EFFECTS OF GLYCOPRYROLOATE AND ATROPINE COMBINED WITH ANTACID ON GASTRIC ACIDITY

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SUMMARY

Glycopyrrolate, atropine or saline were administered i.v. with oral magnesium trisilicate 1 h before induction of anaesthesia to patients about to undergo Caesarean section. Both anticholinergics greatly reduced gastric acidity. It is suggested that glycopyrrolate should be used in combination with antacid therapy before obstetric anaesthesia and puerperal tubal ligation because of its prolonged duration of action, effect on gastric secretion and failure to cross the placental barrier.

Despite recent advances in anaesthesia and a great reduction in frequency of postoperative morbidity and mortality, aspiration of acidic gastric contents still accounts for a considerable number of deaths associated with obstetric anaesthesia. The eighth Confidential Enquiry into Maternal Deaths in England and Wales, 1973–1975 (Tomkinson et al., 1979) reported that 13 deaths were caused by inhalation of stomach contents. Nine of these patients had received routine antacid therapy and yet subsequently died of Mendelson's syndrome.

A competent anaesthetist using a safe technique, particularly during induction, with application of cricoid pressure and rapid tracheal intubation is obviously a prerequisite, but despite this, reduction in gastric acidity is still a valuable safeguard. Simple antacid regimes may not achieve sufficient neutralization of stomach contents in every patient and anticholinergic drugs and, recently, cimetidine have been assessed for ability to reduce gastric acidity. We report here the effects, in patients undergoing Caesarean section, of combined administration of antacid with either atropine or the newer quaternary ammonium anticholinergic, glycopyrrolate.

METHODS

Patients

Healthy female patients about to undergo elective Caesarean section were studied after giving consent. None was given drugs with pronounced anticholinergic activity in the preceding 24 h.

Anaesthetic technique

All patients received magnesium trisilicate mixture BPC 20 ml orally about 60 min before induction of anaesthesia. At the same time, they received 1 ml of either sodium chloride injection, atropine injection 0.4 mg ml⁻¹ or glycopyrrolate 0.2 mg ml⁻¹ i.v. Patients were allocated randomly to the three treatment regimes which were administered under double-blind conditions. Following preoxygenation, induction of anaesthesia was performed with methohexitone 1 mg kg⁻¹, cricoid pressure and suxamethonium 100 mg. An endotracheal tube was inserted and anaesthesia maintained with nitrous oxide and oxygen. Relaxation was maintained with alcuronium 15 mg. Immediately after delivery, ergometrine 0.5 mg was given to increase uterine tone and phenoperidine 2 mg to deepen the level of anaesthesia. Atropine 1.2 mg and neostigmine 5.0 mg were given to antagonize residual neuromuscular blockade at the end of the operation.

Assessment

Gastric juice was aspirated immediately after induction and immediately before antagonism of the neuromuscular block. Fetal heart rate was recorded with a Sonicaid before administration of the drug under study and at 10-min intervals until delivery; neonatal heart rate was measured 10 min after delivery. The Apgar score was recorded 1 min and 5 min after delivery.

RESULTS

One hundred and twenty-seven patients took part in the study; they were well matched for age, weight and time from administration to induction of the drugs under study (table I). Distribution of gastric pH and the mean values immediately
Table I. Details of the patients studied (mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Atropine</th>
<th>Glycopyrrolate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>42</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>29±1.1</td>
<td>28±0.7</td>
<td>27±0.9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72±1.4</td>
<td>72±1.6</td>
<td>73±1.7</td>
</tr>
<tr>
<td>Time from pre-med. to induction (min)</td>
<td>64±1.8</td>
<td>63±1.9</td>
<td>60±2.3</td>
</tr>
</tbody>
</table>

following induction and before antagonism of the neuromuscular block are shown in figure 1. The difference in frequency between both anticholinergic groups and the placebo group was significant \( (P<0.00001 \) after induction; \( P<0.005 \) before antagonism of neuromuscular block; Fisher's exact test). It was not possible to obtain gastric juice samples from every patient studied.

Fetal heart rate in both anticholinergic groups and the placebo group did not change significantly (mean change < 3 beat min⁻¹ from the pre-administration value). Similarly, there was no significant difference in mean neonatal heart rate or in Apgar scores between the three groups.

**DISCUSSION**

The present study has shown that the co-administration of atropine and glycopyrrolate with magnesium trisilicate provides acceptable gastric pH immediately before anaesthesia and after antagonism of neuromuscular blockade. It also confirms the unsatisfactory control of acidity produced by magnesium trisilicate alone which has been suggested previously (Peskett, 1973).

The overall frequency of patients in our study with a pH of less than 2.5 after having received magnesium trisilicate 20 ml (35%) is similar to that reported by Taylor and Pryse-Davies (1966) in a control series of patients (42%).

