Biolife 5(4):578-584
AN INTERNATIONAL QUARTERLY JOURNAL OF BIOLOGY & LIFE SCIENCES
ISSN (online): 2320-4257
www.biolifejournals.com
BIOLIFE ORIGINAL ARTICLE

Screening for Chronic Hepatitis B Virus Infection in Patients With Malignancies and Assessment of the Impact of Malignancies on the Response To Preemptive Treatment of Chronic Hepatitis B Virus

Abd Elfatah Fahmy Hanno, Mohamed Sobhy Elshazly, Abbas Mohamed Omar, Hossam Eldin Fathy Ahmed, Mohamed Mahmoud Mohamed Ismaail

Tropical Medicine Department, Alexandria University.
Clinical Oncology and Nuclear Medicine Department, Alexandria University.

Email: hhbb_2010@yahoo.com

ABSTRACT

The prevalence of hepatitis B virus (HBV) infection in patients with malignancies especially haematological malignancies is increased compared with the general population worldwide. HBV reactivation is common following chemotherapy and is associated with a high mortality despite prompt anti-viral treatment. HBV reactivation may necessitate interruption of chemotherapy with adverse prognostic consequences for the haematological disease. All candidates for chemotherapy and immunosuppressive therapy should be tested for HBV markers prior to immunosuppression, All HBsAg-positive patients should receive ETV or TDF or TAF as treatment or prophylaxis, HBsAg-negative, anti-HBc positive subjects should receive anti-HBV prophylaxis if they are at high risk of HBV reactivation according to EASL guidelines 2017. The aim of this study was to screen for chronic Hepatitis B virus infection in patients with Malignancies recruited from Oncology department in Main Alexandria University Hospital and assessment of the impact of malignancy on the response to preemptive treatment of chronic Hepatitis B virus with Nucleoside analogue (Entecavir 0.5mg). The study was conducted on 500 patients recruited from Oncology department screened for CHB virus infection and those who suffered from CHB were called group I and treated with Entecavir 0.5mg tab and treatment response was compared to group II patients which included 20 control patients suffering from chronic Hepatitis B virus being treated with Nucleoside analogue (Entecavir 0.5mg). In both groups 100% patients was successfully treated with Entecavir 0.5mg tab daily and all the patients met the criteria of virological response to treatment (undetectable PCR after 6 months of treatment) and no virological breakthrough or treatment failure was reported. Also there was statistically significant reduction in AST, ALT, Total and Direct bilirubin levels in both groups with Entecavir 0.5mg tab treatment daily. Percentage of patients suffering from chronic HBV in Oncology department at Alexandria Main University Hospital is 4.6 % and the effectiveness of Entecavir 0.5mg tab in treatment of chronic HBV in patients with malignancies is comparable to patients without malignancies.

Keywords: Hepatitis B virus, Preemptive treatment, Entecavir, Malignancies.

INTRODUCTION

An estimated 240 million persons are carriers of hepatitis B virus (HBV) in the world today; of these, 75% reside in Asia and the Western Pacific. Effective vaccines against HBV have been available since the early 1980s, but perinatal and early life exposures continue to be major sources of infection in high-prevalence areas.[1]

Hepatitis B is the chief cause of cirrhosis and HCC in the world today, and nationwide vaccination has been shown to diminish greatly the number of new cases of infection and HCC.[2] Universal hepatitis B vaccination is likely to have the greatest impact on liver disease–related mortality in future generations.

How to Site This Article:
Abd Elfatah Fahmy Hanno, Mohamed Sobhy Elshazly, Abbas Mohamed Omar, Hossam Eldin Fathy Ahmed, Mohamed Mahmoud Mohamed Ismaail (2017). Screening for Chronic Hepatitis B Virus Infection in Patients with Malignancies and Assessment of the Impact of Malignancies on the Response to Preemptive Treatment of Chronic Hepatitis B Virus. *Biolife*. 5(4), pp 578-584. doi: 10.5281/zenodo.7393362
Received: 5 October 2017; Accepted; 26 November2017; Available online : 5 December 2017

The age at which a person becomes infected with HBV is a principal determinant of the clinical outcome. HBV infection in adults with an intact immune system is likely to cause clinically apparent acute hepatitis B; only 1% to 5% of these persons become chronically infected.[3]

By contrast, as many as 95% of infected neonates become chronic HBV carriers because of immunologic tolerance to the virus. In adults, fulminant liver failure caused by acute hepatitis B occurs in less than 1% of cases, but this group still accounts for 5% of all cases of acute liver failure and approximately 400 deaths annually in the United States.

