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Original Article

Gut firmicutes changes after laparoscopic one anastomosis gastric bypass surgery

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Abstract

Background and aims: Bariatric surgery may cause anatomical changes in the digestive system and alter the distribution of gut microbes. We aim to evaluate the changes of Firmicutes after the laparoscopic one anastomosis gastric bypass/mini gastric bypass (OAGB/ MGB) surgery.

Methods: Fifty patients with morbid obesity were operated on with OAGB/ MGB. Demographic data and Firmicutes counts in stool samples were obtained before, 6, and 12 months after the surgery. The logarithm of Firmicutes colony count based on 10 was used for analysis. Paired T-test, ANCOVA model, and Pearson correlation tests were used for statistical analysis.

Results: 70.6% of our patients were female. The percentage of Excess weight loss (%EWL) and excess BMI loss (%EBMIL) were 44.06%±9.84 and 42.56%±5.29 respectively at the 6-month follow-up and 67.55%±5.56 and 70.81%±7.25 respectively at the 12-month follow-up. The Firmicutes count was dropped from 1.57 to 1.44 at 6-month (p=0.01) and 1.32 at 12-month (p=0.02) follow-up. ANCOVA model after adjustment for age, sex, preoperative BMI, and delta-BMI did not show a significant difference for either the 6- or 12-months data (p=0.74 and 0.59, respectively). Pearson correlation test found no relationship between Firmicutes count change any weight-related variables.

Conclusion: The Firmicutes count was significantly decreased after OAGB/MGB. However, no significant relationship was found between weight loss and Firmicutes count.

Keywords: Gastric Bypass, Firmicutes, Bacteroidetes, Obesity, Microbiota, Bariatric surgery

Introduction

Although the exact mechanisms and relationships of gut microbiota and obesity are unknown, numerous studies have highlighted that the gut microbiota communicates with host organs by using several pathways that ended to obesity. Changing the intestinal microbiota was associated with bodyweight increase and fat mass development in animal models (1-3).

Bariatric surgery has become a prominent therapeutic option for morbid obesity. Although there is no doubt that gastric bypass surgery has a positive effect, clinical results can't be explained solely by the mechanism of caloric restriction or malabsorption (4). Some studies have been shown that bariatric surgery changes the gut microbiome and these changes are leading to weight loss (5, 6). Some studies have demonstrated an increase in gut microbiota richness and associations between gut microbiota and WAT genes a fter Roux-en-Y Gastric Bypass (RYGB) in obesity. RYGB changes the environmental and systemic factors of the digestive system that can deeply affect the combination of intestinal microbiota. (7). The literature lacks sufficient data about changes in gut microbiota and its mechanisms after other gastric bypass surgeries. Mechanistic studies have shown that gastrointestinal tract microbiota can affect both sides of the energy balance equation; namely, as a factor influencing energy utilization from the diet and as a factor affecting host genes that regulate energy expenditure and storage (8).

The human intestine has billions of bacteria. Bacteroidetes and Firmicutes, which consist of more than 90% of all phylogenetic types, are the two dominant parts of the bacteria in the human. Recent studies in animal models and humans reported that the microbial-community composition is affected by body fat storage. Comparing the distal gut microbiota of people with morbid obesity and normal anthropometric indexes revealed that a significantly greater proportion of Firmicutes are seen in people with obesity than in normal controls (9). Morbid obese patients had more Firmicutes and fewer Bacteroidetes than normal patients. Also, when volunteers with morbid obesity took a low-fat or low-carb diet for one year and lost 25% of their weight, the Firmicutes ratio decreased in their colon and the Bacteroidetes increased significantly (10).

Therefore, for this study, we aimed to assess the Firmicutes count in the feces of bariatric surgery candidates before and after the laparoscopic OAGB/MGB and evaluate whether there is any relationship between weight loss and the Firmicutes count change.

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Methods

Patient Selection: Fifty bariatric candidates were referred to our bariatric surgery center. All patients evaluated for bariatric surgery based on the American Society for Metabolic and Bariatric Surgery guideline: BMI ≥40 kilograms/square meter (kg/m^2) without any co-morbidities (e.g. hypertension, type 2 diabetes mellitus, or obstructive sleep apnea syndrome). Patients were excluded if they had acute or chronic inflammatory diseases, infectious diseases, viral infection, cancer, and/or known alcohol consumption. Clinical and demographic data including height, weight, and BMI were assessed before the surgery, 6 and 12 months after the surgery. Protein pump inhibitors were prescribed for all of them to prevent any gastric reflux symptoms.

