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Title

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Permalink

<https://escholarship.org/uc/item/3mx0062t>

Journal

Surgery for Obesity and Related Diseases, 13(10)

ISSN

1550-7289

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Publication Date

2017-10-01

DOI

10.1016/j.soard.2017.09.231

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Peer reviewed

ANTI-DIABETIC EFFECTS OF ILEAL TRANSPOSITION SURGERY ON OBESE MICE

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Background and objective: On the basis of the nutrient passage patterns, bariatric surgery is broadly divided into restrictive, malabsorptive, and/or metabolic procedures. It has been postulated that the early entry of nutrients into the distal small intestine after Roux-en-Y or other intestinal bypass procedures elicits a neuroendocrine response that causes improved glucose homeostasis, which is called “ileal break” mechanism. Ileal transposition (IT) is a hindgut procedure that produce weight loss and improve glycemic control by translocating a segment of the distal ileum proximally to the upper jejunum without altering the length of gastrointestinal tract or gastric restriction. The antidiabetic mechanisms of IT remain poorly understood. Ileal transposition has not been performed in the mouse model because of difficulty in constructing a functional small bowel anastomosis. The aim of this study was to evaluate the optimal surgical technique to construct an IT procedures in the mouse model and to examine the anti-diabetic effects of IT surgery on high-fat diet (HFD) induced obese mice.

Methods: For IT procedure, 4-cm segment of distal ileum was transected and repositioned 3.2cm distal to the ligament of Treitz. Small bowel reconstruction was performed end-to-end (n=5), end-to-side (n=5) or side-to-side (n=12) with a single layer continuous 10-0 suture. The side-to-side group was divided to either a 0.4 cm enteroenterostomy anastomotic technique (n=5) vs a 0.6 cm enteroenterostomy anastomotic technique (n=7). For IT-sham procedure (n=4), animals received intestinal transections and reanastomoses without change in location. Survival rate, body weight change and glucose metabolism were observed after surgery.

Results: There was a 100% mortality in end-to-end group, end-to-side group, and side-to-side with 0.4cm anastomosis group. Mortality was secondary to anastomotic obstruction 2 to 3 weeks after surgery. There was a 57% (4/7) survival rate in the mice with 0.6cm side-to-side enteroenterostomy anastomosis, which showed significant body weight loss and improved daily blood glucose after surgery compared to IT-sham group. Oral glucose tolerance test performed after surgery showed significantly decreased in total area under the curve for blood glucose in the IT group compared to IT-sham group (10238±1856 vs 15545±2360 (mg/dl)*min at 2 weeks, 9210±1774 vs 16660±5183 (mg/dl)*min at 4 weeks, respectively).

Conclusion: This is the first report establishing the technical feasibility of IT surgical procedure on mice. This study will open a novel avenue and opportunity to further study the mechanisms underlying IT surgery by using specific knockout mice.