Four phases of chronic HBV infection have been described: immune tolerance, immune clearance, the inactive carrier state, and reactivation. These phases usually occur in perinatally acquired HBV while patients who acquire HBV in adulthood usually experience immune clearance, inactive carrier state and/or reactivation. Patients who acquire the infection in the perinatal period often have high serum levels of HBV DNA without biochemical evidence of active hepatitis and are considered to be immune tolerant to HBV.[4]

Pre-therapeutic causal relationship between chronic HBV infection and liver disease has to be established and an assessment of the severity of liver disease needs to be performed. In addition, all first degree relatives and sexual partners of patients with chronic HBV infection should be advised to be tested for HBV serological markers (HBsAg, anti-HBc, anti-HBs) and to be vaccinated if they are negative for these markers.[5]

Therapy must ensure a degree of virological suppression that will then lead to biochemical remission, histological improvement and prevention of complications. The ideal end point is HBsAg loss, which however is infrequently achievable with the currently available anti-HBV agents. A more realistic end point is the induction of sustained or maintained virological remission.[6]

Drugs available for the treatment of CHB include IFN, PEG-IFN and six NAs. NAs for HBV therapy can be classified into nucleosides (lamivudine, telbivudine, emtricitabine, entecavir) and nucleotides (adefovir and tenofovir).[7]

The prevalence of hepatitis B virus (HBV) infection in patients with Malignancies especially haematological malignancies is increased compared with the general population worldwide. HBV reactivation is common following chemotherapy and is associated with a high mortality despite prompt anti-viral treatment.[8] HBV reactivation may necessitate interruption of chemotherapy with adverse prognostic consequences for the haematological disease. Chemotherapy-induced immune suppression may lead to increased HBV replication.[9] Immune reconstitution within the weeks and months following recovery from chemotherapy may be associated with a flare of hepatitis B manifested by hepatocellular injury. Risk factors associated with HBV reactivation include detectable hepatitis B surface antigen (HBsAg), HBV DNA, Hepatitis B e (HBeAg) antigen, antibodies to hepatitis B core antigen (anti-HBc), treatment with Corticosteroids or Rituximab, young age and male gender.[10]

Therefore, all candidates for chemotherapy and immunosuppressive therapy should be screened for HBsAg, anti-HBs and anti-HBc prior to immunosuppression treatment.[11]

Vaccination of HBV seronegative patients is recommended. Higher doses or reinforced vaccine may be required to achieve anti-HBs response in immunocompromised patients.[12]

Patients with chronic hepatits B should be treated with ETV, TDF or TAF, similarly to the immunocompetent patients.[13]

In contrast, the optimal management of patients with chronic HBV infection, but without chronic hepatitis, remains controversial. Prophylactic administration of LAM has been shown to reduce the risk of HBV reactivation and the associated morbidity and mortality, but a residual risk of HBV reactivation remains approximately in 10% of chronic HBV patients with low viremia (HBV DNA<2,000 IU/ml) and in a higher proportion of those with higher viremia levels. As recent studies suggest that ETV or TDF can be successfully used in such patients, prophylaxis with ETV, TDF, TAF is recommended in this setting.[14] Prophylaxis should continue for at least 12 months (18 months for rituximab-based regimens) after cessation of the immunosuppressive treatment and discontinued only if the underlying disease is under remission.

The aim of this study was to screen for chronic Hepatitis B virus infection in patients with malignancies recruited from Oncology department in Main Alexandria University Hospital and assessment of the impact of malignancy on the response to preemptive treatment of chronic Hepatitis B virus with Nucleoside analogue (Entecavir 0.5mg).[15]

