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Outcome of Transarterial Chemoembolization (TACE) in Patients with Hepatocellular Carcinoma

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Abstract

Background: Transarterial Chemoembolization (TACE) is recommended as a treatment for unresectable Hepatocellular Carcinoma (HCC) in patients with normal compensated liver. The efficacy of TACE in cirrhotic patients with compromised liver function is unknown.

Aim of Study: To evaluate the outcome following Transarterial Chemoembolization (TACE) in patients with unapplicable locoregional therapy in Hepatocellular Carcinoma (HCC).

Patients and Methods: This Prospective Cohort study conducted on 50 patients with HCC at Tropical Medicine and Gastroenterology Department Qena University Hospital.

Results: 56% of patients reached complete response within one month of treatment in mean duration of follow-up of 58.28 months, 66% of patients had recurrence 40% in <1 year and 26% 1-2 years, 34% of recurrence were target tumor progression, 20% intrahepatic new lesion and 12% both, total deaths were 46% of patients.

Conclusions: TACE offers a reasonable palliative therapy for HCC.

Key Words: *Transarterial Chemoembolization (TACE) – HCC.*

Introduction

HEPATOCELLULAR carcinoma (HCC) is the most common primary hepatic malignancy and the fifth most common cancer worldwide **[1]**.

Only a minority of patients with HCC (25%) were found suitable for the current curative treatment options, i.e., surgical resection, liver transplant, and percutaneous ablative therapies. Therefore, palliative management forms the mainstay of therapy for most of the patients with relatively advanced disease **[2]**.

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Transarterial Chemoembolization (TACE) is the standard of care for intermediate stage hepatocellular carcinoma (HCC) in patients that are not candidates for surgical resection or tumour ablation **[3]**.

Patients and Methods

This Prospective Cohort study conducted on 50 patients with HCC at Tropical Medicine and Gastroenterology Department Qena University Hospital from 1/4/2017 to 30/5/2018.

Inclusion criteria:

Patients with associated Child's A or B cirrhosis, normal main portal vein, less than 50% involvement of liver by HCC, and patients willing for therapy and follow-up. Some patients of BCLC A, who were unsuitable for ablative therapy or surgery, were also included.

Exclusion criteria:

Extra hepatic disease; coagulopathy; biliaryobstruction; comorbid illness like coronary artery disease, congestive heart failure, chronic renal failure, etc.; and a previous history of encephalopathy/upper gastrointestinal bleed in the last 6 months.

Methods: Liver and renal function test. Abdominal ultrasonography. Complete blood count, Prothrombin time, concentration & INR, Alpha feto protein, CT abdomen with contrast, was done follow-up of outcome of patients treated by TACE by CT abdomen with contrast, alpha feto protein, liver function tests and complete blood count.

Study outcome measures:

a- *Primary (main):* Efficacy of trance arterial chemoembolization in treatment HCC with un applicable locoregional therapy.

b- *Secondary (subsidiary):* Role of Triphasic CT Abdomen in follow-up patient with HCC treated with TACE.

Results

This study was conducted on 50 patients with HCC with mean age of studied patients was 62 years and 62% of them were males and 38% were females. HCV represented the etiology of disease in 54% of patients HBV in 26% and 20% had other etiology (alcoholic 4%, autoimmune 4%, NAFLD 6% and cryptogenic 6%) Fig. (1).

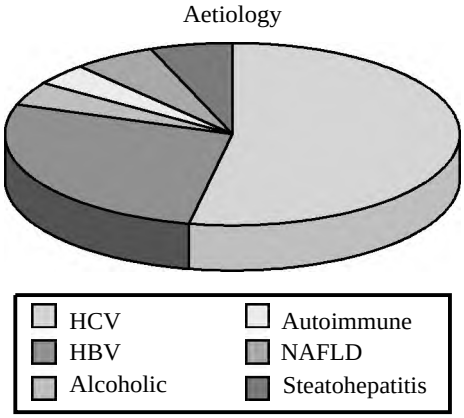

Fig. (3): Distribution of the studied cases according to Aetiology of liver disease.

