

Maintenance of efficacy after duodenal–jejunal bypass liner explantation in the first NHS EndoBarrier service

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Abstract

EndoBarrier®, a 60 cm endoscopically implanted proximal intestinal liner, reduces weight and HbA_{1c} over 1 year. We report the outcomes of the first 12 patients who completed 6 months post EndoBarrier removal in the first NHS EndoBarrier service. All patients were obese (body mass index 41.7±9.8 kg/m²) with diabetes for 10–25 years and 75% were on insulin therapy. All patients (age 52.4±9.3 years) were advised to institute behavioural changes during the implant period (1 year) and maintain them thereafter. Implantation of EndoBarrier for 1 year reduced weight (17.6±8.9 kg, $p<0.001$), HbA_{1c} (26.7±20.8 mmol/mol, 2.4±1.9%, $p=0.001$), systolic blood pressure (14.1±16.1 mmHg, $p=0.011$) and median total daily insulin dose from 104 to 48 Units/day ($p=0.024$) ($n=9$). Six months post EndoBarrier removal, 75% of patients sustained the metabolic improvement achieved with EndoBarrier; insulin dose requirement continued to fall and four of the nine insulin-treated patients discontinued insulin. Of the three patients whose weight/glycaemic control worsened, two had depression and one became immobile after explantation due to ill health unrelated to EndoBarrier treatment. Most (93.8%) of our patients stated that they would be extremely likely to recommend our service to friends and family. These data are encouraging for wider establishment of NHS EndoBarrier services.

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Introduction

EndoBarrier® (GI Dynamics, Boston, USA), also known as the duodenal–jejunal bypass liner, is a 60 cm long impermeable

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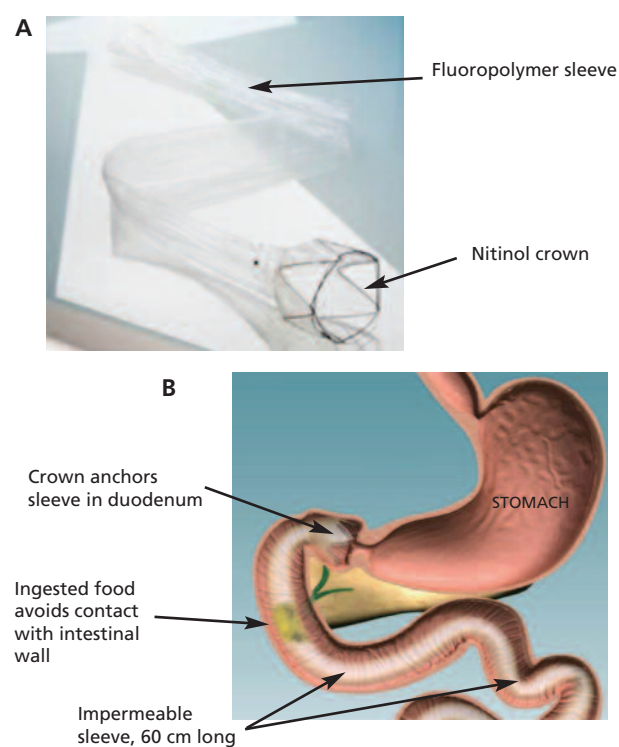
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Figure 1. (A) The Endobarrier device and (B) a diagram of the device in situ



Adapted from http://www.diabetologists-abcd.org.uk/Research/What_Endobarrier.htm.

fluoropolymer sleeve which is implanted by endoscopy into the first part of the small intestine where it remains for about 1 year (Figure 1). It is held in place by a nitinol anchor, such that food passes through it without coming into contact with the small intestine, thereby interfering with the normal digestive processes that occur in this region.¹ The endoscopic insertion and removal of EndoBarrier are day case procedures, performed in less than an hour under general anaesthesia. This form of reversible bariatric procedure has been shown to reduce weight and improve glycaemic control in patients with diabetes and obesity.²⁻⁵ REVISE-Diabetes (Randomisation to Endobarrier alone Versus with

Incretin analogue in SustainEd Diabetes), an Association of British Clinical Diabetologists (ABCD) UK-funded, multicentre, randomised controlled trial (ISRCTN00151053) led by our institution supports these observations. Additionally, preliminary data on the first year of treatment with the EndoBarrier device combined with liraglutide therapy showed benefit on HbA_{1c} and weight/body mass index (BMI), liver fat and cardiovascular risk, as measured by the UK Prospective Diabetes Study (UKPDS) risk engine v2.⁶⁻⁹ However, there is uncertainty regarding the extent to which EndoBarrier-induced improvements are maintained following its removal. Despite the growing evidence of benefits, EndoBarrier treatment has not been tried as a routine NHS service.

