Percutaneous Hepatic Perfusion for Primary and Secondary Liver Tumors- Interventional Radiology Initial Experience

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Introduction:

The prevalence, morbidity, and lack of effective systemic treatments for liver tumors (primary and secondary) have spawned efforts to establish more organ-specific techniques. Since the majority of dose-limiting toxicities for systemic chemotherapies are not hepatic, organ-specific techniques that would prevent systemic exposure could potentially allow for higher dosing regimens for neoplasms of the liver.

Using a procedure pioneered by Ausman over forty years ago, several institutions are currently using isolated hepatic perfusion (IHP) to treat unresectable liver tumors. Despite the improved response rates seen in IHP, several drawbacks exist including: mean operative time of greater than 8 hours, mean hospital stay of 12 days, an overall mortality of approximately 4%, and treatment limited to a single application.

Percutaneous hepatic perfusion (PHP) attempts to provide the potential efficacy of IHP without these drawbacks. The procedure uses a double balloon venous catheter to isolate hepatic venous outflow, allowing regional perfusion of the liver. Blood that flows into the catheter lumen is pumped through charcoal filtration circuit to remove the therapeutic agent and then returned to systemic circulation. The report seeks to address technical issues, venous and arterial anatomical variants and the specific set-up related to interventional radiology and radiology practice, encountered using PHP with melphalan in phase I trials for patients with primary and secondary liver tumors.

Material and Methods:

At present, under an IRB approved protocol, a total of 62 treatments have been performed on 25 patients (out of 29 enrolled), from August 2001. The proposed goal is 4 treatments per patient. Primary tumors were: ocular melanoma (n=10); Cutaneous melanoma (n=2); Biliary carcinoma (n=3); Neuroendocrine (n=4); sarcoma (n=1); breast (n=1); colorectal (n=1); renal cell (n=1), adrenal (n=1), and peri-ampullary (n=1) carcinoma.

The procedure is performed under general anesthesia and takes about 3 hours. Using real time ultrasound, fluoroscopy and sterile Seldinger technique, a 5 or 6 F right common femoral artery sheath, a 10F right internal jugular vein sheath, a right 18F common femoral vein Delcath sheath and a 7F triple lumen left internal jugular vein catheter are placed. The patient is then fully heparinized to therapeutic ACT levels. Using a 4 or 5 F Cobra C-2 / Simmons 1 catheters /and/ microcatheters the superior mesenteric artery and celiac arteries are accessed for evaluation of portal vein patency and angiographic detail. During the patient's first session, the gastroduodenal artery is documented and embolized using

coils, to prevent reflux of the high dose melphalan and injury of small bowel. The common/ proper hepatic artery is catheterized, and melphalan (1.5 mg/kg) is infused during 30 minutes. Hepatic venous hemofiltration is achieved by placement of a double-balloon, IVC filter catheter system (Delcath system, Delcath Inc. Stamford, CT), isolating and diverting the hepatic venous outflow through an external activated charcoal filter(Delcath systems, Inc.) and back into the systemic circulation via the right internal jugular vein for another 30 minutes. Drug levels were assessed at baseline (0), 5, 10, 15 and 30 minutes after from the hepatic artery, before and after hemofiltration from the hepatic veins and from systemic blood to determine hepatic and systemic toxicity, and filter efficiency.

Results:

A total of 62 treatments were performed on 25 patients. The procedure was aborted in 4 other patients secondary to: direct drainage of the hepatic veins into the right atrium(n=1); sclerosed hepatic artery from previous IHP therapy(n=1); IVC longer than catheter system available(n=1) and insufficient hepatic venous outflow flow rates(n=1).Other arterial and hepatic venous outflow anatomical variants were encountered including: duplicated gastro-duodenal artery, aberrant hepatic arterial supply, accessory hepatic artery, replaced hepatic artery, hepatic arterial spasm, hepatic venous outflow tract draining directly into the right atrium, and a narrowed IVC (from near-by tumor and from previous irradiation to the liver). Also, several minor complications related to heparinization (hemorrhage into metastasis, venous access site hematomas) and high dose melphalan (low white count and low platelets) are described.

Conclusion:

This report seeks to address technical issues related to interventional radiology and radiology practice, encountered using PHP with melphalan in phase I trials for patients with primary and secondary liver tumors.

Delivery of melphalan is possible via this percutaneous system, is relatively safe with minor complications related to high-dose heparin, and with limited manageable systemic toxicity. From the interventional radiology technique stand-point it has proven to be a safe procedure, supporting continuing further clinical studies using this percutaneous approach.