Reduction of gastric acid secretion on a low-salt diet and furosemide

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The management of peptic ulcer essentially consists of the neutralization or the reduction of gastric hydrochloric acid (HCl) by the use of antacids, anticholinergics, or by surgery. The drugs are partially effective, and surgery, with its known hazards, has a limited application. Johnston (1965), in a review of the various medical methods for the reduction of gastric acid secretion, concluded that none was satisfactory. An accidental observation of the relief of symptoms of duodenal ulcer in a patient while on a low-salt diet, advised for a different reason, prompted the present study.

MATERIAL AND METHODS

Twelve patients with active duodenal ulcer and six healthy controls, a total of 18 subjects, were studied. Seventeen were males and one female. The gastric secretory response was studied either by the augmented histamine test (AHT) (Kay, 1953) or by the histamine infusion test (HIT) (Lawrie, Smith, and Forrest, 1964; Desai, Borkar, and Jeejeebhoy, 1967). In overnight fasting subjects, a 14 to 16 French Levine tube was passed under fluoroscopic control along the greater curvature of the stomach with the tip of the tube placed at the right border of the vertebral column. The patients were

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instructed to lie on the left side and not to swallow saliva during the period of collection. The gastric secretion was collected by intermittent hand suction. After aspirating the fasting contents, 50 mg mepyramine maleate was injected intramuscularly and the basal secretion collected for half an hour. Histamine acid phosphate was then injected subcutaneously (AHT) or given in an infusion of 5% glucose (HIT). In the AHT the collection of gastric secretion was done for one hour after the injection of histamine. In the HIT, four 15-minute samples were collected after a 'steady state' was reached and pooled. The total acidity in the gastric samples was titrated against freshly prepared N/10 NaOH using phenolphthalein as the indicator and expressed as m-equivalents per hour of HCl (Lawrie and Forrest, 1965; Desai *et al*, 1967).

In the first group of seven subjects (Table I), the acid output was measured, on admission, by the AHT (histamine 0.04 mg/kg body weight). The test was repeated after a period of nine to 20 weeks (mean period = 14 weeks) on a low-salt diet. A low-salt diet meant the avoidance of common salt (NaCl) in food. No other dietary restrictions were imposed and no drugs prescribed. In subject no. 1 (control), the acid output was measured on six occasions, before and after maintenance on a low-salt diet, with an interval of 15 days between two successive tests. In the second group of 11 subjects, the HCl output was measured, on admission, by the HIT (histamine 0.04 mg/kg body weight/hour in subjects weighing more than 50 kg and a dose of 2.0 mg/hour in

TABLE I
GASTRIC ACID OUTPUT (AHT) BEFORE AND AFTER LOW-SALT DIET

No.	Age (yr)	Subject	HCl (m-equiv/hr)		
			On Admission	After Salt Depletion	Difference
1	30	Control	43.81 ¹	27.7 ¹	-16.1
2	24	Duodenal ulcer	53.0	21.2	-31.8
3	36	Duodenal ulcer	28.4	22.8	-5.6
4	40	Duodenal ulcer	36.9	33.5	-3.4
5	50	Duodenal ulcer	41.8	18.7	-23.1
6	54	Duodenal ulcer	29.8	24.6	-5.2
7	54	Duodenal ulcer	17.41	15.41	-2.0

t = 2.870 df = 6 P < 0.05

¹Average of six serial tests.

All subjects were males.

TABLE II

GASTRIC ACID OUTPUT (HIT) BEFORE AND AFTER FUROSEMIDE

No.	Age (yr)	Subject	HCl (m-equiv/hr)		
			On Admission	After Salt Depletion	Difference
1	22	Control	31.1	28.2	- 2.9
2	25	Control	25.6	21.0	- 4.6
3	30	Control	16.2	18.2	+ 2.0
4	45	Control	15.4	12.4	- 3.4
5	35	Control	17.0	9.9	- 7.1
6	39	Duodenal ulcer	25.7	16.3	- 9.0
7	30	Duodenal ulcer	29.0	18.0	- 11.9
8	36	Duodenal ulcer	25.4	32.3	+ 6.9
9	45	Duodenal ulcer	43.0	24.2	- 18.8
10	40	Duodenal ulcer	15.0	4.8	- 10.2
11	30	Duodenal ulcer	43.2	31.4	- 11.8

t = 3.0 df = 10 P < 0.02
All males except case 1.