We therefore aimed to evaluate whether the experience acquired through the REVISE-Diabetes study could translate into establishment of a safe and effective NHS EndoBarrier service for patients with diabetes, and investigate whether improvements achieved during the first year of EndoBarrier treatment could be maintained during the 6 months after removal of the device.

Methods

An NHS EndoBarrier service for patients with suboptimally controlled type 2 diabetes and obesity was designed and implemented in October 2014 (see Box 1). Typically, patients had HbA_{1c} >58 mmol/mol (7.5%) and BMI >30 kg/m², although HbA_{1c} <58 mmol/mol (7.5%) was sometimes accepted if it was felt that the lower HbA_{1c} was being caused by insulin treatment but that the insulin was maintaining the obesity.

On establishment of the service, patients referred for EndoBarrier treatment were assessed and advised of behavioural changes which would improve the likelihood of success of the treatment while the device was in situ and following its removal. Patients were also given standard mandatory advice in relation to EndoBarrier treatment – namely, on insertion of the EndoBarrier to adhere to a liquid diet and then pureed food diet for the first fortnight and to avoid consuming large volumes of fluid or food. This is to allow the EndoBarrier to settle into place without the crown tearing the duodenum and precipitating gastrointestinal (GI) haemorrhage. To reduce the risk of GI haemorrhage, patients were also prescribed a high-dose proton pump inhibitor (omeprazole 40 mg twice daily) throughout the implant period.

The first 12 patients to enter this NHS EndoBarrier programme were followed from pre-implantation (baseline) up to 6 months after device removal. Body weight, HbA_{1c}, systolic blood pressure and liver function (alanine aminotransferase (ALT)) were monitored throughout the study. Baseline data were compared with follow-up data using the paired t-test for parametric data and the

Table 1 Baseline characteristics (mean±SD) of the first 12 NHS patients to have completed 6 months post EndoBarrier

Parameter	N=12
Age (years)	52.4±9.3
Sex (% male)	33.3
Ethnicity (% Europid)	41.7
BMI (kg/m ²)	41.7±9.8
HbA _{1c} (mmol/mol)	81.6±22.5
(%)	9.6±2.1
*Diabetes duration (years)	17.0 (9.7-24.7)
Taking insulin (%)	75.0
*median (interquartile range)	

Wilcoxon signed-rank test for non-parametric data. Patient baseline characteristics are summarised in Table 1.

Results

Between October 2014 and December 2016, 62 of 140 referrals (44%) to the EndoBarrier service were accepted for treatment and 45 devices were implanted. Table 2 shows outcomes for the first 12 patients after 1 year of treatment and at 6 months following removal of the EndoBarrier. After 1 year with the implant in situ there were significant reductions in weight, HbA_{1c} and systolic blood pressure (mean±SD decrease 17.6±8.9 kg, 26.7±20.8 mmol/mol, 2.4±1.9% and 14.1±16.1 mmHg, respectively). Liver function improved and, in the nine patients on insulin, the median total daily insulin dose fell from 104 to 48 Units/day (p=0.024) with three patients no longer requiring insulin therapy.

Following EndoBarrier removal, nine (75%) of the 12 patients sustained the improvements achieved during the implantation period. However, in the remaining three patients, weight and glycaemic control deteriorated, leading to the group data at 6 months after removal of the EndoBarrier apparently regressing to levels achieved 6 months after implantation (Figure 2). Investigation of these three patients revealed that, following EndoBarrier removal, one patient developed depression and received counselling organised by her primary care provider. Another patient had previously unrecognised depression diagnosed whilst the EndoBarrier was in situ and was treated with mirtazapine. His mood improved, as did his appetite, and he failed to lose weight over the treatment period and gained weight following explantation. The weight gain was exacerbated by increasing his insulin dose to maintain glycaemic control. During the 6 months following EndoBarrier removal the third patient was unable to work when he developed a diabetic foot ulcer and this, combined with arthritic pain, rendered him immobile, resulting in weight regain.

