

The EndoBarrier as a Novel Minimally Invasive Treatment of Type 2 Diabetes and Obesity: A Literature Review and Case Series of over 50 patients.

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Abstract : Surgical intervention is now the most effective treatment for patients with type 2 diabetes (T2DM) and severe obesity. There is currently a lack of minimally invasive technology to effectively treat obesity and T2DM. The Duodenal-jejunal bypass sleeve (EndoBarrier Gastrointestinal Liner) is an endoscopically inserted device that aids weight loss and immediately improves glycaemia through neurological and endocrine mechanisms. Firstly, we conducted a review of articles published on MEDLINE involving more than 300 patients to ascertain metabolic outcomes and safety profiles of the EndoBarrier. Secondly, in our own clinical series we implanted the EndoBarrier into 57 patients from January 2011 to December 2012. Most previous studies reported 11.9%-23.6% excess weight loss (EWL) at 12-weeks, while one study showed 47% EWL at 52-weeks. Most studies did not report changes in HbA1c as a marker of glycaemia. In our own clinical series, HbA1c improved from $8.04 \pm 0.14\%$ (mean \pm SEM) to $6.50 \pm 0.18\%$, a reduction of $1.54 \pm 0.15\%$ with an average weight loss of 14.80 ± 2.38 kg representing $29.50 \pm 3.82\%$ EWL. Only 1 device had to be removed early due to migration. There were no other major postoperative side effects. The EndoBarrier shows promise as a minimally invasive device treatment for T2DM and obesity. The review of the literature demonstrated consistent efficacy and safety. However, randomized controlled trials are now needed to ascertain whether the EndoBarrier is superior to other forms of treatment and whether the benefits will persist. Our results confirmed that this non-permanent device resulted in substantially improved glycaemia and body weight without the side effects associated with surgery.

INTRODUCTION

In recent years, obesity has reached epidemic status on a global scale. With around 300 million females and 200 millions males falling under the obese category¹, the WHO declared this as the largest chronic health problem in adults². Categorized by a Body Mass Index (BMI) greater than 30 kg/m², obesity plays a significant role in the occurrence of type 2 diabetes³. Weight loss in patients with type 2 diabetes is associated with improved glycemic control⁴. Surgical intervention is now the most effective modality with which to treat severe obesity⁵. Despite resulting in maintainable weight loss, surgical methods have been shadowed by fairly high re-operative rates and variable long-term weight loss results⁶. As a result, numerous strategies have been employed in an effort to provide long-term weight loss results.

Weight loss in the Type 2 diabetes mellitus setting is difficult to manage. To date invasive surgical procedures like the laparoscopic banding, sleeve gastrectomy and gastric bypass have proven to be effective⁷. However, patients fear surgery and its permanency. Recently, an alternative, non invasive, method with promising trial results in the settings of isolated weight loss and in type 2 diabetes, has surged to the forefront of our pursuit for a resolution, attracting more patients and bariatric specialists into exploring the EndoBarrier.

This duodenal-jejunal bypass sleeve is a minimally invasive technology that can be used as a method of inducing pre-operative weight loss⁸ which has been shown to positively correlate with long-term post-operative weight loss⁹.

THE DUODENAL-JEJUNAL BYPASS SLEEVE

Endoscopically and fluoroscopically inserted, the duodenal-jejunal bypass sleeve (DJBS, EndoBarrier Gastrointestinal Liner; GI Dynamics Inc., Lexington, Massachusetts, USA) is an impermeable fluoropolymer sleeve. Once inserted, it is reversibly fixated to the duodenal bulb and extends 60 cm into the small bowel, usually terminating in the proximal jejunum¹⁰.

The sleeve allows the transit of chyme from the stomach through to the jejunum without contact with the duodenal wall resulting in biliary and pancreatic fluids passing between the gut wall and outer surface of the liner only mixing with chyme once it exits at the distal end of the liner. This process encourages weight loss through hormonal triggers that lead to increased satiety and insulin sensitivity, mimicking the features of a Roux-en-Y bypass¹¹.



Figure 1: Image of EndoBarrier

Contained within a capsule, the EndoBarrier is introduced in the duodenum endoscopically. With relative technical ease, the sleeve is then deployed distally into the proximal jejunum under fluoroscopic control. Benefits include: no incisions and the fact that insertion takes only a few hours in hospital¹². It is the only endoluminal technology to be studied in human subjects that works in this way¹³.

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 Received on 25.07.14 Accepted on 04.10.14

By aiding patients regain metabolic control of Type II diabetes and aid in weight loss¹⁴, the EndoBarrier is in a new class of treatment that bridges pharmaceutical innovation with surgery.

EXPERIMENTAL SECTION

Efficacy and Safety

For the EndoBarrier, a technology still in its infancy, we do not have a large selection of data series in the literature.

A review of articles published on MEDLINE involving more than 300 patients was conducted to ascertain metabolic outcomes and safety profiles of the EndoBarrier. In addition we analysed results from our own clinical series, where the EndoBarrier was implanted into 57 patients from January 2011 to December 2012.

Every study used excess weight loss (EWL) as their primary outcome measure. The first reported human case series was by Rodriguez *et al* in 2008, which showed a 12-week EWL of 23.6%¹⁵. In four other studies (Table 1) EndoBarrier was trialled in a randomised fashion against either sham endoscopic procedures or low energy diets. Three of these studies showed 12-week EWLs ranging from 11.9% to 22%^{10,16,17} and greater weight loss compared with controls to statistically significant levels.

