NICE guidance

Photodynamic therapy for Barrett's oesophagus

Interventional procedures guidance
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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with

those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

1 Guidance

1.1 Current evidence on the efficacy of photodynamic therapy (PDT) for patients with Barrett's oesophagus with high-grade dysplasia (HGD) is adequate, provided that patients are followed up in the long term. There are no major safety concerns, although there is a risk of oesophageal stricture, and photosensitivity reactions are common. This procedure may be used in patients with Barrett's oesophagus with HGD provided that normal arrangements are in place for clinical governance, consent and audit.

1.2 Current evidence on the efficacy and safety of PDT in patients with Barrett's oesophagus with either low-grade dysplasia (LGD) or no dysplasia is inadequate in quality and quantity, and the balance of risks and benefits is not clear. Therefore, for these patients, the procedure should be used only with special arrangements for clinical governance, consent and audit or research.

1.3 Clinicians wishing to undertake PDT in patients with Barrett's oesophagus with either LGD or no dysplasia should take the following actions.

- Inform the clinical governance leads in their Trusts.
- Ensure that patients and their carers understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended.
- Audit and review clinical outcomes of patients with Barrett's oesophagus other than HGD having PDT (see section 3.1).

1.4 Patient selection should be carried out by a multidisciplinary team experienced in the management of the condition.

1.5 PDT for Barrett's oesophagus should only be carried out by endoscopists with specific training in this procedure.

2 The procedure

2.1 Indications and current treatments

2.1.1 Barrett's oesophagus is characterised by abnormal epithelium of the oesophagus. In some patients, metaplasia and dysplasia could progress to oesophageal adenocarcinoma.

2.1.2 Cancer risk is higher for patients who have Barrett's oesophagus with high-grade dysplasia (HGD; some of whom may already have developed early-stage cancer) than for those with low-grade dysplasia (LGD) or no dysplasia. Patients with HGD are usually offered oesophagectomy, or frequent endoscopic surveillance and re-biopsy (to detect neoplastic changes early) followed by oesophagectomy. Endoscopic treatments aiming to remove or ablate abnormal epithelium include endoscopic mucosal resection and different ablative treatments.

2.1.3 Patients with LGD or no dysplasia are usually offered regular endoscopic surveillance and re-biopsy (with the aim of detecting potential progression to HGD or cancer).

2.2 Outline of the procedure

2.2.1 Photodynamic therapy (PDT) is carried out as an inpatient procedure, with the patient under intravenous sedation. A photosensitising agent is injected intravenously and is activated by illuminating the selected area with a laser inserted into the oesophagus. The photosensitising agent absorbs the light and forms high-energy oxygen molecules that cause necrosis of the Barrett's epithelium through a photochemical effect. For extensive Barrett's oesophagus, more than 1 treatment session may be required.

2.2.2 Patients are advised to avoid exposure to bright light and direct sunlight for several weeks after the procedure to minimise risk of photosensitivity reactions.

2.3 Efficacy

Sections 2.3 and 2.4 describe efficacy and 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 overview.

2.3.1 A randomised controlled trial (RCT) of 208 patients with HGD treated by PDT and omeprazole or omeprazole alone reported absence of HGD in 75% (104 out of 138) and 36% (25 out of 70) of patients respectively at 18-month follow-up ($p<0.0001$) and in 48% and 4% of patients at 5-year follow-up ($p<0.0001$).

2.3.2 An RCT of 72 patients without dysplasia treated by PDT or argon plasma coagulation (APC) reported complete response (reversal of columnar to squamous epithelium) in 50% (17 out of 34) and 97% (33 out of 34) of patients respectively at 12-month follow-up ($p<0.0001$).

2.3.3 The RCT of 208 patients treated by PDT and omeprazole or omeprazole alone reported adenocarcinoma development in 15% (21 out of 138) and 29% (20 out of 70) of patients respectively during 5-year follow-up.

2.3.4 The Specialist Advisers listed key efficacy outcomes as reversal of dysplasia and metaplasia, and prevention of progression to adenocarcinoma.

2.4 Safety

2.4.1 One patient died 3 days after PDT treatment, with transmural oesophageal necrosis without perforation, in an RCT of 40 patients (13 with single-dose PDT versus 13 with two-dose PDT versus 14 with APC).

2.4.2 Oesophageal stricture was reported in 36% (49 out of 138), 3% (1 out of 34), 33% (20 out of 60), 15% (2 out of 13), and 27% (35 out of 131) of patients treated by

PDT in RCTs of 208, 72, 60, 26 and a non-randomised controlled trial of 199 patients respectively. Most were treated successfully with dilatation but 2 patients had perforation requiring oesophagectomy, as a result of dilatation.

2.4.3 Dysphagia was reported in 19% (absolute figures not stated) of patients treated by PDT in the RCT of 208 patients (symptom timing not stated).

2.4.4 Photosensitivity reactions within 90 days occurred in 69% of patients in the PDT arm of the RCT of 208 patients (absolute figures not stated). Photosensitivity reactions occurred in 15% (5 out of 34) and 15% (2 out of 13) of patients in RCTs of 72 and 26 patients respectively, and in 60% (77 out of 129) of patients in the non-randomised controlled trial of 199 patients.

2.4.5 In the RCT of 72 patients treated by PDT or APC, buried glands were reported in 24% (4 out of 17) and 21% (7 out of 33) of patients respectively (difference reported as 'not significant').

2.4.6 Specialist Advisers listed anecdotal adverse events as pain and inflammation, ulceration and severe hypotension after PDT with 5-aminolevulinic acid. They considered theoretical adverse events to include decompensation in patients with cirrhosis of the liver, and skin and retinal damage due to photosensitisation.

3 Further information

3.1 This guidance requires that clinicians undertaking the procedure for low-grade dysplasia (LGD) or no dysplasia make special arrangements for audit. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion).

3.2 This guidance should be read in conjunction with NICE's guideline on Barrett's oesophagus and stage 1 oesophageal adenocarcinoma: monitoring and management.

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the overview.

Information for patients

NICE has produced information for the public on this procedure. It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.