Reports on the effects of glycopyrrolate alone on gastric acidity is equivocal. Keating, Black and Watson (1978) showed that glycopyrrolate 0.4 mg i.m. given to non-obstetric patients 60 min before operation had very little effect on gastric pH. Similarly, Stoelting (1978) showed that administration of morphine and glycopyrrolate 0.2 mg was not significantly different from administration of morphine alone in decreasing gastric acidity immediately following induction. However, Baraka and others (1977) demonstrated in parturient patients that administration of glycopyrrolate 0.4 mg i.m. produced a reduction in gastric acidity which was significantly different from that produced by atropine.

These differences in published data are difficult to explain but may be related to differences in patients studied and routes of administration. Although Baraka and others (1977) found a significant effect of glycopyrrolate, the dose they used was twice that (0.2 mg) normally used for premedication and would be likely to produce an unpleasant antisialagogue effect for a considerable duration after operation. We administered antacid and anticholinergics together to determine any synergism which would permit reduction of the amount of anticholinergics administered before operation and to use a route of administration which provides complete availability of the drugs. In addition, we administered the anticholinergics 60 min before induction; a period which, according to Baraka and others (1977), is necessary to achieve maximum effect. The significant findings presented are in good agreement with those of Boatright and others (1970), who administered glycopyrrolate with a magnesium hydroxide–aluminium hydroxide antacid mixture to paediatric patients and showed marked
synergism between the two drugs. The samples with high gastric pH obtained in our placebo group may have resulted from regurgitation of duodenal contents into the stomach.

Although both atropine and glycopyrrolate were equally effective in the present study, glycopyrrolate possesses theoretical advantages in obstetric anaesthesia. Because it is a quaternary ammonium compound, it is highly lipophobic and penetrates with difficulty through lipid membranes such as the blood–brain and placental barriers. Proakis and Harris (1978) showed that, in the dog, a peak fetal serum: maternal serum concentration ratio of only 0.04 was achieved after the administration of glycopyrrolate, whereas this ratio was 1.0 after the administration of atropine. Heyman and others (1976) showed clinically that glycopyrrolate 0.4 mg administered to the mother had no significant effect on fetal heart rate, whereas the administration of atropine 0.8 mg produced a significant increase in fetal heart rate.

In conclusion, we have shown that both glycopyrrolate and atropine administered i.v. with oral magnesium trisilicate produce a more favorable gastric pH. On a theoretical basis, glycopyrrolate offers greater safety to the fetus and, having a longer duration of action, is thus the preferred anticholinergic agent for use in obstetric anaesthesia. Antacid therapy with magnesium trisilicate alone is unsatisfactory for use in routine premedication of obstetric patients and anaesthetists should administer an anticholinergic, preferably glycopyrrolate, i.v. 1 h before anaesthesia rather than giving it immediately before induction.

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REFERENCES


EFFETS DU GLYCOPRYROLATE ET DE L’ATROPIE COMBINES AVEC UN ANTACIDE SUR L’ACIDE GASTRIQUE

RESUME

Il a été administré du glycopyrrolate, de l’atropine ou de l’eau physiologique par voie intraveineuse, de même que du tri-silicate de magnésium par voie buccale, une heure avant l’induction de l’anesthésie à des patientes sur le point de subir une césarienne. Les deux anticholinergiques ont grandement réduit l’acidité gastrique. Ceci laisse penser que le glycopyrrolate doit être utilisé en combination avec un traitement antacide avant toute anesthésie pour une intervention obstétrique et pour toute ligature tubulaire puerpérile, en raison de sa durée prolongée, de son effet sur la sécrétion gastrique et du fait qu’il ne traverse pas la barrière placentaire.

AUSWIRKUNGEN VON GLYCOPRYROLAT UND ATROPIN IN VERBINDUNG MIT EINEM SÄUREBINDENDEN MITTEL AUF DIE MAGENSÄURE

ZUSAMMENFASSUNG


EFFECTOS DEL GLICOPYRROLATO Y DE LA ATROPINA EN COMBINACION CON ANTACIDO SOBRE LA ACIDEZ GASTRICA

SUMARIO

Se administraron intravenosamente glicopirrolato, atropina o soluciones salinas, junto con trisilicato de magnesio via oral,
una hora antes de la inducción de la anestesia a pacientes a punto de ser sometidos a sección de cesárea. Los dos anti-colinérgicos redujeron en gran medida la acidez gástrica. Se sugiere que el glicopirrolato debiera usarse en combinación con terapia antiácida antes de la anestesia obstétrica y de la ligación puerperal de los tubos, a causa de su prolongada actividad, su efecto en la secreción gástrica y de la inhabilidad para cruzar la barrera de la placenta.