EFFECTS OF GLYCOPRYRROLATE AND CIMETIDINE ON GASTRIC VOLUME AND ACIDITY IN PATIENTS Awaiting Surgery

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SUMMARY

Glycopyrrolate or cimetidine was administered before operation to patients undergoing elective surgery. After the induction of anaesthesia, the stomach contents were retrieved and the volume and pH measured. Neither drug diminished the volume of gastric contents compared with control. Glycopyrrolate produced little diminution in hydrogen ion concentration. Cimetidine caused a marked increase in pH with a mean $[H^+] = 3.2 \times 10^{-5}$ g litre$^{-1}$ compared with $1.4 \times 10^{-5}$ g litre$^{-1}$ in the controls and $1.1 \times 10^{-5}$ g litre$^{-1}$ in the glycopyrrolate group. Seventy-seven per cent of the patients receiving cimetidine had a pH greater than 2.5.

Mendelson (1946) showed that the exudative oedema, which is the principal pathological consequence of pulmonary aspiration of gastric contents, is a result of the irritant effect of acid. When the pH of the aspirate is greater than 2.5, the clinical course is less severe (Tebeaut, 1952; Cameron, Anderson and Zuydema, 1967).

Various methods of increasing the pH of gastric contents before the induction of anaesthesia have been tried (Taylor and Pryse-Davis, 1966; Crawford, 1971; Salem et al., 1976; Baraka et al., 1977; Hester and Heath, 1977). Anticholinergic drugs inhibit the production of gastric juice, but to a variable degree. However, they have a range of other effects—increasing heart rate, delaying gastric emptying and reducing the tone of the cardiac sphincter (Misiewicz, 1973).

Cimetidine is a recently developed receptor antagonist. It inhibits histamine-stimulated gastric acid secretion with no other significant effects (Circular, 1976).

We have measured the effects of an anticholinergic, glycopyrrolate, and cimetidine on the volume and pH of the gastric contents of adult patients awaiting surgery.

PATIENTS AND METHODS

The patients were undergoing general, orthopaedic, urological, gynaecological or plastic surgery at Tripler Army Medical Center. All gave informed consent to the study. Only patients who were to have a tracheal tube inserted were included. There were three random groups. All were given sedation before operation, most receiving hydroxyzine and pethidine, approximately 1 h before surgery. The control group (15 patients) received no other drug at that time. The second group (21) received glycopyrrolate 0.4 mg i.m. and the third group (31) had received cimetidine 300 mg orally on the night before surgery, and at 05.45 a.m. and 4-hourly thereafter until the time of the preoperative sedation; 24 patients received one morning dose and seven received two.

The control and cimetidine groups received atropine 0.4 mg i.v. immediately before induction of anaesthesia. The anaesthetic technique was not standardized, but in all patients anaesthesia was induced with thiopentone, and the trachea was intubated with the aid of suxamethonium, preceded by a small dose of tubocurarine. As soon as a stable anaesthetic state was obtained, an 18-FG-Salem nasogastric sump tube was passed into the stomach, and the gastric contents were aspirated using a 60-ml syringe. Auscultation over the epigastrium during the insufflation of 20 ml of air was performed to verify the position of the nasogastric tube in the stomach. Aspiration was performed with the patient supine, then tilted onto the left, and then the right side, and again in the head-down position in an attempt to empty the gastric contents as completely as possible (Hester and Heath, 1977). The volume of the samples was measured to the nearest 5 ml in a volumetric cylinder and the pH was measured using a calibrated Beckman pH Meter-Zeromatic SS-3.
RESULTS
The control group had an average gastric juice volume of 23 ml. Mean $[\text{H}^+]$ was $1.4 \times 10^{-2}$ g litre$^{-1}$ (table I), (pH 1.85). Sixty per cent of these had pH less than 2.5 (fig. 1, table II).

The patients premedicated with glycopyrrolate showed little difference from the control group. The average volume was 21 ml and mean $[\text{H}^+]$ was $1.1 \times 10^{-2}$ g litre$^{-1}$, (pH 1.94). Sixty-six per cent had pH less than 2.5.

The group premedicated with cimetidine showed no significant change in volume of gastric contents (mean zone), but a striking reduction in $[\text{H}^+]$, to $3.2 \times 10^{-3}$ g litre$^{-1}$ (pH 2.5). Twenty-three per cent of the patients in the group had pH less than 2.5.

Of the seven patients who received two doses of cimetidine, pH was less than 2.5 in only one.

DISCUSSION
Neither glycopyrrolate nor cimetidine reduced significantly the volume of the gastric contents compared with the controls.

