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Gastroileostomy for controlling body weight and lipid profile: An experimental rat model

Behrouz Keleidari[a], Mohsen Mahmoudieh[a], Rastin Mohammadi Mofrad[b], Shahab Shahabi[a,*], Erfan Sheikhbahaei[c]

[a] Fellowship of Laparoscopic Surgery, Department of Surgery, Minimally Invasive Surgery and Obesity Research Center, Alzahra University Hospital, Isfahan University of Medical Sciences, Isfahan, Iran
[b] General Surgeon, Minimally Invasive Surgery and Obesity Research Center, Alzahra University Hospital, Isfahan University of Medical Sciences, Isfahan, Iran
[c] Student Research Committee, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

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ABSTRACT

Objective: there is a direct correlation between development of obesity and elevated lipid profile. Restrictive and malabsorptive mechanisms along with stimulating neuroendocrine signals are major components of current bariatric surgeries. Higher weight loss is achieved by a malabsorptive operation compare to other bariatric procedures. In this study, we aim to investigate the early effects of gastroileostomy on weight reduction and lipid profile in rat model.

Materials and methods: Gastroileostomies with side-to-side anastomosis were performed on 15 male New Zealand rats. Blood samples were obtained at baseline and one week after the surgery. Blood samples were analyzed for lipid profiles.

Results: The data showed that gastroileostomy leads to a significant decrease in weight (330 ± 15 vs. 240 ± 25 g before and after surgery, respectively; $p = 0.04$). The levels of triglycerides decreased in plasma (99.21 ± 29.012 mg/dl before and 95.64 ± 48.668 mg/dl after the surgery respectively; $p = 0.807$). Total cholesterol (71.14 ± 13.416 mg/dl vs. 72.64 ± 22.455 mg/dl; $p = 0.813$) and LDL (12.96 ± 4.853 mg/dl vs. 15.36 ± 5.665 mg/dl $p = 0.121$) had no significant changes after the operation.

Conclusion: Based on the results of this study, gastroileostomy is effective for weight reduction but has no statistically significant change on lipid profiles in a short time. Therefore, this surgery is a promising surgery for weight reduction like other methods of bariatric surgery.

1. Introduction

Obesity and pathologic weight gain have been increasing prevalently and have become a worldwide problem recently (Soriano-Maldonado et al., 2016; Mansour et al., 2016). Overweight and obesity are associated with an increased risk of developing certain metabolic abnormalities such as type 2 diabetes mellitus and cardiovascular diseases such as hypertension and myocardial infarction (Soriano-Maldonado et al., 2016), which are related to hyperlipidemia and insulin resistance (Al-Thani et al., 2016).

Although the exact mechanism of obesity remains a matter of debate, there is a direct correlation between development of obesity and elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL), and triglycerides (TG) and an inverse relationship with high-density lipoprotein cholesterol (HDL) (Carbajo et al., 2016). The risk of developing morbidity and mortality rises with increasing adiposity, while weight loss can reduce this risk and improves medical conditions like diabetes mellitus (Nayak et al., 2016). Therefore, since obesity and pathologic weight gain are the most frequent chronic metabolic diseases with great impact on public health, researches for novel methods in preventing and treating these disorders continues (Carbajo et al., 2016).

Currently, treatment options to control obesity and pathologic weight gain have focused on controlling metabolic disturbances using "bariatric surgery" (Carbajo et al., 2016). Bariatric surgical procedures affect weight loss through three major mechanisms: restriction, malabsorption, and sending neuroendocrine signals (Lim et al., 2010; Rubino et al., 2004).

* Corresponding author. Alzahra University Hospital, Sofe blvd., Isfahan, Iran.
E-mail addresses: keleidari@med.mui.ac.ir (B. Keleidari), mahmoudieh@med.mui.ac.ir (M. Mahmoudieh), rastinmohammadimofrad@yahoo.com (R.M. Mofrad), shshahabi@yahoo.com (S. Shahabi), E.shikhbahaei@edc.mui.ac.ir (E. Sheikhbahaei).

