HYPERGLYCEMIA INDUCES INTESTINAL SUCRASE ACTIVITY IN SUBTOTALY PANCREATECTOMIZED RATS

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Summary

The effects of experimental diabetes, hypertonic glucose infusion, and subsequent insulin administration on the sucrase activity of the small intestine were studied using intestinal segments completely excluded from luminal continuity by construction of Thiry-Vella fistulas in rats. Eight weeks after subtotal pancreatectomy, the rats contracted insulin-deficient diabetes mellitus, and sucrase activity was enhanced in both the Thiry-Vella loop and in the proximal jejunum in continuity. Subcutaneous injections of insulin during the last 4 weeks maintained the enzyme activity in the control range in both segments. There was a positive correlation between sucrase activity and blood glucose level in the pancreatectomized rats. Hyperglycemia in normal rats induced by intravenous infusion of 30% glucose solution over 48 hours enhanced the sucrase activity in the jejunum. Furthermore, insulin administration with a glucose solution inhibited the enhancement of enzyme activity. These findings suggest that hyperglycemia itself might play an important role in the diabetic increment of sucrase activity.

Key Words: Subtotal pancreatectomy, Thiry-Vella fistula, Hyperglycemia, Intestinal sucrase activity.

Introduction

Increased glucose absorption has been reported in the small intestine of patients with diabetes mellitus1). Cerda et al.2) also reported elevated disaccharidase activities in small intestinal mucosal biopsies taken from cases with diabetes mellitus and chronic exocrine pancreatic insufficiency. These findings were confirmed in the small intestinal mucosa of rats with experimental diabetes induced by alloxan, streptozotocin, or subtotal pancreatectomy3-11). These changes in intestinal function might exert a harmful influence on postprandial hyperglycemia after carbohydrate ingestion in diabetic patients. Recently, the use of a disaccharidase inhibitor was advocated as an adjunct in the treatment of diabetes to improve postprandial metabolic profile by decreasing the digestion and absorption of sucrose and starch12).

The increment in activity of intestinal disaccharidases could result from changes in either intraluminal factors (food intake3,4), pancreatic-biliary secretion2,13) or extraluminal factors (blood flow, hormones5-8,14-17), nerve...
impulses). The fact that these enzymes increased even after pair feeding\(^4\), after parenteral feeding\(^9\), or in the Thiry-Vella intestinal loop\(^10\) in experimental diabetic animals suggested that the enhancement of enzyme activities in diabetes was independent of intraluminal factors. Previous studies have examined the regulatory roles of several trophic hormones (gastrin\(^{14,15}\), glucocorticoid\(^5\), secretin\(^{16,17}\) and insulin\(^{6-8}\)) for intestinal disaccharidases, and demonstrated that among these hormones, insulin reversed or markedly diminished the enhancement of enzyme activities in diabetic animals\(^6-8\)). However, previous experiments were carried out mainly in the intestines of orally fed diabetic animals. Such conditions could not exclude the influence of the direct effects of intraluminal nutrients or digestive enzymes and the indirect effects of enteral feeding, such as the release of gastrointestinal hormones and neural factors.

In this study, we examined the effects of pancreatectomy diabetes and insulin administration on intestinal sucrase activity using the intestinal segment of the small intestine completely isolated from luminal continuity by construction of a Thiry-Vella loop. We also studied the effects of hyperglycemia induced by intravenous glucose infusion and of intestinal perfusion with a glucose solution on sucrase activity in nondiabetic intact rats to elucidate the mechanism involved in the enzyme induction.

**Materials and Methods**

1) Materials

Male albino rats of the Wistar strain, weighing 170–220 g, were obtained from the Shizuoka Agriculture Laboratory, Shizuoka, and fed with laboratory chow (MR-3-A, Nippon Nosan Co., Yokohama). Glucose oxidase, peroxidase, saccharose, maleic acid, glucose, and phloridzin were purchased from commercial sources. An infused glucose solution was made from 50% glucose solution (Terumo Co. Ltd., Tokyo).

2) Animal treatment

Animals were divided into five groups:

- **Group 1**: Splenectomy (control) \((n = 11)\)
- **Group 2**: Subtotal pancreatectomy \((n = 10)\)
- **Group 3**: Subtotal pancreatectomy treated with subcutaneous lente insulin \((n = 6)\)
- **Group 4**: Splenectomy with insulin administration \((n = 6)\)
- **Group 5**: No treatment (Thiry-Vella loop only) \((n = 5)\)

All animals had free access to the laboratory chow for 8 weeks after surgery\(^{11,18}\).

**Subtotal pancreatectomy**

Subtotal pancreatectomy (more than 95%) was performed by the modified method of Scow\(^{19}\), under 40 mg/kg intraperitoneal pentobarbital anesthesia, after overnight fasting. The remaining pancreatic tissue between the common bile duct and the duodenum (parabiliary segment) was partially cauterized by an electric surgical knife to ensure the onset of contraction of diabetes mellitus\(^{18}\). Splenectomy was performed at the same time to ease the operative method of subtotal pancreatectomy.

**Excluded intestinal loop**

A Thiry-Vella fistula was constructed by the modified method of Olsen\(^{19}\) at the time of the pancreatectomy. The jejunum was divided at 10 cm and 25 cm distal to the ligament of Treitz, and this 15 cm segment with intact blood and nerve supply served as the Thiry-Vella loop, and each end of the segment was brought out and sutured to the abdominal wall. An end-to-end anastomosis restored the continuity of the remaining small bowel.

**Insulin treatment**

Insulin treatment was performed subcutaneously with 4 IU lente insulin (NOVO) at