Prevention of postoperative nausea and vomiting with transdermal hyoscine in children using patient-controlled analgesia

E. Doyle, G. Byers, L. R. McNicoll and N. S. Morton

SUMMARY

We have studied 40 children aged 6-14 yr undergoing abdominal surgery under general anaesthesia with extradural block; they were allocated randomly to receive transdermal hyoscine (loading dose 140 µg, followed by 5 µg h⁻¹) or placebo for the duration of postoperative analgesia with PCA morphine. There was a significant (P < 0.001) reduction in the incidence of postoperative nausea and vomiting in the treated group compared with the placebo group during the first 48 h after operation. The treated group also had a significantly increased incidence of sedation (P < 0.02) and dry mouth (P < 0.01). (Br. J. Anaesth. 1994; 72: 72-76)

KEY WORDS


Postoperative nausea and vomiting (PONV) occurs in 40-100% of patients [1-5]. The causes include the effects of premedicant drugs, anaesthetic agents, postoperative analgesics (especially opioids), the surgery itself and the susceptibility of the patient. PONV appears to be a significant problem in patients who use patient-controlled analgesia (PCA) for postoperative pain relief [6] and, although distressing for a number of children using this form of postoperative analgesia, PONV appears to be less of a problem in children using PCA than it is in adults [7-10].

Several agents with different modes of action are used commonly to treat PONV, including phenothiazines, butyrophenones, antihistamines, dopamine antagonists and anticholinergics. Children are sensitive to the extrapyramidal effects of some of these drugs [11].

The anticholinergic agent, hyoscine, has been shown to have an antiemetic effect when given i.m. [12, 13]. There is also a preparation of hyoscine in the form of a plaster for transdermal application (Scopoderm TTS (Ciba)) which contains hyoscine 1.5 mg. This releases hyoscine 140 µg soon after application, followed by 5 µg h⁻¹ for up to 72 h while the plaster is in place, giving an average absorption rate of hyoscine 500 µg in 72 h. The preparation has been shown to have a significant antiemetic effect in motion sickness [14-16]. Transdermal application of hyoscine offers potential advantages in the prevention of PONV. It produces steady, small plasma concentrations of hyoscine [17] and avoids the problems of a short half-life, brief duration of action and large peak plasma concentrations which occur after i.m. injection. In paediatric practice the avoidance of i.m. injections is a particular advantage [18].

We have undertaken a prospective, placebo-controlled, double-blind assessment of the efficacy of transdermal hyoscine in preventing PONV in children using PCA morphine after abdominal surgery.

PATIENTS AND METHODS

The study was approved by the local Ethics Committee and informed written consent was obtained from the parents of children participating in the study. We studied 40 children aged 6-14 yr undergoing abdominal surgery. Exclusion criteria included inability to operate a PCA machine, unsuitability for extradural anaesthesia and the use of centrally acting or antiemetic drugs within the previous 1 week. Based on previous studies showing the efficacy of this preparation of hyoscine in reducing PONV, we calculated a 90% probability of finding a difference between the groups which would be significant at the 5% level. Patients were instructed before operation in the use of a PCA machine for postoperative analgesia.

A standard anaesthetic technique was used for all patients. Premedication comprised diazepam 0.3 mg kg⁻¹ orally, 2-4 h before operation. Anaesthesia was induced with propofol 3 mg kg⁻¹ (plus lignocaine 0.2 mg kg⁻¹) and vecuronium 0.1 mg kg⁻¹. The trachea was intubated and the lungs ventilated with 67% nitrous oxide in oxygen, with 0.5-2.0% isoflurane as indicated clinically. The patient was
then turned to the lateral position and a single extradural injection of 0.25% bupivacaine 2 mg kg⁻¹ (maximum 75 mg) given in the lumbar region. At the end of surgery, residual neuromuscular block was antagonized with neostigmine and glycopyrronium in appropriate doses.

Patients were allocated randomly, by means of computer-generated randomization, to two groups of 20 patients. Group H (hyoscine) received a hyoscine patch and group P (placebo) received an inactive patch. After the induction of anaesthesia and before the start of surgery, patients in group H had a hyoscine patch applied to the skin in the left postauricular area and this was covered with an Elastoplast dressing. Patients in group P had the dressing alone applied to the postauricular skin.

