The effect of anticholinergic drugs on the electrolyte content of gastric juice

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SYNOPSIS Gastric secretion was stimulated by insulin hypoglycaemia and the effect of increasing doses of anticholinergic drugs on the volume, acid, and electrolyte content of gastric juice was studied. The sodium and potassium output was depressed to a far less extent than the acid output and the drop in volume of secretion and acid output after anticholinergic drugs is almost entirely due to decreased acid secretion. With increasing anticholinergic suppression of the volume of secretion, there is a marked fall in potassium output and a lesser fall in sodium output. The potassium concentration showed a slight fall and there was a rise in sodium concentration.

The effect of various anticholinergic drugs on gastric acid secretion has been studied by many workers. The acid concentration and output so investigated represents the amount of parietal secretion remaining after dilution and partial neutralization by the alkaline component, chiefly mucus and sodium and potassium chloride and bicarbonate. Hence it is of some interest to know the effect of anticholinergic agents on the electrolyte content of gastric juice; as far as can be ascertained, this has not been previously studied.

METHODS

The patients studied were psychiatric patients having insulin coma therapy. All were free of gastrointestinal disease. Their repeated treatment enabled many observations to be made on the same patient. A Cleland tube was passed when the patient became comatose, coma being considered to be present when patients no longer responded to painful stimuli and bilateral extensor plantar responses were present. Continuous suction was applied for about 15 minutes to remove the gastric residue and two 15-minute specimens were collected during the last 30 to 45 minutes spent in coma. Blood sugar estimations were done initially but were discontinued when it was found reproducible control results were obtained under the above conditions, whatever the actual blood sugar level found. Patients were included in this study only if the control secretory rates were high (>3 ml./min.) and the specimens were not bile-stained.

The series of anticholinergic drugs included atropine, propantheline, oxyphenycyclimine, and propionyl atropine methyl nitrate. These were administered orally two to two and a half hours before the onset of coma.

From the design of the experiments, maximal hypoglycaemic stimulation was considered to be present because the patients were comatose from hypoglycaemia during the period gastric secretion was collected. That this is a constant base line from which to assess changes is shown by the fact, discussed later in this article, that in 10 control observations on three patients the standard deviation was only 3.7% of the mean secretion under these circumstances. A greater error than this could be expected, however, when the volume of secretion was small. It is appreciated that the time of maximum action of the drugs administered varied and would not necessarily coincide with the time of collection of gastric juice. It is seen in Table I, however, that the control secretions were relatively constant for each patient and it is reasonable to assume that the change after the drugs was due to the anticholinergic drug administered. The different responses after drugs were a manifestation of different pharmacological effects related to the potency of the drug, its dose, and the time relationship of the time of collection to the time of its maximal action. All that is of importance in this investigation is that the changes in secretion in the studies after the drugs are due to the drug alone and not to other factors. Which of the four drugs was used is irrelevant in view of the information sought.

The acid concentration was estimated using phenol red as indicator. Schales and Schales method was used in the estimation of chloride. The sodium and potassium concentrations were determined using an Eel flame photometer.

RESULTS

The results from the three patients studied are given in Table I; the findings from one patient are represented graphically in Figure 1. The findings

