What is hepatic arterial infusion (HAI) therapy?

Hepatic arterial infusion therapy is a treatment for colorectal liver cancer. It uses a drug delivery system to infuse cancer-fighting medication on a continuous basis directly into the liver, the most common place for colon cancer to spread.

HAI therapy is based on the principle of improving therapeutic value by targeting the site of the tumor while minimizing systemic exposure and resultant side effects. HAI therapy commonly uses a small, surgically implantable pump and a catheter that carries the drug from the pump to the hepatic artery.

How is HAI therapy used in fighting cancer?

HAI therapy is used for site-specific drug delivery of chemotherapy for patients with colorectal liver cancer. Each year 160,000 cases of this disease are diagnosed in the United States. Half of these patients will suffer recurrence after initial therapy and it is estimated that, for 70 percent of those who suffer recurrence, their colon cancer will spread, or metastasize, to the liver.

After surgery to remove liver tumors, HAI therapy holds great promise for keeping the cancer in check. Estimates indicate that approximately 12,000 patients who develop liver tumors from colorectal cancer each year in the United States might benefit from HAI therapy.

What are the benefits of HAI therapy for patients with colorectal liver cancer?

Numerous studies conducted over the last 15 years suggest that HAI therapy — administered alone or in combination with systemic chemotherapy after the surgical removal of liver tumors — can significantly extend the lives of appropriately selected patients with advanced colorectal liver cancer, decrease the recurrence of disease in the liver and improve quality of life.

According to a study published in the December 30, 1999 issue of the *New England Journal of Medicine*, researchers at Memorial Sloan-Kettering Cancer Center in New York found that treating advanced colorectal liver cancer patients with a combination of standard systemic chemotherapy and HAI therapy following the surgical removal of their liver tumors improved survival rates and decreased recurrence of liver disease at two years after surgery compared with patients treated only with standard systemic chemotherapy. In other words, the combined treatments produced significantly better outcomes than standard systemic chemotherapy alone. Side effects were similar between the two groups, though the combined therapy group had a higher occurrence of diarrhea.

After two years, 85 percent of the patients who received the combined treatments were still alive, and nearly 90 percent of patients in the same group were found to have no recurrence of disease in the liver. Of those treated with chemotherapy alone, only 69 percent were alive after two years, with 57 percent having had no recurrence of tumors in the liver.
While some older studies on HAI therapy reported mixed results in tumor response and survival rates, new techniques — including the evolution of treatment methods and fully implanted drug infusion systems — make HAI therapy a viable treatment option for appropriately selected patients.

What are the risks associated with HAI therapy?
There are risks associated with HAI therapy, such as:

- Complications that can occur with surgery, such as infection, fluid build-up around the implant site, skin erosion over the site of the implant, incision breakdown, or drug delivered to organs other than the liver.
- Drug toxicity and medication side effects. The most common reported side effects for FUDR are nausea, vomiting, diarrhea, and intestinal inflammation.
- A disruption in therapy if the pump or catheter is damaged by improper handling or filling; drugs or uses not intended for the pump; plugging or tearing the catheter; or manipulating the pump or catheter through the skin (manipulation can result in moving the catheter or pump from its intended site).
- Overdose or underdose of medication if the pump is damaged by impact to the body in the area of the pump, as in strenuous exercise or contact sports.
- Overdose or underdose of medication if the pump is damaged or prolonged exposure to temperature or pressure changes occurs.

Patients should talk with their doctors about side effects that may occur with this therapy and their specific drug regimens.

How does HAI therapy increase the efficacy of chemotherapy drugs for colorectal liver cancer?
Liver tumors derive their blood supply largely from the hepatic artery, whereas normal liver cells derive most of their blood supply from the portal vein. Infusion of chemotherapy directly into the hepatic artery thus exposes the cancer to high drug concentrations while reducing exposure of normal liver tissue to the medications.

How does HAI therapy differ from traditional therapies used to treat colorectal liver cancer?
Traditional chemotherapy is usually delivered by mouth [pills] or intravenously [IV]. The Medtronic IsoMed Infusion System safely and accurately delivers high concentrations of the cancer-fighting agent floxuridine (FUDR) on a continuous basis directly to the liver via the hepatic artery, which is the primary blood supply for liver tumors.

Does HAI therapy reduce the side effects of chemotherapy?
HAI therapy allows a greater concentration of the drug to reach the tumor in the liver with a lower drug exposure to tissues outside of the liver and potential decrease in side effects. The
liver filters up to 99 percent of the chemotherapy drug out of the body, thereby reducing systemic exposure.

**How is HAI therapy administered using the IsoMed Constant-Flow Infusion System?**

The Medtronic IsoMed Constant-Flow Infusion System consists of a pump and a catheter. The pump is surgically placed beneath the skin of the abdomen and its catheter is immobilized in the hepatic artery by two nonabsorbable ties. The pump delivers a constant, prescribed dose of chemotherapy through the catheter and is refillable during a relatively quick and painless outpatient procedure. To refill the pump, a syringe is inserted through the skin and into the refill septum in the pump. When the syringe is depressed, the drug flows from the syringe into the pump’s drug reservoir.

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