Before the patient left the recovery area, the PCA machine was connected (Graseby PCAS). The solution used consisted of morphine 1 mg kg⁻¹ diluted in 50 ml of normal saline to give a dilution of 20 μg kg⁻¹ ml⁻¹. The PCA machine was attached to the side arm of a Cardiff one-way valve incorporated into the i.v. infusion cannula. The settings used were a bolus dose of 1 ml (20 μg kg⁻¹), with a lockout interval of 5 min. There was no background infusion. If necessary, the patient was given increments of morphine 50 μg kg⁻¹ in the recovery area.

After operation, the patient breathed air. We used a monitoring procedure described previously [19]; this involved a high dependency level of nursing care with hourly recordings of SpO₂, ventilatory frequency, sedation score, pain score and nausea score. The number of demands made and the volume of solution infused by the PCA machine were recorded hourly. PCA was discontinued when the patient was able to take oral analgesics and there was a consistent decline in analgesic use.

Pain was scored using a four-point, self-reporting score which has been validated previously [20]: 0 = no pain; 1 = not really sore; 2 = quite sore; 3 = very sore.

Children were not woken from sleep unless the nurse suspected oversedation; "A" was recorded on the chart at these times. Sedation was scored using a four-point scale: 0 = eyes open spontaneously; 1 = eyes open to speech; 2 = eyes open to shake; 3 = unrousable.

Nausea and vomiting were scored using a four-point scale: 0 = no nausea or vomiting; 1 = nausea only; 2 = vomited once in the past 1 h; 3 = vomited more than once in the past 1 h.

The patient was questioned on each day after operation for the presence of dry mouth and blurred vision. All assessments were made by staff who were unaware if the patient had received hyoscine or placebo.

Prochlorperazine was prescribed for use in both groups if an antiemetic was considered necessary to treat persistent nausea or vomiting. The hyoscine or placebo patches were removed at the time of discontinuation of PCA.

Results were analysed using the unpaired t test for patient data, the Mann-Whitney U test for pain scores and morphine consumption and chi-square tests for comparisons of events between groups.

### RESULTS

Patient data and details of surgery and morphine consumption are shown in Table I. Of the laparotomies performed, six in group H and seven in group P involved bowel surgery.

There was a significant reduction in the incidence of PONV in group H compared with group P (P < 0.001) during the period of postoperative use of PCA (Table II) (for the purposes of analysis, PONV was considered to be present if a nausea score other than 0 was recorded at the hourly recordings). There was a significant antiemetic effect of hyoscine in patients aged less than 10 yr and in those aged 10 yr or more. There was also a significant reduction in the number of patients who complained of PONV at any time during the postoperative period in group H (P < 0.05) compared with group P (Table II). Six patients in group P and three in group H vomited on one or more occasions.

When the antiemetic effect of hyoscine was analysed for each 24-h period of use there was a significant (P < 0.01) antiemetic effect during the first 24 h of use, a significant (P < 0.01) antiemetic effect in group H compared with group P during the second 24 h after operation and no significant antiemetic effect in group H compared with group P during the third 24 h after operation (Table III).

Two patients in group P received one dose each of prochlorperazine (Stemetil) i.v. during PCA usage.

There were no significant differences between the groups in pain scores at any time during the postoperative period.

#### Table I. Patient data and details of morphine consumption (mean (SD))

<table>
<thead>
<tr>
<th></th>
<th>Group H</th>
<th>Group P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>6/14</td>
<td>7/13</td>
</tr>
<tr>
<td>Age (months)</td>
<td>134 (76-169)</td>
<td>122 (86-171)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>39.5 (13.4)</td>
<td>36.9 (11.9)</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>101 (41)</td>
<td>108 (44)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>80 (36.4)</td>
<td>79 (40.4)</td>
</tr>
<tr>
<td>Duration of PCA use (h)</td>
<td>50 (9.9)</td>
<td>48 (14.6)</td>
</tr>
<tr>
<td>Morphine consumption (μg kg⁻¹ h⁻¹)</td>
<td>1410 (734)</td>
<td>1190 (872)</td>
</tr>
<tr>
<td></td>
<td>27.6 (12.5)</td>
<td>22.9 (11.0)</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nephrectomy</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Pyeloplasty</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mitrofanoff</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Reimplantation of ureters</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Bladder neck repair</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Laparotomy</td>
<td>6</td>
<td>11</td>
</tr>
</tbody>
</table>

#### Table II. PONV in groups H and P: incidence during PCA usage (assessed by hourly nausea scores) and at any time in the postoperative period. †For difference in group H compared with that in group P

