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Small intestinal interventions including barriers, duodenal mucosal resurfacing, and other small bowel strategies

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ABSTRACT

Bariatric surgery has revolutionized obesity treatment. There remains, however, a large demand for less invasive and potentially cheaper or even reversible procedures that impart a similar effect on obesity and its related comorbidities. Endoluminal Bariatric Therapies, such as endoluminal sleeves or barriers, duodenal mucosal resurfacing technology, and magnetic anastomoses may emerge to fill this gap. To date, their safety profiles and the reported success with regard to both weight loss and diabetes control have proven favorable, yet need to be further studied before widespread adoption. The following review will discuss in detail these procedures and the literature supporting their continued development and potential clinical applications.

1. Introduction

Bariatric surgery has emerged as an effective intervention to treat and even cure morbid obesity and its related comorbidities such as diabetes, hypertension, hyperlipidemia, depression, infertility, coronary artery disease, and obstructive sleep apnea [1-10]. However, owing to a multitude of factors, such as access to bariatric surgeons, insurance coverage issues, patient fears and perceptions, lack of referrals from primary care physicians, and the underlying risks associated with the Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy, only approximately 1% of the eligible population undergoes bariatric surgery [11]. For this reason, coupled with the increasing epidemic of obesity, there remains a considerable need for effective nonsurgical treatment modalities to address this serious potentially life-threatening disease. Intensive lifestyle intervention has been shown to result in only a modest 5% long-term weight loss [12-14]. Thus, novel endoscopic therapies that are minimally invasive and associated with less morbidity than surgery could be the answer for many morbidly obese patients [15-19].

Currently available endoscopic technology attempts to mimic the effects of bariatric surgery or has been developed based on existing understanding of weight loss physiology. These endoscopic therapies can serve as the primary treatment modality or can be used as a bridge to bariatric surgery. The potential for endoscopic bariatric therapies to promote weight loss before bariatric surgery is significant because it has been shown that preoperative weight loss before RYGB or vertical sleeve gastrectomy improves the technical complexity of the surgery and shortens the operative time by decreasing visceral fat volume, liver volume, and abdominal wall thickness. Also, improvements in cardiovascular and respiratory status as well as decreased thromboembolic risk occur with preoperative weight loss [16]. Furthermore, some of these procedures offer the benefit of reversibility and can be very cost-effective [15-19]. In the following review, 3 emerging small bowel endoscopic bariatric procedures will be discussed: endoluminal barriers or sleeves, duodenal mucosal resurfacing, and magnetic anastomoses (Figure).

2. The role of the small bowel in weight loss and diabetes

Early explanations for weight loss after bariatric surgery are focused on malabsorption and restriction as the primary etiologies for successful sustained weight reduction. More recent studies, however, have disproven those theories and have demonstrated that the physiology of weight loss is much more complex. Exact understanding of the neurohormonal control of hunger and weight as well as the role of the proximal small bowel, especially the duodenum, in the regulation of glycemic control, insulin secretion and resistance, and gastric motility remains somewhat elusive. A multitude of peptides are released by enteroendocrine cells (EECs) of the gastrointestinal (GI) tract in response to stimulation by luminal nutrients, including glucagon-like polypeptide (GLP-1), oxyntomodulin, peptide YY (PYY), ghrelin, and gastric inhibitory peptide (GIP). These peptide hormones have been

