NICE guidance

Photodynamic therapy for brain tumours

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 safety and efficacy of photodynamic therapy (PDT) for brain tumours is limited in both quality and quantity. Therefore, this procedure should only be used in the context of randomised controlled trials with well-defined inclusion criteria (specifying the tumour type for inclusion in the trial) and treatment protocols, and with collection of both survival and quality of life outcomes.

2 The procedure

2.1 Indications and current treatments

2.1.1 Brain tumours may be primary tumours or metastases from tumours elsewhere in the body. Primary brain tumours are graded using a World Health Organization (WHO) classification from I (least aggressive) to IV (most aggressive). Patients with high-grade tumours often have a poor prognosis.

2.1.2 The symptoms of a brain tumour are determined by its location and size. Depending on its location in the brain, a tumour can cause limb weakness or speech disturbance. Any brain swelling caused by a tumour can result in raised intracranial pressure, which can lead to headache, vomiting and reduced consciousness.

2.1.3 Some patients can be treated by surgical resection, with the aim of reducing symptoms and improving prognosis. Non-surgical treatment options include chemotherapy and radiotherapy. A combination of these treatments may be

used, or surgery may be followed by chemotherapy and radiotherapy.

2.2 Outline of the procedure

2.2.1 Photodynamic therapy is usually carried out with the patient under general anaesthesia, at the same operation as surgical resection, when as much of the tumour has been removed as possible. A photosensitising agent is injected, usually intravenously, although direct injection into the tumour is also possible. The photosensitising agent is activated by illuminating the selected area with a laser source. The photosensitising agent absorbs the light and forms high-energy oxygen molecules that interact with the brain tissue to cause tumour necrosis through a photochemical effect. Occasionally, repeated photodynamic therapy (PDT) sessions are performed after surgery via access maintained through the skull. To minimise the risks associated with skin photosensitivity, patients are advised to avoid exposure to bright light and direct sunlight for several weeks after the procedure.

2.2.2 This guidance refers to the therapeutic use of PDT and not to PDT-guided resection.

2.2.3 Various devices and photosensitising agents can be used for this procedure.

2.3 Efficacy

Sections 2.3 and 2.4 describe efficacy and safety outcomes which were available in the published literature and which 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 27 patients with newly diagnosed glioblastoma and a Karnofsky score of 60 or greater (on a scale where 100 is 'perfect health' and 0 is 'death') reported an increase in mean survival in 13 patients who received PDT after surgery compared with 14 patients treated by surgical resection alone (52.8 weeks and 24.1 weeks respectively; p=0.001). A case series of 112 patients treated by PDT following surgical resection reported

median survival of 30 weeks in patients with gliomas and 24 weeks in patients with metastatic carcinoma (follow-up not stated). A case series of 136 patients treated by PDT following surgical resection reported that median survival from initial diagnosis was 76.5 months for patients with primary anaplastic astrocytoma and 14.3 months for patients with glioblastoma multiforme (p=0.001), with a minimum follow-up of 3 years. Duration of survival was not associated with the location of the tumours in the brain (p=0.54). A case series of 26 patients with recurrent glioblastoma (WHO grade IV) treated by PDT following surgical resection reported median survival of 8.5 months.

2.3.2 The case series of 26 patients reported that median time to disease progression was 6 months.

2.3.3 The RCT of 27 patients reported an improvement in mean Karnofsky score from 60 to 80 points in the PDT after surgery group but no change from 70 points in the surgical resection group (follow-up not stated; $p<0.05$).

2.3.4 The Specialist Advisers considered key efficacy outcomes to include overall and progression-free survival, completeness of resection and quality of life.

2.4 Safety

2.4.1 In the case series of 112 patients, 3% (3 out of 112) died after the operation, 1 of pulmonary embolism and 2 of tumour cavity haemorrhage. Deep vein thrombosis occurred in 4% (4 out of 112), infection (not otherwise specified) in 4% (4 out of 112), and cerebrospinal fluid leak in 1% (1 out of 112) of patients (no further details stated).

2.4.2 The case series of 26 patients reported transient oedema of the treated area in 4% (1 out of 26) of patients.

2.4.3 Across three case series, sunburn due to light exposure occurred at a rate of between 2% (2 out of 112, 2 out of 136) and 8% (2 out of 26).

2.4.4 The Specialist Advisers considered adverse events associated with PDT for brain tumours to include cerebral oedema, raised intracranial pressure, hypersensitivity

reactions and skin photosensitisation. They stated that additional theoretical adverse events include damage to the normal brain and cerebral blood vessels, stroke, and compromising of further treatments by increasing the sensitivity of the brain to their toxic side effects.

3 Further information

3.1 NICE has published technology appraisal guidance on temozolomide for the treatment of recurrent malignant glioma (brain cancer) and carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma, and a cancer service guideline on improving outcomes for people with brain and other central nervous system tumours.

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.