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The Influence of Hypercalcemia on Gastric Secretion and Serum Gastrin Concentration in Intact and Thyro-parathyroidectomized Rats

HENRY JOHANSSON, URBAN KRAUSE, FOLKE NILSSON and GUDMAR LUNDQVIST

From the Departments of Surgery, Clinical Research II, and Clinical Chemistry, University Hospital, Uppsala, Sweden

ABSTRACT

Gastric acidity and serum gastrin concentration were measured in thyro-parathyroidectomized and sham-operated rats after calcium infusion. A moderate hydrogen ion decrease, and unchanged chloride ion concentration and plasma gastrin level were demonstrated in both experimental groups, indicating a different calcium-gastrin mechanism from that in man.

INTRODUCTION

The relationship between parathyroid hormone, calcium level and gastric secretion has been the subject of studies in both human and animals. The suspicion that patients with hyperparathyroidism have an increased incidence of peptic ulcer (Dent et al., 1972) has made such investigations especially justified.

Hypercalcemia may stimulate gastric secretion in man by liberating gastrin (Rosato et al., 1973). In the dog, however, the serum gastrin concentration did not change during infusion of calcium (Reeder et al., 1970). On the contrary, some inhibition of gastric acid secretion may occur (Allen & Elliott, 1971). Another aspect of interest is a possible interhormonal relation between gastrin and calcitonin—gastrinstimulating calcitonin secretion, calcitonininhibiting gastrin and gastric acid secretion (Sizemore et al., 1973).

The purpose of this investigation was to study gastric acidity and serum gastrin concentration in the rat after intravenous administration of calcium. The study was specially performed to analyse whether intact rats reacted in any way different from thyro-parathyroidectomized animals with respect to gastric secretion and plasma gastrin in response to calcium stimulation.

MATERIAL AND METHODS

The material consisted of 28 male albino rats (Sprague-Dawley) weighing about 250 g. The animals were divided into two groups: Thyro-parathyroidectomized rats ($n=14$), and Sham-operated rats ($n=14$).

Plasma gastrin concentration was monitored in 10 animals of each group. Gastric secretion was determined in 4 rats from each group. A chronic gastric fistula (Arnthorsson, 1972) was performed 1 week before the collection of gastric juice.

The experiments were conducted after a fasting period of 18 hours and started 2 weeks after the thyro-parathyroidectomy and sham-operation, respectively.

Calcium was given in a dose of 2.6 mg/100 g b.w. in a volume of 0.5 ml and administered by continuous infusion at a rate of 0.1 ml/min.

Plasma gastrin and calcium concentrations were determined 15, 30, 60, 90, and 120 minutes after the start of the calcium infusion. Gastric juice was collected between 0–2 and 2–4 hours.

Gastrin was measured by a solid phase radiommunoassay (Lundqvist et al., to be published). The antiserum used (No. 2604) was obtained from Dr J Rehfeld, Copenhagen, and its binding capacity and cross-reactivity are presented in detail elsewhere (Rehfeld et al., 1972). Human Synthetic Gastrin I (ICI Chemicals, England) was used for iodination and standards. The results are therefore expressed as ng equivalents of gastrin per ml. Serum calcium was determined in a Perkin-Elmer atomic absorption spectrophotometer.

The collected gastric juice was analysed for volume, hydrogen ions (0.1N NaOH titration with bromthymol blue as indicator), and chloride ions (mercury titration with diphenylcarbazone as indicator).

RESULTS

The thyro-parathyroidectomized animals showed markedly low serum calcium values 2 weeks after the operation ($M=2.7$; S.E.$=0.1$ mEq/l) in relation

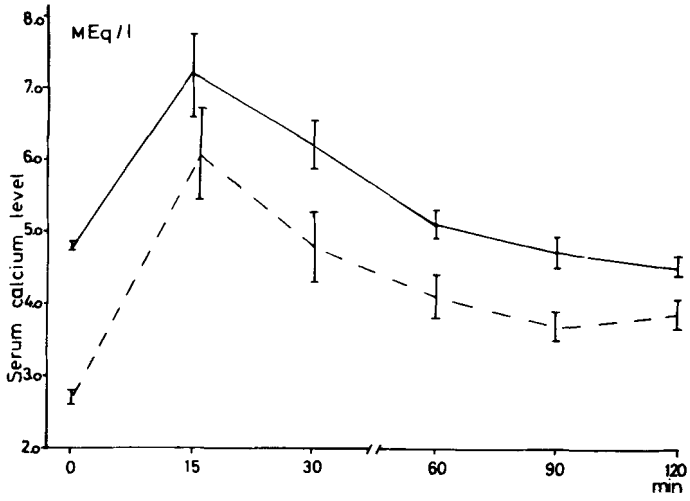

Fig. 1. Mean serum calcium level after intravenous infusion of calcium in a dose of 2.6 mg per 100 g b.w. The bars represent S.E. - - -=Thyro-parathyroidectomized rats. —=Sham-operated rats.

