CARDIOVASCULAR EFFECTS OF GLYCOPYRROLATE AND BELLADONNA DERIVATIVES IN OBSTETRIC PATIENTS*

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GLYCOPYRROLATE is a new anticholinergic quarternary ammonium compound (see figure) reported to reduce gastric acidity more efficiently than belladonna derivatives and to cause "minor" cardiovascular responses.[1-3] The effect on gastric pH in parturient women of glycopyrrolate 0.4 mg. has been compared with that of atropine 0.6 mg.[2] We used this dosage regime to compare the cardiovascular effects of glycopyrrolate and atropine or scopolamine premedication in healthy women undergoing elective cesarean section or postpartum bilateral tubal ligation.

METHOD

The anesthesiologist assigned to the particular patient selected the anticholinergic drug and one of two of the authors (D.M.D. or S.F.D.) evaluated cardiovascular responses. After control electrocardiogram and noninvasive brachial arterial pressure had been obtained, the premedication (glycopyrrolate 0.4 mg., atropine 0.6 mg., or scopolamine 0.6 mg.) was injected intravenously. During the next 10 minutes, while the patient was being preoxygenated, heart rate was recorded every minute and blood pressure was taken twice at irregular intervals. Induction of anesthesia was then accomplished by the intravenous injection of ketamine 50 mg.—

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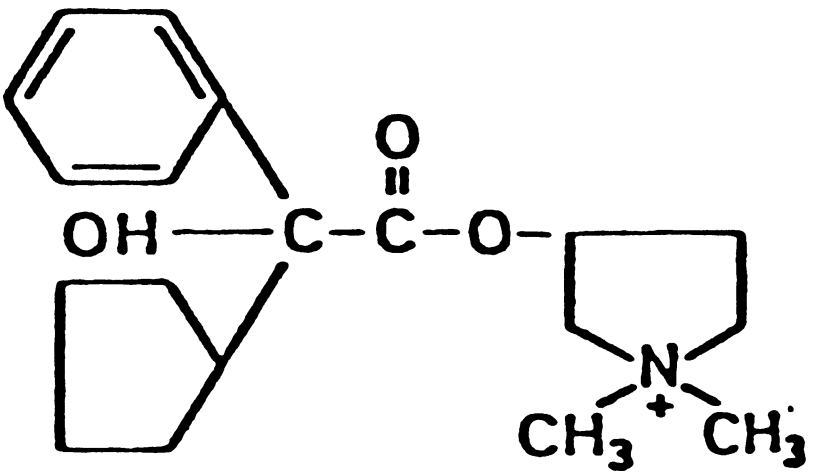

Chemical formula of glycopyrrolate: 3[(cyclopentylhydroxphenylacetyl) oxy]-1,1-dimethyl-pyrrolidinium bromide.

thiopental 100 to 125 mg. (45 seconds apart) in parturient and of thiopental 250 mg. in puerperal women. Heart rate and blood pressure were again recorded immediately following endotracheal intubation, facilitated by the intravenous administration of 100 mg. of succinylcholine. Student's t-test for paired variables was used for the statistical analyses.

RESULTS

Thirty-five women undergoing cesarean section and 34 undergoing tubal ligation were observed; 23 got glycopyrrolate, 24 atropine, and 22 scopolamine. Maximum increases in heart rate initiated by the premedications occurred 4 to 6 minutes after injection and were statistically significant with all three drugs (Table I). Increases were greater following atropine (35% and 41%, respectively) than after glycopyrrolate (27% and 37%, respectively) or scopolamine (29% and 38%, respectively), but these differences were not statistically significant. Maximum heart rates following endotracheal intubation were only slightly higher than the peak rates before induction of anesthesia but atropine produced a further statistically significant rise in the postpartum women (Table I). Similarly, mean arterial pressure increased more markedly with atropine than with the other

TABLE I. MEAN HEART RATES BEFORE INJECTION OF ONE OF THREE ANTICHOLINERGIC PREMEDICANT DRUGS AND MEAN MAXIMUM RATES FOLLOWING INJECTION AND AFTER ENDOTRACHEAL INTUBATION

Procedure	*Drug*	*# Pts.*	*I*	*II*	p^1	*III*	p^2
Cesarean section	Glycopyrrolate	12	86.8 ± 10.7	110.4 ± 16.8	*	118.0 ± 20.4	N.S.
	Atropine	12	84.3 + 16.5	113.6 ± 17.4	†	125.5 ± 18.6	N.S.
	Scopolamine	11	87.6 ± 16.9	113.1 ± 18.0	*	114.6 ± 15.0	N.S.
Tubal ligation	Glycopyrrolate	11	87.1 ± 16.0	118.9 ± 11.2	†	124.7 ± 12.4	N.S.
	Atropine	12	80.5 ± 10.0	113.5 ± 18.6	†	130.7 ± 14.4	‡
	Scopolamine	11	85.0 ± 16.0	117.6 ± 16.0	†	123.9 ± 15.7	N.S.

* = < .01
† = < .001
‡ = < .05
I = control, II = maximum prior to induction of anesthesia, III = after endotracheal intubation, p^1 = difference between I and II, p^2 = difference between II and III

TABLE II. MEAN ARTERIAL PRESSURES BEFORE INJECTION OF ONE OF THREE ANTICHOLINERGIC PREMEDICANT DRUGS AND AFTER ENDOTRACHEAL INTUBATION.

Procedure	*Drug*	*# Pts.*	*Control*	*After E.I.*	*p*
Cesarean section	Glycopyrrolate	12	98.3 ± 10.3	113.5 ± 13.6	*
	Atropine	12	94.2 ± 18.3	117.7 ± 16.7	*
	Scopolamine	11	95.1 ± 11.1	110.4 ± 18.6	†
Tubal ligation	Glycopyrrolate	11	95.5 ± 7.7	108.4 ± 14.9	‡
	Atropine	12	91.4 ± 7.7	110.5 ± 9.9	§
	Scopolamine	11	90.9 ± 9.7	106.3 ± 13.2	*

* = < .01
† = < .02
‡ = < .05
§ = < .001
E.I. = endotracheal intubation

two anticholinergics in both groups of patients (Table II) but, again, the differences among the three drugs were not statistically significant.

DISCUSSION

Our data do not support the statement that the cardiovascular effects of glycopyrrolate are "minor." In our patients the effects approximated those of scopolamine, and atropine produced a slightly greater response. Similar results were recently reported after intramuscular administration of the same premedications in healthy adults scheduled for minor gynecologic

surgery or electroconvulsive therapy: increased heart rates before anesthesia occurred with all three drugs but were most marked after atropine, and amounted to a mean of 42%.[3] This agrees closely with the 41% rise seen in our postpartum women. Atropine is known to have a more prominent action on central parasympathetics whereas scopolamine preferentially affects the peripheral system.

Responses to endotracheal intubation were similar in parturient and postpartum women, although the former received a ketamine-thiopental sequence for induction and the latter only barbiturate. Ketamine has properties resembling heightened sympathetic activity and causes increases in heart rate and systemic blood pressure. Our findings support the clinical impression that the addition of a small dose of thiobarbiturate to a reduced dose of ketamine mitigates the circulatory effects of the agent.

SUMMARY

In equal antisialogogue doses, circulatory effects of glycopyrrolate are similar to those of scopolamine, and should not be described as minor. Glycopyrrolate offers an advantage only in patients in whom circulatory responses must be depressed and the potential excitement of scopolamine avoided.

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