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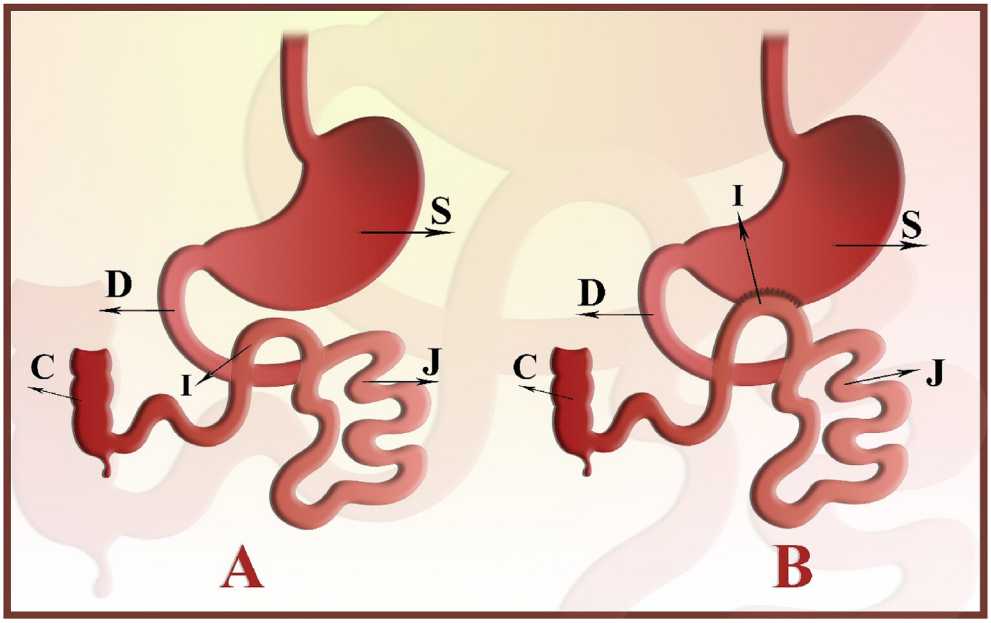

Figure 1. a schematic view of normal gastrointestinal anatomy (A.) and gastroileostomy (B.) in our study with side-to-side anastomosis of ileum to gastric antrum. S. Stomach, D. duodenum, J. jejunum, I. ileum, C. colon.

Restrictive procedures like sleeve gastrectomy, limit caloric intake by reducing the stomach's reservoir capacity. In these procedures, solid food intake is limited by restriction of stomach size, while the absorptive function of the small intestine remains intact. Additionally, Ghrelin secretion from gastric fundus decreases (Bosnic, 2014; Mechanick et al., 2008).

Malabsorptive procedures decrease the effectiveness of nutrient absorption by shortening the length of the functional small intestine. Profound weight loss can be achieved by a malabsorptive operation, depending upon the effective length of the functional small bowel segment. However, the benefit of greater weight loss can be counterpoised by significant metabolic complications, such as various micronutrient deficiencies and metabolic disturbances (Bosnic, 2014; Mechanick et al., 2008).

Bariatric surgery may change intestinal morphology and the subcellular organization of enterocytes as well as the expression of functional proteins in enterocytes and alter their metabolism (Dupre et al., 2004).

Although there are various types of bariatric surgery, laparoscopic sleeve gastrectomy (LSG) laparoscopic Roux-en-Y gastric bypass (LRYGB), and one-anastomosis or minigastric bypass (OA/MGB), there is lack of sufficient evidences to guide the development of valid and reliable protocols to select one surgery (Mechanick et al., 2008; UK Prospective Diabetes Study (UKPDS) Group, 1998). Single anastomosis sleeve Ileal (SASI) is a new therapeutic approach introduced by Santoro et al. composed of a sleeve gastrectomy with side-to-side gastroileal anastomosis. SASI has two components; the sleeve gastrectomy is the restrictive part and the gastroileal anastomosis sending neuroendocrine signals. In recently published clinical researches on limited number of patients, SASI was effective for significant weight loss, controlling T2DM, and normalizing lipid profile without any nutrient deficiencies after two years follow-up (Mahdy and Schou, 2016; Salama et al., 2017). However, there is not enough convincing evidence suggesting the therapeutic effects and complications of SASI.

