Chemo-Occlusion for the Treatment of Liver Cancer
A New Technique Using Degradable Starch Microspheres

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Summary

The use of particulate embolic agents combined with regional chemotherapy in the treatment of hepatocellular carcinoma and metastatic liver cancer has been widely investigated over the past decade. The rationale for the use of such agents is to provide vascular blockade, resulting in a reduced or halted blood flow. This increases the in situ time, tumour exposure and, thus, efficacy of any coadministered cytotoxic drug. Of all the embolic agents and techniques available, degradable starch microspheres (DSMs) are the agents that have been evaluated most extensively. DSMs are non-toxic, are readily degradable and provide temporary vascular occlusion. Phase II and III clinical trials have demonstrated the efficacy of DSM when coadministered with chemotherapeutic drugs (chemo-occlusion), as measured by tumour response. Indeed, compared with drug therapy alone, a significantly greater tumour response is associated with chemo-occlusion, for patients with either hepatocellular carcinoma or metastatic liver cancer.
The use of combination or multimodular therapies have, in recent years, been investigated. The therapeutic benefits associated with chemo-occlusion would suggest that this technique might have a potential application as an adjuvant, or neoadjuvant therapy, for example, in reducing tumour recurrence after surgical resection in hepatocellular carcinoma, or downstaging a tumour prior to surgical resection, respectively. Furthermore, comprehensive management of patients with liver metastases and potential extrahepatic involvement may well be achieved by a combination of DSM chemo-occlusion and systemic chemotherapy. Large, randomised trials are, however, required to access more fully the clinical benefits associated with chemo-occlusion, such as, quality of life, time to tumour progression and survival.

Regionally occlusive techniques administered with cytotoxic agents have also shown potential in the treatment of alternative cancers, for example, breast and pancreatic carcinomas. However, these therapies require further evaluation.

The use of foreign bodies injected into the circulation to induce embolism was first proposed at the beginning of this century (Dawbarn 1904). However, it was not until the early 1980s that it became the subject of extensive research (Young 1981). Embolisation has been employed for various diagnostic and therapeutic purposes, but perhaps has been investigated most widely as treatment for tumours. Embolisation of the vascular tree, which supplies blood to the tumour region, is a technique used to elicit either permanent vascular blockade, and thereby promote tumour necrosis, or temporary embolisation to enhance the therapeutic efficacy of a coadministered anticancer drug. The latter technique is referred to as chemoembolisation.

The benefits of such treatment are, however, confined to a single body region, and are limited by the blood supply to and the normal tissue tolerance of the infused region. The liver, therefore, is an obvious organ to which regional chemotherapy may be applied. In humans, the blood supply to liver tumours greater than 2mm in diameter is obtained from the hepatic artery, whilst the normal liver parenchyma is supplied mainly from the portal circulation (fig. 1). Consequently, the efficacy of embolic agents in the treatment of primary and metastatic liver cancer has been investigated.

An agent that has undergone considerable research in recent years is degradable starch microspheres (DSM), which unlike most other embolic agents has a unique ability to provide brief, transient occlusion. This article reviews relevant data concerning the current clinical use of DSM in the treatment of cancer, highlighting liver cancer, in particular.

1. Treatment of Liver Cancer

The natural course of hepatocellular carcinoma has not altered dramatically over the past few decades despite advances in diagnostic and therapeutic techniques. Life-expectancy for patients with primary and secondary liver tumours is extremely poor, being approximately 6 months (Moosa et al. 1991). Surgical resection, whilst curative in 10 to 20% of patients (Moosa et al. 1991), is of limited value because few patients (30%) have tumours that are surgically resectable (Witte et al. 1991).

An alternative approach for treatment of liver cancer is to administer systemic chemotherapy. However, very few patients with primary or metastatic tumours respond to chemotherapy (Falkson et al. 1984, 1990; Kemeny et al. 1992; Lai et al. 1990). Even in patients who demonstrate a response (approximately 20%) [Kemeny 1992], median survival is only 5 to 7 months after diagnosis, thereby demonstrating that systemic chemotherapy alone is not sufficiently effective and that alternative treatment options are required (Falkson et al. 1984, 1990; Lai et al. 1990; Kemeny 1992; Kemeny et al. 1992).

1.1 Regional Arterial Infusion Chemotherapy

Chemotherapy delivered by regional arterial infusion provides obvious benefits in the treatment of tumour. This technique provides a more direct delivery of the cytotoxic drug to its site of action.