ANTACID ANTICHOLINERGIC REGIMENS IN PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION

DAVID M. DEWAN, A. SCOTT WHEELER, FRANCIS M. JAMES III,
HERBERT M. FLOYD AND LEONARD RHYNE

ABSTRACT

The pH and volume of gastric contents were examined in 60 patients undergoing elective Caesarean Section under thiopentone, nitrous oxide-oxygen, succinylcholine anaesthesia. All patients received Gelusil® 30 ml per os preoperatively, while 20 were given atropine $7 \mu\text{g}\cdot\text{kg}^{-1}$ and another 20 glycopyrrolate $4 \mu\text{g}\cdot\text{kg}^{-1}$ intramuscularly along with Gelusil®. Following tracheal intubation, gastric fluid was sampled through an orally placed 18 French Salem Sump tube.

After Gelusil® alone, the mean gastric fluid pH was 4.54 ± 2.45 (SD) while it was significantly higher following the combined use of antacid and atropine (6.78 ± 1.20) or antacid and glycopyrrolate (6.42 ± 1.72), ($P < 0.01$). Differences in gastric fluid volume between the groups were insignificant.

All three regimens produced a gastric pH greater than 2.5 when given less than 75 minutes before sampling. When the premedication to sampling interval exceeded 75 minutes the addition of atropine or glycopyrrolate decreased the incidence of gastric pH less than 2.5 from 47 per cent in patients given Gelusil® alone to 6 per cent and 14 per cent, respectively. In comparison to Gelusil® alone, this difference was significant with atropine ($P < 0.05$) but not with glycopyrrolate. Atropine and glycopyrrolate respectively produced 6 per cent and 7 per cent incidences of pH lower than 2.5 combined with gastric volume greater than 25 ml, which were significantly lower than was observed with Gelusil® alone ($P < 0.05$).

This study demonstrates that the addition of atropine or glycopyrrolate to Gelusil® premedication provides additional protection against the consequences of aspiration, especially when the premedication to anaesthetic induction period is prolonged.

KEY WORDS: PREMEDICATION, antacid, atropine, glycopyrrolate; CAESAREAN SECTION, acid aspiration.

ASPIRATION of gastric contents remains a leading cause of maternal mortality. Recent maternal mortality statistics from Great Britain showed the risk of death from anaesthesia among parturients to be between 1/6000 and 1/7500 operations.¹ This death rate included 36 deaths associated with general anaesthesia of which 16 or 44 per cent involved aspiration of gastric contents. Since between 90 per cent and 100 per cent of these anaesthetic deaths had a preventable fac-

tor, clearly there remains much room for improvement in the area of aspiration.¹

Laboratory work indicates that the pH and volume of the aspirate are critical factors in determining the degree of pulmonary injury produced by aspiration.^{2,3} Gastric contents exceeding a volume of 0.4 ml/kg with a pH below 2.5 are more likely to cause sequelae if aspirated. Therefore, either increasing gastric pH or decreasing gastric volume improve the prognosis when aspiration occurs. Antacid therapy effectively increases gastric pH but does not always produce a pH above 2.5.⁴ The anticholinergic agent glycopyrrolate both raises pH and decreases gastric volume, but also does not always raise the pH above 2.5.⁵ We therefore examined the efficacy of combining glycopyrrolate with an antacid to determine whether this combination presents advantages over the use of either the antacid alone or over the more com-

David M. Dewan, M.D., Assistant Professor; A. Scott Wheeler, M.D., Associate Professor; Francis M. James III, M.D., Professor; Herbert M. Floyd, M.D., Assistant Professor; Department of Anaesthesia. Leonard Rhyne, Ph.D., Professor, Department of Family Practice and Community Medicine; Bowman Gray School of Medicine of Wake Forest University, Winston-Salem, North Carolina 27103 U.S.A.

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Requests for reprints to Dr. Dewan.