The present study was carried out on 500 patients of any age or sex with malignancies recruited from Oncology department at Main Alexandria University Hospital who were screened for Chronic HBV infection and then patients who suffered from Chronic HBV were treated with Nucleoside analogue (Entecavir 0.5mg), 23 patients were given Entecavir 0.5mg daily, 5 of them were given Entecavir 1-3 months before chemotherapy and the rest were given Entecavir in concomitant with chemotherapy, PCR and routine investigations were done on 0, 3, 6 months to assess the response to treatment and that was compared to another 20 control patients suffering fom chronic HBV without malignancies being treated with Nucleoside analogue (Entecavir 0.5mg) and that was done to assess the impact of malignancy on the response to preemptive treatment of chronic HBV with Nucleoside analogue (Entecavir 0.5mg).[16]

Aim of the Work

The aim of this study was to screen for chronic Hepatitis B virus infection in patients with Malignancies recruited from clinical Oncology department in Main Alexandria University Hospital and assessment of the impact of malignancy on the response to preemptive treatment of chronic Hepatitis B virus with Nucleoside analogue (Entecavir 0.5mg).

PATIENTS AND METHODS

Five hundred patients with malignancies recruited from clinical Oncology department at Main Alexandria University Hospital were screened for Chronic Hepatitis B virus infection with HBsAg and HBcAb by ABON Rapid Test.

Patients who tested positive for HBsAg (n = 23) and another 20 control suffering from chronic HBV infection were subjected to the following:

1. Detailed history taking and thorough clinic al examination.
2. Laboratory investigations:
   - Routine investigations: CBC, blood urea, serum creatinine.
   - Liver enzymes and Liver function tests: Aspartate transaminase and Alanine transaminase, total and direct bilirubin, prothrombin activity, INR, total protein, and serum albumin.
   - HBsAg and total HBcAb (by ABON Rapid Test) for screening patients with Malignancies.
   - HBcAb (IgM and IgG) and HBsAb for HBsAg positive and/or total HBcAb positive patients.
   - HBeAg and HBeAb for HBsAg positive and HBcAb LgG positive patients, and HBsAg negative, HBcAb IgG positive and HBsAb negative patients (Occult HBV infection).
   - PCR for HBV in serum for HBsAg positive and HBcAb LgG positive patients, and HBsAg negative, HBcAb IgG positive and HBsAb negative patients (Occult HBV infection) at 0, 3, 6 months while treated with Nucleoside analogue (Entecavir 0.5mg).

1. Body mass index (BMI) was calculated at the beginning of HBV treatment and after 6 months of treatment by the following formula: BMI = weight in Kg / (height in meter)^2
2. Radiological studies:
   - Ultrasound study of the abdomen and pelvis to assess the liver, spleen, presence of ascites and other signs of portal hypertension in patients with Malignancy and chronic Hepatitis B virus infection.

RESULTS

Statistical analysis of the data obtained from the present study revealed the following results:

In group I;

PCR for hepatitis B virus was above detection limit for 21 out of 23 (91.3%) patients before starting HBV treatment, then it was above detection limit for 4 out of 23 (25%) patient after 3 months of receiving Entecavir 0.5mg tab daily, then no patient was above detection limit after 6 months of receiving treatment of HBV (Entecavir 0.5mg). This Decrease in PCR for HBV is statistically significant p = 0.047.

In group II:

PCR for hepatitis B virus was above detection limit for 20 out of 20 (100%) patients before starting HBV treatment, then it was above detection limit for 5 out of 20 (25%) patient after 3 months of receiving Entecavir 0.5mg tab daily, then no patient was above detection limit after 6 months of receiving treatment of HBV (Entecavir 0.5mg). This Decrease in PCR for HBV is statistically significant p = 0.043

In both groups 100% patients was successfully treated with Entecavir 0.5mg tab daily and all the patients met the criteria of virological response to treatment (undetectable PCR after 6 months of treatment) and no virological breakthrough or treatment failure was reported.

PCR of HBV in group I was higher in AML patient 5.20 x 10^4 , Non-Hodgkin's lymphoma (NHL) patients (n = 10) with mean 4.42 ± 10.09 x 10^4, Hodgkin's lymphoma (HL) patients (n = 5) with mean 4.35 ± 6.40 x10^4 than Chronic myeloid leukemia (CML) patients (n = 3) with mean 0.40 ± 0.07 x 10^4, Cancer Rectum patient 1.20 x $10^4$and Bronchogenic carcinoma patient 0.27 x 10^4. Effect of different types of malignancies on PCR cannot be assessed due paucity of cases.