Investigational procedures such as gastroileostomy also work by malabsorption, but produce more weight loss compared with other surgical procedures. The small bowel reconfiguration provides additional mechanisms favoring weight loss (Mechanick et al., 2008).

To the best of the authors' knowledge, the current study is the first experimental data that assesses weight reduction effects of gastroileostomy in rat model as a promising model for treatment of overweight and obesity. The present study was conducted to evaluate the efficacy of gastroileostomy on weight reduction and lipid profiles.

2. Materials and Methods

2.1. Animals

Fifteen healthy male New Zealand rats with the same weight (the mean and standard deviation (mean ± SD) were 330 ± 15 g) were obtained from Central Laboratory of our University. None of the rats had a history of surgery or other medical interventions. The animals were maintained under controlled conditions in a pathogen-free environment under constant ambient temperature and humidity with free access to food and water. The rats fasted overnight (at least 6 h) before the surgery. All procedures were conducted in agreement with the National Institutes of Health Guide for Care and Use of Laboratory Animals.

2.2. Interventions

Gastroileostomies were performed on 15 male rats after an overnight fast. Surgery for all subjects was carried out under the same standard conditions by one person. Anesthesia was induced and maintained with 0.1 mg/kg ketamine (Ketamine Hydrochloride Rotexmedica, Germany).

While anesthetized, each rat was laid in the supine position on a surgical table and the abdominal skin was shaved using hair removal cream (Veet ®, French) and disinfected with 10% betadine. Under sterile conditions, a 4.5 cm midline incision with a No. 10 scalpel was made on the abdomen. A piece of peritoneal surface was removed from the abdominal wall with surgical scissors. Gastroileostomy surgery was performed in all animals by anastomosing 1 cm of gastric antrum to terminal ileum (side-to-side). We measured the whole small intestine, find the ileum, and create an upward loop from its distal one-third, about 10 cm from ileocecal part (Figure 1). For anastomosing, a single layer running technique with absorbable poly-p-dioxanone suture (4/0, Monoplus®) was used. The opening of the anastomoses was tested with an index finger. Finally, the incised area of the skin and fascia were repaired by silk suture (4/0 Taft, Yazd, Iran) and the rats were left at a

suitable temperature (23°C–25 °C) to regain consciousness. All animals were kept on the same regular diet after the surgery. The study period was seven days after surgery. Silk sutures were removed on day 5 of treatment, under general anesthesia.

Blood samples were obtained from the vein in medial cantus at the base line and one week after the gastroileostomy.

2.3. Outcome assessment

The efficacy endpoint was any reduction in body weight and serum TC, LDL, and TG.

Any side effects of the intervention, including adverse effects related to systemic anesthesia, local infection, anastomosing leakages, and death, were assessed by the same surgeon using a questionnaire.

2.4. Statistical analysis

Mean ± SD values were determined for serum TC, LDL, and TG levels at base line and one week after the surgery. For comparison of two mean ± SD values, paired Student's t-test was used. P value of < 0.05 was considered to be significant.

3. Results

The experiments were performed with 15 male New Zealand rats. One of the 15 animals did not regain consciousness after the surgery and expired.

One week after the gastroileostomy, body weights on the same standard diet decreased significantly compared to baseline (330 ± 15 g to 240 ± 25 g before and after the surgery, respectively; $p = 0.04$).

Serum TG level decreased from 99.21 ± 29.012 mg/dl to 95.64 ± 48.668 mg/dl, but this reduction was not significantly different ($p = 0.80$). TC (71.14 ± 13.416 mg/dl vs. 72.64 ± 22.455 mg/dl; $p = 0.813$) and LDL (12.96 ± 4.853 mg/dl vs. 15.36 ± 5.665 mg/dl; $p = 0.12$) had no significant changes after the operation (Table 1).

4. Discussion

In this pre-clinical experiment, we found rapid weight reduction after gastroileostomy.

The goals of bariatric operations include maximizing weight loss and maintaining or achieving nutritional health, while preventing micronutrient deficiencies and lean body mass loss (Bosnic, 2014; Mechanick et al., 2008).

The LSG, which is the most commonly performed bariatric procedure in certain regions, does not involve intestinal bypass but can still lead to certain nutritional deficits (Mahdy and Schou, 2016; Salama et al., 2017).

