A Phase I Feasibility Study of Hepatic Arterial Melphalan Infusion with Hepatic Venous Hemofiltration using Percutaneously Placed Catheters in Patients with Unresectable Hepatic Malignancies


* Surgery Branch, NCI; and **Diagnostic Radiology Department, NIH, Bethesda, MD

Abstract

Primary and metastatic liver cancer is a significant clinical problem without effective therapies for the vast majority of patients. There are approximately 130,000 new cases of hepatocellular carcinoma (HCC) and liver cancer in the United States annually, with approximately 40% of patients presenting with unresectable disease, and 30% of patients with tumors not surgically resectable. Primary or metastatic liver cancer is usually treated with systemic chemotherapy for unresectable primary hepatocellular carcinoma (HCC) and extensive metastases representing the life associated morbidity. Further treatments are prevented by postoperative adhesions around the vena cava and hepatic veins. The occlusion of these major vessels limited the introduction of hepatic arterial drug delivery. High level of regional tissue levels is advantageous to the drug dose-response of active anticancer drugs. In the present study, we used percutaneously placed catheters to create a segmental hepatic arterial and venous isolation to deliver chemotherapy in the liver.

Methods and Materials

From July 2009 to March 2011, a total of 20 procedures were performed on 10 patients (5 men, 5 women; mean age 66 ± 6.8 years) with unresectable primary or metastatic liver cancer. The procedure was approved by the Institutional Review Board of Mayo Clinic and all patients signed informed consent. Primary or metastatic liver tumors were assessed with computed tomography (CT) and/or magnetic resonance imaging (MRI) before the procedure. A hepatic arteriogram was performed before the procedure to confirm the absence of arterial blockage, enabling some flow from the lower IVC to the right atrium. In the procedure, melphalan is infused into the IVC and the outflow line of the filtration circuit is connected to the venous effluent (HVE) through an activated charcoal filter (Delcath Systems, Inc.) then to the systemic circulation. Melphalan and its metabolites are filtered and removed. The patient is kept at bedrest and monitored for 12 hours after the procedure. If the patient is hemodynamically unstable, the patient is taken off study.

Results

From July 2009 to March 2011, a total of 20 procedures were performed on 10 patients (5 men, 5 women; mean age 66 ± 6.8 years) with unresectable primary or metastatic liver cancer. The procedure was approved by the Institutional Review Board of Mayo Clinic and all patients signed informed consent. Primary or metastatic liver tumors were assessed with computed tomography (CT) and/or magnetic resonance imaging (MRI) before the procedure. A hepatic arteriogram was performed before the procedure to confirm the absence of arterial blockage, enabling some flow from the lower IVC to the right atrium. In the procedure, melphalan is infused into the IVC and the outflow line of the filtration circuit is connected to the venous effluent (HVE) through an activated charcoal filter (Delcath Systems, Inc.) then to the systemic circulation. Melphalan and its metabolites are filtered and removed. The patient is kept at bedrest and monitored for 12 hours after the procedure. If the patient is hemodynamically unstable, the patient is taken off study.

Conclusions

This study has demonstrated that catheter-based percutaneous hepatic arterial and venous isolation is feasible and safe for patients with unresectable primary or metastatic liver cancer. The isolated hepatic arterial and venous isolation technique allows delivery of chemotherapy to a specific liver lobe, while the filtrate is removed from the liver and treated with activated charcoal. The isolated hepatic arterial perfusion (IHP) technique, used in this study, is an advantageous drug delivery method for patients with unresectable primary or metastatic liver cancer.

Figure 1: Diagram of the Delcath System. Melphalan is administered directly into the hepatic artery. A pre-filter is used to remove microparticulate matter that could otherwise be retained in the filtration system. A hepatic vein filter is placed just prior to the effluent to remove particles that are not captured by the hepatic vein filter. The effluent is then routed to the collection chamber. The patient is maintained on heparin through the intravenous catheter to prevent thrombus formation. The catheter is removed after 24 hours. The procedure is repeated every 28 days.