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In Healthy Humans, Chronic Physiological Hyperglycemia affects Insulin Ability to Reduce the Level of Glucagon in the Blood

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Abstract

Type 2 diabetes mellitus is characterised by hyperglucagonemia. We looked at how insulin and hyperglycemia, both of which are common in those who can tolerate glucose normally, affected the suppression of plasma glucagon levels. Hyperglucagonemia contributes to fasting as well as postprandial hyperglycemia in type 2 Diabetic mellitus. Multiple studies have shown that impaired suppression of glucagon following a meal is a characteristic feature of type 2 diabetes mellitus and contributes to the hyperglycemia.

Keywords: Hyperglycemia • Insulin ability • Glucagon

Introduction

Type 2 diabetes mellitus is characterised by hyperglucagonemia. We looked at how insulin and hyperglycemia, both of which are common in those who can tolerate glucose normally, affected the suppression of plasma glucagon levels. Hyperglucagonemia contributes to fasting as well as postprandial hyperglycemia in type 2 Diabetic mellitus. Multiple studies have shown that impaired suppression of glucagon following a meal is a characteristic feature of type 2 diabetes mellitus and contributes to the hyperglycemia [1].

Description

Although some research indicates that glucagon may potentially be released from the small intestine, glucagon is produced and secreted by the pancreatic alpha cells. Many circulating and paracrine variables affect glucagon secretion. Low plasma glucose levels trigger the alpha cell's intrinsic autoregulation, which in turn stimulates glucagon release. Insulin and somatostatin secretion from the beta and delta cells, respectively, act in a paracrine manner to control glucagon secretion during hyperglycemia. While some research has shown that glucagon release can be inhibited by both glucose and insulin. Mice lacking insulin receptors in pancreatic alpha cells show modest hyperglycemia and hyperglucagonemia in the postprandial state and increased glucagon release in response to L-arginine stimulation, supporting an insulin role in reducing glucagon secretion [2].

It has been established that glucotoxicity significantly contributes to both decreased insulin secretion and skeletal muscle insulin resistance. In those with type 2 diabetes, reducing plasma glucose levels with insulin or SGLT2 inhibitors enhances beta cell activity and insulin sensitivity. The malfunctioning of pancreatic alpha cells has been linked to glucotoxicity in rats, however studies on how prolonged hyperglycemia affects glucagon output in humans have not been conducted. In the current investigation, we looked at how persistent physiological hyperglycemia affected the ability of glucose and insulin to control glucagon secretion in healthy NGT patients.

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36 healthy individuals who are normal glucose tolerators were participants. Following a 3-step euglycemic insulin clamp, 16 participants received a glucose infusion for 48 hours to increase their plasma glucose concentration by about 50 mg/dl. Twenty individuals underwent a 2-step hyperglycemic clamp after receiving a 72-hour glucose infusion. According to medical history, physical exam, and screening blood, all participants had normal liver, heart, and kidney function. Clinical and metabolic features of the 20 subjects who participated in the 2-step hyperglycemic clamp after a 72-hour glucose infusion and the 36 healthy participants with normal glucose tolerance who underwent a 3-step euglycemic insulin clamp before and after a 48-hour glucose infusion. The fasting and 2-hour plasma glucose concentrations of each participant were also normal [3].

The main finding of the present investigation is that 48 hours of physiologic hyperglycemia decreases insulin's ability to reduce the level of plasma glucagon. The plasma glucagon/insulin ratio decreased throughout the euglycemic insulin clamp because a higher plasma insulin concentration was needed to produce the same decrease in plasma glucagon concentration during each of the three insulin clamp phases. The main hormones that work quickly to maintain normoglycemia are the blood glucose-lowering insulin and the blood glucose-raising glucagon. Adrenaline contributes by preventing the release of insulin, promoting the release of glucagon, and directly imitating the glucose-raising effects of glucagon.

In diabetes, inadequate or incorrect insulin production is the most common cause of hyperglycemia. This striking comment demonstrates the growing understanding that glucagon underlies significant diabetic symptoms. Yet, glucagon dysregulation is not just limited to the excessive production of the hormone that elevates blood sugar levels and exacerbates hyperglycemia in diabetics. When glucagon secretion is not properly driven by hypoglycemia, glucose counterregulation is hampered, which is a far more harmful component [4].

It would seem that the range of hypoglycemic glucose concentrations is best for regulating glucagon secretion. A physiological function of the hormone is suggested by the hyperglucagonemia in diabetes, which may reflect a stimulatory component in the effect of high glucose concentrations on glucagon release. The control of glucagon secretion by glucose values ranging from those indicative of hypo- to hyperglycemia is consequently included in this review [5].

There are fundamentally different theories about how glucose regulates glucagon secretion, despite the fact that research over the past few decades has greatly increased our understanding of the molecular mechanisms by which pancreatic -cells recognise glucose and how subsequent signalling results in the release of insulin. It is frequently asserted that the nervous system controls glucagon secretion more significantly during hypoglycemia [6].

Conclusion

Hepatoportal and cerebral sensors are necessary for control by the autonomic nervous system. The sympathetic system, which mostly secretes noradrenaline,

the parasympathetic system, which primarily secretes acetylcholine, and the adrenal medulla, which primarily releases adrenaline, are the three main autonomic inputs to the beta cells. However, given that recent findings have revealed that human islets are significantly less innervated than rat islets, the significance of pancreatic islet innervation in the regulation of glucagon secretion should be viewed with caution. It is also evident that in isolated Langerhans islets and perfused pancreas, glucagon secretion is controlled by glucose without neurological effect. The regulation of glucagon release within the islet will be the current area of emphasis. It has been suggested that this regulation involves both intrinsic -cell mechanisms and autocrine and paracrine interactions with other islet cell types. It is likely that these processes participate in the control of glucagon release, as will become clear in this review, and that their relative significance varies with the level of glucose in the blood.

Acknowledgement

None.

Conflict of Interest

None.

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