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PRE AND POST TRANSARTERIAL CHEMOEMBOLISATION ASSESSMENT IN LIVER TUMOR BY MULTIPHASIC CT ANGIOGRAPHY: A PROSPECTIVE OBSERVATIONAL STUDY

Medical Science

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ABSTRACT

Background: Transarterial chemoembolization (TACE) is the most common treatment modality for treating patients of large unresectable hepatocellular carcinoma (HCC).

Materials and Methods: A total of 28 patients of HCC were included. Multiphasic computed tomography (CT) scan was done to see the feeding vessel and its feasibility for chemo embolization. Conventional TACE was done using doxorubicin 50-75 mg and 10 ml lipiodol followed by gelfoam embolization with standard protocol. Drug eluting beads (DEB)-TACE was also used in some patients.

Results: Out of 28 patients, right hepatic artery was main feeding vessel in most of the patients, mean tumor feeding artery diameter was 1.61mm and mean tumor size was 5.47 cm. After three months of follow up mean tumor necrosis was 93.75% (p value <0.01), and mean alpha fetoprotein was 30.89IU/ml with p value of <0.01 (mean baseline was 6625.28IU/ml). Conclusions: Multiphasic CT scan is a very good tool for tumor vascularity description and the basic step of successful TACE. TACE is a safe and effective procedure and has become an established palliative treatment for unresectable HCC.

KEYWORDS

TACE, HCC, Multiphasic CT.

INTRODUCTION

Hepatocellular carcinoma is one of the most common malignancy and fifth most common cancer worldwide.[1,2] The occurrence of hepatocellular carcinoma varies widely depending on geographic location. Whereas incidence in the Western world is less than two per 100,000 males, it is currently 40-60 per 100,000 males in Africa and parts of the Far East. According to available data from Indian Council of Medical Research (ICMR) the age adjusted incidence rate of hepatocellular carcinoma (HCC) in India for men ranges from 0.7 to 7.5 and for women 0.2 to 2.2 per 100,000 population per year. The male: female ratio for HCC in India is 4:1. The age of presentation varies from 40 to 70 years. According to another study the incidence of HCC in cirrhotic patients in India is 1.6% per year. [3]

HCC is frequently the long term sequel of chronic viral infection mainly hepatitis B & C. In India HCC has a peculiar variation in terms of epidemiology and the stage of disease at diagnosis. HBV infection is predominant and is responsible for 35-60% of HCC in India. [4-11]

Despite the numerous existing strategies to treat HCC, the 5-year survival rate remains below 12%.[12] In developing nations, survival rates are as low as 5%.[13] Surgical resection, transplantation and ablation are potentially curative treatment options for HCC.[14] Unfortunately, only a minority of patients are eligible for these treatments at the time of diagnosis.[15] For patients presenting with more advanced disease, several treatments have been developed to slow disease progression. These include many liver-directed therapies, such as bland transarterial embolization (TAE), conventional transarterial chemoembolization

(cTACE), drug-eluting beads TACE (DEB-TACE) and yttrium-90 (Y^{90}) radio embolization.[16,17,18,19] The principle of TACE/TAE revolves around the basic concept of dual blood supply of the normal liver. Liver tumors derive 90% of their blood from the hepatic artery.[20-23] Park et al conceptualized carcinogenesis of HCC as a multistep process involving parenchymal arterialization, sinusoidal capillarization and development of unpaired arteries (a vital component of neo angiogenesis).[24] Embolization induces ischemic necrosis of tumor causing a failure of the transmembrane pump, resulting in a greater absorption of agents by the tumor cells. Tissue concentration of agents within the tumor is more than 40 times that of the surrounding normal liver. [27,28,29]

This study is needed for the assessment of liver tumor by multiphasic CT scan and to see the effectivity of transarterial chemoembolization on Indian patients.

AIMS AND OBJECTIVES

1- Assessment for HCC by multiphase CT angiography for tumor vascularity description, and analysis of feeding vessel.
2- To see the impact of transarterial chemoembolization on HCC by multiphase CT angiography for residual contrast enhancement, tumor necrosis and decrease in lesion size.

MATERIAL AND METHODS

This study was a prospective observational study conducted at a tertiary centre, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow in patients diagnosed with hepatocellular carcinoma over the period of one and half year. Patients diagnosed with hepatocellular carcinoma reporting to our institute were subjected to clinical, biochemical and radiological examination. TACE was performed in those who fulfilled the inclusion criteria. Follow up assessment was done with multiphase CT scan of liver after 1, 3 and 6 months.

