RAPID COMMUNICATION

Secretion of Gastrin and Calcitonin after Ingestion of Meat Extract in Patients with Peptic Ulcer

KANJI NOZAKI, SHIN-ICHI NODA, SABURO OBI, YOSHIKI NISHIZAWA,
HIROTOSHI MORII AND MASAHISA WADA

*Second Department of Internal Medicine,
Osaka City University Medical School, Abeno, Osaka 545*

Synopsis

Serum gastrin and calcitonin were determined after administration of meat extract to patients with peptic ulcer in order to investigate what role gastrin and calcitonin are playing in peptic ulcer. Serum gastrin levels were elevated after ingestion of meat extract in 9 out of 11 patients with peptic ulcer. Serum calcitonin (CT) levels were elevated rather gradually in 7 subjects. It was suggested that increased endogenous gastrin levels may have stimulated the release of CT.

When salmon calcitonin (SCT) was administered intravenously at a dose of 100 MRCu before administration of meat extract, the rise of gastrin and CT was suppressed in 67% of cases as to gastrin and in 43% as to CT.

Calcitonin (CT) has been recognized as a hypocalcemic agent secreted from C-cells in mammals. Recently, it was shown by Care *et al.* (1971) and Cooper *et al.* (1971) that the release of CT was increased by administration of a small dose of synthetic pentagastrin in pigs. Pancreozymin (Care *et al.*, 1971) and glucagon (Avioli *et al.*, 1969; Roos *et al.*, 1975) were also shown to stimulate secretion of CT. In this report, it was investigated whether the increased secretion of endogenous gastrin which was stimulated by ingestion of meat extract stimulates the secretion of CT in patients with peptic ulcer.

Eleven patients with peptic ulcer with ages between 25 and 67 were fasted overnight and a gastric tube was inserted into the stomach. Then 100 ml meat extract (condensed beef consommé, Nichiro Heinz Co.) which contains 2% protein, 0.4% carbohydrate, 0.12% fat, 0.005% calcium

and 0.024% phosphate was administered into the stomach through a gastric tube and patients were kept right side down for 15 min.

Blood samples were obtained before and 15, 40, 65, 90, and 115 min after the administration of meat extract. Serum was separated immediately after bleeding and kept at -20°C until use. Serum gastrin and CT levels were measured by the method of double antibody radioimmunoassay. Anti-gastrin rabbit serum and anti-human CT rabbit serum were made at Teikoku Pharmaceutical Co., Japan. Radioiodination of synthetic human gastrin (ICI, U.K.) and synthetic human CT (Teikoku Pharmaceutical Co.) were carried out by the modified method of Hunter and Greenwood (1962). The range of CT measurement was between 0.012 and 25 ng/ml and that of gastrin between 0.01 and 10 ng/ml. Serum calcium levels were determined by Webster's method (Webster, 1962) and phosphate by modified Fiske-Subbarow's method (Phosphor B-Test

Wako, Japan).

Serum gastrin and CT secretion was stimulated after administration of meat extract in 9 (80%) out of 11 patients as to gastrin and 7 (64%) out of 11 patients as to CT. Meat extract caused the mean serum gastrin concentration to increase from the initial level of 89.3 pg/ml to 122.9 pg/ml at 20 min after administration of meat extract. Mean serum CT concentration increased from the initial level of 45.3 pg/ml to 52.4 pg/ml. In 4 out of 5 patients who showed immediate increase of serum gastrin levels, CT was increased gradually after administration of meat extract. (Fig. 1(a)) On the other hand, in 5 out of 6 patients whose gastrin levels did not rise

markedly at 20 min after administration of meat extract, serum CT levels did not show significant changes. (Fig. 1(b)) While the basal level of serum gastrin was significantly higher in patients with gastric ulcer (111.4 ± 12.6 pg/ml) than that in patients with duodenal ulcer (50.5 ± 3.2 pg/ml), the percentage of patients with gastric ulcer in the group with immediate response of gastrin (80%) was higher than that in the group with delayed or no response of gastrin (50%). In all subjects, serum calcium and phosphate levels did not change significantly.

