METABOLISM OF GLUCAGON AND ITS PATHOPHYSILOGICAL ROLE IN METABOLIC DISORDERS

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Plasma levels of pancreatic glucagon were determined in control individuals as well as in patients with several disease states, by radioimmunoassay using Dr. Unger's 30K antiglucagon serum. Unbound glucagon was separated with dextran-charcoal.

Plasma level of the glucagon in I7 controls (mean ± SD) was 8I ± 4I pg/ml, whereas the levels in 34 patients with diabetes mellitus, 70 patients with various liver disorders, I8patients with uremia and 8 children with cyclic vomiting and positive ketone body in the urine were I67 ± 97 pg/ml, 325 ± 363 pg/ml, 395 ± I75 pg/ml and 378 ± I34 pg/ml respectively.

These values are significantly higher than that of controls. Average insulin level in the children with cyclic vomiting was significantly lower than that of controls.

Glucagon levels were ditermined during 50g oral glucose tolerance test in patients with diabetes mellitus, liver disorders as well as normal controls. In control individuals decrease of glucagon level was observed at 30 minutes after glucose administration, whereas in patients with diabetes mellitus, liver cirrhosis and chronic hepatitis, increase of the level was observed at this time.

These results imply that I) glucagon is catabolized at the kidney, 2) there is a mechanism increasing blood glucose to the normal level by increasing glucagon secretion and dereasing insulin secretion in children with cyclic vomiting, and 3) impaired secretion of the glucagon may be exist in diabetic and patient with some liver diseases.

Biological Activity of Iodinated SHG by Using Lactoperoxidase

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It was been reported that the radioiodination of Gastrin by Chloramine T (C.T.) resulted in the loss of biological activity. In this report, we studied the biological activity of iodinated Synthetic Human Gastrin I (SHG) by using Lactoperoxidase through Schild's rat and the radio-receptor binding of this iodinated SHG to the crude membrane of canine gastric corposal mucosa.

Methods : SHG (from Calbiochem.) was iodinated by the minor modification of the Hunter-Greenwood's method with C.T. and of Miyachi's method with Lactoperoxidase. In the latter, the radioiodination was performed by using 0.5μg to 1μg of Lactoperoxidase against 1μg of SHG, 1mCi of $Na^{125}I$ and 63ng of H_2O_2 in 0.4M acetate buffer pH 5.6 Iodinated SHG was then purified with Sephadex G-25 and Biogel P-6 columnchromatography. In order to study the biological activity of iodinated SHG, (1) acid output abilities of I-SHGs, which were prepared by two ways of cold iodination, were determined using Schild's rat, and (2) the binding specificities of both ^{125}I-SHG to the crude membrane of canine gastric corposal mucosa were determined after incubations with 1mg membranes of 800 to 10000 x g fraction in the presence of 5μg original SHG.

Results : In acid output abilities, I-SHG by C.T. method resulted in 86.8 ± 18.7 % (S.D.) loss, however I-SHG by Lactoperoxidase method reserved 83.2 ± 7.4 % (S.D.) activity of the original SHG (n=3). Further, approximately 4 % of both ^{125}I-SHG by C.T. and Lactoperoxidase were found to bind with crude membrane preparations. However, the addition of 5μg of original SHG caused 36.2 ± 4.6 % (S.D.) displacement of ^{125}I-SHG binding in only that by Lactoperoxidase method (n=3).

From these observations, ^{125}I-SHG by Lactoperoxidase method was considerd to retain biological activity , and might be useful for the further receptor binding studies.