PCR of HBV in group I was below detection limit for all patients after 3 months of treatment except for 2 HL patients and 2 NHL patients and that may be related to very high level of PCR of HBV for those patients before beginning of treatment.

In group I:

There was statistically significant reduction in AST level with mean 271.13 IU/dl before starting HBV treatment and with mean 24.73 IU/dl after 6 months of treatment with Entecavir 0.5mgtab daily. There was also statistically significant reduction in ALT level with mean 303.43 IU/dl before starting HBV treatment and with mean 27.73 IU/dl after 6 months of treatment with Entecavir 0.5mgtab daily.

In group II:

There was statistically significant reduction in ALT level with mean 501.85 IU/dl before starting HBV treatment and with mean 27.65 IU/dl after 6 months of treatment with Entecavir 0.5mgtab daily. There was also statistically significant reduction in ALT level with mean 576.75 IU/dl before starting HBV treatment and with mean 28.25 IU/dl after 6 months of treatment with Entecavir 0.5mgtab daily.

In group I:

There was statistically significant reduction in Total Bilirubin level with mean 3.51 ± 1.20 mg/dl before starting HBV treatment and with mean 0.81 ± 0.21 mg/dl after 6 months of treatment with Entecavir 0.5mgtab daily. There was also statistically significant reduction in Direct Bilirubin level with mean 1.54 ± 0.53 mg/dl before starting HBV treatment and with mean 0.25 ± 0.07 mg/dl after 6 months of treatment with Entecavir 0.5mgtab daily.

In group II:

There was statistically significant reduction in Total Bilirubin level with mean 1.46 ± 0.82 mg/dl before starting HBV treatment and with mean 0.64 ± 0.19 mg/dl after 6 months of treatment with Entecavir 0.5mgtab daily. There was also statistically significant reduction in Direct Bilirubin level with mean 1.26 ± 0.32 mg/dl before starting

Table-1. Comparison between the two studied groups according to PCR for HB virus

PCR for HB virus (x10^4)	HBV				Test of Sig.	P
	With Malignancy		Without Malignancy			
	No.	%	No.	%		
Before HBV treatment	**(n = 23)**		**(n = 20)**			
Below detection limit	2	8.7	0	0.0	□ □ □ □ □ □	FE p= 0.491
Over detection limit	**21**	**91.3**	**20**	**100.0**		
Min. – Max.	0.08 – 32.80		1.08 – 3450.0		U = 67.00*	<0.001*
Mean ± SD.	3.52 ± 7.55		389.74 ± 826.06			
Median	0.602		5.99			
After 3 months	**(n = 23)**		**(n = 20)**			
Below detection limit	19	82.6	15	75.0	□ □ □ □ □ □	FE p= 0.711
Over detection limit	**4**	**17.4**	**5**	**25.0**		
Min. – Max.	0.12 – 0.85		0.42 – 1.34		U = 3.00	0.086
Mean ± SD.	0.40 ± 0.31		0.75 ± 0.41			
Median	0.31		0.53			
p_1	0.047*		0.043*			
After 6months	**(n = 22)**		**(n = 20)**			
Below detection limit	22	100.0	20	100.0	□	-
Over detection limit	**0**	**0.0**	**0**	**0.0**		

	N	PCR for HB virus (x10^4) in group I (Before HBV treatment)		
		Min. – Max.	Mean ± SD.	Median
Tumor				
Acute myeloid leukemia	1	5.20		
Breast Cancer	1	Below detection limit		
Bronchogenic carcinoma	1	0.27		
Cancer Rectum(post colectomy)	1	1.20		
Chronic myeloid leukemia	3	0.36 – 0.48	0.40 ± 0.07	0.36
Hodgkin's lymphoma	5	0.08 – 15.60	4.35 ± 6.40	1.25
Non-Hodgkin's lymphoma	10	0.08 – 32.80	4.42 ± 10.09	0.46

	N	PCR for HB virus (x10^4) in group I (after 3 months)		
		Min. – Max.	Mean ± SD.	Median
Tumor				
Acute myeloid leukemia	1	Below detection limit		
Breast Cancer	1	Below detection limit		
Bronchogenic carcinoma	1	Below detection limit		
Cancer Rectum(post colectomy)	1	Below detection limit		
Chronic myeloid leukemia	3	Below detection limit		
Hodgkin's lymphoma	2	0.12 – 0.32	0.22 ± 0.14	0.22
	3	Below detection limit		
Non-Hodgkin's lymphoma	2	0.30 – 0.85	0.58 ± 0.39	0.58
	8	Below detection limit		

