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First human experience with endoscopically delivered and retrieved duodenal-jejunal bypass sleeve

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Abstract

Background: We report the first human experience with an endoscopic duodenal-jejunal bypass sleeve (DJBS) in a community hospital.

Methods: The DJBS is a 60-cm sleeve anchored in the duodenum to create a duodenal-jejunal bypass. In a 12-patient prospective, open-label, single-center, 12-week study, the device was endoscopically implanted, left in situ, and retrieved. The study included 5 men and 7 women, with a mean body mass index of 43 kg/m^2. Of the 12 patients, 4 had type 2 diabetes. The primary endpoints were the incidence and severity of adverse events. The secondary outcomes included the percentage of excess weight loss and changes in co-morbid status.

Results: The DJBS was endoscopically delivered and retrieved in all patients (mean implant/explant time of 26.6 and 43.3 min, respectively). Of the 12 patients, 10 were able to maintain the device for 12 weeks and 2 underwent explantation after 9 days secondary to poor device placement. Several self-limited adverse events were possibly or definitely related to the device, including 6 episodes of abdominal pain, 18 of nausea, and 16 of vomiting, mainly within 2 weeks of implantation. Two partial pharyngeal tears occurred during explantation. Implant site inflammation was encountered in all patients. No device-related event was considered severe. The average percentage of excess weight loss for the 10 patients with the device in place for 12 weeks was 23.6%, with all patients achieving at least 10% excess weight loss. All 4 diabetic patients had normal fasting plasma glucose levels without hypoglycemic medication for the entire 12 weeks. Of these 4 patients, 3 had decreased hemoglobin A_{1c} of $\geq$.5% by week 12.

Conclusion: The DJBS can be safely delivered and removed endoscopically and left in situ for 12 weeks. The device had a favorable safety and encouraging efficacy profile. Randomized prospective trials are warranted. (Surg Obes Relat Dis 2008;4:55–59.)

Keywords: Bariatric; Endoluminal; Diabetes; Obesity; Duodenum

The 1998 National Institutes of Heath Panel on Weight Loss recommended that patients attempt to lose 10% of their body weight before undergoing surgery for weight loss [1]. Current strategies range from commercial diets to staged approaches [2]. Although each of these methods has merit, considerable limitations exist. Diets carry little risk but are invariably unsuccessful. Staged approaches are paradoxical in that high-risk patients are exposed to two surgical procedures rather than one. Given these limitations, novel preoperative weight loss strategies are desirable.

We recently reported our animal experience with an endoscopically delivered and retrieved, reversible duodenal-jeju-

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Fig. 1. DJBS implant.

nal bypass sleeve (DJBS) [3]. The DJBS contains an implant that is endoscopically delivered and anchored in the proximal duodenum and a sleeve that is extended into the jejunum (Fig. 1). Chyme passes through the sleeve, creating an intestinal bypass/biliopancreatic diversion without the need for stapling or anastomosis. The device has not yet received Food and Drug Administration approval. This report details our first human experience with the DJBS.

Methods

In a 12-patient, prospective, open-label study, the device was endoscopically placed, left in situ for 12 weeks, and endoscopically retrieved. Patients were enrolled in the study after they were deemed candidates for gastric bypass in accordance with the 1991 National Institutes of Health guidelines [1]. The device was used to enhance the preoperative weight loss. The primary endpoints were the incidence and severity of adverse events. The secondary endpoints included the percentage of excess weight loss and changes in co-morbid status. Type 2 diabetes mellitus (T2DM) was considered improved if the patient had a reduction in fasting plasma glucose or hemoglobin A_{1c} or a decrease in the frequency or dosing of medications. T2DM was considered to have resolved if the fasting plasma glucose and hemoglobin A_{1c} had normalized and the patient no longer needed diabetes medication. Hypertension was considered improved if the systolic and/or diastolic pressure components had decreased or the patients had been able to reduce or discontinue medical therapy. Hypertension was considered to have resolved if the systolic and diastolic components were normal and the patient no longer required medication. Hyperlipidemia was considered improved if the patient had a decrease in laboratory values or a reduction or discontinuation of medical therapy. It was considered to have resolved if the laboratory values were normal and the patient no longer required medication.

All patients provided written informed consent, and the hospital ethics committee approved the study. All participants had undergone a baseline evaluation, including history and physical examination, upper endoscopy, fasting blood tests, and a nutritional assessment. During all study-specific visits, the safety and efficacy data were recorded using approved study forms.