Studies reporting weight loss outcomes following the use of the EndoBarrier

Author and Year	Type of Study	Number of subjects	12-Week EWL (%)
Rodriguez <i>et al</i> 2008 ^[15]	Case Series	12	23.6
Tarnoff <i>et al</i> 2009 ^[16]	Randomised trial	25 (vs. 14 diet control)	22.0 (vs. 5.0; P < 0.001)
Gersinet <i>et al</i> 2010 ^[17]	Randomised trial	25 (vs. 26 sham control)	11.9 (vs. 2.7; P < 0.05)
Schouten <i>et al</i> 2010 ^[10]	Randomised trial	26 (vs. 11 diet control)	19.0 (vs. 6.9; P < 0.002)
Escalona <i>et al</i> 2012 ^[18]	Single arm, open-label, prospective trial	39	47.0 (52-week EWL) P < 0.0001

Abbreviations EWL - excess weight loss

The results, especially the levels of EWL are encouraging, and suggest the effective use of the device as a method for inducing pre-operative weight loss before definitive surgery.

The single arm prospective open-label study by Escalona *et al* uses 52-week EWL as their primary end point. A mean EWL of 47.0% occurred in the 24 subjects that completed the 52-week programme¹⁸.

A similarly designed study to Escalona *et al's*, used 52-week HbA1c as their primary endpoint. Results showed a decrease in HbA1c of $2.1 \pm 0.3\%$ ¹⁹.

These studies suggest that the EndoBarrier may be able to be used as an independent weight loss and diabetes therapy rather than a pre-operative weight loss primer. All four of the studies had complications that caused either a failed implant or early extraction of the device. Anatomical difficulties were the reasons for failed implantation¹⁷. Abdominal pain, sleeve migration, anchor dislocation, sleeve obstruction and haematemeses triggered the need for early extractions in the studies^{10,15-17}. Additionally, in the first case series (Rodriguez *et al*. 2008), upon removal of the sleeve after twelve weeks, oesophageal mucosal and oropharyngeal tears were noted, this was classified as minor surgical trauma.

In our own clinical series, a part of a multicentre UK trial with encouraging results in terms of weight loss and control of type II diabetes (57 patients, January 2011 - December 2012), HbA1c improved from $8.04 \pm 0.14\%$ (mean \pm SEM) to $6.50 \pm 0.18\%$, a reduction of $1.54 \pm 0.15\%$ with an average weight loss of $14.80 \pm$

2.38 kg representing $29.50 \pm 3.82\%$ EWL. Only one device had to be removed early (3 months) due to migration. There were no other major postoperative side effects. Results are encouraging as the majority experienced clinically significant weight loss, with evidence of reduced insulin resistance.

As the EndoBarrier is still very much in its infancy²⁰, it should be noted that these complications are anticipated. However, they will certainly become less common as the practical procedure of the implantation process becomes more familiar to the surgeon.

Furthermore, it is believed that EndoBarrier may also positively impact cardiovascular risk factors by reducing lipid levels and blood pressure²¹.

The Future

The possibility of using the EndoBarrier as a treatment of type 2 diabetes mellitus independently with weight loss as a secondary outcome was thought of after the first series published on EndoBarrier use revealed a resolution of type II diabetes mellitus in 3 out of 4 affected subjects¹⁵. Furthermore, the difference in weight loss between diabetic and non-diabetic patients was identical which further provided interest in the use of the EndoBarrier as an independent treatment of type 2 diabetes mellitus.

The Brazilian study done by De Moura EG *et al*. last year provided authentication for this belief. At the end of their 52 week study, substantial reductions in fasting blood glucose, fasting glucose and HbA1c were reported in 13 patients¹⁹. This notion claiming the reverse of diabetes after EndoBarrier treatment will however have to be examined under randomised trials before it gets as widely recognized as its effect on weight loss.

In the interest of future protocols, it is also noteworthy to state the maximization of benefits obtained from the device once the treatment is coupled to a multidisciplinary support program. Components of this program include: behavior modification, nutritional counseling and exercise regimes. Similarly to any other type of bariatric mediation, patient compliance will play a critical part on any success that the EndoBarrier may have.

CONCLUSION

As the first endoluminal device to effectively cause weight loss through malabsorption in obese patients, the EndoBarrier shows promise as a minimally invasive device treatment for type 2 diabetes mellitus and obesity. The review of the literature demonstrated consistent efficacy and safety. Despite the EndoBarrier being associated with some minor problems regarding implantation as well as complications requiring early extraction, the increased use of the device will show a reduction in complication rate.

Randomised controlled trials are now needed to ascertain whether the EndoBarrier is superior to other forms of treatment and whether the benefits will persist. Our results confirmed that this non-permanent device resulted in substantially improved glycaemia and body weight without the side effects associated with surgery. There hasn't been a study that has looked at the effects of the EndoBarrier beyond one year, and as a result the long-term effects of weight loss and diabetes control must be studied further.

Endobarrier use as a treatment to reverse type II diabetes mellitus independently of weight loss will require further

investigation, however, preliminary results from studies are favourable. The EndoBarrier certainly has the potential to revolutionise the way in which we can effectively and safely manage weight loss and type II diabetes mellitus.

Acknowledgments

Conflicts of Interest : The authors declare no conflict of interest.

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