

Electrochemical Therapy of 74 Cases of Liver Cancer

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ABSTRACT

Ninety-four patients with primary liver cancer have been treated with electrochemical therapy (ECT) in our hospital. Seventy-four cases were followed up for more than one year, 12 cases for less than one year, and 8 cases were lost. Seventy-four cases of stage II and III liver cancer were divided into three groups. Group A received ECT only, group B received ECT plus transcatheter hepatic artery infusion chemotherapy (TAI) and embolisation (IAE) treatment. Group C received ECT plus systemic chemotherapy. The survival rate at 12 months was 58% for group B patients, which was significantly higher than for group A or C patients. We found ECT to be relatively simple and safe. The main side effect is short-time fever after treatment.

Key words: electrochemical therapy (ECT), liver cancer, embolization, hepatic artery infusion, chemotherapy.

INTRODUCTION

Liver cancer is a common malignant disease in China. Surgery is indicated in the early stages (1), but the therapeutic options are limited in advanced stages (5). Electrochemical therapy (ECT) has been used extensively in China during recent years (3, 4) for treating various malignant tumours including liver cancer (2). This study examines the effect of ECT in liver cancer patients treated at our hospital during a two-year period (from February 1989 to February 1991).

PATIENTS AND METHODS

Seventy-four patients with liver cancer, all confirmed by histopathology or cytology, were included in this study. Forty-one of these had received biopsy of their liver or puncture with thin needles before ECT, and 33 patients were diagnosed by electrochemical intracannular biopsy in connection with ECT prior to treatment. Tumour size was determined by the use of a type B ultrasonic diagnostic set. Liver and kidney function as well as Alpha-fetoprotein (AFP), serum bilirubin and other items were examined by blood analysis. The total number of tumours did not exceed four and focal diameters ranged from 3 to 20 cm. Kidney function was normal. The white blood cell count was greater or equal to $4.0 \times 10^9/L$. The Karnovsky index was greater than or equal to 80. The cases were randomly divided into three different groups. Group A received ECT. Group B received ECT plus transcatheter hepatic artery infusion chemotherapy (TAI) and embolization (IAE) treatment. Group C received ECT plus full body chemotherapy (adriamycin + 5-fluorouracil + mitomycin). Clinical data of the patients in the three groups are presented in Table I.

ECT was performed with a Beijing-made electro-

chemical therapeutic apparatus. After local anaesthesia, platinum electrodes were inserted into the centre of the tumour and its peripheral parts under the supervision of a type B ultrasonic diagnostic set. The electrode in the centre of the tumour was used as the positive electrode and the electrodes in the peripheral parts were made negative. The number of electrodes used depended on the size of the tumour. Under ordinary circumstances two to five electrodes were used. For each treatment, the voltage was set at 8-13 V, the current intensity 40-80 mA, duration of treatment three to five hours, and the electric quantity 400-500 C. The number of treatments varied from two to five with an interval of seven to ten days between each treatment.

A transcatheter hepatic artery infusion (TAI) of cytotoxic drugs plus embolization (TAE) was adopted for treatment of patients randomised to group B. First, a hepatic artery infusion of 60-80 mg of adriamycin and 80-140 mg of cis-platinum was given, followed by a mixture of 10-14 mg of mitomycin and 40% of iodized oil. Cytotoxic agents were then infused slowly through the hepatic artery to the selected tumourous blood vessel. Finally, the nutrient vessel of the tumour was obstructed with a gelfoam embolus. The treatment started on the fourth day after ECT with the same frequency of treatment and the same intervals as in the group A patients.

Systemic cytostatics were administered in the group C patients. The regimen included adriamycin, 40 mg/m² i.v. once a week plus mitomycin 4 mg/m² once a week and 5-fluorouracil 0.5 g/m² twice a week for four weeks during each treatment course. There were one to two courses of chemotherapy with an interval of 40 to 60 days. ECT was conducted during the administration of systemic chemotherapy.

A type B ultrasonic diagnostic set was used for measurement of the tumour size. International stan-

Table I. Clinical data

	Group A (n = 27)	Group B (n = 24)	Group C (n = 24)
Stage II	16	13	13
Stage III	11	11	10
Male/female ratio	17/10	16/8	15/8
Age; mean (range) years	45 (28-62)	45 (34-71)	46 (36-68)
Focal tumour diameter			
> 5 cm	22	19	18
< 5 cm	5	4	6
Focal position			
Right lobe	10	8	8
Left lobe	8	7	9
Both lobes	9	8	7
Elevated AFP levels (>30.1 g/L)	17	14	16
Elevated serum bilirubin levels (>17.1 mol/l)	5	6	4
Mixed ascites	4	5	4

Table II. Relationship between TNM stages and short-term effects in 74 cases of liver cancer

CR = Complete response; PR = partial response; PD = progressive disease; NC = no change.