Conversely, bypass procedures including LRYGB are known to cause micronutrient malabsorption (Bosnic, 2014; Mechanick et al., 2008; Elder and Wolfe, 2007).

Each technique has some advantages and disadvantage. LRYGB is fully reversible; however, the irreversible LSG is a faster and simpler procedure with potentially less dumping (Samuel et al., 2006; Tucker et al., 2007; Rizvi, 2016).

Table 1
Rats body weight and lipid profile before and after the gastroileostomy surgery.

P	After	Before	Variables
0.04	240 ± 25	330 ± 15	Weight (grams)
0.813	72.64 ± 22.455	71.14 ± 13.416	TC (mg/dl)
0.80	95.64 ± 48.668	99.21 ± 29.012	TG (mg/dl)
0.12	15.36 ± 5.665	12.96 ± 4.853	LDL (mg/dl)

There are technical difficulties involved in performing LRYGB in severely obese patients, and such patients may have limited success from LRYGB attributed to pouch dilation and loss of restriction at the gastrojejunal anastomosis over time (Samuel et al., 2006; Rizvi, 2016). The gastroileostomy resembles the SASI surgery without performing the restrictive component, sleeve gastrectomy. According to newly published clinical research with limited patients, SASI decreases fasting blood sugar (FBS), glycosylated hemoglobin A (HbA1c), and lipid profile until two years after the surgery continuously and progressively without nutrient deficiency (Mahdy and Schou, 2016; Salama et al., 2017). More compelling evidences are needed in this area to show the clinical applicability of this procedure.

Therefore, a simple technique with fast efficacy and minimal complications is favorable.

We chose gastroileostomy because, unlike other bariatric surgeries and anti-metabolic procedures, it has a more rapid weight loss with less physiological complications.

In a gastroileostomy, the duodenum and jejunum are excluded so the amount of food reaching the ileum after meal is increased.

Compared with the gastrojejunostomy, in LRYGB, gastroileostomy anatomy (connection between the stomach pouch and ileum) is associated with less dumping physiology, and causes less unpleasant symptoms such as lightheadedness, nausea, diaphoresis and/or abdominal pain, and diarrhea when a high-sugar meal is ingested (Campos et al., 2016; Keidar et al., 2013; Roth et al., 2009).

Shortening of the food retention time in the GI tract after gastroileostomy is also thought to decrease body weight after meals. Results from randomized clinical trials in this operation topic are limited. During the time of the study, weight decreased significantly at 7 days, which corroborates with the findings of other studies that analyzed the impact of surgical obesity treatment on these variables and demonstrates the effectiveness of this procedure on loss of body weight (Brolin et al., 2002; Kellum et al., 1990). We also observed a decrease in TG levels in rats with an experimental gastroileostomy.

It is hypothesized that bariatric surgeries may change intestinal morphology and alter the concentration of adipokines, such as tumor necrosis factor (TNF), which play an important role in the development of metabolic complications associated with obesity (Miller et al., 2011).

Additionally, other metabolic effects associated with caloric restriction, such as improved insulin sensitivity, might also have anti weight-gain effects (Holdstock et al., 2005).

Hormones such as glucagon, like peptide-1, and cholecystokinin, which are increased after bariatric surgeries including gastroileostomy, may promote an anorectic state (Bullo et al., 2007).

Regarding weight reduction, LRYGB or malabsorptive surgeries such as gastroileostomy have been shown repeatedly to have better outcomes than purely restrictive procedures (Heilbronn et al., 2006).

It is difficult to estimate the reduction of serum cholesterol in patients who lose weight, primarily due to reduced synthesis or lower absorption. Therefore, more experimental and clinical studies are necessary to determine the exact mechanism and outcomes.

The limitations of our study include the relatively small sample size and the un-controlled study design, which may omit the side effects related to general anesthesia and midline laparotomy.

5. Conclusion

Based on the results of this study, gastroileostomy may be an effective surgical method for weight reduction. Consequently, further studies are needed to clarify its effectiveness in similar cases in humans and to define its adverse effect and complication. The authors recommend further clinical studies evaluating the efficacy and safety of this surgery to find the most efficient and safe surgical technique that can be used in a human model.

Conflicts of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.obmed.2019.100096.

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