Efforts to Resurrect EndoBarrier for Use in Obese With Diabetes

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Efforts are being made to kick-start further development of a duodenal-jejunal bypass liner, the EndoBarrier (GI Dynamics), this time specifically for use in obese patients with type 2 diabetes, after some issues with the device in earlier trials.

The device lost its CE Mark in Europe in 2017 and its listing on the Australian Register of Therapeutic Goods in 2016 because of issues with quality assurance documentation. Although approved in some South American countries, it is not being distributed there.

Meanwhile, the device is currently limited to investigational use in the United States. In 2015, the company stopped enrollment in the ENDO trial at the recommendation of the independent data and safety monitoring board when there were seven cases of liver abscess (a 3.5% incidence).

"We believe hepatic abscess risks can be mitigated by a change in the EndoBarrier instructions for use with different medication regimens, inclusion/exclusion criteria, and improved patient care," Scott Schorer, president and chief executive officer, GI Dynamics, told *Medscape Medical News* in an email.

"The company is currently focused on obtaining US Food and Drug Association (FDA) approval for a new EndoBarrier clinical trial in the United States, and on obtaining a new CE Mark," he added. The company anticipates FDA approval for a new study may come in the third quarter of 2018, and the CE Mark may be obtained in 2019.

As previously reported, the device is a plastic tube that is inserted (and later removed) endoscopically. While in place, food bypasses part of the intestine, and studies have shown this can induce weight loss.

A new meta-analysis shows that it may also help improve glycemic control in patients with obesity and type 2 diabetes. These findings were published in the May issue of *Diabetes Care* by Pichamol Jirapinyo, MD, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, Boston, Massachusetts, and colleagues.

Focusing on Obesity With Type 2 Diabetes

For the meta-analysis, researchers identified 14 studies (nine observational and five randomized trials) of the device that included obese patients with type 2 diabetes. "This systematic review and meta-analysis is the first to focus on a patient population with obesity and concomitant type 2 diabetes," they observe.

In the 388 patients, mean HbA_{1c} decreased by 1.3% after the device was in place for a mean 8.4 months compared with baseline.

The researchers acknowledge that between-study heterogeneity is a limitation of the meta-analysis and the glycemic effect was not always durable.

However, they note that not all patients had maximized the medical therapy for diabetes. "Nevertheless, most studies report a decrease in medication dosages and/or discontinuation of antidiabetes medication including insulin. Therefore, the change in HbA_{1c} reported...is likely conservative and possibly underestimates the true effect on glucose homeostasis."

Weight loss appeared to be durable. At device removal, patients had lost a mean 11.3 kg compared with baseline (in 10 studies and 352 patients).

Six months after device removal, patients had lost a mean 7.1 kg (in three studies and 104 patients), and at 12 months patients had lost a mean 10.7 kg (in two studies and 80 patients).

Gut Hormone Changes, Safety

The changes in gut hormones were largely similar to those seen after Roux-en-Y gastric bypass (RYGB) surgery.

Levels of glucagon-like peptide 1 and peptide YY increased, similar to what is seen after RYGB. Levels of glucose-dependent insulinotropic peptide decreased (whereas these levels may increase or decrease after RYGB), but ghrelin levels increased, whereas they decrease after RYGB.

In the nine studies that reported adverse events, abdominal pain, nausea, and vomiting were most common.

A total of 55 of 350 patients (15.7%) had a serious adverse event, which included gastrointestinal bleeding (16 patients), hypoglycemia (8 patients), acute pancreatitis (6 patients), sleeve migration, severe abdominal pain, liver abscesses (4 patients, none required surgery), anchor perforation, sleeve obstruction, esophageal perforation during explantation, acute cholecystitis and duodenal fistula, ulceration at the duodenal bulb, and dehydration.

Less than 1% of patients required surgery to address adverse events, and there were no deaths.

Moving Forward With EndoBarrier

Schorer emphasized that in almost 4000 procedures since 2009, the rate of hepatic abscess was about 1% with EndoBarrier, and there were no deaths or long-term safety issues.

The company has revised its quality assurance documentation system, he stressed, adding, "GI Dynamics believes EndoBarrier to be safe and effective, with strong clinical benefit outweighing the risk."

In their article, Jirapinyo and colleagues conclude: "Moving forward, small bowel [endoscopic bariatric and metabolic therapies] may have implications as an adjunct therapy to pharmacotherapy and lifestyle intervention for the care of patients with obesity and concomitant [type 2 diabetes]."

The authors have reported no relevant financial relationships.

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