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Gastro Jejunal Inner Lumen Bypass Device Inhibits the Growth of Pigs

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Abstract

The EndoBarrier has a weak point caused by a Teflon membrane, which completely inhibits the movement of water and food. We developed a new type of gastro jejunal inner lumen bypass device (GJB) using an artificial net that has a hole instead of a membrane.

We inserted a net in the gastric antrum-duodenum–jejunum via open laparotomy. The growth of pigs with long nets was suppressed compared with the sham operation. However, there were no differences in blood biochemistry or anatomical findings at autopsy between the groups. As a result, GJB can control the growth of pigs without requiring dietary restriction.

Keywords: Bariatric surgery; EndoBarrier; Gastro jejunal inner lumen bypass devices (GJB)

Introduction

Obesity is a risk factor for cardiovascular disease, type II diabetes, stroke, cancer and Alzheimer's disease [1-5]. Obese individuals need to lose weight. However, weight loss attempts are frequently unsuccessful. As a result, surgical treatment has emerged as an effective treatment for patients with obesity. Commonly performed procedures include Roux-en-Y gastric bypass, sleeve gastrectomy, and biliopancreatic diversion/duodenal switch [6]. However, several short- and long-term complications may occur with these procedures, including anastomotic leaks, bleeding, infection, dumping syndrome and malabsorption of micronutrients (e.g., iron, calcium, and vitamins). Furthermore, the procedure is irreversible [7,8]. As a result, at the time of biliary and pancreatic carcinoma surgery, future reconstruction may be very complicated.

To avoid an irreversible procedure, several recent human studies have used the EndoBarrier Gastrointestinal Liner, which is a 60 cm impermeable fluoropolymer, Teflon membrane that is fixated to the duodenum and extends into the small intestine; it usually terminates in the proximal jejunum. The EndoBarrier is minimally invasive and fully reversible and is effective for weight loss; it can also improve diabetes (greater reductions in glycated hemoglobin; HbA1c) [9-12]. However, on 31 July 2015, a medical device company and the U.S. Food and Drug Administration (the FDA) announced the decision to discontinue the U.S. EndoBarrier therapy trial for the treatment of obese patients because of a higher than anticipated incidence of hepatic abscesses from bacterial infections of the liver (GI Dynamics Press Release - July 30, 2015, GI Dynamics Concludes ENDO Trial).

To solve these problems, we developed new type of gastro jejunal inner lumen bypass device (GJB) with a longer length using an artificial net. We have a patent pending (2014-068503, PTC/JP2015/57361).

The difference between the Teflon membrane of the EndoBarrier and our GJB net is that our net has holes, allowing for free movement of water and food at the surface of the intestinal mucosa, indicating that digestion and absorption are not completely inhibited at that location. So it may prevent obstruction of the ampulla of Vater which impairs the flow of bile and causes hepatic abscess from the bacterial infection of the liver.

Methods

Four-to-five-week-old male Landrace, Large white and Duroc (LWD) pigs with an average body weight of 7-8 kg from Seiko animal industry Co., Ltd. (Gifu, Japan) were included in this study. Pigs were housed in separate pens at a constant temperature under a light-dark cycle. They had free access to food, semi-solid animal feed (for growing animals) (Winny Cline, NOSAN Co., Yokohama, Japan), and water. The pigs were fed the same amount of feed, which was based on the Japanese Feeding Standard for pigs (Japan Livestock Industry Association, 2005), every day. All pig experiments were approved by the university committee on animal research, and the pigs received humane care in accordance with the National Institutes of Health publication 86-23, the "Guide for the Care and Use of Laboratory Animals."

Laparotomy, gastrostomy and enterotomy were performed, and a catheter (New Enteral feeding tube, COVIDIENTM, Co., Tokyo, Japan) was inserted into the jejunum and extended into the gastric

antrum of the stomach. The end of the GJB was then connected to the introduction catheter, and the catheter was removed from the enterotomy (Figure 1). The oral side of the GJB was fixed to the full-thickness gastric wall by non-absorbable prolene 2-0 suture (4-8 stitches). The jejunum side of the GJB was also weakly fixed by absorbable vicryl 5-0 suture (1-2 stitches). Finally, the laparotomy, gastrostomy and enterotomy were completed, and the area was irrigated with saline. The sham operation consisted of laparotomy and gastrotomy with repair. Control pig was bred without undergoing an operation during the same period. After surgery, the pigs were provided free access to water and food after approximately 15 h.