Microbiologic Measurement: The amount of gut Firmicutes was profiled from fecal samples by real-time quantitative polymerase chain reaction (PCR). Stool samples were obtained in the morning before breakfast. The samples were self-collected in sterile boxes and stored at -20°C within 4 hours. Then samples were stored in the laboratory in 200 milligrams (mg) of aliquot and solution -80°C until further analysis. We replicated the protocol used by Guo et al. (9). After counting the colonies, we used its logarithm in the base of 10 to simplify its analysis.

Surgery Details: After inducing general anesthesia, preparation, and draping, laparoscopic OAGB/MGB surgery was started with standard protocol. A small gastric pouch with a 50-60 milliliter capacity was created with a stapler. The small intestine was measured from the Treitz ligament to reach a 180 centimeter (cm) biliopancreatic limb. This segment was then attached to the pouch and a vertical or slightly oblique omega-loop, isoperistaltic, antecolic, and side-to-side gastrojejunostomy was created (11). After checking for any leak from the anastomosis site with a methylene-blue dye test, the incision sites were sutured, dressed with gazes, and the patient was sent to the recovery room. All patients were treated with intravenous antibiotics for one day and continued with an oral antibiotic for 5 days. Patients were put on oral clear liquids and soups on the first postoperative day, which turned to soft puree and blended foods if they did not have any problem like nausea/vomiting. The patients were allowed to start oral protein and multivitamin supplementation meals on the second day after the surgery.

Statistical analysis: All data were analyzed by the IBM SPSS statistical package version 20.0 (Chicago, IL, USA). Kolmogorov-Smirnov test was used to evaluate the normal distribution of the variables. A paired T-test was used to compare each quantitative variable in two situations (pre and postoperatively). One ANCOVA model was used for delta-difference in Firmicutes count between baseline and either of the 6-month or 12-months results after being adjusted for cofounding variables. Age, sex, preoperative BMI, and delta-BMI were entered to the ANCOVA model all together. Pearson correlation test was used to evaluate the relationship between weight change and Firmicutes counts before and after the surgery. The Pearson correlation coefficient is not reported in case of finding no significant relationship. P-value (2-tailed) of < 0.05 was considered statistically significant.

Results

About 70.6% of our patients were female. Our 50 bariatric candidates aged 37.79±8.98 years (range: 21-56). Mean, Standard deviation, and ranges of weight, BMI, and Firmicutes count before and after the surgery are summarized in Table 1.

Percentage of Excess weight loss (%EWL), total weight loss (%TWL), and excess BMI loss (%EBMIL) were 44.06%±9.84, 25.04%±4.40, and 42.56%±5.29, respectively at the 6-month follow-up and 67.55%±5.56, 33.52%±3.94, and ۷۰.81%±7.25 respectively at the 12-month follow-up.

No significant difference was found by ANCOVA model and after adjustment was used for age, sex, preoperative BMI, and delta-BMI for neither the 6 nor 12 months data (p=0.74 and 0.59, respectively).

Pearson correlation test did not show any relationship with changes in Firmicutes count and any weight-related variable (delta-weight, delta-BMI, %EWL, %TWL, or %EBMIL) in OAGB/MGB candidates for neither the 6 nor 12 months data.

Table 1. Comparison of the weight, BMI and Firmicutes count before and after the laparoscopic OAGB/MGB surgery

Variables*	Before (n=50)	6 months (n=50)	P†	12 months (n=50)	P†
Weight (kg)	132.50±15.44 (110-160)	105.64±9.47 (95-120)	<0.001	77.81±10.29 (65-99)	<0.001
BMI (kg/m^2)	49.86±7.25 (40-58)	35.90±3.86 (32-45)	<0.001	26.03±5.62 (22-30)	<0.001
Firmicutes count (log10)	1.57±0.29 (1.01-2.40)	1.44±0.19 (1.00-1.85)	0.01‡	1.32±0.31 (1.02-1.41)	0.02‡

OAGB/MGB: one anastomosis gastric bypass/mini-gastric bypass, kg: kilograms, kg/m^2: kilograms per square meter.
*All variables are shown with mean and standard deviation. The ranges are put in parenthesis.
† Paired t-test was used for the analysis. P<0.05 was considered statistically significant.
‡ No significant difference was found by ANCOVA model and after adjustment was used for age, sex, preoperative BMI, and delta-BMI.