Table-2. Comparison between the two studied groups according to liver enzymes

	Liver Enzymes	HBV		Test of Sig.	P
		Group I	Group II		
AST (U/L)	**Before HBV treatment**	**(n = 23)**	**(n = 20)**		
	Min. – Max.	21.0 – 832.0	213.0 – 1253.0	U = 97.0*	0.001*
	Mean ± SD.	271.13 ± 277.61	501.85 ± 287.98		
	Median	149.0	416.50		
	After 6 months	**(n = 22)**	**(n = 20)**		
	Min. – Max.	14.0 – 41.0	17.0 – 44.0	U = 170.50	0.212
	Mean ± SD.	24.73 ± 7.34	27.65 ± 7.77		
	Median	23.0	27.0		
	% of change	↓77.44 ± 25.01	↓ 93.33 ± 3.10	U =106.0*	0.004*
	^{wx}p	<0.001*	<0.001*		
ALT (U/L)	**Before HBV treatment**	**(n = 23)**	**(n = 20)**		
	Min. – Max.	29.0 – 911.0	287.0 – 1400.0	U = 91.0*	0.001*
	Mean ± SD.	303.43 ± 299.42	576.75 ± 314.37		
	Median	169.0	452.50		
	After 6 months	**(n = 22)**	**(n = 20)**		
	Min. – Max.	18.0 – 43.0	17.0 – 45.0	U = 213.0	0.860
	Mean ± SD.	27.73 ± 6.32	28.25 ± 8.63		
	Median	26.50	26.50		
	% of change	↓80.51 ± 18.28	↓94.18 ± 2.78	U =92.0*	0.001*
	^{wx}p	<0.001*	<0.001*		

t, p: t and p values for Student t-test for comparing between the two groups
U, p: U and p values for Mann Whitney test for comparing between the two groups
^{t}p: p value for Paired t-test for comparing between 0 and 6
^{wx}p: p value for Wilcoxon signed ranks test for comparing between 0 and 6
*: Statistically significant at p ≤ 0.05

Table-3. Comparison between the two studied groups according to total bilirubin and direct bilirubin

		HBV		U	P
		Group I	Group II		
Total Bilirubin (mg/dl)	**Before HBV treatment**	**(n = 23)**	**(n = 20)**		
	Min. – Max.	0.50 – 5.50	0.70 – 3.90	48.50*	<0.001*
	Mean ±SD.	3.51 ± 1.20	1.46 ± 0.82		
	Median	3.40	1.20		
	After 6 months	**(n = 22)**	**(n = 20)**		
	Min. – Max.	0.40 – 1.10	0.30 – 1.0	115.50	0.008*
	Mean ±SD.	0.81 ±0.21	0.64 ±0.19		
	Median	0.80	0.60		
	% of change	↓68.59 ± 36.56	↓49.08 ± 20.25	64.50*	<0.001*
	^{wx}p	<0.001*	<0.001*		
Direct Bilirubin (mg/dl)	**Before HBV treatment**	**(n = 23)**	**(n = 20)**		
	Min. – Max.	0.90 – 3.0	0.95 – 2.30	160.50	0.089
	Mean ±SD.	1.54 ± 0.53	1.26 ± 0.32		
	Median	1.40	1.18		
	After 6 months	**(n = 22)**	**(n = 20)**		
	Min. – Max.	0.10 – 0.40	0.10 – 0.32	146.0	0.051
	Mean ±SD.	0.25 ± 0.07	0.19 ± 0.09		
	Median	0.20	0.18		
	% of change	↓83.81 ± 3.37	↓84.54 ± 6.92	168.50	0.194
	^{wx}p	<0.001*	<0.001*		

U, p: U and p values for Mann Whitney test for comparing between the two groups
^{wx}p: p value for Wilcoxon signed ranks test for comparing between 0 and 6
*: Statistically significant at p ≤ 0.05

HBV treatment and with mean 0.19 ± 0.09 mg/dl after 6 months of treatment with Entecavir 0.5mgtab daily.

