NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedure consultation document

Electrical stimulation of the lower oesophageal sphincter for treating gastro-oesophageal reflux disease

Gastro-oesophageal reflux disease or GORD causes symptoms such as heartburn, regurgitation, chest pain and nausea. It is caused by several conditions, such as hiatus hernia, that disturb the function of the lower oesophageal sphincter, which is the ring of muscle separating the oesophagus from the stomach. Electrical stimulation of the lower oesophageal sphincter applies low energy electrical impulses to the sphincter in repeated sessions, with the aims of strengthening it and reducing acid reflux. In this procedure, small electrodes are implanted in the sphincter using keyhole surgery, and connected to a stimulator, which is placed under the skin of the abdomen.

The National Institute for Health and Care Excellence (NICE) is examining electrical stimulation of the lower oesophageal sphincter for treating gastro-oesophageal reflux disease and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about electrical stimulation of the lower oesophageal sphincter for treating gastro-oesophageal reflux disease.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.
- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the Interventional Procedures Programme process guide, which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 6th August 2015

Target date for publication of guidance: September 2015

1 Provisional recommendations

1.1 Current evidence on the safety and efficacy of electrical stimulation of the lower oesophageal sphincter for treating gastro-oesophageal

reflux disease (GORD) is limited in quantity and quality. Therefore, this procedure should only be used in the context of research.

1.2 NICE encourages clinicians to enter patients into controlled clinical trials. These should provide a clear description of patient selection, and details of adjunctive medical and surgical treatments. Outcomes should include GORD symptoms, quality of life and objective measurements of gastric reflux. Efficacy, device durability, the need for surgical treatment for GORD in the longer term (at least 2 years) and all complications should be reported. NICE may update the guidance on publication of further evidence.

2 Indications and current treatments

2.1 Gastro-oesophageal reflux disease (GORD) is a common problem. It is caused by several conditions that disturb the sphincter function at the lower end of the oesophagus, such as hiatus hernia. Symptoms of GORD can be broadly grouped into those directly related to reflux episodes, such as heartburn, regurgitation, chest pain and nausea, and those symptoms caused by complications of reflux disease, including dysphagia and respiratory difficulties. Repeated episodes of GORD can damage the lining of the oesophagus and lead to oesophageal ulceration, oesophageal stricture and Barrett's oesophagus.

2.2 The standard treatments for patients with symptomatic GORD are lifestyle modification and drug therapy. Patients who have refractory symptoms, who develop complications despite medication or who develop intolerance to medication may be considered for anti-reflux surgery (usually laparoscopic fundoplication). Several endoscopic techniques (such as

endoscopic radiofrequency ablation or endoscopic injection of bulking agents) have also been used.

3 The procedure

3.1 Electrical stimulation of the lower oesophageal sphincter aims to strengthen a weak or improperly functioning lower oesophageal sphincter muscle, to restore the anti-reflux barrier between the stomach and oesophagus, by using low energy electrical impulses.

3.2 With the patient under general anaesthesia, 2 electrodes and a lead are implanted into the sphincter muscle using a laparoscope under endoscopic guidance. The lead is passed through the abdominal wall and is secured to a stimulator, which is implanted in a subcutaneous pocket in the abdominal wall.

3.3 The stimulator automatically delivers impulses of about 3 mA to 8 mA to the electrodes in repeated 30-minute sessions. The patient does not feel the stimulation. The stimulator is programmed and controlled wirelessly to adapt it to specific patient needs (for example, related to diet and lifestyle).

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

4.1 A case series of 25 patients with gastro-oesophageal reflux disease (GORD) treated by electrostimulation of the lower oesophageal sphincter (LOS), with a 2-year follow-up, reported median percentages of days and nights with heartburn at baseline ‘off

proton pump inhibitors (PPIs)' (defined as 10 days after the patients had started electrostimulation and had stopped taking PPIs) and at follow-up. The evaluations used a 14-day symptom diary kept by the patients. Median percentages of days with heartburn were 92% at baseline 'off PPIs', 14% at 6 months, 13% at 12 months and 7% at 24 months ($p<0.001$ for all times versus baseline 'off PPIs'). Median percentages of nights with heartburn were 71% at baseline 'off PPIs', and 0% at 6, 12 and 24 months ($p<0.001$ for all times versus baseline 'off PPIs').

4.2 The case series of 25 patients reported median percentages of days with symptoms of regurgitation of 66% at baseline 'off PPIs', and 0% at 6, 12 and 24 months ($p<0.001$ for all times versus baseline 'off PPIs'). Median percentages of nights with regurgitation were 31% at baseline 'off PPIs', and 0% at 6, 12 and 24 months ($p<0.01$ for all times versus baseline 'off PPIs').

4.3 The case series of 25 patients reported dysphagia caused by GORD in 38% (9/24) of patients at baseline 'on PPIs' and in 71% (17/24) at baseline 'off PPIs'. Dysphagia was reported in 13% (n=23) of patients at 12-month follow-up, and in 5% (1/21) at 24-month follow-up (level of significance not stated).