to the sham-operated animals (M=4.8; S.E.=0.1 mEq/l).

The mean serum calcium concentrations obtained after calcium infusion are demonstrated in Fig. 1.

The plasma gastrin concentrations after calcium infusion are illustrated in Fig. 2. Calcium infusion did not significantly alter the plasma gastrin concentration in thyro-parathyroidectomized or in sham-operated animals.

A moderate decrease in the hydrogen ion concentration in gastric juice was found 2–4 hours after the calcium infusion both in thyro-parathyroidectomized and sham-operated animals. The chloride ion concentration in the gastric juice was unaffected during the collection period (Table I).

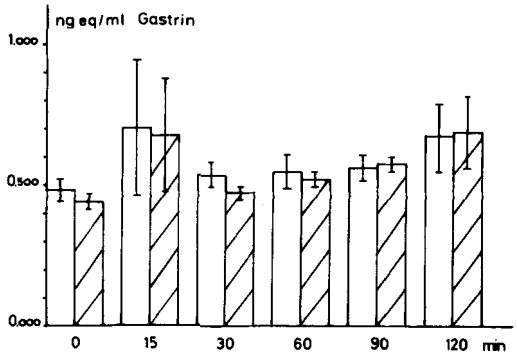

Fig. 2. Plasma gastrin after intravenous infusion of calcium in a dose of 2.6 mg per 100 g b.w. Mean values with S.E. are given.
▨=Thyro-parathyroidectomized rats.
□=Sham-operated rats.

DISCUSSION

If calcium has any effect on gastric acid secretion the mechanism would operate by facilitating acetylcholine release (Rubin, 1970) and/or by liberating gastrin. In patients with the Zollinger-Ellison syndrome the secretory response to hypercalcemia is accentuated (Passaro & Basso, 1970). These findings may suggest that hypergastrinemia could be a mediator of the acid secretory response to calcium.

In our studies the calcium infusion resulted in a marked hypercalcemia, which was not accompanied by any changes in the plasma gastrin levels, however. The gradually appearing decrease in the calcium level in the sham-operated animals after the calcium infusion was finished (rebound effect) may indicate a sufficient endogen thyrocalcitonin release.

Exogenous thyrocalcitonin was found to inhibit gastric secretion in the cat (Nordgren et al., 1974).

Table I. *Hydrogen- and chloride ion concentration (mEq/l) in gastric juice after intravenous infusion of calcium in a dose of 2.6 mg per 100 g b.w. Mean values with S.E. are given*

Collection period	H^+	Cl^-
Thyro-parathyroidectomized rats (n=4)		
0–2h	93.8±3.5	118.6±10.2
2–4h	60.9±7.2	106.4±10.8
Sham-operated rats (n=4)		
0–2h	86.0±16.8	127.8±3.6
2–4h	67.2±10.8	127.1±6.8

The presumed endogenous calcitonin release in our experiments could not be the main cause of the moderately decreased hydrogen ion concentration. The decrease in hydrogen ions was similar for thyro-parathyroidectomized animals, where no endogenous thyrocalcitonin release more than a possible ectopic one could be anticipated, and for sham-operated rats. The induced hypercalcemia *per se* might, however, be responsible for this effect. Öhrn et al. (1974), also in experiments in the rat, found a diminished hydrogen ion concentration after administration of both parathyroid hormone and vitamin D.

Calcium may increase the release of gastrin in man. From our experiments, however, with no change in the serum gastrin concentration after calcium infusion, it seems justified to conclude that such a mechanism does not exist in the rat.

These findings call attention to the importance of not uncritically transposing physiological information between species in the complex relations between calcium, parathyroid hormone, calcitonin, gastrin and gastric secretion.

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Address for reprints:

F. Nilsson, M.D.
Department of Surgery
University Hospital
S-750 14 Uppsala
Sweden