DISCUSSION

An estimated 400 million persons are carriers of hepatitis B virus (HBV) in the world today; Hepatitis B is the chief cause of cirrhosis and HCC in the world today, and nationwide vaccination has been shown to diminish greatly the number of new cases of infection and HCC.[1]

Patients at risk of HBV reactivation are those with haematological malignancies (or solid malignant tumours) who are candidates for chemotherapy but also patients with non-malignant diseases, such as immune thrombocytopenic purpura (ITP) or autoimmune haemolytic anaemia, which require continuous immunosuppressive therapy.

Our study was conducted on 500 patients with malignancies recruited from clinical Oncology department at Main Alexandria University Hospital who were screened for Chronic Hepatitis B virus infection and those who were tested positive for HBs Ag or HBc Ab (IGg) (n = 23) were tested for HBeAg, HBeAb, PCR for HBV, Liver function tests and Ultrasound study of the abdomen and pelvis to assess the liver, spleen, presence of ascites and other signs of portal hypertension and then these patients received preemptive treatment with Nucleoside analogue (Entecavir 0.5mg) before (n = 7) and during (n = 16) chemotherapy for 6 months.

Another 20 control patients suffering fom chronic Hepatitis B were subjected to the same work up of the other group and then were treated with Nucleoside analogue (Entecavir 0.5mg) for 6 months.

PCR for HBV, Liver function tests and routine investigations were done at 0, 3 and 6 months while on Entecavir 0.5mg tab to assess the impact of malignancies on the response to preemptive treatment of CHB, we depended on the results of investigations taken after the use of Entecavir 0.5mg to assess the effect of treatment on these investigations.

In our study, after screening of 500 patients suffering from different types of malignancies in Alexandria main university hospital with HBsAg and HBcAb IgG, 21 patients tested positive for HBsAg and HBcAb, 8 with NHL, 6 with HL and 4 with leukemia, and 2 patients were tested positive for HBcAb only (occult HBV infection) and was going to be on Rituximab based chemotherapy, so 23 out of 500 (4.6%) cases were recommended for preemptive treatment according to recent EASL Guidelines 2017[17], therefore screening for HBV infection in patients suffering from malignancies is recommended specially those with lymphoma or leukemia.

Also our results showed that, there was statistically significant decrease in AST, ALT, total bilirubin and direct bilirubin levels in both groups after 6 months of treatment of HBV with Entecavir 0.5mg tab once daily. Also it showed that, there was statistically significant increase in serum total protein and Albumin levels after treatment of CHB virus with Entecavir 0.5 mg tab for 6 months, however percentage of increase was higher in group I and that may be mostly related to improvement of general condition of the patient with treatment of malignancy and so improvement of appetite and nutritional status of the patient. There was also statistically significant reduction in serum urea and creatinine levels after 6 months of treatment of HBV in group I more than that in group II and that may be mostly related to improvement of the general condition of the patient with treatment of malignancy and so improvement of appetite and so rehydration of the patient.

The current results were in consistent with the EASL guidelines 2017[17] which stated that pre-emptive treatment with Entecavir is indicated for all HBsAg positive patients however lamivudine has been shown to reduce risk oh HBV reactivation and associated morbidity and mortality, a residual risk of HBV reactivation remains approximately in 10% of chronic HBV patients with low viremia (<2000 IU/ml) and in higher proportion of those with higher viremia level. As recent studies suggest that ETV or TDF can be successfully used in such patients,[18] so prophylaxis with ETV, TDF, TAF is recommended in this setting. Prophylaxis should continue for at least 12 months (18 months for rituximab-based regimens) after cessation of the immunosuppressive treatment and discontinued only if the underlying disease is under remission. Liver function tests and HBV DNA should be tested every 3 to 6 months during prophylaxis and for at least 12 months after NA withdrawal as a large proportion of HBV reactivations develops after NA discontinuation.[19-21]

Similarly the results of the present work were in agreement with AASLD guidelines[22] which stated that Antiviral prophylaxis is recommended for HBV carriers at the start of cancer chemotherapy and for 6 months after completion of chemotherapy if baseline HBV DNA <2.000 IU/ mL level and should continue treatment until they reach treatment endpoints as in immunocompetent patients if baseline HBV DNA level is >2.000 IU/mL; Lamivudine or Telbivudine can be used if the anticipated duration of treatment is short (<12 months) and baseline serum HBV DNA not detectable. Tenofovir or entecavir is preferred if longer duration of treatment is anticipated.

