EFFECT OF INTRAVENOUS INFUSION OF SOMATOSTATIN ON GASTRIC, PANCREATIC AND BILIARY SECRETION IN THE RAT

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Summary

The effect of somatostatin (GH-RIH) on gastric, pancreatic and biliary secretion was examined in the anesthetized rats.

Intravenous infusion of the hormone, in graded doses ranging from 1 to 16 μg/kg/hr, produced a dose-dependent inhibition of pentagastrin, 1.5 μg/kg/hr, induced acid secretion, reaching about 54% of control level at the dose of 16 μg/kg/hr. Somatostatin, 4, 16 and 64 μg/kg/hr, inhibited the pancreatic juice volume stimulated by intravenous injection of secretin, 1 μl/kg, as a bolus. Somatostatin, 2, 8, 32 and 128 μg/kg/30 min, did not change the bile flow rate in control period. Somatostatin may play a physiological role in the regulation of the secretory process of the stomach and pancreas.

Key Words: somatostatin, Ghosh-Lai's rat, Love's rat, gastric and pancreatic secretion.

Introduction

Somatostatin, a growth-hormone release inhibiting hormone, isolated originally from ovine hypothalamus by Brazeau et al.1) was found in the rat stomach and pancreas in high concentrations, similar to that in the brain5).

The intravenous infusion of this hormone inhibits the release of growth hormone1,9), TSH4), insulin5,6), glucagon6,7), gastrin8,9), secretin10) and CCK-PZ11).

These informations suggest that somatostatin may play a physiological role in the regulation of the secretory process of the stomach and pancreas.

The present study was performed to investigate the effect of somatostatin on gastrointestinal secretions in the anesthetized rats.

Materials and Methods

Female Wistar albino rats weighing 200–250 g were used in the experiments. The animals were not starved, and were anesthetized by a single intramuscular injection of urethane (0.7 ml/100 g body weight of a 25% solution). Body temperature of the rat was maintained at 36±1°C by means of a rectal probe and a warming system throughout the study. Bilateral femoral veins were cannulated for injections and infusions.

The effect of somatostatin on gastric secretion was tested in the Ghosh-Lai rat preparation18,19). The rat stomach preparation was perfused with a phosphate-citrate buffer in saline
of pH 6.6 at 36°C using an automatic peristaltic pump that delivered the buffer at a rate of 1 ml/min. The 15-min aliquots of perfusate were collected continuously, and used for the determination of acid and pepsin contents. Acid output was determined by titration to pH 7.0 with 0.01 N NaOH using an automatic titrator assembly. Pepsin activity was measured by the method of Anson-Mirsky\textsuperscript{(14)}. The results were calculated as the output during every 30 min period. The results were also expressed as the percentage of the outputs of acid and pepsin occurring in the period immediately before somatostatin infusion. Gastric secretion was stimulated by an intravenous infusion of pentagastrin (ICI, England), 1.5, 3 and 6 μg/kg/hr. Somatostatin (Synthetic cyclic peptide; Yajima H, Chem Pharm Bull 23: 1956, 1975) was infused for one hour in graded doses of 1, 4, 8 and 16 μg/kg/hr.

The effect of somatostatin on pancreatic secretion was tested in the Love-Tachibana rat preparation\textsuperscript{(15,16)}. In tests measuring the maximal pancreatic flow of the preparation with secretory stimulant, secretin was injected using an incremental 30 min step-dose method. Pancreatic secretion was stimulated by an intravenous injection of secretin (Eisai, Japan), 1 u/kg, to about 80% of the maximum output. Secretin was given as a bolus injection at the beginning of each 30 min period. In some cases, two secretin dosages, 0.25 and 0.5 u/kg as a bolus, were used as the stimulant. Pancreatic juice was collected every 30 min and the volume was measured. The effect of addition of somatostatin on these pancreatic responses was studied. Somatostatin was added in graded doses of 4, 16 and 64 μg/kg/hr.

The effect of somatostatin on the secretion of bile was studied by the Love-Tachibana's method\textsuperscript{(15,16)}. The bile flow, through a complete outer drainage, was measured for one 15 min basal and eight 15-min secretions during somatostatin infusion. Somatostatin was infused in graded doses of 2, 8, 32 and 128 μg/kg/30 min.

All the experiments were statistically evaluated with Student's t test for non-paired values, p<0.05 being taken as level of significance. The mean with asterisk in the figure was significantly different from that during the control period before somatostatin infusion.

Results

In this Ghosh-Lai rat preparation, the mean outputs of gastric acid and pepsin in the steady state in response to pentagastrin at the dose of 1.5 μg/kg/hr were 29.2±4.7 μEq/30 min and 293.4±55.2 μg tyrosine/30 min, each.

The infusion of somatostatin, 16 μg/kg/hr, during submaximal stimulation of gastric secretion by pentagastrin, 1.5 μg/kg/hr, produced a significant inhibition of gastric secretion (Fig. 1). The acid output was reduced by 75% at a dose of 16 μg/kg/hr.

![Fig. 1](image-url)

The results were calculated as the output during every 30 min period and all outputs were expressed in the ratio of the response during the period before the infusion of somatostatin. (mean ± S.E. of the mean) The statistical difference is calculated from the level before somatostatin infusion.