All 12 patients underwent general anesthesia. During the procedure, fluoroscopy and endoscopy were used to deliver the device. The implant was delivered using an over-the-wire catheter system and was contained within a capsule at the distal end of the catheter. Once the capsule was placed in the duodenum, an inner catheter was pushed and the bowel negotiated with the aid of an atraumatic ball attached to the distal end of the catheter. The sleeve was attached to the catheter, which pulls the sleeve out of the capsule. Once the sleeve was fully deployed, the anchor was deployed from the capsule to sit within the duodenal bulb. The anchor is self-expanding, and the barbs engage the tissue to prevent movement. Contrast was flushed to ensure patency of the sleeve (Fig. 2). The sleeve and ball were detached from the catheter, and the catheter was removed from the bowel, leaving the implant in place. The total procedure and fluoroscopy times were recorded, as were any procedure-related adverse events.

All patients were hospitalized for 24 hours and maintained on a liquid diet for 1 week. The diet was then advanced to puree and then solid food at weeks 2 and 4, respectively. After discharge, the patients were evaluated weekly for the first 8 weeks, at 10 and 12 weeks after implantation, and then again 72 hours after device removal.

For the 12-week follow-up period, the patients were closely evaluated with a combination of serum testing, history, physical examination, and adverse event monitoring. Plain abdominal films and upper gastrointestinal studies with contrast were occasionally used to evaluate device position and assess for patency.

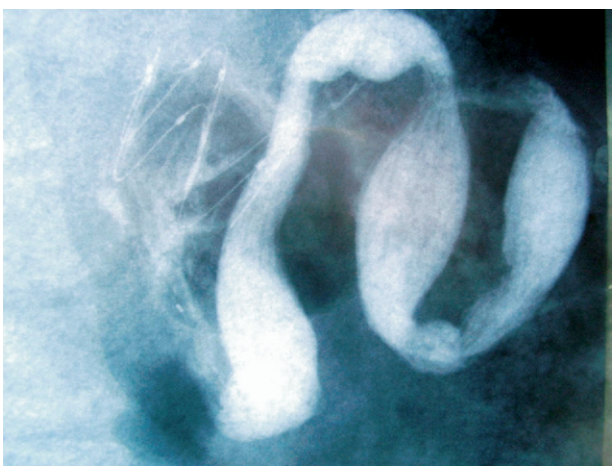

Fig. 2. Contrast study showing patency of sleeve.

The patients received weight loss counseling before implantation and at each follow-up visit during the in vivo period. All patients were advised to consume a 1000-calorie low-fat diet. Although no food logs were used, the patients were asked to rate their desire for food and feelings of satiety at each visit compared with before implantation. No patient was lost to follow-up.

During the explantation procedure, a combination of fluoroscopy and endoscopy was used for retrieval. Retrieval was accomplished by first collapsing the anchor by grabbing 1 of the proximal drawstrings using a custom grasper. Once collapsed, the anchor was pulled inside a custom retrieval hood placed on the end of the endoscope. The hood served to protect the tissue from the barbs during withdrawal, thus precluding the need for an overtube. The total procedure and fluoroscopy times were recorded, as were any adverse events.

Follow-up endoscopy and clinical assessment were performed 72 hours after removal of the implant. Surveillance was done of the stomach and the duodenum.

Results

Of the 12 patients, 5 (41.7%) were men and 7 (58.3%) were women. The mean age was 41 years (range 28–54), and the mean body mass index (BMI) was 43 kg/m^2 (range 35–51). The mean starting weight was 115.7 kg (range 89–142). Of the patients who completed the study, 6 had at least 1 co-morbid condition. Of these 6 patients, 4 had T2DM, 4 had hypertension, and 3 had hyperlipidemia.

Twelve implants were attempted and completed. The mean implant time was 26.6 minutes (range 20–51), with a mean fluoroscopy time of 14.5 minutes (range 9.0–19.7). The time required for implanting the device was relatively constant across all 12 implants. Twelve explants were performed. The mean explant time was 43.3 minutes (range 17–182), with a mean fluoroscopy time of 10.7 minutes (range 2.2–23.8).

Two procedure-related adverse events occurred in 2 patients: 1 oral-pharyngeal mucosal tear and 1 esophageal mucosal tear. These events both occurred during device removal. No event was considered serious by the investigator.

A total of 71 adverse events were reported in the 12 patients during the in vivo period. Of these events, 55 (78%) were possibly or definitely related to the device. These events included 6 reports of abdominal pain, 1 of diarrhea, 1 of a gastrointestinal mucosal disorder/esophageal tear, 12 of implant site inflammation, 18 of nausea, 16 of vomiting, and 1 of a oral-pharyngeal mucosal tear. Most episodes of abdominal pain, nausea, or vomiting occurred during the first week of the study. None of these events were considered severe by the investigator. All events were rated mild or moderate, and all were self-limited.

