Seven out of the first eight patients in the ABCD EndoBarrier® in obstructive sleep apnoea (End-OSA) study no longer require continuous positive airway pressure ventilation (CPAP) after 3 months treatment with EndoBarrier®


ABCD Autumn Meeting, London
10/11/2017
Obstructive sleep apnoea
A Vicious Cycle

Obesity

- Reduced physical activity
- Insulin resistance
- Increased ghrelin levels

OSA

- Fat deposit in UAW lumen
- Reduced tracheal traction
- Oval UAW shape
- Fat deposit in UAW muscle

G Pillar et al Diabetes care 2008, 31(2)
OSA & Obesity

• Weight loss can improve or even cure OSA, though results are variable [1,2,3]
• Bariatric surgery can cause significant weight loss and bring benefit to patients with OSA
• But it is invasive and is not without significant complications and it is relatively expensive

1- Greenstone M, Hack M. Obstructive sleep apnoea. BMJ. 2014 Jun 17;348:g3745
EndoBarrier® – implantable duodenal-jejunal liner

- Fluoropolymer wall
- Nitinol Anchor

- 60 cm impermeable sleeve
- Minimally invasive
Objectives

Primary objective
• To assess whether a significant number of patients with diabetes, obesity and moderate OSA lose so much weight with EndoBarrier® treatment that their OSA improves to such an extent that they no longer require CPAP treatment

Secondary objectives
• Improvements in AHI, symptoms of OSA and reduction in CPAP pressures
• To assess the extent of improvement in glycaemic control, weight, cardiovascular risk factors, composite scores of Non-Alcoholic Fatty Liver Disease (NAFLD) severity and requirement for diabetes treatments, including insulin
• To assess the association of changes in circulating testosterone levels and insulin sensitivity before and after EndoBarrier® treatment in males.
• To assess effect on quality of life of EndoBarrier® treatment in patients with diabetes and moderate OSA.
• To assess the sustainability of primary outcome and of the other secondary outcomes during the year following explantation of EndoBarrier®.
Outcome Measures

Primary endpoint/outcome
• Patients no longer fulfilling NICE criteria for CPAP treatment

Secondary endpoints/outcomes
• AHI
• OSA symptoms
• CPAP pressures
• HbA1c
• Fasting plasma glucose
• Weight and Body Mass Index (BMI)
• Composite scores of NAFLD severity derived from age, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), BMI, platelets, and serum albumen
• Circulating free testosterone, fasting insulin and C-Peptide in males
• Blood pressure
• Diabetes treatment including need for insulin
• Quality of life scores (EQ-5D)
• Sustainability of primary outcome and of the secondary outcomes during the year following explantation of Endobarrier
Study design:
Response to intervention

Trial Registrations:
ISRCTN33788132
EUDRACT2016-001920-78
Study design: Selection Criteria

Inclusion Criteria:

- Moderate OSA on CPAP fulfilling NICE criteria (AHI 15-29 events/hr) with symptoms
- Prediabetes (HbA1c 42-48mmol or confirmed T2DM (HbA1c ≥ 48mmol/mol)
- Obesity BMI ≥ 30 and ≤ 45 Kg/m2
- Age ≥ 18 years
- Capable of giving informed consent
NICE

• Mild OSA : AHI<15 events/hr
• Moderate OSA : AHI 15-29 events/hr
• Severe OSA : AHI ≥30 events/hr
Exclusion Criteria

- abnormal intestinal anatomy
- contraindication to oesophagogastrroduodenoscopy
- previous bariatric surgery or bowel surgery
- active infection
- anticoagulation therapy
- coagulopathy INR >1.3
- estimated Glomerular Filtration rate (eGFR)<30
- known portal hypertension
- uncontrolled cardiovascular disease
- lactating or pregnant females
- excess anaesthetic risk
- patients on regular non-steroidal anti-inflammatory agents
- Aspirin or other anti-platelets for cardiovascular secondary prevention
Baseline characteristics (n=10)

<table>
<thead>
<tr>
<th>characteristic</th>
<th>value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53.5 ± 10.5</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>Females (80%)</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td>Caucasian (50%)</td>
</tr>
<tr>
<td>T2DM pt’s (n)</td>
<td>8</td>
</tr>
<tr>
<td>Pre-diabetes pt’s (n)</td>
<td>2</td>
</tr>
<tr>
<td>Mean Wt (kg)</td>
<td>102.2 ± 11.7</td>
</tr>
<tr>
<td>Mean BMI (Kg/m²)</td>
<td>37.6 ± 2.8</td>
</tr>
<tr>
<td>Mean HbA1c (mmol)</td>
<td>66.3 ± 17.7</td>
</tr>
<tr>
<td>Mean AHl (events/hr)</td>
<td>19.0 ± 4.0</td>
</tr>
<tr>
<td>Duration of OSA {Median(IQR) years}</td>
<td>1.5 (1.0-2.4)</td>
</tr>
</tbody>
</table>
Results: Weight (n=9)

Baseline mean weight: 102.2 ± 11.7 kg
3 Months mean weight: 95.2 ± 13.2 kg

* - 7.0 ± 3.2 kg (p < 0.001)
Results: Mean BMI (n=9)

<table>
<thead>
<tr>
<th>Mean BMI (Kg/m²)</th>
<th>Baseline</th>
<th>3 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.5 ± 2.8</td>
<td></td>
<td>34.9 ± 3.5 *</td>
</tr>
<tr>
<td></td>
<td>34.9 ± 3.5 *</td>
<td>2.6 ± 1.3 kg/m²</td>
</tr>
</tbody>
</table>

* - 2.6 ± 1.3 kg/m² (p<0.001)
Results - Mean HbA1c (n=9)

Baseline: 66.3±17.7
3 Months: 55.2±17.3*

*- 11.1±12.0mmol (p=0.026)
Mean AHI (n=10)

Baseline: 19.0 ± 4.0 events/hr
3 Months: 10.7 ± 5.0 events/hr

*p=0.002

* 8.3 ± 6.0 events/hr
Sleep Studies (n=10)

**AHI (events/hr)**

- **BL**: 19.0 ± 4.0
- **3M**: 10.7 ± 5.0

* - 8.3 ± 6.0 events/hr (p=0.002)

**Epw Sleep Score**

- **BL**: 12.8 ± 5.3
- **3M**: 4.2 ± 3.0

* - 8.6 ± 4.1 (p=0.000)
Body Fat Measurements (n=9)

- Neck: BL 8.6±6.1 (p=0.003) compared to 1.07±1.7 (p=0.09) after 3M.
- Waist: BL 4.5±6.6 (p=0.073) compared to 110±10 (p=0.073) after 3M.
- Hip: BL 110±10 (p=0.073) compared to 110±10 (p=0.073) after 3M.
CPAP Discontinued

- 3 Mths: 7/10 (70%)
- 6 Mths: 1/10 (10%)
- A/w 6 Mths SS
SAE

• Small perforation of Oesophagus in one participant at 6 months during EndobARRIER removal
Conclusion

• Although these are preliminary results, EndoBarrier® has been effective in OSA pts in allowing 8 out of the first 10 patients to discontinue their CPAP
• Associated glycaemic and weight benefits
For many more examples see: [http://www.diabetologists-abcd.org.uk/Endobarrier/Birmingham_Endobarrier_patients.pdf](http://www.diabetologists-abcd.org.uk/Endobarrier/Birmingham_Endobarrier_patients.pdf)

If you would like to discuss more about starting an NHS EndoBarrier service at your hospital contact Dr Bob Ryder ([bob.ryder@nhs.net](mailto:bob.ryder@nhs.net)) or talk to him at this meeting.