NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional procedures consultation document

Melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic cancer in the liver

Cancer can start in the liver (primary) or spread to it from another part of the body (metastases). The chemotherapy drug (melphalan) used to treat it can cause side effects in other parts of the body. In this procedure, the blood flow from the liver to the rest of the body is diverted (hepatic vein isolation) while the drug is delivered directly into the liver (percutaneous hepatic artery perfusion). Blood leaving the liver is taken out of the body and filtered to remove the drug, then returned. The aim is to destroy the cancer with a very high dose of the drug (chemosaturation) without causing side effects in the rest of the body.

NICE is looking at melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic cancer in the liver. This is a review of NICE's interventional procedures guidance on chemosaturation via percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic cancer in the liver.

NICE's interventional procedures advisory committee met to consider the evidence and the opinions of professional experts, who are consultants with knowledge of the procedure.

This document contains the draft guidance for consultation. Your views are welcome, particularly:

- comments on the draft recommendations
- information about factual inaccuracies
- additional relevant evidence, with references if possible.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Issue date: November 2020

This is not NICE's final guidance on this procedure. The draft guidance may change after this consultation.

After consultation ends, the committee will:

- meet again to consider the consultation comments, review the evidence and make appropriate changes to the draft guidance
- prepare a second draft, which will go through a resolution process before the final guidance is agreed.

Please note that we reserve the right to summarise and edit comments received during consultation or not to publish them at all if, in the reasonable opinion of NICE, there are a lot of comments or if publishing the comments would be unlawful or otherwise inappropriate.

Closing date for comments: 17 December 2020

Target date for publication of guidance: April 2021

1 Draft recommendations

1.1 Evidence on the safety of melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for cancer or metastases in the liver shows there are serious but well-recognised complications:

- For patients with metastases in the liver from ocular melanoma, there is some evidence of short-term tumour response. For these patients, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. Find out what special arrangements mean on the NICE interventional procedures guidance page.
- For patients with primary liver cancer or metastases in the liver that are not from ocular melanoma, evidence of efficacy is inadequate in quality and quantity. For these patients, this procedure should only be used in the context of research. Find

out what only in research means on the NICE interventional procedures guidance page.

1.2 Clinicians wishing to do melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for patients with metastases in the liver from ocular melanoma should:

- Inform the clinical governance leads in their healthcare organisation.
- Give patients (and their families and carers as appropriate) clear written information to support shared decision making, including NICE's information for the public.
- Ensure that patients (and their families and carers as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.
- Audit and review clinical outcomes of all patients having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion).
- Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve.

1.3 Healthcare organisations should:

- Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for every patient having this procedure.
- Regularly review data on outcomes and safety for this procedure

1.4 The procedure should only be done in specialist centres by a multidisciplinary team that includes an interventional radiologist, an anaesthetist and a clinical perfusion scientist trained and experienced in the procedure.

1.5 Further research should be in the form of randomised controlled trials against current best practice. It should report details of patient selection, concurrent therapies and techniques, and adverse events, including those related to chemotherapy.

2 The condition, current treatments and procedure

The condition

2.1 The most common types of primary liver cancer are hepatocellular carcinoma (also known as hepatoma) and cholangiocarcinoma. However, cancer in the liver often metastases from other sites such as the lung, colon, stomach and eye (particularly ocular melanoma).

Current treatments

2.2 Treatment for primary or metastatic cancer in the liver depends on the location and stage of the cancer and how much liver function is preserved. Treatment options include surgical resection, thermal ablation, systemic chemotherapy, transarterial chemoembolisation, isolated hepatic perfusion and selective internal radiation therapy. In patients with primary liver cancer, surgical removal with curative intent and liver transplantation may be possible. For most patients with liver metastases, treatment with curative intent is not possible.

The procedure

2.3 Melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation is done under general anaesthesia. A high dose of melphalan chemotherapy is delivered directly into the hepatic artery. Blood leaving the liver is diverted out of the body and filtered to reduce the level of melphalan before being returned to the circulation. The aim is to allow high doses of

melphalan chemotherapy to be used, which would otherwise not be tolerated because of severe systemic side effects.

2.4 An infusion catheter is inserted into the femoral artery and guided into the hepatic artery. The femoral vein is cannulated and a multi-lumen, double-balloon catheter is inserted into the inferior vena cava and across the hepatic veins. The balloons are inflated so that all blood leaving the liver through the hepatic veins enters the catheter rather than the systemic circulation. High doses of melphalan are infused directly into the liver through the hepatic artery infusion catheter over about 30 minutes. Blood leaving the liver passes through an extracorporeal filtration system to remove most of the melphalan and is returned to the circulation through a catheter in the internal jugular vein. Full anticoagulation with heparin is needed throughout the procedure.

2.5 The procedure causes significant changes in the patient's haemodynamic status, which must be managed by the anaesthetic team with support from a clinical perfusion scientist.

3 Committee considerations

The evidence

3.1 NICE did a rapid review of the published literature on the efficacy and safety of this procedure. This comprised a comprehensive literature search and detailed review of the evidence from 11 sources, which was discussed by the committee. The evidence included 1 randomised controlled trial, 1 non-randomised comparative study and 9 case series (including 2 studies looking at the same patient population). It is presented in table 2 of the interventional procedures overview. Other relevant literature is in the appendix of the overview.

3.2 The committee considered the key efficacy outcomes to be: overall survival, progression-free survival, quality of life and downstaging of cancer.

3.3 The committee considered the key safety outcomes to be: procedure-related complications (including bleeding, thrombosis and cardiovascular events), bone marrow or haematological toxicity, and death.

3.4 NICE received 1 submission from a patient organisation.

Committee comments

3.5 The filter used in this procedure is designed for use with melphalan.

3.6 The committee noted that the toxicity of the procedure is principally related to how efficiently the melphalan is removed and prevented from entering the systemic circulation.

3.7 The technology has changed over time, and the newest filter may be associated with less haematological toxicity.

3.8 The procedure is used for unresectable liver cancer.

3.9 There are other emerging therapies for treating liver cancer and metastases.

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Chair, interventional procedures advisory committee
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