As regard differences of different parameters pre and post TACE as regard Alpha-fetoprotein level was decreased after treatment with significant differences p-value <0.001, ALT level had insignificant differences between pre and post p-value 1.00, also Total bilirubin level had insignificant differences pre and post p-value 0.197, Albumin level decreased after TACE twit significant differences p-value <0.001, INR level had insignificant differences p-value 0.311, as regard platelet level it increased after TACE with significant differences p-value <0.001, Child-Pugh score increased after TACE with significant differences p-value <0.001 (Table 1).

Mean numbers of tumors pre TACE was 1.47 and size of largest tumor was 4.22cm, 60% of patients had child pugh score A,40% had score B .56% of patients reached complete remission within one month of TACE in mean duration of follow-up 58.28 months, 66% of patients had recurrence 40% in <1 year and 26% 1-2 years .34% of recurrence were target tumor progression, 20% Intrahepatic new lesion and 12% both, total deaths were 46% of patients (Table 2).

Table (1): Comparison between pre and post TACE according to different parameters (n=50).

	Pre TACE	Post TACE	Test of sig.	*p*
Alpha-fetoprotein:				
Min. - Max.	980.0-4500.0	990.0-4350.0	Z=	<0.001*
Mean ± SD.	2101.32±810.46	2064.50±782.93	4.447*	
Median	2006.0	1950.0		
ALT (IU/L):				
Min. - Max.	24.0-76.0	25.0-76.0	Z=	1.000
Mean ± SD.	39.0±14.45	39.84±14.56	0.000	
Median	33.50	34.0		
Total bilirubin (mg/L:)				
Min. - Max.	0.77-1.66	0.76-1.66	*t*=	0.197
Mean ± SD.	1.09±0.22	1.09±0.22	1.309	
Median	1.04	1.05		
Albumin (g/dL):				
Min. - Max.	3.0-4.80	3.0-4.80	*t*=	<0.001*
Mean ± SD.	3.81±0.62	3.70±0.60	7.104*	
Median	3.80	3.70		
INR:				
Min. - Max.	1.0-1.30	1.0-1.21	Z=	0.311
Mean ± SD.	1.12±0.11	1.10±0.09	1.012	
Median	1.07	1.08		
Platelet (X 10³/µL)				
Min. - Max.	97.0-160.0	100.0-170.0	Z=	<0.001*
Mean ± SD.	116.12±18.26	123.42±18.26	6.175*	
Median	110.50	115.0		
Child-Pugh score:				
Min. - Max.	5.0-7.0	5.0-9.0	*t*=	<0.001*
Mean ± SD.	6.0±0.90	7±1.03	7.286*	
Median	6.0	7.0		

Table (2): Assesment of response in the studied cases according to different parameters (n=50).

	No.	%
Complete remission in 1 month:		
No	22	44.0
Yes	28	56.0
Mean duration of follow-up (month):		
Min. - Max.	35.0-70.0	
Mean ± SD.	58.28±11.19	
Median	63.0	
Total recurrence:		
No	17	34.0
Yes	33	66.0
Time of recurrence (n=33):		
<1 year	20	40.0
1-2 years	13	26.0
The characteristics of recurrence at first timing (n= 33)		
Target tumor progression	17	34.0
Intrahepatic new lesion	10	20.0
Both	6	12.0
Total death:		
No	27	54.0
Yes	23	46.0

As regard unuvariate and multivariate analysis factors had significant effect on outcome, gender, pre-TACE Child-Pugh score, number of tumors, size of largest tumor and Child-Pugh class had significant effect on univarite analysis but by multivariate only Child-Pugh class had significant effect (Table 3).

Table (3): Univariate and multivariate analysis for the parameters affecting recurrence (n=50).