<table>
<thead>
<tr>
<th></th>
<th>Group H</th>
<th>Group P</th>
<th>χ², P</th>
</tr>
</thead>
<tbody>
<tr>
<td>During PCA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>29</td>
<td>69</td>
<td>21.3, &lt; 0.001†</td>
</tr>
<tr>
<td>Absent</td>
<td>646</td>
<td>554</td>
<td></td>
</tr>
<tr>
<td>Any time after op.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>6</td>
<td>14</td>
<td>4.9, &lt; 0.05†</td>
</tr>
<tr>
<td>Absent</td>
<td>14</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>
Although the majority of nausea scores in our study were lower than 4% to 34% [7-10], compared with 38-82% in adults [6,21,22]. The incidence of PONV in groups H and P during the first, second and third 24-h periods after operation is shown in Table III. There was no significant difference between the groups in the number of occasions on which patients were considered to be excessively sedated (sedation scores of 2 = eyes open to shake; 3 = unrousable) was significantly (P < 0.02) greater for score 2 in group H (table IV). There were no sedation scores of 3 in either group.

There was no significant difference between the groups in the number of occasions on which SpO₂ readings less than 94% were recorded (table IV). One patient in group H was excluded from this analysis because he was receiving supplementary oxygen as a result of a pneumothorax produced during a nephrectomy. The number of occasions on which patients were considered to be excessively sedated (sedation scores of 2 = eyes open to shake; 3 = unrousable) was significantly (P < 0.02) greater for score 2 in group H compared with that in group P.

The use of propofol as an induction agent, followed by inhalation agents, causes less PONV than thiopentone [23-25] and it has been suggested that propofol has antiemetic effects [26]. Avoidance of preoperative opioid premedication and intraoperative opioids is likely to reduce total opioid consumption. An extradural block provides analgesia into the postoperative period and reduces the requirements for PCA morphine in the early postoperative period.

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It has been suggested that transdermal hyoscine should be applied several hours before surgery [27], so that therapeutic plasma concentrations are attained perioperatively. It is possible that a more marked antiemetic effect would have been found if we had done this rather than apply the patches at induction of anaesthesia. The time to first tolerating oral fluids is often regarded as a useful indicator of the duration and impact of PONV, but it is not a precise indicator, as it is influenced by individual ward routines, and for this reason was not adopted in our study.

Other studies of the efficacy of transdermal hyoscine in the prevention of PONV are contradictory. Two studies [21,22] used transdermal hyoscine in combination with PCA after intra-abdominal gynaecological surgery without regional block. The first [21] found a reduction in PONV immediately after operation and on the third day after operation. The treated group required 50% of the number of supplementary doses of antiemetic as those in the placebo group. Preoperative opioids were omitted and fentanyl was given during operation. The other study [22] found a significant antiemetic effect of transdermal hyoscine compared with placebo and a reduced need for supplementary droperidol in the treated group. There was no opioid premedication and fentanyl was given during operation.

Two studies [28, 29] in patients receiving extradural morphine for postoperative analgesia showed that transdermal hyoscine had a significantly greater antiemetic effect than placebo, with a reduced requirement for supplementary antiemetics. One of these [28] examined patients undergoing intra-abdominal gynaecological surgery with general anaesthesia and intraoperative extradural block and the other [29] was in women undergoing Caesarean section with extradural block.

Transdermal hyoscine has also been found to be effective after orthopaedic and plastic surgery [30]. In contrast, Koski and colleagues [31] found no effect of transdermal hyoscine on the incidence of PONV in female patients. However, this study was not well controlled. Tigerstedt, Salmela and Aromaa [32] also found transdermal hyoscine was no more effective than placebo or intraoperative droperidol in preventing PONV. In this study, a range of surgical procedures was involved, the hyoscine patch was applied only 50 min before surgery, an opioid premedication was given in addition to intra-
operative fentanyl, and postoperative analgesia was with i.m. opioids.

The finding of an increased incidence of dry mouth in our patients in group H is in keeping with operative fentanyl, and postoperative analgesia was.

Other studies have reported visual disturbances induced by hyoscine used for both travel sickness [14] and after operation [5, 21, 31–33]. We found no difference in the incidence of this symptom between groups H and P. This may be because children are less affected, or because this symptom is less troublesome to children.

Psychoisis has been reported after transdermal hyoscine [34, 35] in adults and children. It is unusual, and treated easily by removal of the patch and cleaning of the skin.

In summary, we have found a useful antiemetic effect of transdermal hyoscine during the first 48 h after operation in children undergoing abdominal surgery with balanced anaesthesia when postoperative analgesia was provided by PCA morphine. Use of the hyoscine patch was associated with an increase in the incidence of sedation and dry mouth.

ACKNOWLEDGEMENT

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REFERENCES