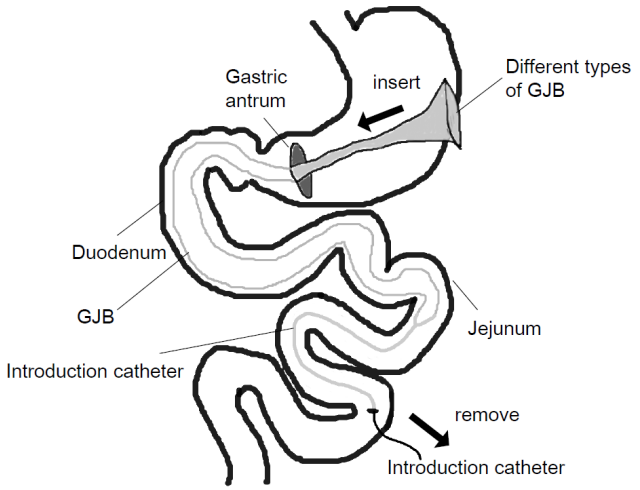

Figure 1: How to insert the GJB.

The following nets were used in this study for the GJB: a plastic net, which is used as an orange package in Japan (made of polyethylene, Morishita Inc., Okayama, Japan, 5-10 mm hole); knit fabric net, which is used as nylon stockings (ATSUGI Co., Ltd., Kanagawa, Japan, 1-2 mm hole); and a nonwoven net, which farmers initially used to keep insects off plants (made of polypropylene, Dio Chemicals, Ltd., Tokyo, Japan, less than 1 mm hole) (Figure 2). The diameter of the net was 20 mm, and the lengths of the short nets were as follows: plastic net (45 cm), knit fabric net (70 cm), and nonwoven net (45 cm). The lengths of the long net were as follows: plastic net (115 cm), knit fabric net (109 cm), and nonwoven net (125 cm). Every week after surgery, we checked the animals' body weights (Figure 3). Additionally, serum total protein, albumin (Alb), total cholesterol, triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), magnesium (Mg) and calcium (Ca) were measured by standard laboratory methods (Table 1). After five weeks, the pigs were killed and autopsied, and we observed the intraperitoneal cavity, the inside of the stomach and the intestine.

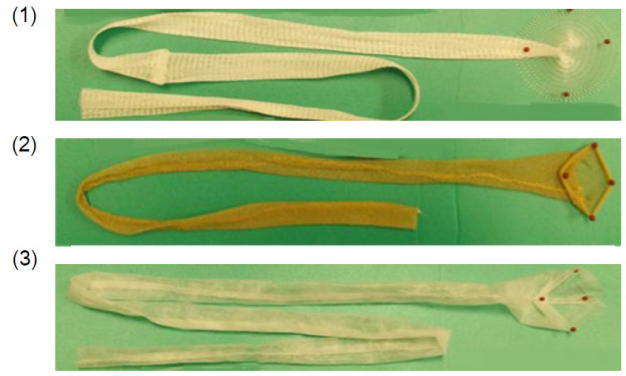

Figure 2: The different GJB types. (1) Plastic net (Short 45 cm, Long 115 cm). (2) Knit fabric net (Short 70 cm, Long 109 cm). (3) Nonwoven net (Short 45 cm, Long 125 cm).

