UPDATE: Endobarrier® for type 2 diabetes mellitus with obesity

The Endobarrier® (GiDynamics) is a 60 cm long impermeable sleeve-like device, placed endoscopically into the small intestine for up to 12 months. By creating a physical barrier to food absorption and probably affecting gut hormone production it is designed as a treatment for patients with type 2 diabetes with obesity.

Background

Endobarrier® is designed to be used in patients with type 2 diabetes, which most usually occurs in adulthood, and is often associated with obesity. In 2010 it was estimated that over three million people over the age of 16 in England have diabetes with 85% of these, about two and a half million, having type 2 diabetes.¹

Type 2 diabetes can cause serious complications including heart disease and stroke and may have been the underlying cause in as many as one in ten deaths in adults in Europe in 2010.² Other serious complications of diabetes may include kidney failure, ulceration of the skin of the lower limbs due to nerve damage, amputation and blindness.

The healthcare costs of type 2 diabetes are considerable – the diagnosis brings with it a doubling of cost for each patient as compared with the background population cost. In total type 2 diabetes may account for between 7 and 12% of all National Health Service (NHS) expenditure.³

Current Practice

People with type 2 diabetes need to adjust their diet and lifestyle which may be enough to manage the condition without needing specific medication. However, many patients will need to take tablets and/or insulin to achieve control of their blood glucose level.³ As diabetes is a long term condition this medication will usually need to be continued for life.

Lifestyle changes will be suggested to achieve weight loss although weight loss surgery, (bariatric surgery) for example gastric bypass, may be an option for those with extreme obesity.

New Technology

The Endobarrier®, also known as a duodenal-jejunal bypass sleeve or a gastrointestinal liner, is a novel device. It is a single use 60cm impermeable fluoropolymer sleeve⁴ that is placed endoscopically via the mouth and anchored in
the first part of the small bowel (duodenum) in a procedure that takes around 30 minutes. Endobarrier® receives the contents of the stomach and acts to reduce the uptake of nutrients and calories from the first part of the small bowel (the duodenum and the first section of the jejunum).

There is some controversy about Endobarrier’s® mechanism of action with many patients with type 2 diabetes achieving greater control of their blood glucose, as well as reduced blood pressure and cholesterol levels. It is believed that this effect is similar to that seen in some gastric bypass operations, in particular those that bypass the early small bowel, e.g. Roux-en-Y gastric bypass, and may be related to the activation of hormonal signals from this part of the gut. Endobarrier® also promotes weight loss by reducing intake of calories and this weight loss in itself reduces the symptoms of diabetes.

Endobarrier® received a CE mark in May 2010 and costs approximately £2,750 excluding VAT, plus the costs of implantation and removal. In the United Kingdom it is currently only being used in the context of postmarketing studies in NHS hospitals in London, Manchester and Southampton. It is not yet available, licensed or launched in the United States, Canada or Australia.

**Company update on cost and NHS use - March 2012**

The cost of Endobarrier® remains as stated above. Commercial activity for EndoBarrier® commenced in May 2011 and the device is currently offered at one NHS centre and in several private centres. EndoBarrier® is currently being approved on a named patient basis by the NHS for specific patients in whom continuation of traditional treatment is ineffective or inappropriate. It is now available in Australia and Chile but not yet licensed, launched or available in the United States or Canada.

**Clinical Studies and Research Questions**

A small randomised controlled trial in patients with type 2 diabetes and obesity compared 12 patients implanted with the Endobarrier® with six who underwent sham procedures. There was a greater reduction in HbA1c (the primary endpoint of the trial) at 24 weeks in the Endobarrier® group (-2.4±0.7%) than the sham group (-0.8±0.4%) but this difference did not reach statistical significance. There was a significant difference in the fasting blood glucose at one week (-50 ±18 mg/dl Endobarrier® group, +25 ± 29 mg/dl sham group). This difference was also seen at 12 and 24 weeks although was not statistically significant at those points. All 12 of the patients receiving the Endobarrier® had at least one episode of mild or moderate abdominal pain (64 adverse events in total) but none requested removal of the device.

