Transcatheter Arterial Chemoembolization with Doxorubicin-Eluting Superabsorbent Polymer Microspheres in the Treatment of Hepatocellular Carcinoma: Midterm Follow-up

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ABSTRACT

Purpose: To investigate prospectively the safety, tolerability, and efficacy of transarterial chemoembolization using superabsorbent polymer (SAP) microspheres loaded with doxorubicin for the treatment of hepatocellular carcinoma (HCC).

Materials and Methods: During the years 2006–2011, 64 patients underwent 144 transarterial chemoembolization with SAP microspheres procedures. Most of the patients were staged as Barcelona Clinic Liver Cancer class B (65%). The most frequent underlying liver diseases were hepatitis C (35%) and alcoholic liver disease (28%) resulting in Child-Pugh A (73.4%) or Child-Pugh B (17%) liver cirrhosis. Tumor response was assessed using modified Response Evaluation Criteria in Solid Tumors with magnetic resonance (MR) imaging performed 4–6 weeks after each procedure.

Results: Serious adverse events (n = 9) were ischemic or infectious in nature. Transarterial chemoembolization with SAP microspheres resulted in objective response rates of 67.5%, 44.5%, and 25% after first, second, and third sessions. There were 16 patients (25%) who underwent orthotopic liver transplantation after transarterial chemoembolization with SAP microspheres, of whom 2 experienced recurrent disease. During a median follow-up time of 14 months (range, 2–55 mo), 26 patients (40.5%) died. Median overall and transplant-free survivals were 20.5 months (95% confidence interval, 13.2–27.7) and 18 months (95% confidence interval, 14.2–21.8), respectively.

Conclusions: Transarterial chemoembolization with SAP microspheres has an excellent safety profile in cirrhotic patients, even in the presence of advanced liver disease (Child-Pugh B) or advanced stages of HCC. This treatment produced meaningful tumor response rates as assessed by MR imaging.

ABBREVIATIONS

BCLC = Barcelona Clinic Liver Class, HCC = hepatocellular carcinoma, mRECIST = modified Response Evaluation Criteria In Solid Tumors, OLT = orthotopic liver transplantation, SAE = serious adverse event, SAP = superabsorbent polymer

Patients with hepatocellular carcinoma (HCC) restricted to the liver who retain a patent portal vein branch, preserved liver function, and good performance status should be considered for chemoembolization (1). Drug-eluting microspheres have been developed as an alternative to the conventional technique of chemotherapy

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emulsified with ethiodized oil followed by embolization. Chemoembolization with drug-eluting microspheres has the advantage of combining local and prolonged delivery of chemotherapy with embolization of the blood vessels supplying the tumor. At the present time, there are two drug-eluting microspheres on the market: polyvinyl alcohol–based beads (DC Beads; Biocompatibles Ltd, Farnham, United Kingdom) and superabsorbent polymer (SAP) microspheres (HepaSphere Microspheres [Europe]; QuadraSphere Microspheres [United States]; Merit Medical Systems, South Jordan, Utah). The first comparative trials of DC Beads showed higher response rates (2) and time to progression (3) compared with conventional chemoembolization. A retrospective comparison of conventional chemoembolization with DC Beads suggested a survival benefit for HCC treated with the latter technique (4). Clinical evidence for transarterial chemoembolization with superabsorbent polymer (SAP) microspheres and doxorubicin includes a randomized phase II trial in which this technique resulted in a lower systemic exposure to doxorubicin and fewer systemic side effects compared with conventional chemoembolization (5). A multicenter Italian trial of 50 patients who underwent transarterial chemoembolization with SAP microspheres concluded that the treatment was well tolerated and associated with promising tumor responses after 6–9 months of follow-up (6). This article presents the first midterm follow-up and safety data after treatments with transarterial chemoembolization using SAP microspheres loaded with doxorubicin in a cohort of patients with HCC.

MATERIALS AND METHODS

Study Design and Patient Selection

This prospective case series comprises all patients who underwent transarterial chemoembolization with SAP microspheres during the years 2006–2011 at our center. The study was approved by the medical ethics committee of our institution. Patients had a confirmed diagnosis of HCC based on the European Association for Study of the Liver criteria (7). Other inclusion criteria included nonresectable HCC, ineligibility for curative treatment, and age > 18 years. Exclusion criteria included Child-Pugh C cirrhosis, extrahepatic spread, and extensive portal vein thrombosis. Patients with isolated segmental portal branch tumor thrombosis but a patent portal main branch were considered candidates for inclusion.

Data on patient demographics, etiology, alpha fetoprotein values, and other prior treatments for HCC were collected as well as treatment characteristics, response rates, and serious adverse events (SAEs). SAEs were defined as grade 3 or grade 4 events based on the Common Toxicity Criteria (NCI-CTC Version 2.0) (8). Pain, mild fever, and nausea during the first days after the procedure were classified as postembolization syndrome.

Baseline Demographics

During 2006–2011, we treated 64 consecutive patients with HCC with transarterial chemoembolization with SAP microspheres (Table 1). Most patients were male (> 90%), and the mean age was 65 years. The most common underlying liver diseases were hepatitis C virus

Table 1. Patient Characteristics at Baseline

	Total Cohort (n = 64)	BCLC-A (n = 12)	BCLC-B (n = 42)	BCLC-C (n = 10)	*P* Value
Gender (male/female) (% male)	58/6 (90.6%)	10/2 (80.3%)	40/2 (95.2%)	8/2 (80%)	NS
Mean age (y) (range)	65 (31–83)	66 (49–83)	65 (31–82)	62 (38–78)	
Etiology					NS
HBV (%)	9 (14%)	0 (0%)	6 (14%)	3 (30%)	
HCV (%)	23 (35%)	6 (50%)	13 (31%)	4 (40%)	
Alcohol (%)	18 (28%)	3 (25%)	15 (36%)	0 (0%)	
NAFLD (%)	8 (12.5%)	2 (17%)	3 (7%)	3 (30%)	
Other (%)	6 (9%)	1 (8%)	5 (12%)	0 (0%)	
Child-Pugh					NS
No cirrhosis (%)	6 (9%)	0 (0%)	5 (12%)	1 (10%)	
Child-Pugh A (%)	47 (73.4%)	7 (58%)	31 (74%)	9 (90%)	
Child-Pugh B (%)	11 (17%)	5 (42%)	6 (14%)	0 (0%)	
Child-Pugh C (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Mean MELD (range)	10 (6–26)	11 (7–15)	10 (6–26)	8 (6–14)	NS
Mean AFP in ng/mL (± SD)	8,350.6 (± 50,554)	343.8 (± 772)	148.3 (± 256.6)	52,408 (± 123,824)	.008
AFP > 200 ng/mL (yes/no) (% yes)	44/20	8/4	32/10	4/6	NS
Pretreatment					NS
Total (%)	30	4	22	4	
Resection/RF ablation (%)	22	4	16	2	
Other (%)	8	0	6	2	

AFP = alpha fetoprotein, BCLC = Barcelona Clinic Liver Cancer, HBV = hepatitis B virus, HCV = hepatitis C virus, MELD = model for end-stage liver disease, NAFLD = nonalcoholic fatty liver disease, NS = not significant, RF = radiofrequency.