	Univariate		#Multivariate	
	p	OR (95%C.I)	*p*	OR (95%C.I)
Age	0.967	1.002 (0.922-1.088)		
Gender (female)	0.041 *	4.392 (1.060-18.200)	0.972	1.035 (0.150-7.157)
Aetiology of liver disease:				
HCV	0.279	0.513 (0.154-1.715)		
HBV	0.339	2.029 (0.475-8.660)		
Other	0.766	1.256 (0.280-5.633)		
Alpha-fetoprotein	0.067	1.001 (1.0-1.0)		
ALT (IU/L)	0.147	1.036 (0.988-1.086)		
Total bilirubin (mg/L)	0.128	0.114 (0.007-1.867)		
Albumin (g/dL)	0.590	0.768 (0.294-2.006)		
INR	0.100	0.009 (0.0-2.454)		
Platelet (x10^3/µL)	0.621	1.009 (0.975-1.043		
Pre-TACE Child-Pugh score	0.001 *	0.277 (0.133-0.575)	0.424	4.331 (0.119-157.558)
Number of tumors	0.026*	0.214 (0.055-0.833)	0.229	0.260 (0.029-2.336)
Size of largest tumor	0.020*	2.379 (1.145-4.943)	0.375	0.411 (0.058-2.932)
Child-Pugh class	<0.001*	21.000 (4.522-96.871)	0.047*	0.001 (0.0-0.924)

Discussion

In the present study we aimed to evaluate the outcome following Transarterial Chemoembolization (TACE) in patients with unapplicablelocoregional therapy in Hepatocellular Carcinoma (HCC). 50 patients were included with mean age of studied patients was 62 years and 62% of them were males and 38% were females, HCV represented the etiology of disease in 54% of patients HBV in 26% and 20% had other etiology (alcoholic 4%, autoimmune 4%, NAFLD 6% and cryptogenic 6%).

Llovet JM et al., explained that the main risk factors for developing HCC are well known and include hepatitis B and C virus infection, alcohol intake and ingestion of the fungal metabolite aflatoxin B 1. Additional risk factors such as non-alcoholic steatohepatitis are also emerging **[4]**. Yi SW et al., showed that HCC occurred in 2744 individuals. In the sex-adjusted and age-adjusted analysis, cirrhosis increased the incidence of HCC by 42-fold, followed by hepatitis B virus (21-fold), hepatitis C virus (HCV; 19-fold), male sex (4.3-fold), and each 5-year age increment (1.24-fold) **[5]**.

Kirstein MM et al., study they showed that the first diagnosis of HCC was made at a median age of 63 years (25-75 IQR, 56.25-69.75) in mainly male patients (83.1%). The underlying liver disease was Alcoholic Liver Disease (ALD) in most cases (30.2%), followed by viral hepatitis C (18.6%) and B (13.4%) and non-alcoholic steatohepatitis/fatty liver disease (14%). Liver cirrhosis was diagnosed in 50 patients by imaging, biochemistry and/or histology (76.9%) **[6]**.

In the present study we found that mean numbers of tumors pre TACE was 1.47 and size of largest tumor was 4.22cm, 60% of patients had child pugh score A, 40% had score B.

In Dorn DB et al., 100 patients were Child-Pugh score A and 90 were Child-Pugh class B/C, mean number of tumors was 1.5±0.7 as regard Size of largest tumor was 5.5±3.2 in class A and in class B,C was 3.8±2.0 **[3]**.

In the present study we found that as regard differences of different parameters pre and post TACE as regard Alpha-fetoprotein level was decreased after treatment with significant differences *p*-value <0.001, ALT level had insignificant differences between pre and post *p*-value 1.00, also Total bilirubin level had insignificant differences pre and post *p*-value 0.197, Albumin level decreased after ttt with significant differences *p*-value <0.001, INR level had insignificant differences *p*-value 0.311, as regard platelet level it increased after TACE with significant differences *p*-value <0.001, Child-Pugh score increased after TACE with significant differences *p*-value <0.001.

