EFFECT OF PREMEDICATION WITH DIAZEPAM, MORPINE OR NALBUPHINE ON GASTROINTESTINAL MOTILITY AFTER SURGERY

M. SHAH, M. ROSEN AND M. D. VICKERS

SUMMARY

Premedication with nalbuphine and morphine delayed gastric emptying in the period after operation, but oral diazepam did not. All three drugs delayed co-ordinated intestinal motility, although nalbuphine did so for less than half as long as morphine. This property of nalbuphine, if confirmed, could make it a valuable analgesic drug in the period after operation.

Opioid analgesics and diazepam are administered frequently before surgery. However, opioid drugs delay the rate of gastric emptying when administered during labour (Nimmo, Wilson and Prescott, 1975), and in the period after operation (Nimmo et al., 1978; Ingram and Scheiner, 1981). Diazepam by mouth has also been shown to depress gastric and intestinal motility (Brinbaum, Ben Menachem and Schwartz, 1970). The effect of these drugs when used for premedication is less clear. We have investigated whether a single premedicant dose of diazepam, nalbuphine (an agonist antagonist opioid) or morphine (an agonist opioid) delays gastric emptying or affects intestinal motility in the period after surgery.

PATIENTS AND METHODS

Forty female patients aged 20 – 60 yr and undergoing uterine curettage were studied. None had clinical evidence of gastrointestinal disease; nor were they receiving any medication. Patients were admitted the day before operation and gave informed consent for the procedure. They were allocated randomly to one of five groups: three treatment groups and two control groups:

Group 1. Five patients received diazepam 0.2 mg kg

-1 by mouth 2 h before surgery.

Group 2. Ten patients received nalbuphine 0.2 – 0.3 mg kg

-1 i.m. 1 h before surgery.

Group 3. Ten patients received morphine 0.15 – 0.2 mg kg

-1 i.m. 1 h before surgery.

Group 4. A control group of five patients who had no anaesthetic or medication. Gastric emptying was measured after overnight fasting.

Group 5. Ten patients who acted as controls for co-ordinated bowel action. They were asked to note the time when flatus was first passed passively while resting in bed after overnight fasting.

In groups 1 – 3 the time between arrival in the recovery room and first passing flatus passively was used as a measure of the frequency of purposeful intestinal motility. The nearest practical approximation in the control group (5) was the time interval between 6 a.m. and first flatus. The hour of 6 a.m. was chosen because patients on the wards were awakened at about this time.

Anaesthesia was induced with thiopentone 3 – 4 mg kg

-1 and maintained with nitrous oxide and halothane in oxygen. No myoneural blocking drugs, opioid analgesic drugs or vagolytic drugs were given.

The rate of gastric emptying was assessed by measuring the plasma concentrations of paracetamol after oral intake. This drug is not absorbed until it reaches the small intestine. In groups 1, 2 and 3, paracetamol 20 mg kg

-1 (in tablet form) with 50 ml of water was given as soon as the patient returned to the ward after the anaesthetic. In group 4 the paracetamol was administered after an overnight fast.

Eating or drinking was not permitted for 4 h. Venous blood samples were taken at 30, 50, 70, 90, 110, 130 and 150 min after ingestion of paracetamol. All the patients rested in bed during the period of the study. Plasma paracetamol concentrations were measured by gas-liquid chromatography (Prescott, 1971; Clements et al., 1978). For each patient the chromatograph was calibrated as follows: five known concentrations of paracetamol in blood were analysed and a "best fit" calibration straight line drawn through zero. The residual standard devia-

© The Macmillan Press Ltd 1984
TABLE I. Plasma paracetamol concentrations (μg ml⁻¹) (mean values ± SEM)