TABLE I
AGE, WEIGHT, AND PREMEDICATION TO SAMPLING INTERVAL IN PATIENTS GIVEN GELUSIL®, GELUSIL® PLUS ATROPINE, AND GELUSIL® PLUS GLYCOPYRROLATE. (n = 20 per group.)

	Gelusil	Gelusil + Atropine	Gelusil + Glycopyrrolate
Age (yrs)	24.7 ± 5.1	25.5 ± 5.7	27.6 ± 5.4
Weight (kg)	75.8 ± 13.9	75.9 ± 11.6	75.9 ± 16.1
Sampling Interval (min)	85 ± 17	84 ± 16	85 ± 18

Mean ± Standard Deviation

monly used anticholinergic, atropine, together with the antacid.

METHODS

Sixty healthy term parturients scheduled for elective Caesarean Section under general anaesthesia were included in the study after they had given informed consent. The Human Research Practices Committee approved the protocol. Twenty patients were assigned to each of three premedication regimens: one group received Gelusil®,* 30 ml by mouth; another group Gelusil 30 ml by mouth and atropine 7 µg·kg⁻¹ intramuscularly; and the third group Gelusil 30 ml by mouth and glycopyrrolate, 4 µg·kg⁻¹ intramuscularly. All premedications were given as close to 60 minutes preoperatively as possible.

Anaesthesia was induced with intravenous thiopentone 3 mg·kg⁻¹ and the trachea was intubated after an intravenous bolus of succinylcholine 1.2 mg·kg⁻¹. Nitrous oxide-oxygen (2:1) was then administered while muscle relaxation was maintained with an intravenous infusion of succinylcholine 0.1 per cent. Immediately after delivery of the baby a #18 Salem Sump tube was passed orally and the gastric content was aspirated as completely as possible with a 50 ml syringe. Patient groups were compared for age, weight, interval from premedication to gastric sampling time, gastric volume and pH† using analysis of variance and the Dunkins new multiple range test. The Fischer exact test was employed to determine the significance of the varying incidences. Significance was assumed when $P < 0.05$.

RESULTS

The groups were similar regarding age,

weight, and interval between premedication and sampling (Table I).

Gastric volume did not differ among the groups. Mean pH was lower with Gelusil® alone in contrast to when Gelusil was given with an anticholinergic drug ($P < 0.01$). Atropine and glycopyrrolate in combination with Gelusil produced similar elevations of pH.

Despite the mean pH in all three groups being well above 2.5, thirty-five per cent of patients who had received only Gelusil had a gastric pH less than 2.5. By comparison, the addition of atropine or glycopyrrolate decreased the incidence of pH less than 2.5 to 5 per cent and 10 per cent respectively (Table II). This difference was statistically significant for both atropine and glycopyrrolate.

The three drug regimens were effective for all patients in maintaining pH above 2.5 when the interval between premedication and sampling was less than 75 minutes. When the interval exceeded 75 minutes, 47 per cent of patients who had been given Gelusil had a pH less than 2.5, while the incidence when atropine and glycopyrrolate were used was six per cent and 14 per cent respectively (Table III). In comparison to the Gelusil group, the incidence of gastric pH less than 2.5 was significantly lower in the atropine ($P < 0.05$) but not in the glycopyrrolate group, even though the effects of atropine and glycopyrrolate were similar.

All but one of the patients with a pH less than 2.5 had a gastric volume exceeding 25 ml, which increases the danger of aspiration. The 40 per cent incidence of pH less than 2.5 combined with a volume exceeding 25 ml seen with Gelusil alone was significantly higher in comparison to the six per cent and seven per cent incidences seen with atropine or glycopyrrolate (Table III).

DISCUSSION

Indications for general anaesthesia in obstetrics persist. Aspiration of gastric contents may

*Gelusil® - Warner/Chilcott - each 5 ml contains 200 mg aluminum hydroxide, 200 mg magnesium hydroxide, 25 mg simethicone.

†Fischer Acumet pH Meter, Model 1212.