In Dorn DB et al., they showed that measures of liver function were recorded immediately prior to TACE and 1 month post-TACE. The difference in liver function measurements (pre-to post-TACE) was compared between the Child-Pugh class A and B/C groups. There was a slight, but statistically significant, increase in the Child-Pugh and MELD

scores in the Child-Pugh A group compared with the Child-Pugh B/C group (Child-Pugh score: Δ+0.35 points versus Δ0.0 points, $p<0.001$; MELD score: Δ+0.71 points vs. Δ–0.01 points, $p<0.001$).

Similarly, there was a slight, but statistically significant decrease in the serum albumin in the Child-Pugh A group compared with the Child-Pugh B/C group (Δ–0.21 versus Δ-0.05 g/dl, $p<0.001$). In contrast, there were no significant differences in total bilirubin, INR, creatinine, ascites or encephalopathy measurements between the Child-Pugh groups [3].

In the present study we found that 56% of patients reached complete remission within one month of ttt in mean duration of follow-up 58.28 months, 66% of patients had recurrence 40% in <1 year and 26% 1-2 years. 34% of recurrence were target tumor progression, 20% Intrahepatic new lesion and 12% both, total deaths were 46% of patients.

Paul SB et al., study patients were followed-up for a mean period of 15.6±15.1 months (range: 1-7 months; median: 12 months). A total of 37 (51%) patients died, while the remaining 36 patients were alive at the end of the study. With regard to assessment of local outcome, response could not be assessed in nine patients as they did not undergo follow-up CT scan.

In the present study we found that as regard univariate and multivariate analysis factors had significant effect on outcome, gender, pre-TACE Child-Pugh score, number of tumors, size of largest tumor and Child-Pugh class had significant effect on univarite analysis but by multivariate only Child-Pugh class had significant effect.

Paul SB et al., showed that in Univariate analysis of the predictors for survival identified the Child-Pugh score, serum AFP >1 000ng/ml, BCLC stage, and tumor size as important variables affecting survival post TACE. All these above mentioned variables are basically interrelated and depict the advanced nature of the disease.

The larger the tumor size, the higher the BCLC stage and the poorer the function of the underlying liver (Child's status). However, the presence of vascular invasion and associated portal hypertension did not show any significant effect on the overall survival. On multivariate analysis tumor size emerged as the single most important independent predictor of survival [1]. This finding is similar to the observations made in other studies [7,8].

Conclusion:

After this study of using TACE procedures we found that TACE can be performed safely and may improve the outcome of patients with HCC.

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نتائج الحقن الكبدى الشريانى الكميائى فى المرضى الذين يعانون من سرطان الكبد

سرطان الكبد هو مشكلة عالمية وتختلف البيانات الوبائية من مكان إلى آخر. فى مصر يعتبر سرطان الكبد أحد المشكلات الصحية التى تواجها السلطات الصحية.

فى دراسة نشرت عام ٢٠٠٥ فقد أفادوا عن زيادة بمقدار الضعفين تقريباً فى سرطان الكبد بين مرضى أمراض الكبد المزمنة على مدى عقد من الزمان.

فقط أقلية من المرضى الذين يعانون من سرطان الكبد (٢٥٪) وجدت مناسبة لخيارات العلاج الحالية مثل الاستئصال الجراحى، وزرع الكبد، وعلاجات الكى عن طريق الجلد. لذلك، يشكل العلاج التحفظى الدعامة الأساسية للعلاج بالنسبة لمعظم المرضى الذين يعانون من مرض متقدم نسبياً. وقد تطورت عملية الحقن الكبدى الشريانى الكيميائى على مدى العقدين الماضيين كعلاج فعال وأكثرها استخداماً متحفظاً لسرطان الكبد. هناك عدد من الدراسات المنشورة حول فعالية هذا الأجراء بما فى ذلك تجارب التحكم العشوائية مقارنة نتائجها مع العلاج الداعم. ومع ذلك، فإن معظم هذه التجربة تأتى من البلدان المتقدمة. وقد أوصى بهذا الأجراء من قبل عيادة برشلونة لتصنيف سرطان الكبد كمعيار للاختيار فى حالة أورام متعددة أو كبيرة مع عدم وجود غزو الأوعية الدموية أو انتشار خارج الكبد وأورام لا يمكن الوصول إليها عن طريق الجلد.