Discussion

Laparoscopic OAGB/MGB is an effective, relatively low-risk, and low-failure bariatric procedure. It's acceptable results in weight loss have been confirmed in many articles. In our study, significant weight loss was obtained 12 months after the surgery and it is similar to many other previous studies (12-15). It is now known that the mechanisms of weight loss after the gastric bypass procedures are not explained by mechanical changes and physiologic changes are involved in this process too. The Gastrointestinal (GI) tract is a complex endocrine and metabolic organ thus; altering the GI tract can alter gut physiology and cause metabolic changes such as weight loss.

This study was conducted for the first time to evaluate the effects of laparoscopic OAGB/MGB surgery on gut microbiota changes and its relationship to weight loss postoperatively. In our study, although the amount of Firmicutes was reduced significantly after the surgery, there was no relationship between weight loss and reducing Firmicutes count. This lack of relevance indicates that the mechanism of weight loss following the surgery is complicated and microbial changes in the GI tract after the surgery are not the only possible mechanism or hypothesis for weight loss postoperatively (16). In our study, the amount of Firmicutes dropped significantly 6 and 12 months after the surgery. This finding is consistent with the other studies in other bariatric models (17-22). Several human and animal experiments have been done to understand the mechanism of association between changes in the gut microbiome and weight loss. It has been shown that inflammatory biomarkers (e.g. plasma highly sensitive C-reactive protein (hs-CRP), interleukin-6, and orosomucoid) can be reduced by GI microbial changes. Transfer of the gut microbiota from operated mice to nonoperated, germ-free mice was led to weight loss and fat mass decreased in the recipient due to short-chain fatty acids production (17-22).

Our bariatric candidates operated with standard laparoscopic OAGB/MGB surgery (23-30) and their postoperative results are similar to other studies on RYGB (29). In the animal model study, microbial changes were most evident in the distal intestine, downstream of the surgical anastomosis site. As a hypothesis, it can be concluded that any changes in the GI anatomy can cause microbial changes but more evidence is needed (19). The mechanism why gastric bypass surgery can change the gut microbiome is unclear. After the surgery, the entered foods bypass a large number of gastric acidification parts leading to a reduction of chloride acid flux in the gut. Patients were also under the proton pump inhibitor therapy during the first 3 months, which can also influence the gastric acidity. Therefore, increased pH, with the downstream delivery of bile acids, can contribute to modify the fecal bacteria (18).

An epidemiologic study showed that Firmicutes count and Firmicutes to Bacteroidetes ratio are higher in patients with BMI ranged in obesity category than normal-weight population (16). There was also a statistically significant positive trend for higher hs-CRP in subjects with positive Firmicutes (20). Some researchers believe that gut microbiota alteration may be an initial event leading to altered feeding behavior and/or systemic inflammation, ultimately leading to obesity and metabolic syndrome. In patients with morbid obesity, the Firmicutes are dominant and when they lose weight, the proportion of Firmicutes become more like normal people. Gut microbiota has an important role in energy harvesting, inflammatory signaling, and regulation of the brain-gut axis leading to weight changes. Microbiota can influence weight gain by enhancing energy extraction, creating a smoldering inflammatory response, and by enhancing food intake through stimulation of the brain-gut axis. On the other hand, changing the gut microbiota is leading to weight changes (21). It is unknown why people with morbid obesity have more Firmicutes in their gut. The host gut may have uncharacterized properties that select this bacterial phylum (22). Moreover, the higher caloric intake was associated with a 20% growth of Firmicutes and a 20% reduction in Bacteroidetes, which was directly related to the weight gain (22).

To enhance the quality of further researches in this area, we state a larger study population should be selected, other microbiome profiles with their exact behavioral changes should be addressed postoperatively. We followed our patients for up to 6 months. Long-term results in gut microbiota changes after the surgery should be evaluated too.

Conclusion

OAGB/MGB has excellent weight-loss outcomes during the first and second 6 months postoperatively. This surgery causes significant microbial changes, including significant Firmicutes count reduction that may be a possible hypothesis for weight reduction after the surgery. However, our study did not confirm that hypothesis and no relationship was found between weight loss and Firmicutes count.

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Ethics

An informed written consent was obtained from all of the patients preoperatively. This research was conducted under Helsinki declarations. This study was approved by the Committee on Medical Ethics of Isfahan University of Medical Sciences.

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