Discussion

Our research programme has been translated into an inaugural NHS service, which has demonstrated that the EndoBarrier can be effective in patients with refractory diabetes. There was an

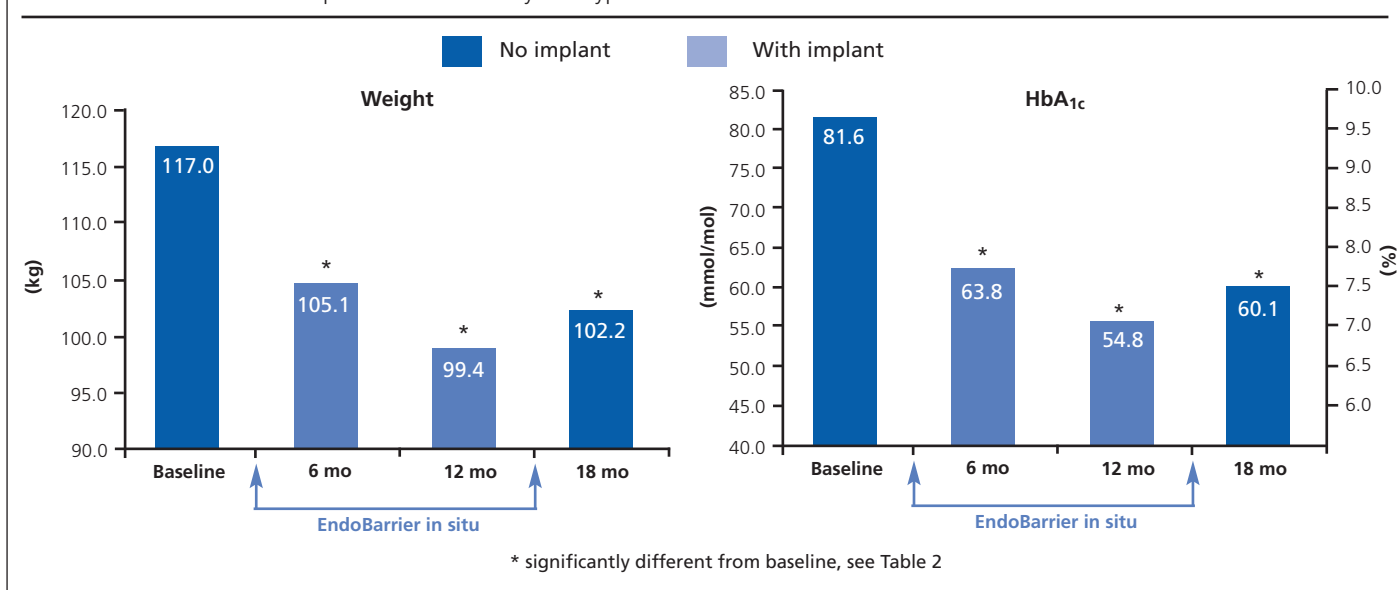
Box 1 Delivering an NHS EndoBarrier service

- Comprehensive 2-year patient pathway designed
- Specialist teams consulted
- Patients consulted
- Management support obtained
- Local service commissioners agreed funding system
- A secure online registry was established (supported by ABCD) to monitor outcomes

Table 2 Effect of EndoBarrier on outcomes after 1 year of treatment and 6 months after EndoBarrier removal in patients (n=12) with type 2 diabetes and obesity^a

Parameter	Baseline	1 year with EndoBarrier	p-value 1 yr vs baseline	6 months post EndoBarrier	p-value 6mo post explant vs baseline
Weight (kg)	117.0±28.3	99.4±28.8	<0.001	102.2±29.8	0.002
BMI (kg/m ²)	41.7±9.8	35.0±9.5	<0.001	36.0±8.8	0.001
HbA _{1c} (mmol/mol)	81.6±22.5	54.8±10.5	0.001	60.1±16.3	0.005
HbA _{1c} (%)	9.6±2.1	7.2±1.0	0.001	7.7±1.5	0.005
Systolic blood pressure (mmHg)	143.8±12.5	129.7±15.2	0.011	135.8±15.5	0.109
ALT (U/l)	28.1±20.5	16.1±9.0	0.05	20.6±13.0	0.31
Insulin daily dose (n=9)	104 (51-120)	*48 (0-67)	0.024	# 10 (0-70)	0.033

^a Values expressed as mean ± SD, except insulin daily dose which is median (IQR); * 3 of the 9 (33%) insulin-treated patients discontinued insulin; # 4 of the 9 (44%) insulin-treated patients discontinued insulin

Figure 2. Mean HbA_{1c} and weight and median insulin dose at baseline and at 6-month intervals after implantation and removal of EndoBarrier in 12 patients with obesity and type 2 diabetes

acceptable safety profile and, following EndoBarrier removal, nine of the 12 patients (75%) were able to sustain the reductions in weight, HbA_{1c} and insulin dose requirement achieved over the 1-year treatment period. We believe patient satisfaction levels were high; in response to the NHS Friends and Family test, 93.8% of our patients stated that they would be extremely likely to recommend our service to friends and family. In addition, several of our patients have actively supported our website chronicling changes in health parameters during and after treatment with EndoBarrier for up to 4 years.¹⁰

