THE EFFECT OF GLYCOPYRROLATE (ROBINUL) ON THE LOWER OESOPHAGEAL SPHINCTER

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PULMONARY ASPIRATION of gastric content with resultant chemical pneumonitis remains a major cause of obstetrical and surgical death.[1] The mechanisms of action of anticholinergic drugs on the lower oesophageal sphincter is of paramount importance to the anaesthetist and his patient. Previous studies have shown a decrease in lower oesophageal sphincter tone following the administration of atropine[2,3] and hyoscine.[4] Glycopyrrolate has been suggested as an alternative to atropine and hyoscine,[5] but to our knowledge its effect on the lower oesophageal sphincter has not been elucidated. This paper concerns our investigations into the effect of glycopyrrolate on the lower oesophageal sphincter in normal control subjects.

SUBJECTS AND METHODS

Oesophageal manometric studies were performed on eight healthy volunteers, aged 18 to 38 years, with their informed consent. Previous history of upper gastro-intestinal surgery or disease precluded entry to the study.

Oesophageal motility studies were performed with the subjects resting quietly in the supine position after a fast of at least eight hours. The motility tube used consisted of three Portex polyethylene No. 54 plastic tubes assembled together at the distal end. Each tube has a single lateral orifice situated at 5 cm, 10 cm and 15 cm respectively from the distal tip.

The catheter consisting of the three tubes was swallowed orally until all recording orifices lay in the stomach. Each tube was continuously perfused with water at a rate of 0.19 ml per minute, using a Harvard constant infusion pump. The tubes were connected separately to three transducers (Beckman Instrument Physiological Transducer, Model 215071) linked to an 8-channel Beckman R411 Dynograph amplifier and recorder.

The catheter was withdrawn slowly, 0.5 cm at a time, until the pressure recordings and their alterations in response to swallowing indicated that all three orifices lay within the oesophagus above the lower oesophageal sphincter. With the catheter in the stomach, three readings of gastric pressures were recorded. Similarly three readings were obtained with the catheter in the sphincter and similarly in the oesophagus. The mean gastric pressure, the mean lower oesophageal sphincter pressure and mean oesophageal pressure from the respective three readings were recorded before and after intravenous injection of glycopyrrolate 0.3 mg. The calculated difference recorded between mean lower oesophageal sphincter pressure and the mean gastric pressure was termed the mean barrier pressure. (Pressures were expressed in kPa above atmospheric pressure.)

The lower oesophageal sphincter normally first relaxes and then contracts during swallowing. This produces fluctuations in the pressure profile obtained, initially giving an abnormally low reading and then an abnormally high value. Any pressure change recorded during swallowing was therefore deliberately excluded and time was allowed for the pressure profile to settle to the previous pre-swallowing level, before continuing with the withdrawal of the catheter.

Respiration was monitored throughout using a tubular pneumograph placed around the subject's chest and connected to the dynograph amplifier and recorder system.

RESULTS

The mean intraluminal pressures obtained appear in Table I. Glycopyrrolate 0.3 mg decreased the mean barrier pressure by 0.88 kPa ($p < 0.005$) (Figure 1).

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TABLE I

MEAN OESOPHAGEAL, LOWER OESOPHAGEAL SPHINCTER, GASTRIC AND BARRIER PRESSURES BEFORE AND AFTER GLYCOPYRROLATE 0.3 mg (kPa)

Pressure site		Basal	Post drug
Oesophageal pressure	mean	0.32	0.43
	SEM	0.07	0.11
Sphincter pressure	mean	4.68	3.77
	SEM	0.30	0.20
Gastric pressure	mean	1.74	1.71
	SEM	0.13	0.15
Barrier Pressure	mean	2.94	2.06
	SEM	0.35	0.22

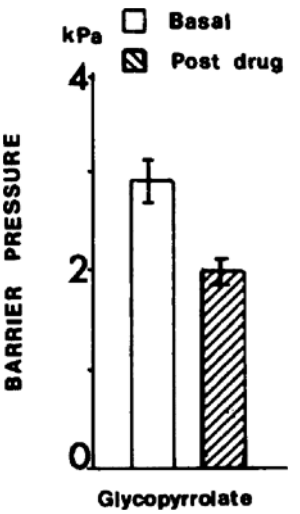

FIGURE 1 Mean barrier pressure in kPa before and after glycopyrrolate which produced a fall of 0.89 kPa ($p < 0.005$). The range around the mean is standard error.

DISCUSSION

The resting tone of lower oesophageal sphincter is currently believed to be the major barrier to gastro-oesophageal reflux.[6] Our results show that glycopyrrolate decreases the barrier pressure (lower oesophageal sphincter pressure minus gastric pressure). Atropine and hyoscine have previously been shown to decrease lower oesophageal sphincter tone,[2,4] whereas the effects of glycopyrrolate in this respect have not been previously reported. Clark and Riddock[7] studied 15 human subjects at operation using a Burge intragastric tube with an inflatable balloon cuff. They reported that atropine given intravenously in a dose of 0.6 mg markedly increased lower oesophageal sphincter tone, and suggested that the drug might thus reduce the likelihood of reflux of acid gastric content. This work has led several authors[8,9] to recommend the use of atropine as a premedicant drug to lessen the dangers of acid regurgitation and aspiration during induction of emergency general anaesthesia. Recent work,[2,10] including our own results in unanaesthetized subjects[3] suggests that this recommendation might not be appropriate.

Glycopyrrolate is a quaternary ammonium compound which is an anti-cholinergic agent. Sun[11] and Moeller[12] reported the first clinical studies on its ability to control gastric acidity. All subsequent papers on glycopyrrolate continue to be related to gastroenterology in the management of peptic ulcers and other disorders associated with gastric hyperacidity. Glycopyrrolate has been found to be a potent antagonizer of the increased salivation induced by neostigmine. As an anticholinergic agent it has, among other properties, the ability to cause dryness of the mouth and larynx. It appears to be free from side-effects. The detrimental effect it has on the lower oesophageal sphincter, demonstrated here, suggests that this drug and also atropine and hyoscine might increase the risk of pulmonary aspiration in patients requiring general anaesthesia. We have previously shown that metoclopramide and atropine when given together antagonize each other at the lower oesophageal sphincter,[3] reversing the relaxant effects of atropine. We are at present studying the combined effects of glycopyrrolate and metoclopramide.

SUMMARY

Regurgitation and inhalation of acid gastric content, with resultant chemical pneumonitis,

remains a common cause of death during anaesthesia.

The effects of intravenous glycopyrrolate 0.3 mg on the lower oesophageal sphincter tone was studied in normal human subjects. Glycopyrrolate decreased lower oesophageal sphincter pressure by 0.88 kPa ($p < 0.005$).

This finding is of clinical importance in the pre-operative preparation of patients presenting for emergency surgery. A drug which decreases lower oesophageal sphincter tone would presumably increase the hazard of gastro-oesophageal reflux and pulmonary aspiration of acid gastric content.

Résumé

La régurgitation de liquide gastrique avec bronchoaspiration et pneumonite chimique demeure une cause de mort anesthésique commune. Nous avons étudié, chez des sujets normaux, les effets d'une dose intraveineuse de 0.3 mg de glycopyrrolate sur le sphincter œsophagien inférieur. Cet agent a abaissé de 0.89 kPa ($p < 0.005$) la pression du sphincter œsophagien inférieur.

Ce résultat est d'importance clinique dans la prémédication anesthésique des malades opérés en urgence. En effet, un médicament qui abaisse le tonus du sphincter œsophagien inférieur peut présumément augmenter le risque de régurgitation gastrique avec bronchoaspiration.

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