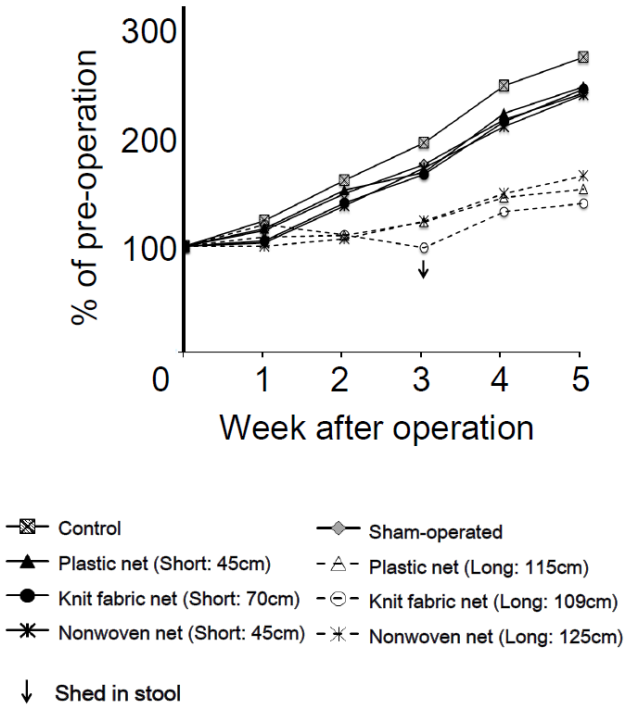

Figure 3: The body weight change observed in the pigs.

Results

After five weeks, the control pig body weight was nearly three times the weight on day 0. Pig undergoing the sham operation had a growth rate depicted in (Figure 3).

The short net inserted pigs

When we conducted the autopsy, the short plastic net (45 cm) and short nonwoven net (45 cm) flowed back from the jejunum into the stomach. The short knit fabric net (70 cm) could not be found inside the stomach or intestine; therefore, we concluded that it may have been shed in the stool.

In the three pigs receiving short net insertions, there were no apparent abnormal findings, such as ulcers of the stomach or intestine, adhesion, or ileus. The body weight of the pigs with the short net increased approximately 2.5-fold at the end of five weeks. It appears there were no differences in the body weight increases of the pigs inserted with short nets compared with the sham-operated pig (Figure 3).

The long net inserted pigs

The long knit fabric net (109 cm) was excreted into the stool three weeks after the operation (technical error of stitches in the stomach). The long plastic and nonwoven nets slightly prevented body weight gain with an approximately 60% growth suppression compared with the sham-operated pig after five weeks.

On autopsy, administered food was observed on the outside and inside of the net. No abnormal findings were seen inside or outside of the intestine. There were no differences in body weight changes, regardless of the hole size, nor were there any differences in blood chemistry results (Table 1).

		Total protein	Alb	Total cholesterol	TG	HDL	LDL	Mg	Ca
		g/dl	g/dl	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl	mg/dl
Control	Pre-operation	4.8	3.3	109	51	49.6	48	2.4	11.7
	5 weeks	4.7	3.6	75	45	34.9	30	1.8	11.1
Sham-operated	Pre-operation	5	3.6	124	66	56.4	55	2.9	12.9
	5 weeks	4.8	4.1	69	19	29.8	30	1.9	11.2
Fabric net (S)	Pre-operation	4.3	3.2	79	23	42.5	28	2.2	12.1
	5 weeks	4.9	3.9	73	26	32.6	30	2	12
Stocking (S)	Pre-operation	4.4	3.1	91	27	49.9	36	2.5	11.9
	5 weeks	4.9	3.4	68	16	29.7	29	1.7	11.1
Nonwoven (S)	Pre-operation	4.8	3	93	12	36.6	48	2.43	11.8
	5 weeks	5.6	3.5	88	18	38.6	43	2.35	12.43
Fabric net (L)	Pre-operation	5.2	3.7	133	74	45	78	2.9	12.2
	5 weeks	5.1	3.4	95	73	42.3	43	2.5	11.6
Stocking (L)	Pre-operation	4.9	3.3	147	85	56.3	76	2.4	11.7
	5 weeks	5.5	4.1	114	118	56.2	44	2.4	11.3
Nonwoven (L)	Pre-operation	4.5	3	150	27	42.8	96	2.7	10.7
	5 weeks	5.2	3.3	116	43	44.9	60	1.9	11.3

Table 1: Blood biochemistry.

