The effect of glucagon on serum gastrin

I Studies in normal subjects

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SUMMARY Serum gastrin has been determined by radioimmunoassay in 13 subjects free of gastrointestinal disease, in the basal state, and following the intravenous injection of 1 mg glucagon. Serum gastrin fell from a mean $\pm$ SEM level of 50.3 ± 6.7 to 9.4 ± 3.3 pg/ml at 30 minutes after injection, significant at $P < 0.005$. This is similar to the response previously reported for secretin and indicates a role for glucagon in the control of gastrin release.

Glucagon has been shown to inhibit both basal and pentagastrin-induced gastric acid secretion in man and dog (Dotevall, Kock, and Walan, 1971; Lin and Spray, 1968). Similar inhibition occurs with the hormone secretin (Wormsley and Grossman, 1964; Johnson and Grossman, 1968; Petersen, 1969). Basal serum gastrin becomes lower following secretin injection in normal subjects and patients with chronic pancreatitis (Hansky, Soveny, and Korman, 1971) and recently a preliminary report indicated that intravenous glucagon inhibited the gastrin response to feeding in man and dog (Becker, Reeder, Lerman, and Thompson, 1972).

The structural similarity of glucagon and secretin has prompted the present investigation into the effect of glucagon on basal serum gastrin in normal subjects as measured by radioimmunoassay.

Material and Methods

Thirteen normal subjects, nine males and four females, whose ages ranged from 15 to 46 years, were studied after an overnight fast. All subjects were volunteers free of known gastrointestinal disease, and informed consent was obtained from each.

A 19 gauge court needle was inserted into a forearm vein and kept patent by frequent flushing with a solution of heparin, 1000 units in 20 ml 0.9% sodium chloride. Following the withdrawal of two control samples of blood at -15 and 0 minutes, 1

mg of glucagon (Eli Lilly and Co, Indianapolis, USA) was given by rapid intravenous injection and blood drawn at five, 10, 15, 20, 30, 45, and 60 minutes after the injection. The injection of glucagon caused a feeling of momentary nausea soon after administration in most subjects, but no subject vomited and the reaction only lasted some three to four minutes.

Serum was separated and assayed for gastrin by radioimmunoassay as previously reported (Hansky and Cain, 1969; Hansky *et al*, 1971). Significance of differences in means was assessed by Student's *t* test using standard formulae.

Results

These are shown in the figure. There was a significant fall in serum gastrin from a mean $\pm$ SEM basal level of 50.3 ± 6.7 pg/ml to a level 30 minutes after glucagon of 9.4 ± 3.3 pg/ml with a slow return towards normal. This fall was significant at $P < 0.005$. Although the maximal fall occurred at 30 minutes, there was no significant difference between the levels at 15, 20, and 30 minutes, indicating a rapid effect of glucagon on serum gastrin. The maximal fall occurred at five minutes after injection in one subject, at 15 minutes in four subjects, at 20 minutes in five subjects, and at 30 minutes in three. It fell to unmeasurable levels in nine of the 13 subjects studied.

Discussion

These results indicate that the intravenous injection of 1 mg of glucagon causes a significant fall in serum gastrin within 15 minutes which becomes maximal

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Received for publication 2 March 1973.

Fig Serum gastrin in response to the intravenous injection of 1 mg glucagon in 13 normal subjects. All values are mean $\pm$ SEM.

over the next 15 minutes and then slowly returns towards basal levels. Hansky *et al* (1971) reported a similar fall in serum gastrin after secretin injection but the difference in the two responses is that glucagon has produced a larger fall than secretin. In addition some subjects showed no change with secretin whereas all subjects thus far studied with glucagon have shown a fall in serum gastrin.

The similarity of response is not surprising con-

sidering the number of amino acids which secretin and glucagon share (see table). Indeed seven of the

Secretin	HIS-SER-ASP-GLY-THR-PHE-THR-SER-GLU-LEU . .
Glucagon	HIS-SER-GLN-GLY-THR-PHE-THR-SER-ASP-TYR . .

Table Structure of N terminus of secretin and glucagon

first eight amino acids at the N terminus are identical and perhaps this end of the molecule is responsible for the observed effect on gastrin. Although both glucagon and secretin have a similar effect in suppressing gastric acid secretion, they have opposite effects on pancreatic secretion, secretin stimulating and glucagon inhibiting the release of water and bicarbonate (Dyck, Texter, Lasater, and Hightower, 1970). These facts strengthen the thesis that the N terminus is the critical end for the effect of glucagon on gastrin.

The mechanism responsible for the fall in gastrin remains obscure. The time of fall of gastrin suggests that the mechanism is one of interference with gastrin release but the promotion of excretion of gastrin is a possibility. With this effect on gastrin another mechanism has therefore become apparent in the control of gastric acid secretion by the pancreas. This adds to the complexities which exist in attempting to study the function and interrelationships of the various gastrointestinal hormones and their overall control of digestive processes.

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