TABLE III

GASTRIC ACID OUTPUT IN SIX SERIAL TESTS (AHT) BEFORE AND AFTER SALT DEPLETION IN CASE 1

No.	HCl (m-equiv/hr)	
	On Admission	After Salt Depletion
1	43.0	28.4
2	43.8	28.0
3	44.1	26.9
4	44.3	27.3
5	43.4	28.2
6	44.2	27.4
Average	43.81	27.7

those weighing less than 50 kg). Thereafter, furosemide was administered orally in the dosage of 40 mg twice daily for a period of 10 days. The subjects were on a low-salt diet during the same period. Sixteen to 24 hours after the last dose of furosemide, the HIT was repeated.

RESULTS

Table I shows the HCl output on histamine stimulation (AHT) before and after a low-salt diet. All the seven subjects showed a significant fall in output of HCl ($P < 0.05$). Table II shows the HCl output (HIT) before and after furosemide. Nine of the 11 subjects showed a significant fall in the acid output ($P < 0.02$). In subjects in whom the tests were repeated in order to judge the reproducibility of the results, the mean and SD of the differences of acid output in two tests were 0.11 ± 0.98 m-equiv/hr on AHT and 1.1 ± 0.56 m-equiv/hr on HIT (Desai *et al*, 1967).

DISCUSSION

A significant reduction in the gastric acid output was observed with a low-salt diet alone and in combination with furosemide in 16 out of 18 subjects. This observation may provide a new approach in the management of peptic ulcer.

Taylor (1955) has mentioned that many years ago Kahn produced acid-free gastric juice in animals by prolonged feeding with chloride-free meat. Lahiri (1953) showed a fall in gastric HCl output on a low-salt diet. The possible mechanisms underlying the reduction of HCl secretion, observed in the present study, may be as follows:

1 The formation of HCl by the parietal cells involves the following reaction (Hightower, 1966):

According to the law of mass action, the reduction in the availability of NaCl, one of the reacting masses, can decrease the speed of forward reaction and hence diminish HCl production. A significant rise in basal HCl secretion has been observed in man after intravenous infusions of normal saline (Barreras and Donaldson, 1967). This shows that an increase in the availability of NaCl, the ultimate source of the chloride ion for HCl formation (Hightower, 1966), can step up the speed of the reaction and increase the production of HCl.

2 Salt withdrawal has been shown to increase the circulating levels of aldosterone in man (Leutscher and Axelrad, 1954; Crabbé, Reddy, Ross, and Thorn, 1958; Bledsoe, Island, and Liddle, 1966) and animals (Binnion, Davis, Brown, and Olichney, 1965; Cade and Perenich, 1965). This may act at the level of the parietal cell, altering the rates of ionic transfer and thus depress the formation of HCl. Van Buchem, Doorenbos, and Elings (1956) observed histamine-fast achlorhydria in a patient with primary aldosteronism (Conn's syndrome). Following the removal of the tumour, the patient showed a very high level of HCl secreted.

Inhibition of carbonic anhydrase has been postulated as a mechanism for the reduction of HCl secretion by the stomach on the administration of diuretics such as acetazolamide or chlorothiazide in man (Kramer and Markarian, 1959; Lindner,

Cohen, Dreiling, and Janowitz, 1962) and animals (Ojha and Ahmed, 1967). In the present study, the last dose of furosemide was administered orally 16 to 24 hours before the HIT, by which time it is known to lose its activity (Robson, Kerr, Aschcroft, and Teasdale, 1964). Moreover, furosemide has been shown to have no effect on carbonic anhydrase (Muschaweck and Hajdú, 1964). It is felt that furosemide exerts its action through depletion of sodium chloride.

SUMMARY

A significant reduction in the histamine-stimulated gastric acid output was observed with a low-salt diet alone or in combination with the diuretic furosemide in 16 out of 18 subjects. This observation may afford a new approach in the management of peptic ulcer.

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