Insulin response to glucose in colectomized rats

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A number of studies have delineated the role of enteric factors, often termed the enteroinsular axis, in the modulation of insulin secretion [1~3]. It is generally agreed that one or more of the insulinotropic polypeptide hormones of the intestine (so-called incretin) are involved. The currently postulated incretin includes gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) [4~7]. Investigations on the distribution of GLP-1-like immunoreactivity in the gastrointestinal tract showed highest concentrations in the terminal ileum and colon in the rat [8]. However, the role for the terminal ileum and colon in the enteroinsular axis has remained to be elucidated. In order to elucidate this issue, insulin response to intravenous or intragastric glucose ingestion was investigated in the rat with colectomy in the present study.

Materials and methods

Animals and operation

Male Wistar albino rats weighing approximately 250g (6 — 8 weeks) were used in the present study. The rats were anesthetized with intraperitoneal pentobarbital sodium (40 mg/kg) after an overnight fast. The abdomen was opened and the terminal ileum (3 cm apart from the cecum) and the colon (4 cm apart from the anus) were ligated. The pancreas was carefully removed from the colon. Then the terminal ileum and colon were resected. The polyethylene cannula was inserted into the ileum, and intestinal fluid was drained. In control rats, the abdomen was opened and the polyethylene cannula was inserted into the same portion of the terminal ileum in a similar manner.

Intragastric infusion of glucose

Thirty minutes after the operation, glucose solution (1.5 g/kg in a 20 g solution) was bolus infused into the stomach using a syringe and the blood was drawn at 0, 30, 60, and 120 min from the portal and the femoral vein.

Intravenous infusion of glucose

Glucose solution (0.5 g/kg in a 20% solution) was bolus infused into the left femoral vein, and the blood was drawn at 0, 5, 15, and 30 min from the portal and the right femoral vein. The samples were centrifuged and the plasma was stored at

−20℃until the time of hormone assay. During the studies, the body temperature was maintained at 37℃ with a hot plate.

Measurements

Blood glucose was measured by a glucose oxidase method. Plasma insulin was measured by radioimmunoassay using rat insulin standard. The sensitivity of this assay was 2 μU/ml, and intraassay and interassay coefficients of variation were less than 10%.

Statistics

Data are expressed as means ± SD. Statistical analyses were made using analysis of variance and two-tailed Student's nonpaired *t* teat.

Results

Insulin response to intragastric glucose

As shown in Table 1, portal and femoral blood glucose levels after glucose ingestion were not significantly different between colectomized rats and control rats. Portal and femoral plasma insulin levels were significantly lower in colectomized rats than those in control rats at 30 and 60 min.

Table 1 Blood glucose and plasma insulin response to intragastric glucose

	femoral vein				portal vein			
	0	30	60	120min	0	30	60	120min
control (n=7)								
BG (mg/dl)	110±10	178±25	201±53	165±30	109±10	184±29	184±40	180±32
IRI (μU/ml)	8± 2	43±11	30±6	16±5	24±5	128±46	123±38	67±21
colectomy (n=7)								
BG (mg/dl)	112±10	157±24	221±36	152±33	116±10	158±13	216±28	154±36
IRI (μU/ml)	8±2	28±7*	20±6*	19±5	29±7	64±29*	66±31*	34±15

colectomy : rats resected the terminal ileum and colon
BG : blood glucose, IRI : plasma insulin
*$p<0.05$, significantly different from control.

Insulin response to intravenous glucose

As shown in Table 2, portal and femoral blood glucose responses after the venous infusion were similar in both groups of rats. Femoral plasma insulin level was significantly lower in colectomized rats than those in control rats at 5 and 15

min, and portal insulin level was significantly lower in colectomized rats than those in control rats at 5 min.

Table 2 Blood glucose and plasma insulin response to intravenous glucose

	femoral vein				portal vein			
	0	5	15	30min	0	5	15	30min
control (n = 7)								
BG (mg/dl)	110±10	245±41	216±30	124±19	108±10	237±38	208±35	129±20
IRI (μU/ml)	9±2	29±7	52±12	19±6	25±6	73±22	115±31	55±19
colectomy (n = 7)								
BG (mg/dl)	110±11	270±42	232±39	119±19	116±11	282±49	222±36	125±20
IRI (μU/ml)	9±2	19±5*	30±9*	19± 5	30±8	42±14*	88±24	48±16

colectomy : rats resected the terminal ileum and colon
BG : blood glucose, IRI : plasma insulin
*$p<0.05$, significantly different from control.

Discussion

The present study clearly demonstrated that insulin response to both infusion of intragastric and intravenous glucose was significantly inhibited in rats resected the terminal ileum and colon. Significantly lower level of portal insulin suggests the decrease in insulin secretion from the pancreatic B cell in colectomized rats. Similar degree of insulin response in portal blood and femoral blood indicates that hepatic extraction of insulin is not significantly changed in colectomized rats. Because the concentration of GLP-1 immunoreactivity is markedly higher in the terminal ileum and the colon [8], and because GLP-1 has a strong insulinotropic effect in the rat [9~10], the decreased GLP-1 secretion by colectomy may be involved in the decrease in insulin to glucose in the colectomized rats. Although insulin release in colectomized rats was significantly decreased, blood glucose level in them did not elevate. Such decrease in insulin secretion may not have reached the level for impairing glucose tolerance.

It may be complicated that pancreatic and/or portal blood flow is changed by colectomy, and that other insulinotropic hormone(s) is released from the terminal ileum and/or colon. These issues have remained to be elucidated. I believe that this is the first report suggesting the important role for the terminal ileum and colon in the enteroinsular axis.

Because GLP-1 like immunoreactivity was identified in colorectal enteroglucagon cells in human [11], and because GLP-1 was suggested to be a physiological incretin

in human [12], the terminal ileum and the colon may have an important role in insulin secretion in human as well as in the rat. Further studies should be necessary to resolve this issue.

Summary

Investigations on the distribution of glucagon-like peptide-1-like immunoreactivity, which is one of the most probable candidates for incretin, in the gastro-intestinal tract showed highest concentrations in the terminal ileum and colon. To elucidate the possible role for the terminal ileum and colon in the enteroinsular axis, insulin response to glucose was investigated in rats resected the terminal ileum and colon. Although portal and femoral blood glucose levels after glucose ingestion were not significantly different between colectomized and control rats, portal and femoral plasma insulin responses to intragastric (1.5 g/kg) and intravenous (0.5 g/kg) glucose were significantly reduced in colectomized rats compared with those in control rats. These results suggest that the terminal ileum and/or colon have an important role in enteroinsular axis in the rat.

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(Received August 31, 1993)