PERSPECTIVE

Relation with Glucagon-Like-Peptide-1 Receptor and Extrapancreatic Glucagon

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ABSTRACT

The Glucagon-Like Peptide-1 Receptor (GLP1R) is a receptor protein present on pancreatic beta cells as well as brain neurons. It helps to regulate blood sugar levels by increasing insulin secretion.

The GLP-1RAs have been found to lower body weight and improve glycemic indices. These drugs function by activating GLP-1 receptors in the pancreas, resulting in increased insulin release and decreased glucagon release-both glucose-dependent responses-and a reduced risk of hypoglycemia.

Diabetes is caused by a lack of insulin and an oversupply of glucagon. Extra pancreatic glucagon was identified in dogs, which overturned the prevalent orthodoxy and allowed for detailed examination of the functions of insulin and glucagon in physiology and diabetes, as well as definitive proof about the involvement of glucagon in diabetes. Glucagon was thought to have impacts on many organs prior to his studies, but he was the first to assess the physiological role of glucagon using the effect of glucagon on glucose turnover. He was the first to say that glucagon only affects the liver, contrary to popular perception. He was also the first to quantify insulin secretion physiologically.

INTRODUCTION

Extrapancreatic Glucagon Secretion

Hyperglucagonemia has been demonstrated to contribute considerably to the hyperglycemic state of diabetic patients. Glucagon is thought to be a pancreas-specific hormone. Hyperglucagonemia is hypothesised to be caused by a combination of -cell insensitivity to the suppressive effects of glucose and insulin, as well as decreased insulin production. We tested 10 fully pancreatectomized patients and 10 healthy control participants with a 75-g oral glucose tolerance test and a matched isoglycemic intravenous glucose infusion to see if postabsorptive hyperglucagonemia is a gut-dependent condition. We used novel plasma glucagon analytical methods (sandwich ELISA and mass spectrometry-based proteomics) to show that 29-amino acid glucagon circulates in people without a pancreas and that glucose stimulation of the gastrointestinal tract results in severe hyperglucagonemia [1].

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Pseudo-Hyperglucagonemia in Pancreatectomized Patients

The expression pattern and regulatory role of glucagon (GCG) in colorectal cancer (COADREAD), including Colon Adenocarcinomas (COAD) and rectum adenocarcinomas (RECA), were investigated using publicly accessible data from the TCGA database (READ). R software packages and public web servers were used to conduct statistical studies. Unpaired and paired sample analyses were used to explore the expression pattern and prognostic significance of the GCG gene in pan-cancer and TCGA-COADREAD data. Logistic regression analysis was used to look at the relationship between GCG expression and clinical variables. The predictive relevance of GCG expression for overall survival in COADREAD patients was investigated using a univariate cox regression analysis. Genes that were shown to be substantially linked with GCG were discovered. Functional enrichment analysis and Gene Set Enrichment Analysis were used to identify biological functions and signalling networks [2].

Role of Neuropeptide Gene Glucagon

Even after total pancreatectomy, glucagon is identified in plasma, and whether this glucagon is produced from the gastrointestinal system is debatable. To evaluate plasma glucagon levels in one patient after partial pancreatectomy (one-seventh of the pancreas remaining) and three patients after total pancreatectomy, we used a sandwich Enzyme-Linked Immunosorbent Assay

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(ELISA) and liquid chromatography-high-resolution mass spectrometry. Glucagon levels were shown to be higher in pancreatectomy patients than in healthy people using an ELISA test. Plasma glucagon levels in pancreatectomy patients, on the other hand, were found to be below the lower limit of quantification using liquid chromatography-high-resolution mass spectrometry. Plasma glucagon was found to have a strong connection with plasma glicentin when tested by sandwich ELISA, implying cross-reaction with this gastrointestinal glucagon-related peptide. These findings suggested that when pancreatectomized patients' glucagon levels were measured using a glucagon sandwich ELISA, they falsely showed pseudo-hyperglucagonemia [3].

Extrapancreatic Glucagon

In humans, pancreatic alpha cells are thought to be the only source of glucagon secretion. Glucagon-like immunoreactive material was revealed in the gastrointestinal tract of fully pancreatectomized animals, reopening the subject of an extrapancreatic source of glucagon postulated when a hyperglycaemic substance was discovered in the gastrointestinal tract of dogs and rabbits. Nonetheless, the existence of extrapancreatic glucagon has sparked debate over the years, owing to the difficulty of precisely measuring fully digested 29-amino acid glucagon. Recent improvements in analytical methodologies have improved the sensitivity and specificity of glucagon assays, while technical advancements in mass spectrometry-based proteomics have improved the accuracy of detecting low-abundant peptides like glucagon in human plasma. In this article, we look at fresh evidence on extrapancreatic glucagon secretion in the light of previous research and current analytical discoveries. Extrapancreatic glucagon's source, control, and putative physiological role are also examined, as well as current challenges and knowledge gaps [4].

Effects of Incretin

Incretins are hormonal factors that have been suggested as transmitters of signals from the gut to pancreatic -cells. Incretins include gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). In addition to insulinotropic effects, we have shown that GIP and GLP-1 have direct activities on adipocytes and the kidney, respectively, employing GIP receptor and GLP-1 receptor-deficient mice. GIP and GLP-1 have distinct physiological activities due to tissue-specific differential expression of GIP and GLP-1 receptors, and further comprehensive characterization of the extrapancreatic actions of GIP and GLP-1 is expected, as dipeptidyl peptidase IV inhibitors activate both GIP and GLP-1 signalling [5].

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