TABLE I
EFFECT OF ANTICHOLINERGIC DRUGS ON ACID, CHLORIDE, SODIUM AND
POTASSIUM CONCENTRATION AND OUTPUT

Patient	Vol. (ml.)	H+		Cl-		Na+		K+	
		Concentration (mEq./l.)	Output (mEq.)	Concentration (mEq./l.)	Output (mEq.)	Concentration (mEq./l.)	Output (mEq.)	Concentration (mEq./l.)	Output (mEq.)
1, control	184	92	17.0	133	27.5	29	5.34	15.7	2.90
	181	95	17.2	140	25.4	33	5.97	13.4	2.43
	173	108	18.7	143	24.4	20	3.46	16.0	2.77
After anticholinergic drugs	164	103	16.9	146	24.1	25	4.10	16.4	2.69
	156	95	14.8	135	21.0	25	3.91	13.0	2.03
	137	89	12.2	136	18.6	30	4.15	13.5	1.85
	91	90	8.2	145	13.2	34	3.09	15.9	1.45
	82	83	7.3	134	10.9	36	2.93	13.4	1.10
	80	107	8.5	139	11.1	18	1.48	14.7	1.17
	62	86	5.3	136	8.4	39	2.42	11.8	0.74
	52	72	3.9	113	5.9	38	1.92	12.7	0.66
	39	86	3.4	142	5.6	39	1.53	9.4	0.36
	34	59	2.2	116	4.0	47	1.62	10.0	0.34
2, control	91	96	8.7	154	14.0	43	5.81	12.1	1.10
	88	99	8.7	166	14.6	43	3.78	10.0	0.88
	88	95	8.4	149	13.0	45	3.96	11.2	0.98
	73	99	7.2	150	11.0	38	2.77	12.7	0.93
After anticholinergic drugs	58	60	3.5	128	7.4	50	2.90	12.1	0.70
	28	44	1.2	137	3.8	87	2.44	9.0	0.26
	8	17	0.2	107	0.8	91	0.73	5.0	0.07
3, control	119	100	12.0	149	17.8	30	3.63	14.5	1.72
	98	98	9.6	151	14.8	38	3.74	16.8	1.65
After anticholinergic drugs	99	71	7.0	133	13.2	42	4.20	14.6	1.44
	72	77	5.5	138	9.9	51	3.67	13.6	0.98

¹The results are listed in order of decreasing volume. In the actual experiment the control studies and the studies after drugs were randomized. The volume secreted and the outputs are expressions of secretion during 30 minutes.

are listed in order of decreasing volume of secretion, irrespective of the anticholinergic agent used. The output represents the output during 30 minutes of the hour each patient spent in coma.

Summarizing these results, (1) there was a progressive drop in acid output with decreasing volume of secretion; the acid concentration showed a less marked fall. (2) The sodium and potassium output fell, the potassium output falling to a greater extent than the sodium output. The potassium concentration remained relatively fixed or showed a slight fall with decreasing volume of secretion while the sodium concentration rose.

DISCUSSION

Previous studies have shown that despite the fact that anticholinergic drugs will inhibit the output of acid, the concentration of acid shows relatively little fall (Keeton, Luckhardt, and Koch, 1920; Pollard, 1930; Gray, 1943; Notkin, Forse, and Webster, 1953; Piper, Elliott, Sietsma, and Pryor, 1960). It is possible that the drop in acid secretion could be accompanied by a fall in the output of the alkaline secretion, or the latter could remain relatively un-

changed. Like the acid component, sodium is secreted at a concentration approximately isotonic with plasma (Hollander, 1952; Grossman, 1960) but Grossman (1960) has shown that the secretion of the pyloric antrum, the chief source of the alkaline component, is not influenced by the various drugs that increase gastric secretion. It has also been demonstrated that the sodium output following histamine stimulation varies slightly from individual to individual, compared with the marked variation in acid output found in different individuals (Piper, 1960).

The changes observed here in the concentration of sodium and potassium are consistent with the observed changes in the latter cations with variation in the volume and acid output after histamine. Sodium concentration is inversely related to the acid concentration (Hollander, 1952; Gray, Bucher, and Harman, 1941; Riddell, Strong, and Cameron, 1960) and there is a slight drop in potassium concentration at low volume secretory rates (Riddell *et al.*, 1960). The output responses to increasing doses of anticholinergic drugs show that the latter influences the alkaline component to a lesser extent than the acid secretion and the change in volume after anti-

FIG. 1. Graph showing effect of anticholinergic drugs on the electrolyte output and concentration in gastric juice of one patient (Patient 1).

cholinergic drugs is almost entirely due to diminished acid secretion. It is seen that in Patient 1 (Table I) the drop in the acid output from 17.0 mEq. to 2.2 mEq. was accompanied by a drop in the sodium output from 5.42 mEq. to 1.62 mEq. and the potassium output from 2.90 mEq. to 0.34 mEq. The greater drop in potassium output compared with the sodium output is due to the fact that the concentrations of these cations vary in opposite directions when plotted against the volume of secretion; this suggests that they are secreted by different mechanisms. The drop in acid concentration with low acid secretory rates is no doubt due to neutralization and dilution of the acid secretion by the alkaline component.

In studies such as these, salivary contamination and incomplete collection are a possible source of error. In the present study, because of the use of anticholinergic agents, salivary contamination was least where the volumes of secretion were small and where the effect of contamination would be greatest. It is felt that the error due to the incomplete collection was small; in 10 control observations done on three patients, the coefficient of variation was only 3.7%. A greater error could be expected, however, when the volumes of secretion were small.

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