Discussion

The purpose of the bariatric procedure and EndoBarrier treatment is to reduce body weight in obese people. However, in this study, due to the space constraints of our laboratory, we investigated the effect of growth inhibition on younger pigs instead of conducting research on obese pigs.

The length of the EndoBarrier Gastrointestinal Liner is only 60 cm. It covers only 35 cm of the small intestine. The length of the device may not be sufficient. Furthermore, the EndoBarrier Gastrointestinal Liner is made of the Teflon, which may be a point of weakness. Teflon completely inhibits the movement of water and food, and it may obstruct the ampulla of Vater, preventing the flow of bile and causing a liver abscess. To solve these problems, we envisioned a porous membrane. However, we used nets with different hole sizes (ranging from less than 1 mm to 10 mm) as the gastro jejunal inner lumen bypass device.

We found that long GJB-inserted pigs demonstrated a growth suppression of approximately 60% compared with sham-operated pig. However, compared with the plastic net (5-10 mm) and nonwoven net (less than 1 mm), there was no difference in growth suppression, regardless of the hole diameter. One reason may be that the food the pigs ate is similar to rice gruel. It is easily softened with water and

gastric juice. Therefore, regardless of the sizes of the holes, the food can freely move inside and outside of the net.

On the other hand, there were no differences in blood biochemistry (total protein, albumin, total cholesterol, etc.) between the sham-operated and operated pigs. Therefore, the GJB net seems to inhibit digestion and absorption in a physiologic manner.

This study is the first to demonstrate that inserting different types of artificial nets into the gastro jejunal area inhibits the growth of pigs. These results demonstrate that GJB nets can promote weight loss without requiring dietary restriction.

References

1. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, et al. (2014) Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 384: 766-781
2. Hanson C, Rutten EP, Wouters EF, Rennard S (2014) Influence of diet and obesity on COPD development and outcomes. Int J Chron Obstruct Pulmon Dis 9: 723–733.
3. Finkelstein EA, Fiebelkorn IC, Wang G (2003) National medical spending attributable to overweight and obesity: how much, and who's paying?. Health Aff (Millwood) Suppl Web Exclusives: W3-219-26.
4. Kaplan LM (2005) Gastrointestinal management of the bariatric surgery patient. Gastroenterol Clin North Am 34: 105-125.
5. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, et al. (2004) Bariatric surgery: a systematic review and meta-analysis. JAMA 292: 1724-1737.
6. Buchwald H, Oien DM (2013) Metabolic/bariatric surgery worldwide 2011. Obes Surg. 23: 427-436.
7. Buchwald H, Estok R, Fahrbach K, Banel D, Sledge I (2007) Trends in mortality in bariatric surgery: a systematic review and meta-analysis. Surgery 142: 621-635.
8. Bal BS, Finelli FC, Shope TR, Koch TR (2012) Nutritional deficiencies after bariatric surgery. Nat Rev Endocrinol 8: 544-556.
9. Rohde U, Hedback N, Gluud LL, Vilsboll T, Knop FK (2013) Effect of the EndoBarrier Gastrointestinal Liner on obesity and type 2 diabetes: protocol for systematic review and meta-analysis of clinical studies. BMJ Open 3: e003417.
10. Patel SR, Mason J, Hakim N (2012) The Duodenal-Jejunal Bypass Sleeve (EndoBarrier Gastrointestinal Liner) for Weight Loss and Treatment of Type II Diabetes. Indian J Surg 74: 275-277.
11. Koehestanie P, de Jonge C, Berends FJ, Janssen IM, Bouvy ND, et al. (2014) The Effect of the Endoscopic Duodenal-Jejunal Bypass Liner on Obesity and Type 2 Diabetes Mellitus, a Multicenter Randomized Controlled Trial. Ann Surg 260: 984-992.
12. Schouten R, Rijs CS, Bouvy ND, Hameeteman W, Koek GH, et al. (2010) A multicenter, randomized efficacy study of the EndoBarrier Gastrointestinal Liner for presurgical weight loss prior to bariatric surgery. Ann Surg 251: 236-243.