Arterial Chemo infusion of Hepatocellular Carcinoma

Department of Gastroenterology, Ajou University School of Medicine, Suwon, Korea

Sung Won Cho, M.D.

Advanced hepatocellular carcinoma (HCC) with portal vein thrombosis (PVT) has a poor prognosis. The majority of patients with advanced HCC live on longer than 6 months from the day of initial diagnosis. The only curative treatment for HCC is surgical resection; however, most patients have unresectable HCC at the time of diagnosis because of advanced tumor stage and/or poor hepatic reserve function.

Treatment modalities, which have been used for unresectable HCC include systemic chemotherapy, intra-arterial (IA) chemotherapy, tumor embolization and a combination of the above. Transarterial chemoembolization (TACE) is widely used for the treatment of unresectable HCC. However, PVT in main branch is contraindication for TACE for fear of hepatic failure. IA infusion chemotherapy via implanted port delivery system was reported to have antitumor effect and minimize the risk of hepatic failure. At present, for those with advanced HCC, IA infusion chemotherapy is the main treatment modality.

We investigated the tumor reducing effects of arterial chemoinfusion of 5-Fu+ cisplatin in patients with advanced HCC. Twenty-five patients with advanced HCC and portal vein thrombosis, or large HCC which were unresectable or for which TACE was thought to be ineffective, underwent intra-arterial port implantation. The mean maximal diameter of these tumors was 13.7 (range, 5-21.5) cm, and they were located at the right lobe (n=18), the left lobe (n=3), or throughout the liver (n=4). Tumor thrombosis was detected in the main (n=14), right (n=3) and left portal vein (n=1), the right portal vein and inferior vena cava (n=2), and the inferior vena cava (n=1). The four other patients had no portal vein thrombosis. All intra-arterial port implantations were performed percutaneously in the angiographic ward through the right or left common femoral artery. The port chamber was implanted in the inguinal area and fixed using histoacryl. For intra-arterial chemotherapy, 5-FU (250 mg/day) and CDDP (10 mg/day) were used for five days every four weeks. In order to observe changes in tumor size, follow-up CT scanning was performed every two months. A complete response was achieved in one patient (4%), a partial response in three (12%), and a minor response in four (16%); the overall response rate was 32% and the mean survival period was 7.6 months. This study showed antitumor effect of IA infusion chemotherapy in some patients with advanced HCC.

We performed another study to investigate the effect of arterial chemoinfusion of 5-FU + cisplatin on survival in patients with HCC with major PVT. A total of 102 HCC patients with major PVT were studied retrospectively. Inclusion criteria were adequate performance status, liver cirrhosis of Child-Pugh A or B, serum bilirubin less than 3 mg/dL, serum creatinine less than 1.4 mg/dL, and absence of refractory ascites. Patients were divided into three groups. Group 1 was 24 patients treated with conservative management. Group 2 were 25 patients treated with systemic intravenous chemotherapy of FAM or FEC regimen. Group 3 were 53 patients
treated with IA chemotherapy. Arterial infusion of a chemotherapeutic agent consisted of the daily administration of cisplatin (10 mg for 5 days) and the subsequent infusion of 5-FU (250 mg for 5 days). This procedure was repeated at 4 week intervals. Mean number of cycles of IA chemotherapy was 3 and ranged from 1-11 cycles.

The median survival of IA chemotherapy group was found to be significantly longer (6 months) than that of conservative treatment group (2 months) or systemic chemotherapy group (4 months) (p=0.003), and one-year survival rates were 21%, 0%, 4%, respectively. These results suggest that IA chemotherapy can prolong survival in HCC patients with major PVT. We investigated the relationship between tumor response to IA chemotherapy and survival to clarify the survival benefit of IA chemotherapy. Ten of 38 patients (26.3%) and 5 of 17 patients (29.5%) were assessed as having response to IA chemotherapy when evaluate at 3 and 8 months after therapy.

One-year survival rate of responder and non-responder evaluated at 3 and 8 months after therapy were 48% and 14% (p=0.01), 75% and 41% (p=0.01), respectively. These results indicated survival benefit of IA chemotherapy in responders.

We identify prognostic factors influencing survival in patients treated with IA chemotherapy. The favorable factors were female sex (p=0.000), Child class A (p=0.003), low alkaline phosphatase level (p=0.015). At least three or four serial course of chemotherapy may be needed to achieve tumor response. The patients with the good hepatic reserve function of underlying liver may have more chance of improved survival. IA chemotherapy may be harmful to patients with decompensated cirrhosis due to chemotherapy-induced deterioration of hepatocellular function. Other favorable factors were nodular type tumor (p=0.04), and only one major branch involvement of the PV (p=0.05) and good tumor enhancement on CT (p=0.04). HCC patients with high vascular tumors might have favorable responses due to increasing local concentration of drugs. We concluded that, intra-arterial infusion of 5-FU and cisplatin may increase survival in advanced HCC patients with favorable prognostic factors.

This therapy can be tried as a treatment option for the management of HCC with major PVT. Prospective, randomized study should be needed to confirm the survival benefits of arterial chemo infusion therapy in advanced HCC.

References


Present Position:
Professor of Medicine Dept. of Gastroenterology Ajou University School of Medicine, Suwon, Korea

Education
1984-1994  Medical Degree Yonsei University College of Medicine
1982-1986  Master of Medicine, The Graduate School, Yonsei University
1990-1994  Doctor of Philosophy, The Graduate School, Soon Chun Hyang University

Employment
1980-1984  Internship and Residency Dept. of Internal Medicine
            Soon Chun Hyang University Hospital, Seoul
1984-1985  Research Fellow Dept. of Gastroenterology
            Soon Chun Hyang University Hospital, Seoul
1985-1989  Instructor Dept. of Gastroenterology
            Soon Chun Hyang University School of Medicine, Seoul
1990-1993  Assistant Professor Dept. of Gastroenterology
            Soon Chun Hyang University School of Medicine, Seoul
1994-1995  Associate Professor Dept. of Gastroenterology
            Soon Chun Hyang University School of Medicine, Seoul
1995-1997  Associate Professor Dept. of Gastroenterology
            Ajou University School of Medicine, Suwon
1998-Present Professor of Medicine Dept. of Gastroenterology
            Ajou University School of Medicine, Suwon

Overseas study
1987-1989  Research Fellow, Liver Section Academic Department of Medicine,
            Royal Free Hospital, London
Memberships

Korean Society of Internal Medicine,
Korean Society of Gastroenterology,
Korean Association of the Study of the Liver,
Korean Society of Gastrointestinal Endoscopy,
Korean Study of Group of Hepatocellular carcinoma,
European Association for the Study of the Liver.

Major research interests

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