ANALGESIA AFTER HIP REPLACEMENT SURGERY: COMPARISON OF NALBUPHINE WITH MORPHINE

J. P. H. FEE, M. M. BRADY, G. FURNESS, M. CHAMBERS AND R. S. J. CLARKE

Nalbuphine hydrochloride is a semi-synthetic agonist-antagonist opioid analgesic with a low potential to induce respiratory depression [1, 2]. Its analgesic potency has been reported as 0.5-0.9 that of morphine [3, 4]; it has been used with some success in the management of pain after a variety of surgical procedures [3-5]. The analgesic effect of nalbuphine in the treatment of pain after hip replacement has not been evaluated fully; we report a comparative study of the analgesic and sedative effects of nalbuphine and morphine in patients undergoing this procedure.

METHOD AND RESULTS

Following approval by the local Medical Ethics Research Committee and after informed consent, we studied 80 patients (ASA grades I or II) who were not receiving opioid, sedative or antidepressant therapy. Each patient received either nalbuphine 0.3 mg kg\(^{-1}\) or morphine 0.15 mg kg\(^{-1}\) by random allocation on a double-blind basis. One hour before operation each patient received premedication with 0.03 ml kg\(^{-1}\) of the coded drug by i.m. injection into vastus lateralis. The drug concentrations were 10 mg ml\(^{-1}\) and 5 mg ml\(^{-1}\) for nalbuphine and morphine, respectively.

Anaesthesia was standardized and consisted of thiopentone, pancuronium and isoflurane and nitrous oxide in oxygen. Opioids were not given during operation. All patients received Dextran 70 during surgery with additional i.v. fluids and blood products as required. Systemic arterial pressure, heart rate and ECG were monitored continuously.

Immediately after operation, the residual analgesic effect was assessed by a trained nurse observer who was not informed of the treatment used. As soon as a patient expressed a need for analgesia, a second dose of the same coded drug was administered by the observer and additional assessments made at 30-min intervals for 2 h and at 1-h intervals thereafter up to 6 h. If analgesia proved unsatisfactory after a second injection, a third dose of coded drug could be given after a minimum of 3 h. Inadequate pain relief within 3 h of each postoperative injection was deemed "failed analgesia" and patients were given morphine to provide effective analgesia.

Pain intensity was assessed by the patient as nil, moderate or severe. Analgesia was assessed by the nurse observer and graded as slight, moderate or complete. At the same time, sedation was assessed
TABLE 1. Number of patients receiving nalbuphine (n = 40) or morphine (n = 40) with pain intensity (patient assessed) and analgesia (nurse assessed) at the postoperative times shown. N = Nalbuphine; M = morphine

<table>
<thead>
<tr>
<th>Time after operation (h)</th>
<th>N</th>
<th>M</th>
<th>N</th>
<th>M</th>
<th>N</th>
<th>M</th>
<th>N</th>
<th>M</th>
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</thead>
<tbody>
<tr>
<td>Pain intensity</td>
<td></td>
<td></td>
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<tr>
<td>Severe</td>
<td>34</td>
<td>32</td>
<td>16</td>
<td>5</td>
<td>15</td>
<td>4</td>
<td>14</td>
<td>5</td>
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<tr>
<td>Moderate</td>
<td>0</td>
<td>0</td>
<td>14</td>
<td>24</td>
<td>12</td>
<td>15</td>
<td>14</td>
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<tr>
<td>None</td>
<td>6</td>
<td>8</td>
<td>10</td>
<td>11</td>
<td>13</td>
<td>21</td>
<td>12</td>
<td>20</td>
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<tr>
<td>Analgesia</td>
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<tr>
<td>Slight</td>
<td>33</td>
<td>29</td>
<td>14</td>
<td>4</td>
<td>12</td>
<td>4</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Moderate</td>
<td>1</td>
<td>3</td>
<td>14</td>
<td>22</td>
<td>13</td>
<td>12</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Complete</td>
<td>6</td>
<td>8</td>
<td>12</td>
<td>14</td>
<td>15</td>
<td>24</td>
<td>18</td>
<td>24</td>
</tr>
</tbody>
</table>

by the observer and recorded as fully awake, drowsy, very drowsy or asleep. Nausea and vomiting occurring during the study period were noted. Differences between the two treatments were assessed using Mann–Whitney U tests and Fisher's Exact Test.

There were no significant differences between the two treatment groups in respect of age, weight, gender or duration of operation. Of the 80 patients studied, six who received nalbuphine and eight who received morphine did not require further analgesia during the study period. For statistical purposes these were graded as having no pain. In contrast, analgesia "failed" in 10 of those who received nalbuphine compared with only two in the morphine group (P < 0.05). These 12 patients were graded as having severe pain during the study period.

Morphine reduced pain intensity (assessed by patient) to a greater extent than nalbuphine at 2 and 3 h (P < 0.02); at 1 h, three times as many of those with severe pain had received nalbuphine rather than morphine (table I). Analgesia (assessed by nurse) showed a similar trend in favour of morphine. There were no significant differences in sedation scores between the drugs. At 1 h, 15 of the nalbuphine group and 11 of the morphine group were either very drowsy or asleep, but by 2 h this had increased to 17 and 20 patients, respectively. Six patients in the nalbuphine and nine in the morphine group experienced emetic symptoms. These tended to occur early after nalbuphine and late after morphine (mean (SD) times of onset 0.8 (1.1) h and 2.7 (1.5) h respectively (P < 0.02)).

COMMENT

Intermittent i.m. injection of analgesic drugs is the standard method of providing postoperative pain relief outside the recovery ward. In this study of the analgesic efficacy of nalbuphine and morphine, the intensity of pain experienced by patients receiving nalbuphine was markedly greater than when morphine was given. This difference was apparent 1 h after the first postoperative injection and became more pronounced with time (table I). Thus at 2 h, 10% of the morphine group still had severe pain compared with 37.5% in the nalbuphine group. The times to peak plasma concentrations after the i.m. injection of nalbuphine and morphine have been shown to be similar, as have the elimination half-lives of the two drugs (approximately 5 h) [6]. Thus the differences in effect cannot be explained easily on a pharmacokinetic basis. Furthermore, the earlier onset of emetic sequelae in the nalbuphine group was accompanied by a marked lack of analgesic efficacy compared with morphine over the study period.

A recent study comparing the dose requirements of nalbuphine and morphine, when self-administered i.v. for postoperative pain, concluded that morphine 10 mg was equivalent to nalbuphine 15 mg [4]. Others have found a similar relationship in terms of peak analgesic effect [3].
Despite allowing for a potency of only 50% that of morphine, we found that nalbuphine was markedly less successful than morphine in alleviating postoperative pain following hip replacement surgery.

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REFERENCES


