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Effects of different foods on blood glucose and lipid in type 2 diabetes mellitus in a rat model

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ABSTRACT

Background: This study investigated the effects of duodenal-jejunal bypass (DJB) and new biliopancreatic diversion (NBPD) on blood glucose and lipid levels in type 2 diabetes mellitus (T2DM). An additional goal was to explore the potential mechanism or mechanisms underlying the therapeutic effects of surgery on T2DM.

Methods: Rats were fed a high-fat, high-glucose diet and then were intraperitoneally injected with streptozotocin, 35 mg/kg, to induce T2DM. Then, 33 T2DM rats were randomly assigned to one of three groups, a DJB group, an NBPD group, or a sham group. Fasting body weight, fasting glucose, and 2-h postprandial glucose were measured before and after surgery. Then, the rats were intragastrically administered lipid emulsion, peanut oil, glucose, starch, and Ansul, and blood glucose and lipid levels were measured.

Results: One week after surgery, 2-h postprandial glucose decreased from 24.41 ± 2.28 mmol/L before surgery to 19.87 ± 4.07 mmol/L after surgery in the DJB group, and from 25.88 ± 1.91 mmol/L before surgery to 20.34 ± 5.76 mmol/L after surgery in the NBPD group. After intragastric administration of lipid emulsion, free fatty acid levels increased from 534.60 ± 70.99 to 1082.83 ± 259.67 μEq/L in the DJB group and from 648.33 ± 139.26 to 1258.67 ± 204.18 μEq/L in the NBPD group. After surgery, free fatty acid levels in the DJB group and NBPD group were significantly lower than those in the sham group.

Conclusions: Postprandial blood glucose and lipids decreased after DJB and NBPD, which may be ascribed to postoperative changes in digestion and absorption.

Introduction

The prevalence of diabetes mellitus (DM) rapidly increases with aging, population growth, urbanization, and changes in lifestyle. Over the past three decades, the prevalence of DM has doubled.[1] DM and its complications also significantly increase society's medical burden. Although surgical intervention has achieved favorable efficacy for patients with DM,[2-4] the

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mechanisms underlying the therapeutic effects of surgery on DM are still largely unclear, and surgery is usually only recommended for patients with body mass indexes of at least 35 kg/m^2. Currently, the intestinal hormone hypothesis is widely accepted as the mechanism underlying the therapeutic effects of surgical interventions in DM. There are postintestine hypotheses[5] and preintestine hypotheses.[6] The preintestine hypotheses consider that food stimulation of the proximal jejunum reduces after surgery, which induces decreased secretion of gastric inhibitory polypeptide, thereby improving blood glucose. The postintestine hypotheses consider that postoperative exclusion of the proximal jejunum speeds up the incompletely digested food entering the terminal ileum, which stimulates the secretion of glucagon P-like peptide-1, and thereby improves blood glucose. But both these two hypotheses fail to completely explain the mechanisms underlying the therapeutic effects of surgical interventions[7,8] for DM.

Duodenal-jejunal bypass (DJB),[9] a modified gastric bypass surgery, has been shown to achieve better efficacy than traditional pharmacotherapy in Goto-Kakizaki rats.[9] As for DJB, the therapeutic effects on DM may be ascribed to two factors. First, there is a change in the gastrointestinal tract. After DJB, proximal intestine exclusion may reduce the intestinal absorption area, leading to reduction of nutrient absorption. In addition, food may rapidly enter the terminal ileum. According to the intestine hypothesis, this may cause alteration of intestinal hormones, affecting blood glucose.[6] The second factor underlying the therapeutic effects may be biliopancreatic diversion. After DJB, alteration of the gastrointestinal tract may delay the time and site of mixing bile and pancreatic juice with food, which may then also affect digestion and absorption of food, influencing blood glucose levels.

Our previous study showed that DJB and new biliopancreatic diversion (NBPD)[7] could improve the glucose tolerance levels of Goto-Kakizaki rats.[8] We speculate that the alteration of digestion and absorption is a major contributor to the therapeutic effects of surgery on DM. To investigate this further, we designed a study in which DJB and NBPD could be independently performed in rats with type 2 diabetes mellitus (T2DM). Furthermore, by measuring blood glucose and lipid levels after intragastric administration of different foods before and after surgery, it might be possible to explore the potential mechanisms underlying the therapeutic effects of surgery on T2DM.

Materials and methods

Study design

Animals and animal model

Specific pathogen-free 5-wk-old male Sprague Dawley rats ($n = 60$) were purchased from Shanghai Laboratory Experimental Animal Center and housed in the Experimental Animal Center of Fujian Medical University (laboratory animal use permit no. SYXK [Fujian] 2008-0001).The animals were housed for 1 wk before the study, and given *ad libitum* access to water and food. Then, the rats were fed a high-fat, high-glucose diet (60% common chow, 10% lard, 10% egg yolk powder, and 20% sucrose) at 20-25 g/d for 4 wk. After this, the rats were intraperitoneally injected with 35 mg/kg streptozotocin to induce T2DM. One week later, blood was collected via the tail vein, and rats with random blood glucose levels >16.7 mmol/L were used in subsequent experiments. After establishment of the animal model, the animals were fed with a regular diet.

All animal experiments were complied with the Animal Research: Reporting of *In Vivo* Experiments guidelines and were carried out in accordance with the U.K. Animals (Scientific Procedures) Act, 1986 and associated guidelines, EU Directive 2010/63/EU for animal experiments, or the National Institutes of Health guide for the care and use of laboratory animals (NIH publications no. 8023, revised 1978).

Experimental design

Rats with T2DM were randomly assigned to one of three groups: a DJB group ($n = 12$), an NBPD group ($n = 11$), and a sham group ($n = 10$).

DJB was performed as follows: The duodenum was separated from the stomach, and bowel continuity was interrupted at the level of the distal jejunum, (10 cm from the ligament of Treitz). The distal of the two limbs was directly connected to the stomach (gastrojejunal anastomosis) and the proximal limb carrying the biliopancreatic juices was reconnected downward to the alimentary limb at a distance of 10 cm from the gastrojejunal anastomosis (Roux-en-Y reconstruction).[5] (Fig. 1).

NBPD was performed as follows: NBPD group: (1) a 1-cm intestinal segment was removed at the bile-intestine confluence; (2) the proximal end was anastomosed to the distal duodenum; (3) one end of the intestine at the bile-intestine confluence was closed, and the other end was anastomosed to the jejunum at 20 cm below the ligament of Treitz (Fig. 1).

In the sham group, the duodenum was cut at a point 0.5 cm below the pylorus and then anastomosed.

Measurements of body weight and blood glucose

One wk before surgery and 1, 4, and 10 wk after surgery, rats were deprived of food overnight, and their body weight was measured with an electric balance scale. The fasting glucose level was measured with a blood glucose meter. Then, 2 h after administration of general animal chow, blood glucose was measured.

Measurement of blood glucose level after administration of different foods

Four to 5 wk after surgery, rats were deprived of food overnight, and then received intragastrically administered glucose, starch, and Ansul at 8 kcal/kg sequentially (1 d for one kind of food, intragastric administration via orogastric tube, and the animals were sedated). Blood was collected via the animal's tail vein, and blood glucose was measured 30, 60, 120, and 180 min after intragastric treatment.

Detection of blood lipids after intragastric administration of differing foods

Three to 4 wk after surgery, the rats were once more deprived of food overnight, and blood was collected from the intraocular plexus. Rats were intragastrically fed lipid emulsion, peanut oil, and Ansul at 8 kcal/kg sequentially (1 d for one kind of food, intragastric administration via orogastric tube and the