A study reported in abstract involving 61 people who were obese, 22 of whom also had type 2 diabetes showed that, after 24 weeks of the Endobarrier® being in place, 16 of the people with diabetes had a reduction in the average HbA1c of 1.5% (from an 8.9% baseline). In eight patients the device had to be removed because of complications. Further follow-up at one year of 13 of these patients, reported in abstract, showed that average HbA1c remained similar to the six month level and markers of metabolic function such as insulin, C-peptide, LDL and triglyceride levels were normalised.

A randomised controlled trial of 41 patients with obesity compared Endobarrier® to diet alone. There were ten patients with type 2 diabetes in total, eight in the device group. Reduction in fasting blood glucose and HbA1c were greater for the device group but did not reach statistical significance. Six of the eight patients with diabetes in the device group were able to reduce their diabetic medication after one week. All the patients in the device group had adverse events (mild or moderate) compared with only three in the control group.

A study of 17 patients with obesity and type 2 diabetes, who received the Endobarrier® device as well as a low calorie diet, reported that there was a 29.8% reduction in excess weight after 24 weeks, and a statistically significant improvement in HbA1c (from 8.4 to 7.0%). All but one of the patients was able to reduce their
diabetic medication and there was a rapid increase in insulin sensitivity, sustained for one week after removal of the device.\textsuperscript{11}

A randomised controlled trial of 70 patients with type 2 diabetes and obesity (body mass index \(\geq\)30) is currently underway, with preliminary results expected by the spring 2011.\textsuperscript{12} It is expected that this trial, together with the postmarketing studies in the NHS, will give an updated position regarding the safety of the commercial product.

There are still some outstanding research questions about the Endobarrier\textsuperscript{®} device. It is not clear whether subsequent devices could be implanted after the first is removed, how long the device can be in place without complications occurring and how long the effects upon diabetes might last after removal.

\textbf{Company update on trials - March 2012}


Ongoing research:
Post marketing study in subjects who have type 2 diabetes using the endobarrier™ gastrointestinal liner. \url{http://clinicaltrials.gov/ct2/show/NCT01114438}

One study, in a different patient group, is designed to address the question of whether subsequent devices could be implanted after the first is removed: Study of obese subjects previously implanted with the endobarrier gastrointestinal liner. \url{http://clinicaltrials.gov/ct2/show/NCT01372501}.

\textbf{Potential Impact}

The company states that the Endobarrier\textsuperscript{®} offers immediate but temporary improved control of blood glucose with reductions in weight, blood pressure and blood cholesterol.\textsuperscript{5}

The costs and benefits of Endobarrier\textsuperscript{®} within current NHS practice are difficult to predict. As well as the cost of the device there will be further hospital costs related to the endoscopic placing of the device, and its removal up to one year later. With the large numbers of people who are obese and have type 2 diabetes the potential impact upon healthcare services could be high if a significant proportion received the Endobarrier\textsuperscript{®}. Patients will also need monitoring for complications associated with the device.

Anticipated savings could be the cost of some medication for the period during which the device is in place. There is as yet no evidence of the long term impact of Endobarrier\textsuperscript{®} on weight, blood glucose control or complications of diabetes. The place of Endobarrier\textsuperscript{®} within the pathway of care in type 2 diabetes remains to be determined.

\textbf{Lay summary}

Endobarrier\textsuperscript{®} is a new medical device to treat people who have Type 2 diabetes and are very overweight. It is a tube (like a sleeve) which is 60cms long and is placed through the mouth and stomach to line the first part of the bowel. There it stops food from being absorbed as the contents of the stomach pass through. This may help to treat diabetes, but it is not really clear how it works. The Endobarrier\textsuperscript{®} sleeve is usually removed after about one year. Early studies suggest that it seems to help some people who have diabetes, but more studies are needed to tell us more about how well it works and what the side effects might be.
References


5. Manufacturer’s website www.Endobarrier.com


