A DOUBLE-BLIND COMPARISON OF THE ANTI-EMETIC EFFECT DURING LABOUR OF METOCLOPRAMIDE AND PERPHENAZINE

BY

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SUMMARY

The anti-emetic properties of metoclopramide were investigated by means of a double-blind trial in normal labour in 584 women. The drug was also compared with an established anti-emetic drug, perphenazine. All patients were given pethidine as an analgesic. The incidence of vomiting after metoclopramide 10 mg or perphenazine 5 mg was significantly less than after normal saline. The incidences after perphenazine and metoclopramide were not significantly different. In the three groups studied there was no difference in the parity, length of labour, mode of delivery or Apgar score of the babies.

Metoclopramide (Maxolon) is an anti-emetic pharmacologically unrelated to any other compounds in therapeutic use. It has been found effective in the treatment of nausea and vomiting in a wide variety of conditions. Its use in labour has not previously been reported. The drug has been used for conventional premedication and in the treatment of postoperative vomiting. Bauer (1966) found evidence of an anti-emetic effect of metoclopramide in connection with surgery and Klein, Militello and Ballinger (1968) found a significant anti-emetic action to apomorphine challenge when metoclopramide 0.15–0.3 mg/kg was administered intramuscularly to human volunteers. Handley (1967) showed that intramuscular injection of metoclopramide 20 mg was significantly superior to a placebo in preventing postoperative nausea and vomiting. Jacoby and Brodie (1967), working with dogs, monkeys and rats, found that the drug relieved spasm of the stomach and pyloric sphincter, thus preventing gastric stasis.

In this investigation, a dose of 10 mg metoclopramide was selected as it was the lowest effective dose in human volunteers. Also, because the drug has not been found to have any significant sedative action by previous workers, it was thought that the risks of possible foetal sedation would be minimal.

Perphenazine (Fentazin) 5 mg has been used for the prevention of nausea and vomiting in labour for some years, having been available since Harer first described its use in 1958. However, undesirable side effects such as hypotension and extrapyramidal symptoms have been reported (Heath and McGarry, 1967). The introduction of a new anti-emetic agent with a stimulating effect on propulsive peristalsis of the upper gastro-intestinal tract in man (James and Hume, 1968) seemed worthy of clinical trial in labour.

METHOD

Six hundred women were studied during labour. When analgesia became necessary, pethidine 100 mg was given by intramuscular injection, together with either metoclopramide 10 mg or perphenazine 5 mg, or normal saline 2 ml by the same route. Patients were allocated to one of the three regimes in accordance with random sequence tables. Only patients expected to have a vaginal delivery were included in the trial. Both the doctor and the midwife giving the anti-emetic agent did not know which treatment the patient was receiving. The code giving the names of the contents of the ampoules was not broken until the completion of the trial.

The facts recorded in each case were: parity, drugs given and time of administration, mode of delivery, duration of the three stages of labour, and Apgar score of the baby at 1 and 5 minutes after delivery.
TABLE I

Comparison of metoclopramide and perphenazine in labour. Parity, distribution and length of labour in the three treatment groups.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Primiparae</th>
<th>Multiparae</th>
<th>Primiparae</th>
<th>Multiparae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Metoclopramide</td>
<td>Perphenazine</td>
<td>Placebo</td>
<td>Metoclopramide</td>
</tr>
<tr>
<td>Numbers of patients in each group</td>
<td>100</td>
<td>94</td>
<td>93</td>
<td>96</td>
</tr>
<tr>
<td>Average length of labour (hr)</td>
<td>12.2</td>
<td>11.9</td>
<td>11.9</td>
<td>7.1</td>
</tr>
<tr>
<td>Estimated blood loss (ml)</td>
<td>260</td>
<td>220</td>
<td>231</td>
<td>221</td>
</tr>
<tr>
<td>Average total dose of pethidine (mg)</td>
<td>169</td>
<td>173</td>
<td>179</td>
<td>103</td>
</tr>
<tr>
<td>Forceps and ventouse delivery (%)</td>
<td>13</td>
<td>12</td>
<td>13</td>
<td>8</td>
</tr>
</tbody>
</table>

Any maternal side effects including the occurrence of vomiting were noted. Nausea and retching were not taken into consideration but any vomiting which occurred within 4 hours of administration of the drug was recorded. The same observer saw each of the patients in labour during the trial and was unaware of the drug given. Pethidine 100 mg was repeated when necessary but no further doses of the trial drugs were given.

RESULTS

Sixteen patients were excluded because Caesarean section was required during labour. These patients fell equally into all three groups. The parity, distribution and length of labour in all three groups was the same (table I) as was the amount of blood loss and the type of delivery. The Apgar score of the babies was also the same (table II).

The incidence of vomiting in the three groups is shown in table III. No difference could be detected between metoclopramide and perphenazine but with both drugs there was significantly less vomiting than with the placebo. Statistical analysis was carried out using a Chi-square test. Comparing perphenazine and metoclopramide, \( \chi^2 = 0.8; 0.8 > P > 0.7 \). Comparing metoclopramide and placebo, \( \chi^2 = 5.85; 0.02 > P > 0.01 \). Comparing perphenazine and metoclopramide and placebo, \( \chi^2 = 12.1; P < 0.001 \).

DISCUSSION

Vomiting in labour is a common problem; in this series, 14.1 per cent of the patients given pethidine and placebo vomited. Although the established anti-emetics used in labour in the dosage used have few side effects, Parkinsonism has occasionally been reported in pregnant patients who have been given phenothiazine derivatives and metoclopramide, although this was not seen in this series. The added advantage that metoclopramide increased gastric emptying rate made its use in labour attractive, especially as maternal death due
to inhalation of vomit is still a major problem (Arthure et al., 1969). This trial demonstrates that metoclopramide is an effective drug for reducing the incidence of vomiting in labour and it appears to carry no significant risks for either mother or baby. Metoclopramide is as effective as perphenazine, an anti-emetic drug long used for prevention of vomiting in labour. Further work to establish if gastric emptying time in labour is reduced by the administration of metoclopramide compared with other drugs is currently being carried out.

ACKNOWLEDGEMENTS

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REFERENCES