Complete blood count, liver function tests, and the tests for viral markers of hepatitis B & C infection was done in every patient. Serum alpha fetoprotein (AFP) was estimated using a particular enzyme immunoassay normal (value <20 ng/ml). Upper gastrointestinal endoscopy was done in each case to detect the presence of esophageal varices. Patients with underlying cirrhosis was classified on Child A ,B ,C based on child pugh classification.[19]

Radiological workup including USG abdomen and multiphase CT scan of the liver for establishing the diagnosis, was done. Multiphase CT Angiography was done to assess tumor vascularity, feeding vessel diameter, tumor size, tumor necrosis and arterial anatomy.Digital subtraction angiography (DSA) was perform after CT angiography. TACE was performed through the trans-femoral route. Superior mesenteric artery and celiac axis arteriograms were obtained to begin with. Selective cannulation of the feeding hepatic artery to the tumor was done using 5F simmons/ cobra catheters and 0.035-in. 'J' tip terumo guide wire. Superselective microcatheter was placed in the artery as close as possible to the tumor.

The chemotherapeutic drugs (Doxorubicin 50-75 mg) mixed with 10 ml of iodized oil (lipiodol) or with drug eluting beads (Hepasphere 30-60 micron) were delivered through cannulated feeding hepatic artery. Subsequently, this feeding artery was embolized using gelatin sponge pledgets. This is done to occlude the arterial supply temporarily so that the injected drug mixture can have a prolonged stay in the region of the tumor, facilitating better local effect of the drugs on the tumor and causing tumor necrosis. It also prevents the drugs from moving into the systemic circulation

TACE is offered to patient who fulfill the following inclusion criteria like patient with child's A or B cirrhosis according to Child Pugh criteria, normal portal vein, less than 50% involvement of liver by HCC/ metastasis, patient willing for therapy and follow up and ideally lesions larger than 4 cm. Exclusion criteria included Extra hepatic disease, coagulopathy, biliary obstruction or comorbid illness like coronary artery disease, congestive heart failure, chronic renal failure and h/o upper GI bleed in last 6 month.

STATISTICAL ANALYSIS

This study was conducted in one centre (Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, UP, India) where we included total 30 patients out of which only 28 patients completed the study.

This study was observational study in which all the patient included in the study act as his or her own control. Mean was taken for all attribute and they were compared with baseline value. Clinical characteristics of study patients with required data to calculate score were compared using a chisquare-2 test for qualitative variables, and a student-t test for continuous variables. A p-value of <0.05 is considered significant

OBSERVATION AND RESULTS

All the patients were followed for at least three months after TACE. 6 patients were followed for one year and 13 patients were followed for six months, rest 15 were followed for three months. In our study among all the patients, mean age was 56 yrs, younger one was 36 yrs old and older one was 70 yrs old. Sex distribution in this study was unequal, male patients were represented more than female. Out of 28, males were 22 (78%) and females were 6 (22%).

Liver function test was done at the start of study and during follow up at one month, three month and six months. At baseline only two patients had SGOT value more than three times of upper limit of normal range, one patient had maximum value of 735 IU/L, normal SGOT was found in 6 patients. SGPT was normal in 9 patient and only two patient had value more than three times of upper limit of normal range. Serum Bilirubin was normal in 20 patients and only 8 patients had values higher than normal range. Alkaline phosphatse was higher than normal range in 9 patient and 19 patients had normal values.

All the patients were screened for hepatitis B and C. Total 8 patients were found positive for Hepatitis B, 14 patients were found positive for hepatitis C and 6 patients were non B non C.

AFP level was assessed in all patient at the start of this study and during follow up.

Out of 28 patients, 23 patient were in Child Pugh class A (82.14%) and 5 patient were in class B (17.86%).

BASELINE MULTIPHASIC CT SCAN

Out of 28 patient right hepatic artery was giving main feeding vessel to tumor in 20 patient and left hepatic artery was in 6 patient. Superior mesenteric artery was main feeding vessel in 2 patients. Tumor feeding vessel size –All the feeding arteries were analysed by DSA and CT angiography. In our study mean diameter of feeding artery was 1.61mm (maximum value was 2.5mm and minimum value was 1.1mm). Tumors with good feeding vessel size were necrotised adequately in our study. Lesion size- Mean tumor lesion was 5.47 cm, maximum size in this study was 13cm and minimum size was 2.7cm. Out of 28 only two patient had multiple lesion, rest all had single lesion