TNM	No. of patients	CR	PR	PD	NC	CR + PR (%)
T ₂ N ₁ M ₀	17	4	8	5	0	12 (70.6)
T ₃ N ₂ M ₀	26	4	12	7	3	16 (61.5)
T ₄ N ₂ M ₁	32	2	17	8	4	19 (59.4)
Total	74	10	37	20	7	47 (63.51)

Table III. Curative effects of survival periods

CR = complete response; PR = partial response; NC = no change; PD = progressive disease.

Group	No. of patients	CR	PR	NC	PD	CR + PR (%)	Survival period (months)
A	27	2	10	11	4	44.44	8.5 ± 2.5
B	24	6	15	2	1	87.50	14 ± 2.0
C	23	2	12	8	2	60.87	9 ± 2.5
Total	74	10	37	21	7	63.51	10.5 ± 2.3

dards for appraisal of the curative effects were used. Patients discharged from the hospital were followed-up every two months. All patients presented here were followed up for at least one year. The cause of death was recorded for each case.

RESULTS

The total remission rate for the 74 cases was 63.51% (Table II). There was no remarkable difference in survival between groups A and C ($p > 0.05$), while survival was significantly better for group B ($p < 0.05$; Table III). By the end of February 1992, 9 out of 27 cases in group A, 14 out of 24 cases in group B, and 8 out of 23 cases in group C had survived for more than 12 months, accounting for 33.33%, 58.33% and

34.78%, respectively. There was no obvious difference between the groups in remission rate when the focal diameter of the tumour was less than or equal to 9 cm, and the curative effects were poor when the focal diameter was greater than 9 cm (Table IV). The curative effect was enhanced when the electric charge was increased within a certain range. The relation between curative effects, and survival periods and electric charge is depicted in Tables III and IV, respectively.

When the accumulated electrical quantity used in the treatment of patients in group A reached 400-1000 C, the tumour centre became liquidified in four cases, the focus disappeared in one case and the tumourous body shrank by 50% or more in six cases when the total electrical quantity was 1200-2000 C.

Table IV. The influence of electric quantity (C) and size of tumour on curative effects

CR = complete response, PR = partial response.

Electric quantity (C)	CR + PR			Remission rate (%)
	< 5 cm	5.1-9 cm	> 9 cm	
400-790	2/4	4/7	2/6	47.06 (8/17)
800-990	3/4	5/8	2/7	52.63 (10/19)
1000-1490	4/6	6/8	3/5	68.42 (13/14)
1500-2000	5/5	8/8	3/6	84.21 (16/19)
Remission rate (%)	73.68 (14/19)	74.19 (23/31)	41.67 (10/24)	63.51 (47/74)

Table V. Side-effects of treatment in the three groups

Group of patients	No.	Fever	Stomach pain	Vomiting	Alopecia	Leukopenia	ECG disturbances	Elevation of liver enzymes
A	27	6	4	1	0	0	0	0
B	24	10	6	3	2	3	3	4
C	23	6	4	8	6	6	6	2
Total	74	22	14	12	8	9	9	6

The main side-effect when treating primary liver cancer with ECT was the occurrence of low grade fever (37.5°C-38.2°C) after treatment. The body temperature of most of the patients returned to normal within three days. Side-effects were more pronounced in groups B and C (Table V). Twenty-eight patients suffered from various degrees of pain, but the symptoms disappeared in 21 cases and were alleviated in ten after treatment. There were four cases in group A, five cases in group B, and three cases in group C who showed symptoms similar to those of circumscribed peritonitis. These symptoms disappeared spontaneously within two or three days.

DISCUSSION

The ECT plus TAI plus TAE approach is a treatment formula that destroys the tissue in the centre of the tumour. Oedema in the cathode region causes dystrophy of the tumourous tissue. An additional effect is related to the blockage of the supply of nutrition through blood vessels with TAI and TAE.

We have not been able to find any remarkable difference between pure ECT therapy and the TAI plus TAE therapy in 27 patients with primary liver cancers. Although amalgamated systemic chemotherapy enhanced the remission rate (60.87%) there

was no obvious prolongation of survival ($p > 0.05$). Combined with TAI and TAE, the curative effects of ECT were remarkably enhanced (87.50%). The result shows that the combined topical treatment with ECT as a predominant element is an important way of improving non-operative treatment of primary liver cancer and an effective way of prolonging survival in patients with advanced liver cancer.

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