we have examined the effect of 1% prilocaine 20 ml, plain or alkalinized, or saline, instilled into the knee joint after arthroscopy. Linear analogue scale (LAS) pain scores were assessed at six times after operation and time to first request for analgesia, total analgesic consumption and times to walking unaided and normal activities were recorded. There were no differences in any of these measurements at any time between the groups, except that the group which received intra-articular saline had significantly lower pain scores 8 h after operation than the groups which had alkalinized or plain prilocaine. We conclude that prilocaine, at both pH values, is ineffective in producing postoperative analgesia but as there were patients who received no analgesic agents and who had very little pain, we may also conclude that arthroscopy is not a consistently painful procedure and is not a good model for assessing the efficacy of local anaesthetic agents. (Br. J. Anaesth. 1994; 73: 190–193)

KEY WORDS


Arthroscopy of the knee is commonly performed as a day-case procedure and this requires good pain relief so that patients may go home within a few hours of surgery. Opioid agents are given frequently but are not ideal for day-case surgery because of sedation, nausea and vomiting. Local anaesthetic agents are therefore used often, either intra-articularly, s.c., or both. Despite many studies of the efficacy of this practice, there is little evidence of conclusive benefit [1–11]. Maneuvers to improve the analgesic efficacy of local anaesthetic agents have included using a greater dose [5], placing the agent in a different site in the knee [6, 7], adding adrenaline [8, 9] and adding morphine [10, 11]. Another measure of improving local anaesthetic efficacy is alkalinization, which has been used successfully in other situations, but not intra-articularly [12–20]. The rationale for alkalinization of a local anaesthetic agent is to bring its pH closer to the pKₐ of the drug so that more local anaesthetic agent is un-ionized and therefore able to reach the site of action. This should reduce onset time and improve the quality of the block.

There has been much concern about toxicity from the use of intra-articular bupivacaine because of the vascularity and absorptive potential of the synovium and low therapeutic ratio of bupivacaine [21–28]. Four studies [22, 23, 25, 26] have shown plasma concentrations > 1.1 µg ml⁻¹, a concentration which has produced generalized convulsions in a healthy patient [29]. Prilocaine is considerably less toxic than bupivacaine and has previously been used successfully as the sole anaesthetic agent for arthroscopy [30]. In addition, bupivacaine cannot be alkalinized beyond pH 7.0 because of precipitation and, as its pKₐ is 8.1, only 15% of the drug can be converted to its un-ionized form. On the other hand, prilocaine is stable in solution at pH values near its pKₐ of 7.7 so that about 50% of the drug is un-ionized. We have therefore used prilocaine rather than bupivacaine to assess, in a prospective, double-blind, randomized, placebo-controlled study, the efficacy of alkalinization of the drug for instillation into the knee joint after arthroscopy.

PATIENTS AND METHODS

The study was approved by the hospital Ethics Committee. Sixty-six patients (ASA I or II) gave written informed consent and were instructed in the use of the linear analogue scale (LAS) to assess pain (0 mm = no pain, 100 mm = worst pain imaginable). All patients were unpremedicated and received a standardized general anaesthetic comprising induction with a dose of propofol sufficient to obtund the eyelash reflex and maintenance with spontaneous respiration of isoflurane and 70% nitrous oxide in oxygen. Opioids or non-steroidal anti-inflammatory drugs were not given.

Patients were allocated randomly by means of sealed envelopes to receive saline 20 ml, 1% prilo-
Table I. Patient characteristics (mean (SEM or range)) and type of operations (number) in the three groups

<table>
<thead>
<tr>
<th></th>
<th>Saline group</th>
<th>Prilocaine</th>
<th>Alkalinized</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex (M:F)</strong></td>
<td>12:7</td>
<td>12:7</td>
<td>14:5</td>
</tr>
<tr>
<td><strong>Age (yr)</strong></td>
<td>38.42 (18-77)</td>
<td>42.74 (25-72)</td>
<td>39.05 (21-77)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>73.05 (3.66)</td>
<td>76.95 (3.73)</td>
<td>73.21 (3.01)</td>
</tr>
<tr>
<td><strong>Duration of operation (min)</strong></td>
<td>30.26 (2.31)</td>
<td>22.42 (1.95)</td>
<td>25.21 (3.44)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Meniscectomy</th>
<th>Diagnostic</th>
<th>Synovial biopsy</th>
<th>Curettage patella</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>10</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Prilocaine plain</td>
<td>6</td>
<td>9</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Prilocaine alkalinized</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

As soon as possible after waking, patients recorded pain on a LAS and were asked if they required analgesia. If pain was described by the patient as "severe", ketorolac 30 mg i.m. was given, if "mild" or "moderate", two co-proxamol tablets were given, and if patients said they had no pain, no drug was given until requested. The time of the first requirement for a systemic analgesic agent was noted, hereafter referred to as time to first analgesia. LAS pain scores were repeated after the physiotherapist had mobilized each patient, after the journey home and at 4, 8 and 24 h after operation. Patients were discharged with sufficient co-proxamol for 48 h, told to take them only when needed and asked to record those times on the score sheet. In addition to pain scores and analgesic consumption, patients were asked to record when they were able to walk unaided and when they were back to their normal activities before returning the score sheet.