TABLE II

MEAN GASTRIC VOLUME AND pH ($\pm$ S.D.) AND INCIDENCE (PER CENT) OF GASTRIC pH LESS THAN 2.5 IN PATIENTS GIVEN GELUSIL® 30 ML BY MOUTH, GELUSIL® 30 ML BY MOUTH PLUS ATROPINE $7 \mu\text{g}\cdot\text{kg}^{-1}$ INTRAMUSCULARLY, OR GELUSIL® 30 ML BY MOUTH PLUS GLYCOPYRROLATE $4 \mu\text{g}\cdot\text{kg}^{-1}$ INTRAMUSCULARLY. (n = 20 per group)

	Gelusil	Gelusil+Atropine	Gelusil+Glycopyrrolate
Volume (ml)	37 $\pm$ 22	31 $\pm$ 18	26 $\pm$ 14
pH	4.54 $\pm$ 2.46†	6.78 $\pm$ 1.20	6.42 $\pm$ 1.72
pH < 2.5*	35% (7/20)‡	5% (1/20)	10% (2/22)

*Per cent of patients with gastric pH < 2.5 with (n) representing number of effected patients per group.

†p < 0.01, pH in Gelusil subjects versus pH in both Gelusil + anticholinergic groups.

‡p < 0.05, incidence of pH < in Gelusil® group versus incidence in Gelusil® + atropine and Gelusil® + glycopyrrolate groups.

TABLE III

INCIDENCE (PER CENT) OF GASTRIC pH LESS THAN 2.5 AND GASTRIC pH LESS THAN 2.5 COMBINED WITH GASTRIC VOLUME EXCEEDING 25 ML IN PATIENTS GIVEN GELUSIL® 30 MG BY MOUTH, GELUSIL® PLUS ATROPINE $7 \mu\text{g}\cdot\text{kg}^{-1}$, OR GELUSIL® PLUS GLYCOPYRROLATE $4 \mu\text{g}\cdot\text{kg}^{-1}$ WHEN PREMEDICATION TO SAMPLING INTERVAL EXCEEDS 75 MINUTES*

	Gelusil® (n = 15)	Gelusil+Atropine (n = 16)	Gelusil+Glycopyrrolate (n = 14)
pH < 2.5	47% (7/15)†	6% (1/16)	14% (2/14)
pH < 2.5 and Vol > 25 ml	40% (6/15)‡	6% (1/16)	7% (1/14)

*Incidence is reported as percent of patients with (n) representing number of effected patients per group.

†p < 0.05, incidence of gastric pH less than 2.5 with Gelusil alone vs incidence with Gelusil plus atropine.

‡p < 0.05, incidence of gastric pH less than 2.5 and volume exceeding 25 ml with Gelusil alone vs incidence with Gelusil and atropine and Gelusil with glycopyrrolate.

occur despite all precautions aimed at prevention, including rapid induction of anaesthesia and tracheal intubation accompanied by cricoid pressure. Prophylactic oral antacids have not eliminated the problem. They do not guarantee a pH above 2.5.⁴ Furthermore, aspiration of particulate antacids has produced pulmonary injury in dogs.⁶ Significant pulmonary problems can also follow the aspiration of gastric contents with a pH of 3.5.⁷ Salem's findings that glycopyrrolate ($7.5\text{--}10 \mu\text{g}\cdot\text{kg}^{-1}$) increased pH and decreased gastric volume in children would make its use in obstetrics attractive.⁵ However Baraka,⁸ using 0.4 mg of glycopyrrolate, irrespective of patient weight, failed to observe changes of gastric volume in the parturient, and Stoelting⁹ found volume and pH unchanged when using a standard 0.2 mg dose in non-pregnant adults. Our anticholinergic doses fall between those of Salem and Stoelting and this may explain why there were no statistically significant changes in

gastric volume in our study. Increased doses of glycopyrrolate might have produced significant changes in volume. Furthermore, employing a more accurate method to measure gastric volume such as a dye dilution technique might also have altered our results. Our volumes are, if anything, falsely low.

