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 drugs, 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This document contains the draft guidance for consultation.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.

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 The draft guidance may change after this consultation.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- meet again to consider the consultation comments, review the evidence and make appropriate changes to the draft guidance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: 23 July 2020

Target date for publication of guidance: December 2020

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. There is some evidence of short-term tumour response but evidence on quality of life and survival is inadequate in quality and quantity. Therefore, this procedure should only be used in the context of research.

1.2 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.

1.3 Further research should be in the form of randomised controlled trials against current best practice. It should report details of patient selection, concurrent therapies, technique 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 is 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 9 sources, which was discussed by the committee. The evidence included 1 randomised controlled trial, 1 non-randomised comparative study and 7 case series. 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 Patient commentary was sought but none was received.

Committee comments

3.5 The filter used in this procedure is designed for use with melphalan. The technology has changed over time.

3.6 The committee noted that most of the evidence it reviewed was from patients with metastases in the liver from ocular melanoma, which are often miliary and difficult to resect.

3.7 The committee was informed that the procedure is used for patients with unresectable liver cancer.

3.8 The committee was informed that there are other emerging therapies for treating liver cancer and metastases.

3.9 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.

Tom Clutton-Brock
Chair, interventional procedures advisory committee
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