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>30</th>
<th>50</th>
<th>70</th>
<th>90</th>
<th>110</th>
<th>130</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5</td>
<td>13.9 (5.52)</td>
<td>22.8 (7.04)</td>
<td>12.7 (3.73)</td>
<td>6.3 (3.86)</td>
<td>8.6 (2.42)</td>
<td>7.8 (2.25)</td>
<td>3.4 (2.27)</td>
</tr>
<tr>
<td>Diazepam</td>
<td>5</td>
<td>17.2 (3.78)</td>
<td>16.9 (3.91)</td>
<td>14.6 (2.97)</td>
<td>9.0 (2.59)</td>
<td>7.9 (2.19)</td>
<td>3.2 (2.11)</td>
<td>3.8 (2.11)</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>10</td>
<td>1.8 (1.82)</td>
<td>3.6 (2.63)</td>
<td>3.3 (2.28)</td>
<td>3.5 (2.69)</td>
<td>5.3 (2.04)</td>
<td>5.9 (2.58)</td>
<td>5.3 (1.83)</td>
</tr>
<tr>
<td>Morphine</td>
<td>10</td>
<td>3.2 (2.95)</td>
<td>5.0 (2.94)</td>
<td>9.4 (4.30)</td>
<td>8.9 (2.23)</td>
<td>9.5 (2.08)</td>
<td>9.0 (2.05)</td>
<td>9.0 (2.05)</td>
</tr>
</tbody>
</table>

Patients in groups 1, 2, 3 and 5 were reminded repeatedly to note the time to the nearest 5 min that they first passed flatus. The abdomen of each patient was auscultated 30 and 60 min after arrival in the recovery room (in groups 1, 2 and 3) or at about 6.30 a.m. and 30 min later (in group 5).

The plasma paracetamol concentrations in groups 1 – 4 were compared by one-way analysis of variance at each sampling time. The time intervals to first flatus (TFF) in groups 1, 2, 3 and 5 were compared similarly.

RESULTS

The mean age was 40.1 yr (SEM 1.5) and was similar in all groups.

Mean plasma paracetamol concentrations are shown in figure 1 and table I. The peak plasma paracetamol concentrations occurred about 50 min
after administration in the control group and in those who had received diazepam by mouth. The rate of gastric emptying in these two groups was similar. No clear peak paracetamol concentration occurred in those premedicated with nalbuphine or morphine, in whom there were comparable delays in gastric emptying rate ($P < 0.01$ compared with control).

The mean TFF in the control group was 1.88 h (table II). In all premedicated patients this time was significantly longer than in the controls ($P < 0.01$). There was no significant difference between those premedicated with diazepam or nalbuphine, but in those who had morphine the TFF was significantly longer than in those who received either of the other drugs.

Bowel sounds were heard on auscultation in all patients at 30 min and 60 min after the end of anaesthesia.

**DISCUSSION**

Nausea and vomiting as well as intolerance to oral fluids are problems still encountered in the period after operation, even after minor surgical procedures. Apart from being uncomfortable for the patient, these symptoms may contribute significantly to the risk of aspiration of gastric contents during recovery from anaesthesia.

In this study, morphine and nalbuphine administered as preoperative medication delayed gastric emptying equally after surgery. Oral diazepam did not have this effect. This latter finding is not in agreement with the findings of Birnbaum, Ben Menachem and Schwartz (1970), who measured gastric emptying in volunteers with duodenal ulcers by following the passage of barium, but is similar to the findings of Todd and Nimmo (1983).

There is little information about the effects of opioids on intestinal motility in man. Pentazocine (an agonist antagonist) moderately depressed colonic motility in volunteers although the duration of this effect, an important aspect, was not reported (Danhof, 1967).

In the early phase of this study another measure of intestinal motility was attempted. Volunteers were given oral salazopyrine and the level of sulphapyridine was measured in venous samples at 2-h intervals. Salazopyrine is converted into sulphapyridine by bacteria in the caecum. This method was abandoned because the appearance of sulphapyridine was very variable even in controls, with peak concentrations spread out over 4–6 h. Moreover, sulphapyridine interfered with the measurement of paracetamol concentrations. Therefore, we sought another measure. Bowel sounds are an unreliable indicator of purposeful bowel movement after non-abdominal surgery. However, passing flatus is an accepted clinical indication of purposeful intestinal motility after surgery. This phenomenon has not hitherto been used to compare drug effects.

In this study, this time was prolonged, regardless of the type of premedication. However, there was a markedly greater delay with morphine and relatively less delay with nalbuphine. This cannot be attributed to differences in pharmacokinetics: the elimination half-life of morphine in females is 110 min (Rigg et al., 1978) and about 300 min for nalbuphine (Errick and Heel, 1983).

This suggests that nalbuphine has less effect than morphine in depressing bowel activity, but further studies are required to determine the precise reason for this difference. If confirmed, this would be of substantial importance in the choice of an analgesic for use after surgery.

**REFERENCES**