Also American Gastroenterological Association Institute guidelines (AGA)[23] stated that Antiviral prophylaxis is recommended for patients with high risk for reactivation; HBsAg +ve / anti-HBc +ve or HBsAg –ve / anti-HBc +ve treated with B cell-depleting agents (e.g., rituximab, ofatumumab) and HBsAg +ve / anti-HBc +ve patients treated with either Anthracycline derivatives (e.g., doxorubicin, epirubicin) or Moderate or high dose corticosteroids daily for ≥4 weeks, Antiviral prophylaxis over monitoring is suggested for patients with moderate risk for HBV reactivation; HBsAg +ve / anti-HBc +ve or HBsAg –ve/anti-HBc +ve patients treated with TNF inhibitors (e.g, etanercept, adalimumab, certolizumab, infliximab), Cytokine or integrin inhibitors (e.g., abatacept, ustekinumab, natalizumab, vedolizumab) or TKIs (e.g., imatinib, nilotinib) and HBsAg +ve / anti-HBc +ve patients treated with low-dose corticosteroids for ≥4 weeks HBsAg –ve / anti-HBc +ve patients treated with either Moderate- or high-dose corticosteroids for ≥4 weeks or Anthracycline derivatives (e.g., doxorubicin, epirubicin) and Antiviral prophylaxis is not recommended for patients with low risk for reactivation; HBsAg +ve / anti-HBc +ve or HBsAg –ve/anti-HBc +ve patients treated with; Traditional immunosuppressive agents (e.g.,

azathioprine, mercaptopurine, methotrexate) or Intra-articular corticosteroids. It stated that Antivirals with a high barrier to resistance are preferred over lamivudine and Antivirals should be continued for ≥6 months after immunosuppressive therapy discontinuation.

Conclusion

From the previous results, the following can be concluded:

A. Percentage of patients suffering from chronic HBV in Oncology department at Alexandria Main University Hospital is 4.6 %.
B. Entecavir 0.5 mg tab daily for 6 months is a safe, tolerable drug and effective in reduction of PCR for HBV to below detection limit in immunosuppressed patients with malignancies and also effective in normalization of AST and ALT levels in immunosuppressed patients with malignancies; therefore Entecavir 0.5mg tab daily is effective in preemptive treatment of chronic HBV in immunosuppressed patients with malignancies.
C. It is also concluded that effectiveness of Entecavir 0.5mg tab in treatment of chronic HBV in patients with malignancies is comparable to patients without malignancies.

Conflicts of Interest

Authors declare that there is no conflict of interests regarding the publication of this paper.