الهدف من الدراسة: تحديد فعالية العلاج بالحقن الكبدى الشريانى الكيميائى لعلاج مرضى سرطان الكبد.

المرضى وطرق البحث: اشتملت الدراسة على ٥٠ مريض بسرطان الكبد تم علاجهم عن طريق الحقن الكبدى الشريانى الكيميائى وتم متابعتهم عن طريق تحاليل وظائف الكبد والأشعة المقطعية ثلاثية الأبعاد على البطن بالصبغة وتحليل دلالات أورام الكبد.

الملخص والتوصيات: عدد المرضى الذين اشتملت عليهم الدراسة ٥٠ مريضاً متوسط أعمارهم حوالى ٦٢ عاماً. ٦٢٪ منهم من الذكور و٨٣٪ من الإناث. ٥٤٪ من الحالات مصابة بفيروس الوباء الكبدى سى. ٢٦٪ مصابين بفيروس الوباء الكبدى بى. ٢٠٪ لأسباب أخرى وهى (٤٪ التليف الكحولى، ٤٪ مرض مناعى، ٦٪ التشمع الكبدى غير الكحولى، ٦٪ مجهول السبب ...).

متوسط أعداد الأورام قبل العلاج حوالى ١.٤٧ حجم أكبر ورم ٤.٢٢سم، ٦٠٪ من مجموع المرضي كان على معامل تشايلد من الفئة (أ) ٤٠٪ من الفئة (ب).

فيما يتعلق بالاختلاف فى نتائج التحاليل قبل وبعد الحقن الكبدى الشريانى الكيميائى، على مستوى ألفا فيتو بروتين فقد انخفض بعد العلاج بفارق جوهرى قيمة p أقل من ٠.٠٠١ أما مستوى إنزيم الكبد ألانينالانين لم يتغير بشكل ملحوظ قيمة p حوالى ١.٠٠ أيضاً مستوى البيليروبين (الصفرا) فى الدم لم يتغير بشكل ملحوظ فقيمة p حوالى ٠.١٩٧ مستوى الألبومين انخفض بفارق ملحوظ قيمة p أقل من ٠.٠٠١ أما معدلات السيولة لم تتغير بفارق ملحوظ قيمة p حوالى ٠.٣١١ بالنسبة لمستوى الصفائح الدموية ارتفعت بفارق جوهرى قيمة p أقل من ٠.٠٠١ معامل تشايلد ارتفع بعد العلاج بفارق ملحوظ قيمة p أقل من ٠.٠٠١ ٥٦٪ من المرضى وصلو إلى التعافى الكامل فى خلال شهر واحد من العلاج مع متوسط مدة متابعتهم حوالى ٨٥.٢٨ شهراً، ٦٦٪ من المرضى عاد إليهم المرض (٤٠٪ فى أقل من سنة، ٢٦٪ من سنة إلى سنتين، ٣٤٪ عاد بتقدم فى الورم ٢٠٪ ببؤرة كبدية جديدة و ١٢٪ بالاثنين) مجموع الوفيات حوالى ٤٦٪ من المرضى.

عوامل التحليل أحادى أو عديدى المتغير كانت لها تأثير كبير على النتائج. الجنس، معامل تشايلد قبل الحقن الكبدى الشريانى الكيميائى، عدد الأورام، حجم أكبر ورم، وفئة معامل تشايلد كان لهم تأثير فى التحليل أحادى التغير. أما التحليل متعدد المتغير فتأثرت فقط بفئة معامل تشايلد.

وبذلك نخلص إلى أن الحقن الكبدى الشريانى الكيميائى أمن وممكن أن يحسن من حالة المرضى الذين يعانون من سرطان الكبد ولذلك الاختيار الجيد للمرضى ضرورى لتحسين الاستفادة من الحقن الكبدى الشريانى الكيميائى.