Significance was tested by parametric one-way and two-way ANOVA and unpaired two-tailed Student's t tests where appropriate. Two-way ANOVA was used because there were more males than females in all groups and there were not identical numbers of each type of operation in each group, and therefore the results were adjusted for sex and type of operation. Times to first analgesia were transformed logarithmically before analysis as the original distribution was positively skewed because most patients requested analgesia soon after waking. A non-parametric one-way ANOVA, the Kruskal–Wallis test, was applied to times to walking and normal activities.

RESULTS

Questionnaires were returned by 57 patients (86.4%), 19 in each group. There were significantly more men than women in all groups but there were no significant differences in patient age, weight or duration of operation between groups and when adjusted for sex difference (table I).

The types of operation performed in each group are listed in table I and the trend for slightly longer operations in the saline group, although not significantly so, may be explained by the greater number of meniscectomies in this group. After adjusting for different types of operations in each group using two-way ANOVA, there were still no significant differences in age, weight or duration of operation between the groups.

There were no significant differences between groups after adjusting for sex and type of operation in mean LAS pain scores on waking, after physiotherapy, after the journey home and 4, 8 and 24 h after operation in the saline ( ), plain prilocaine ( ) and alkalinized prilocaine ( ) groups.
There have been many studies of local anaesthetic regimens to relieve postoperative pain after knee arthroscopy [1–11, 21–26, 31]. Chirwa, Macleod and Day [1] showed that 0.25% bupivacaine 20 ml, injected intra-articularly at the end of the procedure, significantly reduced pain scores, morphine requirements and time to first request for analgesia compared with saline. Smith, Van Hemelrijck and White gave 0.5% bupivacaine 30 ml and showed a similar benefit [2]. Two further studies, however, showed no differences in pain scores between 0.25% bupivacaine 30 ml or saline intra-articularly [3, 4]. Doubling the dose of bupivacaine did not improve pain scores or reduce analgesic consumption [5]. A comparison of intra-articular and s.c. bupivacaine showed that the s.c. route was no better than saline but 0.25% bupivacaine 40 ml intra-articularly significantly reduced pain and analgesic use [6]. However, a comparison of femoral nerve block and intra-articular bupivacaine showed that femoral nerve block was better at relieving postoperative pain [7]. Addition of adrenaline to the local anaesthetic produced better pain relief in one study [8] but not in another [9], although the studies did not compare the agent with and without adrenaline. Intra-articular morphine has been found to be no better than saline in two studies [10, 11] although one showed an increase in the time to first request for analgesia but no difference in pain scores [10]. Both these studies found intra-articular bupivacaine to be superior to morphine or saline. Joshi and colleagues compared intra-articular morphine 5 mg with saline, but not a local anaesthetic agent, in knee arthroscopy and found reduced pain scores and consumption of analgesic agents in the group which had morphine [31].

Studies on the effect of alkalinization of bupivacaine are conflicting. Reduction in onset time and increased duration of analgesia were found with alkalinized extradural bupivacaine in labour [12], in brachial plexus block [13] and sciatic nerve block [14]. However, no benefit was found in other studies of alkalinized 0.5% bupivacaine for extradural anaesthesia [15], brachial plexus anaesthesia [16], intercostal nerve block [17] or lower extremity conduction anaesthesia [18]. Alkalinized 0.5% prilocaine was used in 10 volunteers for i.v. regional anaesthesia (IVRA) with decreased onset time, longer duration of analgesia and preference for the alkalinized solution [19]. When 0.75% prilocaine was used for IVRA in 80 patients, alkalinization did not affect onset time but gave significantly less pain on injection, during surgery and 5 min after surgery [20].

In this study we did not show any benefit of alkalinization of prilocaine for instillation into the knee joint after arthroscopy. There were no differences in mean pain scores between the groups at any time except 8 h after operation when intra-articular saline was significantly better than prilocaine. Also, there was no benefit in terms of pain, mobilization or activity with intra-articular prilocaine, whether alkalinized or not, despite a previous study showing benefit with prilocaine in 60 patients for arthroscopy under local anaesthesia [30]. These findings suggest that arthroscopy is not a particularly painful procedure as pain scores in those patients who had no analgesic agent after operation (three in the saline group, one in the prilocaine group and two in the alkalinized group) were low. Thus any potentially analgesic intervention was unlikely to reduce pain scores or analgesic consumption further. There was no difference in the degree of pain between types of operations traditionally thought to be more or less painful, such as meniscectomy and simple diagnostic arthroscopy.

REFERENCES


15. Stevens RA, Chester WL, Schubert A, Brandon D, Clayton B, Spitzer L. pH adjustment of 0.5% bupivacaine has no effect on epidural anesthesia. *Regional Anesthesia* 1989; 14 (Suppl.): 2S, 60.