Of the 45 EndoBarriers implanted in our NHS service, there have been four serious adverse events: three GI haemorrhages and one hepatic abscess. Two of the GI haemorrhages were related to non-compliance with standard mandatory treatment advice and could therefore have been averted. One patient reverted to meals of nor-

mal food during the second week after insertion instead of following the advice given to take small meals of pureed food. He developed melaena and was admitted to hospital with a haemoglobin of 91 g/L; he received a blood transfusion, the EndoBarrier was removed and he made a full recovery. The other patient stopped taking the proton pump inhibitor after 10 weeks because he failed to renew his prescription. He experienced dizziness and melaena and on admission to hospital his haemoglobin was 72 g/L. He also underwent a blood transfusion and EndoBarrier removal and made a full recovery. During the 10 weeks that the EndoBarrier was in situ, he experienced 9.6 kg weight loss, his HbA_{1c} fell from 109 to 47 mmol/mol (12% to 6.5%) and his insulin requirement fell from 140 to 30 Units daily. The third patient presented with a suspected GI haemorrhage 25 days after implantation of his EndoBarrier; he had halved his dose of omeprazole from 40 mg twice daily to once daily.

However, the source of bleeding was not found at endoscopy (duodenitis only with no active bleeding). The omeprazole dose was increased back to 40 mg twice daily and the EndoBarrier remained in situ for the full year of therapy.

The patient with hepatic abscess presented at 6.5 months and responded to drainage of the abscess, antibiotic therapy and early removal of the EndoBarrier at 7 months, by which time he had achieved a weight loss of 18.4 kg. He made a full recovery.

Weight regain is a common challenge for patients who have undergone bariatric surgery. Indeed, weight regain occurs in about half of all patients within 2 years of gastric bypass surgery,¹¹ although after 5 years the average patient regains less than 40% of their excess weight.¹² Thus it is premature to conclude on the long-term effectiveness of this new treatment on the basis of re-assessment just 6 months after removal of the EndoBarrier. Nevertheless, since 75% of the first 12 NHS patients who have completed 1 year of EndoBarrier treatment sustained their significant metabolic improvement 6 months following removal of the device, this is an encouraging result for this new treatment.

It would appear that our cases of GI haemorrhage could have been avoided if the patients concerned had adhered to the advice they were given. Nevertheless, these cases serve as anecdotes to warn patients of the dangers of not 'following the rules'. Thus, with care, serious adverse events can be minimised.

Our patients were not subjected to detailed psychological or psychiatric assessments prior to EndoBarrier treatment. In our experience, many patients report feeling depressed due to their obesity. Indeed, it is our anecdotal experience that patients typically report considerable improvements in wellbeing, energy, fitness and exercise ability as a result of the EndoBarrier supported weight loss. Furthermore, weight loss confers metabolic benefits and reduces the impact of co-morbidities such as obstructive sleep apnoea, raised systolic blood pressure and ALT. Reductions in ALT may reflect reductions in liver fat,⁸ signalling a potential role for EndoBarrier therapy in non-alcoholic fatty liver disease. Observations relating to our cohort of 45 patients to date suggest that it would be fruitful to undertake research of EndoBarrier therapy in diverse areas of obesity-related pathologies. Indeed, a study of EndoBarrier treatment in diabetes with obstructive sleep apnoea, funded by ABCD, is already underway in our institution (End-OSA ISRCTN33788132).

In conclusion, our numbers are small and the duration of follow-up is relatively short, so our results must be interpreted with caution. Nevertheless, these results are encouraging. As endoscopy units and skilled endoscopists are ubiquitous in the NHS, our EndoBarrier service could be readily disseminated with a registry useful for ongoing monitoring nationwide and worldwide.

Conflict of interest Conflict of interest: REJR received consultancy fees from GI Dynamics on one occasion in 2015

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Key messages

- In obese patients with poor glycaemic control and long duration of diabetes, EndoBarrier led to considerable improvement in both weight and glycaemic control during the treatment period
- After the removal of EndoBarrier 75% of the patients were able to maintain the improvement over 6 months. For those on insulin, insulin dose reduced substantially and 44% were able to discontinue insulin
- There was an acceptable safety profile and patient satisfaction levels were high
- These early results are encouraging for EndoBarrier as a treatment for patients with long duration diabetes and obesity who remain with poor glycaemic control despite other diabetes treatments. EndoBarrier may also be beneficial in other obesity related pathologies, such as obstructive sleep apnoea and non-alcoholic fatty liver disease

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