Tissue inflammation was uniformly present in all 12 patients at explantation. The inflammation was limited to the site of the anchor. These changes were noted only on endoscopy. Inflammatory pseudopolyps were a frequent finding at the 72-hour surveillance endoscopy after explantation.

Of the 12 patients, 2 underwent explantation before their scheduled removal date (9 days into the implant) because of excessive abdominal pain and discomfort. No patient in the study experienced migration or obstruction. Similarly, no clinically significant abnormal blood values were reported. No serious adverse events related to the device or the procedure occurred. All events were anticipated in both occurrence and severity.

Weight loss data were available for all 10 patients completing the study. The average percentage of excess weight loss for the 10 patients was 23.6% (range 12.5–41.5%; Fig. 3). All 10 patients were able to achieve $\geq$10% excess weight loss. The average total weight loss was 10.2 kg (range 6.1–16.6). The average baseline BMI was 43 kg/m^2. The average ending BMI was 38.7, for an average decrease in BMI from baseline of 3.8 kg/m^2 (range 2.0–6.2). All patients reported greater satiety and less food volume intake after the device was implanted.

Of the 12 patients, 4 had T2DM, all of whom completed the study. All 4 patients had required oral medication to control their condition at baseline. In 3 of the 4 patients, T2DM had resolved within 24 hours of implantation. One patient showed no improvement. Of the 4 patients with a history of hypertension at baseline, all 4 completed the study. All patients had required oral medication at baseline to control their hypertension. By the end of the study, the hypertension of 1 patient had resolved, 1 patient had improvement, and 2 patients no change. Of the 3 patients with hyperlipidemia, all completed the study. At the end of the study, 2 had improvement and 1 showed no change.

Additional blood tests relevant to safety included measures of serum amylase, liver function tests, complete blood count, routine chemistry, vitamins D and B_{12}, folate, iron, ferritin, and albumin. All laboratory values were normal during the study period, with the exception of transient alterations in serum bilirubin in select patients.

Discussion

Gastric bypass surgery results in anatomic alterations that each may play a role in its mechanism of action. Although continually debated, the restrictive (pouch), hormonal (gastric/duodenal bypass), malabsorptive (jejunal bypass), and neural (partial vagotomy) effects may all variably contribute to the known efficacy profile. Several studies have sought to further delineate these relative contributions. In the attempt to better understand the role of duodenal bypass, Rubino et al. [4] studied duodenal jejunal exclusion in a spontaneous, nonobese rat model of T2DM. That study

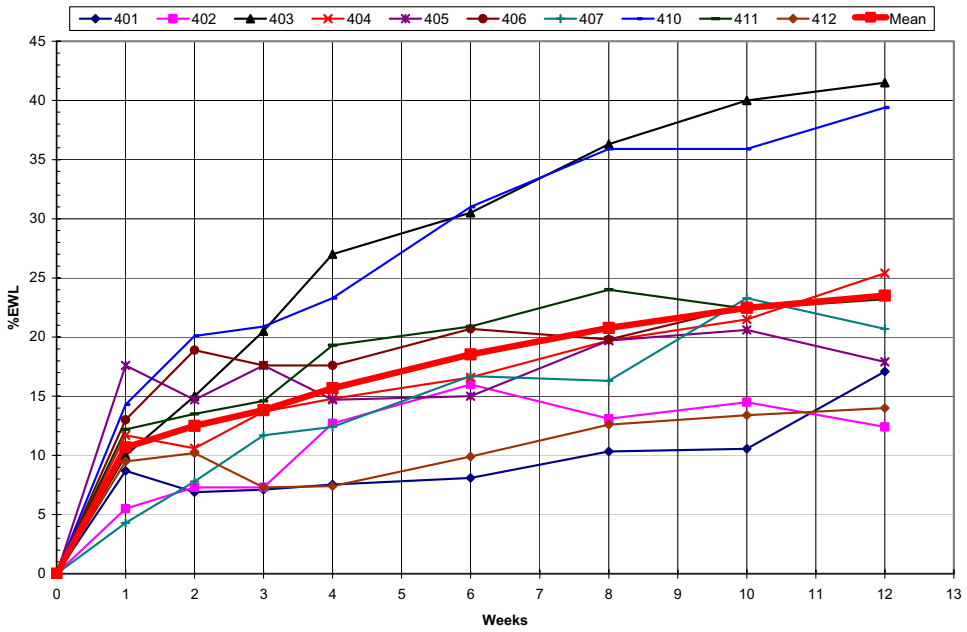

Fig. 3. Percentage of excess weight loss with time for each patient; overall mean also shown.

showed that bypassing the duodenum directly ameliorated T2DM, independently of effects on food intake, body weight, malabsorption, or nutrient delivery to the hindgut. Although still poorly understood, this concept could serve as the physiologic explanation for the rapid restoration of glycemic control seen after gastric bypass and other bariatric procedures. Others have studied the effect of jejunal bypass, for which an alternative, but related, theory is that the enhanced delivery of undigested nutrients to the distal small bowel plays a major role in the improved glycemic control and/or weight loss seen after gastric bypass surgery [5,6].

