Retrospective-Prospective Study on Efficacy & Safety of Entecavir in Chronic Hepatitis B West Asian Patients with Genotype D

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years, interferon, Lamivudine, Adefovir, Telbivudine, Entecavir and tenofovir still used in treatment of chronic hepatitis B. Entecavir and tenofovir are potent antiviral drugs. The treatment with these drugs leads to normalization in liver enzymes, improvement in liver histology, HBsAg and HBeAg loss and undetectable HBV-DNA levels [7,8]. Elevation of the decreased HBV-DNA during treatment is attributed to drug resistance or noncompliance [9].

Entecavir, a new guanosine nucleoside analogue with speciﬁc activity against HBV-DNA polymerase, represents a third agent within the nucleoside/nucleotide HBV polymerase inhibitor class. It has distinct advantages over Lamivudine and Adefovir Dipivoxil: it has a three-step mechanism of action, is the most potent inhibitor of HBV-DNA polymerase, is not associated with any major adverse eﬀects and has a limited potential for resistance. In clinical trials, Entecavir was superior to Lamivudine in all primary endpoints in both nucleoside-naive and Lamivudine-refractory hepatitis B e-antigen (HBeAg)-positive and HBeAg-negative patients [10].

Entecavir should be considered a ﬁrst or second-line treatment option for the management of HBeAg-positive or HbeAg-negative nucleoside -naive or Lamivudine-refractory CHB patients [10].

The study aimed to assess the eﬃcacy and safety of Entecavir in the treatment of chronic viral hepatitis B (CHB) and to check therapeutic end points for Entecavir and its predictors in Kuwait.

Material and Methods

This is a retrospective cohort-longitudinal study to assess the eﬃcacy and safety of Entecavir in the treatment of CHB Asian-Arabic patients (in Kuwait) for 54 months who were nucleosides-naïve and experienced patients, comparing HBeAg positive and HBeAg-ve subgroup. A total of 70 patients were consecutively confronted according to selection criteria (mentioned below) at Gastroenterology centers of Amiri hospital and Al Adan hospital in Kuwait between October 2012 and April 2014.

*Inclusion criteria

- The following patients were included:

Statistical analyses

All data analyses are descriptive. Tabulations by treatment groups are presented for each of the eẌcacy and safety variables. Continuous variables are summarized using the mean and the median values.

count among the two groups (Table 3). In addition, no signiZcant diwerence in the pre-treatment ultrasonographic Zndings was found among the two groups Also, there was no signiZcant diwerences in the pre-treatment HBV-DNA level (Table 4) with a mean ± SD log 10 of 7.9 ± 5.4 and 7.4 ± 5.0 respectively (P=0.237).

	Group(1) N=23		Group(2) N=47		p. value
	Mean	**± SD**	**Mean**	**± SD**	
Mean HBV-DNA Log 10(IU/ml)	7.9 ±	206,084,000.1	28,774,877.94	110,100,715.5	0.237
Genotype (D)	N	%	N	%	
	23	100	47	100	
*This table shows that there was no statistically difference as regards HBV-DNA level in the studied groups and all patients were Genotype					

Table 4: HBV-DNA level and geno-type in the studied groups before start of treatment.

Biochemical response

HXere was a statistically signiZcant improvement in the mean ALT, PLT and S.albumen in HBeAg +ve group throughout the study period (54 months). While, there was no signiZcant changes in LFT or PLT count in the HBeAg -ve group (Figure 1).

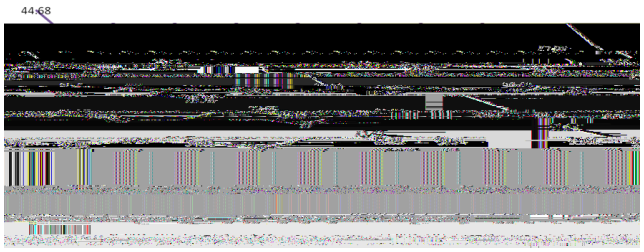

Figure 1: Comparison of LFT between the studied groups before and aner treatment.