The changes in gastric pH, as opposed to the changes in volume, were significant. The addition of glycopyrrolate to Gelusil® increased mean pH and decreased the incidence of a low pH, in contrast to Gelusil alone; but atropine, in the dose used, was equally effective (Tables II, III).

Gelusil alone proved more reliable than had been anticipated. With shorter premedication to sampling times of less than 75 minutes it was 100 per cent effective. Beyond 75 minutes it was much less reliable (Tables II, III). Roberts observed the same 100 per cent effectiveness before 75 minutes when using a combination of

magnesium and aluminum hydroxide.³ The addition of atropine and glycopyrrolate appeared to extend the time of effectiveness of Gelusil. This continued elevation of pH in the face of probable diminishing antacid effect, coincides with the time of maximal effect of glycopyrrolate seen by Baraka.⁸ The continued coverage seen also with atropine may reflect the larger dose used in this study as compared with Stoelting who found no effect with atropine alone.⁹ This longer duration of coverage provides protection during emergence when the patient's airway may once more be unprotected. Since premedication to induction and especially induction to emergence times may be prolonged, the use of anticholinergic appears warranted to provide this longer period of protection.

Glycopyrrolate and atropine do have the disadvantage of decreasing lower oesophageal sphincter tone¹⁰ and so increasing the chances of regurgitation; but properly applied cricoid pressure can overcome this problem.

In summary, the addition of either glycopyrrolate or atropine to a Gelusil® premedication in the parturient undergoing elective Caesarean Section reduces the number of patients with gastric pH less than 2.5, so decreasing the likelihood of aspiration pneumonitis when premedication has been given more than 75 minutes before operation.

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RÉSUMÉ

Le pH et le volume du contenu gastrique ont été mesurés sur 60 femmes anesthésiées au thiopental, protoxyde-oxygène et succinylcholine lors de césariennes en chirurgie réglée. Elles avaient toutes reçues Gelusil® 30 ml per os à la période préopératoire, médication à laquelle furent ajoutés atropine $7 \mu\text{g}\cdot\text{kg}^{-1}$ dans 20 cas et glycopyrrolate $4 \mu\text{g}\cdot\text{kg}^{-1}$ dans 20 autres cas. Après l'intubation endotrachéale, le liquide gastrique fut aspiré à l'aide d'une sonde Salem Fr 18.

Après Gelusil® seul, le pH moyen du liquide gastrique a été mesuré à 4.54 ± 2.45 (ET) alors qu'il fut plus élevé de façon significative à la suite de l'association antiacide-atropine (6.78 ± 1.2) ou antiacide-glycopyrrolate (6.42 ± 1.72), ($P < 0.01$). La différence de volume entre les groupes n'a pas été significative.

Les trois prémédications ont produit un pH gastrique de plus de 2.5 lorsqu'administrées à moins de 75 minutes avant l'échantillonnage. Lorsque l'intervalle entre la prémédication et l'échantillonnage a dépassé 75 minutes l'addition d'atropine ou de glycopyrrolate a diminué l'incidence d'acidité à pH de moins de 2.5 de 40 per cent pour les patientes au Gelusil® seul à 6 pour cent et 14 pour cent respectivement pour les autres prémédications. En comparaison avec le Gelusil® seul, cette différence a été significative pour l'atropine ($P < 0.05$) mais non pour le glycopyrrolate. L'atropine et le glycopyrrolate ont permis de réduire à 6 et 7 pour cent respectivement l'incidence d'acidité plus basse que 2.5 s'associant à un volume gastrique plus grand que 25 ml, ce qui était significativement plus bas qu'avec le Gelusil® seul ($P < 0.05$).

Cette étude tend à démontrer que l'addition d'atropine ou de glycopyrrolate au Gelusil® en prémédication permet une protection additionnelle contre les effets nocifs de l'aspiration lorsque la période qui sépare la prémédication de l'induction se prolonge.