4.4 The case series of 25 patients reported median gastro-oesophageal reflux disease health-related quality of life (GORD-HRQL) scores (interquartile range [IQR]) at baseline of 9.0 (6.0–10.0) when patients (n=24) were still taking PPIs and of 23.5 (21.0–25.3) when patients (n=24) had stopped taking PPIs. The scores improved significantly to 2.0 at 12 months (IQR and number of patients not given) and to 0 (0–3.0) at 24 months (n=21; $p\leq0.002$

versus baseline ‘on PPI’ and ‘off PPI’ score for 12- and 24-month follow-up respectively).

4.5 The case series of 25 patients reported dissatisfaction with GORD control in 71% (17/24) of patients at baseline ‘on PPIs’ and in 92% (22/24) of patients at baseline ‘off PPIs’. At 24-month follow-up, dissatisfaction was reported in none (0/21) of the patients ($p<0.001$ for both groups of patients).

4.6 The case series of 25 patients reported that GORD had an impact on their sleep in 71% (17/24) of patients at baseline ‘on PPIs’ and in 96% (23/24) of patients at baseline ‘off PPIs’. At 12-month follow-up, GORD was reported to have an impact on their sleep by 17% of patients (n=23, absolute numbers not given) and, at 24-month follow-up, by 10% (2/21) of patients.

4.7 The case series of 25 patients reported that the median percentage of the 24-hour period for which there was a distal oesophageal pH of less than 4 was 10% (IQR 8%-13%) at baseline (n=24; defined for this measure as at least 5 days after the patients had started electrostimulation and had stopped taking PPIs) compared against 5% (3%–7%) at 24 months (n=18; p=0.001 versus baseline). At baseline, 96% (23/24) of patients had an abnormal distal oesophageal pH (less than 4 for more than 4% of a 24-hour recording) and, at 24 months, 61% (11/18) had an abnormal pH.

4.8 In the case series of 25 patients, all patients still included in the study (24/24) were taking PPIs for GORD after implantation. At 24 months, 76% (16/21) of patients were not taking any PPIs, 14% (3/21) reported occasional PPI use and 10% (2/21) reported regular PPI use.

4.9 A publication about the case series of 25 patients with GORD treated by electrostimulation of the LOS after only 1 year of follow-up reported that, at baseline (within 6 months before enrolment), 67% (16/24) of patients had LA (Los Angeles classification) Grade A oesophagitis (Grade A to D from less severe to more severe oesophagitis assessed by endoscopy), 25% (6/24) had LA Grade B and 8% (2/24) had LA Grade C oesophagitis. At 12 months, 31% (7/23) of patients had no oesophagitis, 52% (12/23) had LA Grade A, 13% (3/23) had LA Grade B and 4% (1/23) had LA Grade C oesophagitis (p=0.01). Oesophagitis had improved by at least 1 grade in 58% (14/24) of patients at 3 months and in 57% (13/23) of patients at 12 months compared against baseline.

4.10 The specialist advisers listed the following key efficacy outcomes: reduction in symptoms of acid reflux, elimination (remission) of pre-operative GORD-related symptoms assessed by GORD-HRQL questionnaire, subjective and objective maintenance of remission, healing of any pre-operatively noted oesophagitis (assessed according to LA grading), improved 24-hour ambulatory pH studies, and lack of side effects such as dysphagia, bloating, fullness, increased wind and abdominal pain.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

5.1 Trocar perforation of the small bowel during laparoscopy was reported in 1 patient in a cases series of 33 patients with gastro-

oesophageal reflux disease (GORD) treated by electrostimulation of the lower oesophageal sphincter (LOS, results only reported in a conference abstract). It was successfully treated and the device was prophylactically explanted.

5.2 Pain or discomfort in the abdomen was reported on 6 occasions in 6 patients in a case series of 25 patients with GORD treated by electrostimulation of the LOS with a 2-year follow-up; the adverse events were reported as related to the device (no details on timing provided). In addition, 1 patient had transient discomfort in the shoulder and 3 patients had transient nausea or vomiting during the first 24 hours after the procedure.

5.3 Superficial skin infection at the abdominal wall pocket site was reported in 1 patient in the case series of 25 patients.

5.4 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following anecdotal adverse events: deep vein thrombosis and chest infection. They considered that the following were theoretical adverse events: all laparoscopic surgery related adverse events, including port insertion vascular/visceral/ bleeding events; pneumoperitoneum-related cardio-pulmonary complications; oesophageal injury (perforation); dysphagia when hiatal closure is needed; device malfunction/failure; lead migration; and lead erosion.

6 Committee comments

6.1 The Committee considered electrical stimulation of the lower oesophageal sphincter for the treatment of gastro-oesophageal reflux disease to be a promising intervention for a common condition. This underpinned the recommendation for further research, which should provide data to identify subgroups of patients who might derive particular benefit from the procedure.

6.2 For related NICE guidance, see the NICE website.

Bruce Campbell
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