FOLLOW UP RESULTS AFTER ONE MONTH

After transarterial chemoembolization all the patient were followed up at one month. Liver function test (SGOT, SGPT, serum bilirubin, alkaline phosphatase) was done in all patient. Among the entire patients, mean SGOT was 68.48 at one month. Mean SGPT was 56.67 one month after transarterial chemoembolization. Mean bilirubin was 0.88 one month after transarterial chemoembolization. Mean alkaline phosphatase was 167.43 one month after transarterial chemoembolization. Mean AFP was 70.03, one month after transarterial chemoembolization. Average tumor necrosis was 87.85% one month after the TACE .Out of 28 patient 9 patient achieved 100% tumor necrosis, 6 patient achieved 90 % necrosis and rest all achieved less than 90% necrosis.

FOLLOWUP RESULTS AFTER THREE MONTH

After 3 months of transarterial chemoembolization, mean SGOT was 52.45 Mean SGPT was 51.25 three month after trans arterial chemoembolization. Mean bilirubin was 0.81 three month after trans arterial chemoembolization. Alkaline phosphatase was 163.45 three months after trans arterial chemoembolization. Mean AFP was 30.89 at 3 months after transarterial chemoembolization. Average tumor necrosis was 93.75%(p value <0.01) three month after the TACE. Out of 28 patient 9 patient achieved 100% tumor necrosis, 14 patient achieved more than 90 % necrosis and rest all achieved less than 90% necrosis. Our patients tolerated the procedure well. The commonly encountered minor complications post-procedure, were self-limiting and improved in about 5–7 days. Fever developed in 4 patients (10.71%). Nausea and vomiting developed in 19 patients (67.85%), Pain abdomen was found in 10 patients (35.71%). Local site complications in the form mild bruising at vascular access site were seen in 4 patients (14.28%). No serious adverse events were reported during 3 months of follow up.

	N=28	Percentage
Fever	3	10.71%
Nausea and vomiting	19	67.85%
Pain abdomen	10	35.71%
Local site complication	4	14.28%
Abnormal liver fuction	0	0
Ascites	0	0
Tumor lysis syndrome	0	0

CASE-1

44/M patient chronic Hepatitis B +Ve AFP level ~20530, having 3.2cm lesion in segment VII –Complete response following TACE Fig.A pre-TACE arterial phase CT showing enhancing tumor in seg VII. Fig.B showing washout in delayed phase. Fig. C showing tumor blush on angiogram. Fig.D showing Doxorubicin/lipiodol completely filling the tumor with no enhancing residual tumor component.

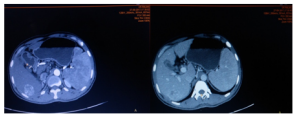

Fig A Fig B

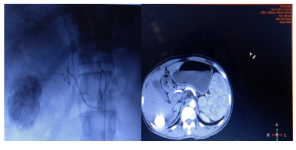

Fig C Fig D

CASE 2

56 yrs/M patient chronic Hepatitis C +Ve having 4 cm lesion in segment VII –Complete response following TACE Fig.A pre TACE arterial phase CT showing enhancing tumor in segment VII. Fig.B showing washout in delayed phase. Fig.C showing angiogram of tumor blush. Fig.D showing Doxorubicin/lipiodol completely filling the tumor with no enhancing residual tumor

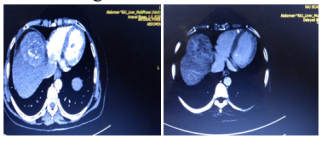

Fig. A Fig. B

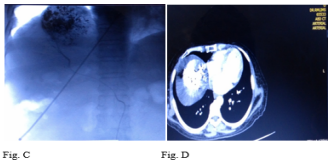

Fig. C Fig. D

CONCLUSION

In our study majority of patient belong to the age group of 56 yrs, majority of them male (almost 78%). Total 8 patients were found positive for Hepatitis B, 14 patients were found positive for hepatitis C and 6 patients were non B non C. Out of 28 patients,23 patient were in Child Pugh class A (82.14%) and 5 patient were in class B (17.86%). After three month of follow up mean tumor necrosis was 95%. Mean alpha fetoprotein was 30.89 (mean baseline 6625.28) three month after transarterial chemoembolization. Mean viral load was 3.5 (baseline 2781.95) three month after transarterial chemoembolization. Liver function become normal in almost all patient three month after transarterial chemoembolization**.** To conclude, Multiphasic CT scan is a very good tool for tumor vascularity description which is the basic step of successful transarterial chemoembolization. TACE is a safe and effective procedure and has become an established palliative treatment for unresectable HCC.

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