The time required for implanting the device was relatively constant. One delivery required additional time because of misplacement and replacement of the device. However, the consistent delivery time signifies the simplicity of the procedure, especially when considering that three different physicians with distinct skill sets placed the devices at differing times. All implants in this study were performed under general anesthesia; however, we believe that conscious sedation will be a viable option as our comfort level with the procedure increases.

Of the 12 implants, 2 were removed before their scheduled date (9 days after implant). We believe this resulted from initial misplacement of the devices during implantation. In both cases, the device was placed too close to the pylorus. In 1 of these 2 patients, we unsuccessfully attempted to push the device distally with the end of the endoscope. Ultimately, both patients complained of persistent and moderate nausea, vomiting, and abdominal discomfort, and the devices were removed.

All remaining patients completed the study per the protocol. Only 1 severe adverse event occurred during the study, which consisted of a report of severe abdominal pain related to preexisting kidney stones. Several other adverse events were noted, all of which were self-limited. The most common of these events included abdominal pain, nausea, and vomiting. We believe that the occurrence of these symptoms in the first 14 days is most reliably explained by early expansion of the anchor. After the first 14 days, the symptoms were most often associated with dietary indiscretion.

The device was patent and stable in all 10 patients. No interference occurred with the ampulla of Vater, as evidenced by the normalcy of the blood test results and the lack of associated symptoms. Several patients had isolated, self-limited abnormalities in the total bilirubin measurements. The significance of this is unknown, but the self-limited nature and lack of associated laboratory abnormalities implies a lack of clinical relevance.

Twelve endoscopic explantations were performed. The mean explant time in the first 2 and last 10 cases was 112 and 29 minutes, respectively. The 2 early cases were associated with difficulty dislodging the anchor from the duodenal wall. The 1 partial oral-pharyngeal tear and 1 esophageal tear that occurred during explantation each occurred in 1 of these first 2 cases. In each instance, failure to properly secure the anchor within the confines of the flexible hood resulted in tearing of the tissue. These events underscore the importance of proper hooding of the anchor.

The 72-hour tissue response was consistent and ranged from mild focal inflammatory changes to diffuse inflammation and superficial mucosal erosions. All patients were noted to have small benign biopsy-proven “pseudopolyps” of unclear etiology. The stability of the anchor diameter after the first 14 days and the acceptable tissue response

indicates that the anchor provides an appropriate balance of mucosal erosion, tissue healing, and device stability.

The 23.6% average excess weight loss and that all 10 patients had >10% excess weight loss are interesting results in the context of a 12-week study that also included counseling. All patients reported enhanced satiety and reduced food volume. This could be explained by any number of mechanisms, including, but not limited to, delayed gastric emptying or other alterations of gastrointestinal physiology. The changes in hypertension and hyperlipidemia were consistent with the degree of weight loss. The T2DM data could have resulted from the effect of the weight loss, but the rapid restoration to normalcy without medications might have been an independent effect of the duodenal bypass.

Conclusion

The results of our study indicate that the DJBS can be safely implanted and explanted during a 12-week period. The preliminary efficacy profile is encouraging and warrants additional investigation.

Disclosures

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at www.SOARD.org.

References

[1] National Institutes of Health. Clinical guidelines on the identification, evaluation and treatment of overweight and obesity in adults. Available from: http:www.nhlbi.gov/guidelines/obesity/obxsum.htm. Accessed May 2007.

[2] Ault A. Two stage gastric surgery is safer for high risk patients. Presented April 3, 2004 at the Sages Annual Meeting (abstract).

[3] Gersin K, Lembo A, Tarnoff M. Chronic in-vivo experience with an endoscopcically delivered and retrieved duodenal jejunal bypass sleeve in a porcine model. Presented April 22, 2007 at the Sages Annual Meeting.

[4] Rubino F, Forgione A, Cummings DE, et al. The mechanism of diabetes control after gastrointestinal bypass surgery reveals a role of the proximal small intestine in the pathophysiology of type 2 diabetes. Ann Surg 2006;244:741–9.

[5] Patriti A, Facchiano E, Annetti C, et al. Early improvement of glucose tolerance after ileal transposition in a non-obese type 2 diabetes rat model. Obes Surg 2005;15:1258–64.

[6] de Paula A, Macedo AL, Prudente AS, et al. Laparoscopic sleeve gastrectomy with ileal transposition—pilot study of a new operation. Surg Obes Relat Dis 2006;2:464–7.