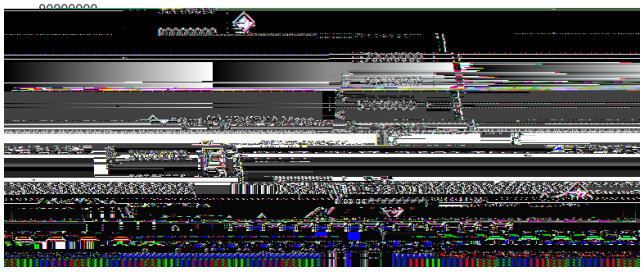

Figure 2: Comparison of HBV-DNA level in the studied groups before and aner the treatment.

HXere was a statistically signiZcant improvement in the mean ALT & AST in the HBeAg +ve compared to the HBeAg -ve group throughout the study period (54 months).

Virological response: HXere was a statistically signiZcant reduction in HBV viral load (Table 5) in the HBeAg –ve compared to the HBeAg +ve group throughout the follow up period (Figure 2).

HXere was a statistically signiZcant reduction in HBV viral load in the HBeAg –ve compared to the HBeAg +ve group throughout the follow up period.

In HBeAg +ve, 19 patients (82.61%) had complete HBV-DNA suppression aner a median period of 7 month. HXe other 4 (17.39%) had showed secondary non-response aner a median period of 24 months, while in HBeAg –ve group; all 47 (100%) had complete HBV-DNA suppression aner a median period of 5 months.

Marker		HBeAg +ve N=23		HBeAg –ve N=47		p. Value
		N	%	N	%	
*HBsAb ion	seroconvert	0	0			

no improvement. At the Meanwhile, 17 patients (73.91%) maintained normal hepatic texture pre and post treatment till the end of follow up period (54 months).

In HBeAg-ve group, 2 (4.24%) showed improvement of US detected pre-treatment hepatomegaly to normal sized liver post-treatment, while 4 (8.48%) showed improvement in texture. On the other hand, 25 (53.19) maintained normal hepatic texture pre and post treatment till the end of follow up period (54 months).

Factors associated with undetectable HBV-DNA ањег 54 months follow up:

As shown in univariate analysis (Table 6); four factors aψected viral load suppression (Age, P=0.0014, ALT, P=0.016, AST, P=0.006, HBeAg–ve, P=0.00), while in multivariate analysis; pretreatment hepatitis Antigen status (HBeAg –ve) was the only independent factor aψecting viral load suppression (OR=16.9, 95% CI 20.287 (0.0-∞), P=0.000).

Variables	**Univariate analysis**		**Multivariate analysis**	
	OR (95%CI)	p. Value	OR (95% CI)	p. Value
Age	6.044 (4.31-15.6)	0.014		0.286
Gender	0.081 (0.54-3.2)	0.837		0.837
Drug History	0.014 (0.65-3.69)	0.906		0.480
Past Medical History	0.162 (1.35- 4.97)	0.689		0.469
ALT	5.751 (0.07-40.91)	0.016		0.529
AST	7.428 (0.58-36.87)	0.006		0.178
T. BiL	2.792 (0.76-9.93)	0.126		0.126
S. AlB	4.53 (602 -34.72)	0.132		0.134
AFP	2.123 (0.27-15.97)	0.699		0.699
U/S Finding	3.372 (0.69-13.58)	0.066		0.217
Seroconversion	0.398 (0.176-1.46)	0.528		0.512
HBeAg negative	16.5 (0.0-∞)	0.000	20.287 (0.0-∞)	0.000
*In Univariate analysis 4 factors affected HBV viral load suppression, while in multivariate analysis the only independent factor was HBeAg –ve.				

Table 6:

ml. The importance of maintaining prolonged HBV-DNA suppression