References

[1]. Kowdley KV, Wang CC, Welch S, et al. Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. Hepatology 2012; 56:422-33.
[2]. Myers RP, Tainturier MH, Ratziu V, Piton A, Thibault V, Imbert-Bismut F, et al. Prediction of liver histological lesions with biochemical markers in patients with chronic hepatitis B. J Hepatol 2003;39:222–30.
[3]. Poynard T, Morra R, Halfon P, Castera L, Ratziu V, Imbert-Bismut F, et al. Meta-analyses of FibroTest diagnostic value in chronic liver disease. BMC Gastroenterol 2007;7:40.
[4]. Marcellin P, Ziol M, Bedossa P, Douvin C, Poupon R, De LV, et al. Noninvasive assessment of liver fibrosis by stiffness measurement in patients with chronic hepatitis B. Liver Int 2009;29:242–7.
[5]. Cardoso AC, Carvalho-Filho RJ, Stern C, Dipumpo A, Giuily N, Ripault MP, et al. Direct comparison of diagnostic performance of transient elastography in patients with chronic hepatitis B and chronic hepatitis C. Liver Int 2012;32:612–21.
[6]. Arena U, Vizzutti F, Corti G, Ambu S, Stasi C, Bresci S, et al. Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology 2008;47:380 384.
[7]. Tassopoulos NC, Volpes R, Pastore G, Heathcote J, Buti M, Goldin RD, et al. Efficacy of lamivudine in patients with hepatitis B e antigen-negative/ hepatitis B virus DNA-p ositive (precore mutant) chronic hepatitis B. Hepatology 1999;29:889–96.
[8]. Marcellin P, Lau GK, Bonino F, Farci P, Hadziyannis S, Jin R, et al. Peginterferon alfa-2a alone, lamivudine alone, and the two in combination in patients with HBeAg-negative chronic hepatitis B. N Engl J Med 2004;351:1206–17.
[9]. Lai CL, Shouval D, Lok AS, Chang TT, Cheinquer H, Goodman Z, et al. Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. N Engl J Med 2006;354:1011–20.
[10]. Menéndez-Arias L, Álvarez M, Pacheco B. 217. Volz T, Allweiss L, Ben MM, *et al.* The entry inhibitor Myrcludex-B efficiently blocks intrahepatic virus spreading in humanized mice previously infected with hepatitis B virus. *J Hepatol* 2013; 58: 861–7.
[11]. Maepa MB, Roelofse I, Ely A, Arbuthnot P. Progress and prospects of ant-HBV gene therapy development. *Int J Mol Sci* 2015; 16: 17589–610.
[12]. Cradick TJ, Keck K, Bradshaw S, Jamieson AC, McCaffrey AP. Zincfinger nucleases as a novel therapeutic strategy for targeting hepatitis B virus DNAs. *Mol Ther* 2010; 18: 947–54.
[13]. Bloom K, Ely A, Mussolino C, Cathomen T, Arbuthnot P. Inactivation of hepatitis B virus replication in cultured cells and in vivo with engineered transcription activator-like effector nucleases. *Mol Ther* 2013; 21: 1889–97.
[14]. Chen J, Zhang W, Lin J, *et al.* An efficient antiviral strategy for targeting hepatitis B virus genome using transcription activator-like effector nucleases. *Mol Ther* 2014; 22: 303–11.
[15]. Boni C, Laccabue D, Lampertico P, *et al.* Restored function of HBV-specific T cells after long-term effective therapy with nucleos (t) ide analogues. *Gastroenterology* 2012; 143: 963–73.
[16]. Giladi H, Ketzinel-Gilad M, Rivkin L, Felig Y, Nussbaum O, Galun E. Small interfering RNA inhibits hepatitis B virus replication in mice. *Mol Ther* 2003; 8: 769–76.
[17]. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol (2017). Curr Opin Virol 2014; 8: 1–9.
[18]. Swapna Gurrapu and Estari Mamidala**.** Medicinal Plants Used By TraditionalMedicinePractitioners in the Management of HIV/AIDS-Related Diseases in Tribal Areas of Adilabad District, Telangana Region. *The Ame J Sci & Med Res*. 2016:2(1):239-245. doi:10.17812/ajsmr2101.
[19]. Hsu C, Tsou HH, Lin SJ, Wang MC, Yao M, Hwang WL, Kao WY, Chiu CF, Lin SF, Lin J, et al. Chemotherapy-induced hepatitis B reactivation in lymphoma patients with resolved HBV infection: a prospective study. Hepatology. 2014;59:2092–100.
[20]. Dong HJ, Ni LN, Sheng GF, Song HL, Xu JZ, Ling Y. Risk of hepatitis B virus (HBV) reactivation in non-Hodgkin lymphoma patients receiving rituximab-chemotherapy: a meta-analysis. J Clin Virol. 2013;57:209–14.
[21]. Matsui T, Kang JH, Nojima M, Tomonari A, Aoki H, Yamazaki H, Yane K, Tsuji K, Andoh S, Andoh S, et al. Reactivation of hepatitis B virus in patients with undetectable HBsAg undergoing chemotherapy for malignant lymphoma or multiple myeloma. J Med Virol. 2013;85:1900–6.
[22]. Zurawska U, Hicks LK, Woo G, Bell CM, Krahn M, Chan KK, Feld JJ. Hepatitis B virus screening before chemotherapy for lymphoma: a cost-effectiveness analysis. J Clin Oncol. 2012;30:3167–73.
[23]. Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH; American Association for the Study of Liver Diseases. AASLD Guidelines for Treatment of Chronic Hepatitis B. Hepatology. 2016;63:261-283.
[24]. Reddy KR, Beavers KL, Hammond SP, Lim JK, Falck-Ytter YT; American Gastroenterological Association Institute. American Gastroenterological Association Institute guideline on the prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy.Gastroenterology. 2015;148:215-219.