When SCT was administered at a dose of 100 MRCu 20 min before ingestion of meat extract, the secretion of gastrin was inhibited in 6 (67%) out of 9 patients in

Fig 1. Percent changes of serum CT levels in types of immediate response (a) and delayed or no response (b) of serum gastrin to meat extract. (a) Basal level of serum gastrin and CT was expressed as 100%. In type of immediate response of serum gastrin to meat extract, serum CT levels were increased in patients, b, e, f, and g. (b) Basal level of serum gastrin and CT was expressed as 100%. In type of delayed or no response of serum gastrin to meat extract, serum CT levels were increased in patient, i only.

whom gastrin secretion was stimulated by ingestion of meat extract, and CT secretion was inhibited in 3 (43%) out of 7 patients who showed increased secretion of CT by meat extract ingestion. (Fig. 2) Serum calcium and phosphate did not show significant

changes even after the administration of CT.

The relationship among serum calcium, gastrin and CT was reported by Becker *et al.* (1973 and 1974). They investigated in cats the effect of calcium and CT on gas-

Fig. 2. Percent changes of serum gastrin and CT levels after administration of meat extract with or without SCT. Basal level of serum gastrin and CT was expressed as 100%. Gastrin secretion was inhibited by SCT in 9 (80%), a, b, c, d, e, f, i, j, and k out of 11 patients. CT secretion was inhibited in 3 (43%), e, f, and i out of 7 patients, a, b, e, f, g, i, and k who showed increased secretion of CT by meat extract ingestion.

trin and gastric secretion. Infusion of calcium into cats brought about dose-related increase in the levels of serum gastrin and stimulated the secretion of gastric acid. On the other hand, intravenous CT infusion strongly inhibited pentagastrin and calcium induced gastric secretion and suppressed calcium induced hypergastrinemia without changing serum calcium levels. It was concluded that calcium may be important in the regulation of gastric secretion, and CT may suppress calcium induced gastric secretion both by suppression of gastric secretion and by direct inhibition of the parietal cell. In man, they also suggested that CT may have a regulatory function in the release or catabolism of the hormone gastrin.

It was shown by Cooper *et al.* (1970) that the administration of a small dose of pentagastrin resulted in a marked, rapid increase in thyrocalcitonin secretion in pigs.

It was suggested in the present investigation that the release of endogenous gastrin induced by meat extract may have stimulated CT release in some subjects whose serum gastrin levels increased after ingestion of meat extract.

Care *et al.* (1971) and Cooper *et al.* (1971) proposed that the presence of calcium in the gastrointestinal tract might have caused secretion of gastrointestinal hormones which, in turn, signaled the thyroid gland to secrete thyrocalcitonin. Although a small amount of calcium was contained in meat extract in the present investigation, it is not known whether calcium ingested with meat extract directly caused CT secretion. Swaminathan *et al.* (1973) reported that glycine or even gastric distension led to the increase of CT secretion in pigs. Although it was suggested that gastrin may have stimulated CT secretion from C-cells in the thyroid gland, the possibility of existence of CT secreting cells in the gastrointestinal tract can not be ruled out. If such cells exist in the gastrointes-

tinal tract, they may be directly stimulated by meat extract administration.

From the fact that CT secretion was inhibited by SCT administration, the mechanism of autoregulation of CT secretion was suggested. However, while some of the patients still retain the regulatory mechanism of CT secretion, the other may have lost such abilities. Although the percentage of patients with gastric ulcer in the group with immediate response of gastrin was higher than that of patients with duodenal ulcer, it is not yet clarified whether the mechanism of gastrin-CT secretion may participate in the pathogenesis of peptic ulcer.

Acknowledgment

We are greatly indebted to Dr. S. Namba., T. Sudo and M. Fujisawa. Teikoku Pharmaceutical Co. in this study.

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