In recent years, the desirability of increasing the pH of the gastric contents towards neutral has been established. A critical level of pH 2.5 has been proposed (Bannister and Satillaro, 1962), above which the sequelae of pulmonary aspiration are minimized; Crawford (1971) has suggested that 3.0 is more appropriate. Anticholinergic agents have been used in an attempt to increase pH of the gastric contents before surgery. Baraka and others (1977), in studying the effects of glycopyrrolate before Caesarean section, found that pH was greater than 2.5 in 66% of cases, whereas atropine produced no significant improvement. Salem and others (1976) found that in 58.1% of children premedicated with glycopyrrolate pH was greater than 2.5. In our study, however, we were unable to demonstrate that glycopyrrolate premedication increased the frequency of gastric pH in the “safe” range.

One weak point in all the investigations cited, including ours, is that the exact location of the gastric tube is not known. Salem and others (1976) found that in 25.4% of patients no gastric juice was obtained; these were included in the pH greater than 2.5 group. In only two of our 67 patients were we sufficiently sure of the location of the tube, in spite of there being no aspirate, to include the results in the study—one in each of the glycopyrrolate and cimetidine groups. The data from five patients were excluded because the location of the tube was in doubt.

In the cimetidine group, there was no reduction in volume of gastric contents, but 77% of these patients had pH values greater than 2.5. Cimetidine will stop the production of gastric acid, but will not influence the pH of the gastric contents already present. Antacid
therapy has been advocated to neutralize gastric acidity (Taylor and Pryse-Davis, 1966; Crawford, 1971), and it has been suggested that such prophylaxis should be routine (Hester and Heath, 1977), but antacid therapy produced "satisfactory" pH values in only 80% of obstetric patients in a study from Bristol maternity hospitals (White, Clark and Stanley-Jones, 1976).

Feldman and others (1977) have reported that an anticholinergic drug augments the inhibitory effects of cimetidine on gastric juice. The combination of antacid therapy, cimetidine and an anti-cholinergic may make a useful prophylactic regime in the preoperative neutralization of gastric acidity, but our results suggest that neither glycopyrrolate nor cimetidine will produce consistently "safe" gastric pH values in the routine surgical patient.

The pitfall in analysing data concerning pH of gastric juice without regard to their logarithmic nature has been pointed out by Tomlin (1978). If the pH values of our cimetidine group are averaged arithmetically, the mean is 5.2 instead of the value of 2.5 derived from averaging the hydrogen ion concentrations. However, the range of hydrogen ion concentrations in studies of gastric acidity is so large that analysis in terms such as standard deviation, which presupposes normal distribution, is not valid. This skewed distribution may be demonstrated most simply by noting the great difference between the mean and median values for hydrogen ion concentration in the cimetidine group and then noting the proximity of the mean and median values obtained by averaging pH values:

<table>
<thead>
<tr>
<th>pH</th>
<th>Mean value</th>
<th>Median value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>3.2 x 10^{-4} g litre^{-1}</td>
<td>6.3 x 10^{-1} g litre^{-1}</td>
</tr>
<tr>
<td>pH</td>
<td>5.2</td>
<td>6.2</td>
</tr>
</tbody>
</table>

It may be that, in studies of this nature, results expressed in terms of pH are more useful clinically. Inspection of the pH distribution histogram certainly suggests an "average" value of 5.2 rather than 2.5.

ACKNOWLEDGEMENTS

We wish to thank Col. Samuel A. Cucinell, M.D., Chief, Clinical Investigation Service, for advice in the preparation of this paper and for review of the statistics, and the nurse anaesthetists of the Anaesthesiology Service for technical assistance.

REFERENCES

WIRKUNGEN VON GLYCOPYRRONIUM-BROMID UND CIMETIDINE AUF DEN MAGENINHALT UND DIE MAGENSÄURE IN CHIRURGISCHEN PATIENTEN VOR DER OPERATION

ZUSAMMENFASSUNG

Glycopyrronium-Bromid und Cimetidine wurden an Patienten, die vor einer ausgewählten Operation standen, verabreicht. Nach der Narkoseeinleitung wurde der Magen ausgehoben und die Menge und die Wasserstoffionenkonzentration gemessen. Keine der beiden Drogen verminderte das Volumen des Mageninhalts, verglichen mit Kontrolluntersuchungen. Glycopyrronium-Bromid bewirkte nur eine sehr kleine Verringerung der Wasserstoffionenkonzentration. Cimetidine verursachte eine bemerkenswerte Erhöhung in der Wasserstoffionenkonzentration mit einem Durchschnittswert \([H^+]\) von \(3,2 \times 10^{-3}\) g liter\(^{-1}\) verglichen mit \(1,4 \times 10^{-2}\) g liter\(^{-1}\) in den Kontrolluntersuchungen, und \(1,1 \times 10^{-2}\) g liter\(^{-1}\) in der Glycopyrronium-Bromid Gruppe. Siebenundsiebzig Prozent der Patienten, die Cimetidine erhielten, hatten eine Wasserstoffionenkonzentration größer als 2,5.