D₅. Measurement F (In Vitro Assay, Gastrin, Secretin and Glucagon)

Responses of Acid Secretion and Serum Gastrin in Peptic Ulcer Patients

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The pathogenesis and pathophysiology of peptic ulcer have not been fully clarified. Gastric acid secretion may be controlled by three functions, namely parietal, vagal and antral. The purpose of this study is to elucidate the relationships of these three functions and the pathophysiologic differences between gastric ulcer and duodenal ulcer. We studied three gastric secretory tests, gastrin test (tetragastrin 4 μg/kg i.m.), insulin test (regular insulin 0.2 u/kg i.v.) and antral function test (meat extract stimulation) in 10 gastric ulcer and 30 duodenal ulcer patients. Acid output and serum gastrin concentration were determined serially. Stimulated acid secretions were significantly higher in duodenal ulcer than in gastric ulcer in all three tests. The difference between duodenal ulcer and gastric ulcer, however, was most remarkable in antral function test, followed in insulin test and lastly in gastrin test. Serum gastrin responses in gastric ulcer were negligible both in insulin test and in antral function test. But, those in duodenal ulcer, were slightly elevated in insulin test, and markedly elevated in antral function test. These results indicate that duodenal ulcer is more vagal dependent than gastric ulcer, but in duodenal ulcer, the antral dependency is more dominant than the vagal dependency. The antral hypersensitivity of gastrin production and the parietal hypersensitivity to gastrin are suggested in duodenal ulcer.

Metabolism of Endogenous Gastrin in Anesthetized Dog

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The determination of serum gastrin levels has become practicable by the introduction of the radioimmunoassay.

While there have been many reports on endogenous gastrin in respect to its behavior in the circulating blood and its physiological properties, gastrin is believed, in its metabolic degradation, to stimulate the acid secretion of the stomach for a certain period, and then lose its biological activity in a short period of time.

So we investigated hepatic, intestinal and renal extraction of endogenous gastrin in anesthetized dogs. Serum gastrin levels were determined using C.I.S. R.I.A. kit, before and after the intravenous
administration of 2-deoxyglucose (2-DG) in a dose of 100 mg/kg.

1) Hepatic clearance value of endogenous gastrin was $102 \pm 2.2\%$ during the control period, and was ranged from $99.2 \pm 2.5\%$ to $107.0 \pm 2.2\%$ after intravenous administration of 2-DG.

2) The extraction rate of small intestine was $19.2 \pm 11.2\%$ during the control period, and was $29.3 \pm 14.1\%$ in stimulating time.

3) The extraction rate of kidney was $33.3\%$ during the control period, and was $27.6 \pm 13.4\%$ in stimulating time.

Radioimmunoassay of Secretin

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Radioimmunoassay of secretin has been studied by using synthetic secretins. Antiserum was produced in 3 rabbits against synthetic porcine secretin (Schwarz-Mann Co.). After 4 consecutive immunizations, specific antibody was detected in all 3 animals through both binding reaction and biologic inhibition (by Dr. Tachibana, Eisai ph. Lab.).

Radioiodination of synthetic 6-Tyrosil secretin, (Schwarz-Mann Co.) was performed by a modified chloramine-T method-reduced reaction time (30 sec.) with chloramine T and whole procedures under cold condition. A Sephadex G-25 column (1.2 x 20 cm) was used for the separation. The initial (organic) elution radioactivity peak with 0.1N HCl was collected and stored at $-20^\circC$. Labeling efficiencies of 200 to 250 $\mu$Ci per $\mu$g were achieved. After storage, significant generation of damaged hormone was observed by Sephadex G-50 gel chromatography. For the removal of the damaged, Talc method was found suitable. Undamaged hormones were absorbed effectively to the Talc and then extracted by acetic acid aceton. Using these antiserum, labeled 6-Tyrosil secretin and standard secretin of Schwarz-Mann Co. origin, possibility of a radio-immunoassay system was investigated. An unequilibrated incubation system was employed for 5 days including preincubation of 3 days, and charcoal dextran absorption system was used for B.F separation. An antibody which gave 1.0 of B/F ratio at $\times 5,000$ final dilution was used. This antibody did not cross significantly with synthetic human gastrin I and cholecystokinin-pancrezymin (both up to 1 $\mu$g). The system could detect 80 pg/tube of secretin which was considered too low to access resting level of circulating secretin. Recently, a highly potent antiserum was obtained (a kind gift from Dr. Chey Rochester), which gave 1.0 of B/F ratio at $\times 600,000$ final dilution. Utilization of this antibody and labeled synthetic secretin (Sqnibb Co.) gave high sensitivity detectable of 25 to 50 pg/ml secretin. This seems quite applicable for clinical study, and further studies will be performed using this new system.