Effect of carbenoxolone sodium on human gastric acid secretion

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SUMMARY Neither basal nor peak acid output changed significantly after treatment for four weeks with carbenoxolone sodium as Biogastrone tablets in patients with gastric ulcer or Duogastrone capsules in patients with duodenal ulcer.

The mechanisms of ulcer healing by carbenoxolone are not fully understood. One of the early controlled trials (Bank *et al.*, 1967) suggested that carbenoxolone may have an inhibitory effect of gastric acid secretion, but later studies have been inconclusive (Table). This problem has, therefore, been re-examined using appropriate preparations of carbenoxolone in patients with gastric ulcer and with duodenal ulcer.

Methods

SUBJECTS

Ten patients with gastric ulcer were given carbenoxolone sodium as Biogastrone tablets 100 mg three times a day for four weeks. Ten patients with duodenal ulcer were given Duogastrone capsules 50 mg four times a day for four weeks.

TESTS

Basal and peak acid output after pentagastrin were

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Received for publication 4 March 1977

measured by standard methods (Baron, 1963a). The patient fasted overnight and a nasogastric tube was positioned fluoroscopically in the body of the stomach. The stomach was emptied, and 15-minute collections of gastric juice were then made by continuous pump and intermittent hand suction. After a basal hour pentagastrin, 6 µg/kg was injected intramuscularly, and four further 15-minute collections were made. Volume, pH, and titratable acidity (to pH 7) were measured. Peak acid output (mmol/h) was calculated by doubling the sum of the two highest consecutive 15-minute periods of acid output after pentagastrin.

Acid tests were done before, and the morning after the end of, the four-week course of treatment with carbenoxolone. The significances of differences were calculated non-parametrically by Wilcoxon's matched-pairs signed-rank test.

Results (Figure)

The basal and peak acid outputs of the patients with gastric and duodenal ulcer were similar to those previously reported (Baron, 1963b). After treatment with carbenoxolone as Biogastrone basal acid out-

Table Effect of carbenoxolone sodium on human gastric acid secretion

Source	Subjects	n	Drug	Dose (mg/day)	Duration (weeks)	BAO	PAO (reduction %)	Stimulant
Bank <i>et al.</i> (1967)	GU	11	Biogastrone	{ 300 200	1 3		24	Augmented histamine
Cocking and MacCaig (1969)	GU	11	Placebo				13	
	GU	16	Biogastrone	{ 300 150	1 4		16 13	Augmented histamine
Berstad <i>et al.</i> (1970)	DU	2	Carbenoxolone	200	2 min	Inconstant		
	Controls	3	Intraduodenal					
Geismar <i>et al.</i> (1973)	GU	13	Biogastrone	{ 300 150	1 3		P < 0.05	Augmented histamine
Ottenjann and Rösch (1970)	GU	7	Placebo	{ 300 150	1 3	NS	NS	
			Biogastrone	{ 300 150	1 3	NS	NS	
Baas <i>et al.</i> (1975)	Controls	6	Biogastrone	300	1	NS	NS	Pentagastrin
Domschke <i>et al.</i> (1975)	Controls	10	Biogastrone	300	6 d	NS	NS	Pentagastrin
Gordon <i>et al.</i> (1975)	Controls	6	Biogastrone	{ 300 150	1 2	< 0.05

Figure Basal (○) and peak (●) acid output after pentagastrin in 10 patients with duodenal ulcer (DU) before and after a four-week course of Duogastrone 200 mg/day and 10 patients with gastric ulcer (GU) before and after a four-week course of Biogastrone, 300 mg/day. By Wilcoxon matched-pairs signed-ranks test, $P > 0.1$ for each of the four comparisons shown.

put fell in five, and peak acid output in seven, of 10 patients. After treatment with carbenoxolone as Duogastrone basal acid output fell in seven, and peak acid output in five, of 10 patients.

The changes in basal and peak acid output after a four-week course of carbenoxolone in patients with gastric or duodenal ulcer were not statistically significant.

Discussion

Basal acid output shows obvious variation on repeated tests on the same subject with coefficients of variation over 50% (Baron 1963a, 1970). Peak acid output has excellent repeatability with coefficients of variation of only 8 to 9% (Baron 1963a, 1970). On repeated testing over periods of weeks both basal and peak acid output occasionally show distinct spontaneous increases or reductions (Baron, 1970),

as in this series of patients treated with carbenoxolone.

Carbenoxolone had no significant systematic effect on basal and peak aspirated acid output, which represents the sum of acid secretion into the stomach minus pyloric loss and neutralisation by saliva and duodenal juice. Admittedly, no allowance was made in the present studies for these three errors, so that it is theoretically possible, though highly unlikely, that carbenoxolone both reduced gastric acid secretion and reduced salivation, pyloric loss, and reflux.

Conclusion

The absence in this series of any significant changes in basal or peak acid output after carbenoxolone given for four weeks to patients with gastric or duodenal ulcer makes it improbable that carbenoxolone has an inhibitory effect on gastric acid secretion, or that its ulcer-healing effect could be related to inhibition of gastric acid.

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