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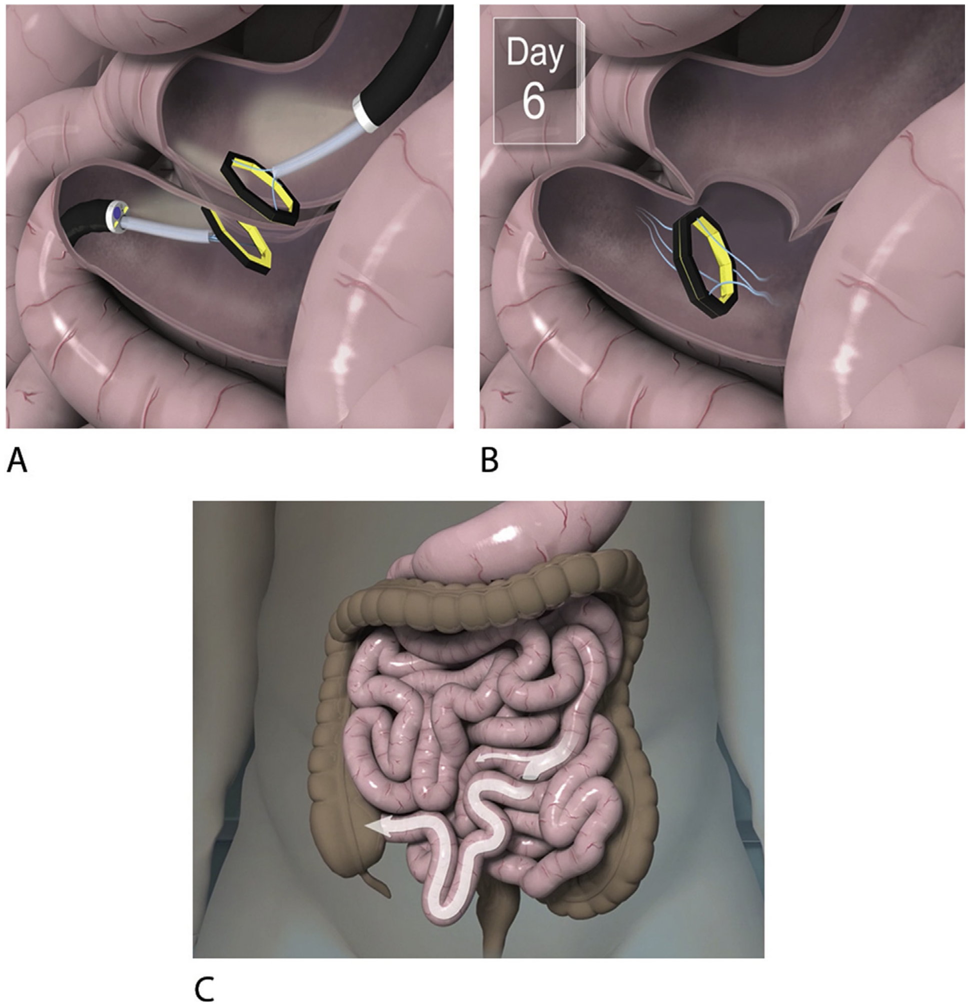

Fig. Pictured is the incisionless anastomosis system (IAS) by GI Windows. (A) Magnets are deployed endoscopically and coupled. (B) The mated magnets pass naturally after the creation of the anastomosis. (C) The enteral diversion has been created and chyme now bypasses a large portion of small bowel.

implicated in weight loss physiology owing to observed actions either peripherally or centrally in the gut-brain axis. Several of these peptides, all cosecreted by L cells located along the GI tract, GLP-1, oxyntomodulin, and PYY, which are elevated in patients following RYGB, induce satiety and decrease caloric intake [20-22].

This is summarized as the hindgut hypothesis, which explains that the expedited delivery of nutrients to the distal intestine alters a physiologic signal, perhaps one or all of these peptides, and subsequently results in weight loss and enhanced glucose metabolism [23]. Although GLP-1 and PYY have been correlated with weight loss after bariatric surgery, studies are controversial or lacking with regard to the peptides' involvement in glucose homeostasis after surgery [21,24,25]. In addition to regulating weight, many studies have demonstrated that the proximal small bowel plays an important role in glucose homeostasis, and thus alterations can lead to the development of diabetes. This idea is corroborated by the fact that most obese patients experience early resolution of diabetes after RYGB, usually long before significant weight loss occurs [22,23,26].

In contrast to the hindgut hypothesis, the foregut hypothesis states that the exclusion of nutrients from the duodenum and proximal jejunum is what drives improved glycemic control and weight loss. The peptides implicated in this theory are ghrelin (released by gastric epithelial cells) and GIP (secreted by K cells in the duodenum). Ghrelin, also known as the hunger hormone, is an appetite-stimulating hormone that peaks prior to eating and falls after meals. It has also been implicated in glucose homeostasis. The effect of bariatric surgery on ghrelin levels has been inconclusive, with some studies reporting an increase, some a decrease, and some no change in plasma levels. The peptide GIP has an incretin (insulin-like) effect and increases energy expenditure. Studies have yet to elucidate the role of GIP after bariatric surgery [20].

The results of a study by Rubino et al. favor the foregut hypothesis in diabetes control. They demonstrated, in a surgical diabetic rat model that tested the foregut hypothesis of duodenal-jejunal bypass (DJB) against the hindgut hypothesis of gastrojejunostomy, that bypassing the proximal small intestine (DJB) results in improved glucose tolerance compared to expedited delivery of nutrients to the distal bowel gastrojejunostomy. They hypothesized the following regarding the development of insulin resistance and diabetes: “in predisposed individuals, chronic stimulation of the proximal small bowel to certain nutrients may create an imbalance between incretin and anti-incretin signals” [23]. In addition, in a study comparing obese patients with and without hyperglycemia, Verdam et al determined by measuring plasma protein levels that small intestinal enterocyte mass and enterocyte turnover is increased in obese diabetic patients. They hypothesized that the increased enterocyte mass might result in