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Research Article

Entecavir for Treatment of Chronic HBV Infection, Real-Life Data from Saudi Arabia

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Abstract

Background: Chronic hepatitis B virus (HBV) infection is one of the most common causes of chronic liver disease worldwide. Untreated disease can lead to cirrhosis, hepatocellular carcinoma (HCC) and mortality in a significant proportion of affected patients. Two potent nucleotide(side) inhibitors (entecavir and tenofovir) are widely used to control HBV and subsequently prevent its complication. The efficacy and safety of entecavir have been assessed in several clinical and real-life trials in western countries however no data from Saudi Arabia and middle east region.

Objective: To assess the efficacy of entecavir in treatment of chronic HBV in Saudi Arabia where the predominant genotype is genotype D.

Patients and Methods: A retrospective chart review for HBV infected patients who were treated with entecavir between June 2008 and June 2015 in Prince Sultan Military Medical City was carried out. We included all HBV patients treated with entecavir whether naive or treatment exposed, e Ag positive and e Ag negative and cirrhotic and non cirrhotic patients. Patients with acute HBV infection were excluded. Relevant data were collected and analyzed descriptively and inferentially with SPSS version 17.

Conclusion: Entecavir is highly effective in controlling HBV infection in a large cohort of Saudi patients. It has an excellent safety profile and can be considered as one of the first line options for treatment of HBV infected cirrhotic and non cirrhotic patients.

Keywords: *Hepatitis B Virus (HBV); Hepatocellular Carcinoma (HCC); Entecavir*

Introduction

Worldwide, almost 400 million people are suffering from chronic hepatitis B virus (HBV) [1]. In Saudi Arabia, most patients with chronic HBV are infected with genotype D [2]. Patients with chronic HBV may suffer from cirrhosis and hepatocellular carcinoma when they left untreated [3,4]. Chronic HBV is considered to be as an important cause of morbidity and mortality, with 1,000,000 deaths and 470,000 cases of hepatocellular carcinoma annually, and currently accounts for 5 - 10% of cases of liver transplantation [5,6]. Chronic HBV goal of therapy is to reach a continues viral suppression, which reduce the chances of progression to cirrhosis and hepatocellular carcinoma [5].

Various drugs such as, standard interferon, pegylated interferon alfa, lamivudine, adefovir, tenofovir, telbivudine and entecavir have been approved by the FDA for management of patients with chronic HBV [7].

Aim of the Study

In this study we aim to assess the efficacy of entecavir in treatment of chronic HBV in Saudi Arabia where the predominant genotype is genotype D.

Methodology

A retrospective chart review for HBV infected patients who were treated with entecavir between June 2008 and June 2015 in Prince Sultan Military Medical City was carried out. We included all HBV patients treated with entecavir whether naive or treatment exposed, e Ag positive and e Ag negative and cirrhotic and non cirrhotic patients. Patients with acute HBV infection were excluded.

Relevant demographic, biochemical, radiological, histological and serological data were collected and analyzed descriptively and inferentially with SPSS version 17. The primary end point was viral suppression below 2000 iu/ml. Secondary endpoints were ALT normalization, e Ag loss, s Ag loss, overall survival and safety of treatment.

Results

A total of 439 patients included in the trial. The mean age at time of presentation was 46.7 ± 14.9 years and 72.2% were males. E Ag was positive in 24.6% and 73% were treatment naive. One third of patients (32%) were cirrhotic at the time of diagnosis and one forth of these patients had signs of decompensation. After a median follow up of 26 months (3 - 72), 50%, 65% and 88% of patients had undetectable HBV DNA after 6, 12, and 24 months of treatment respectively while 95% of them had HBV DNA below 2000 iu/ml at the end of follow up. E Ag loss and seroconversion was achieved in 30 and 20% respectively while S Ag loss occurred in 2.7%. Normalization of ALT was achieved in 90% of patients and in those who had persistently high ALT, a co-existing fatty liver disease was found in most of them. Overall survival at 5 years was 90% with significant difference between cirrhotics and non cirrhotics (83% vs 99%, p = 0.001). The drug was well tolerated and there was no discontinuation related to adverse events.

Variable	Subgroups	% Mean± SD
Age		46.7 ± 14.9 years
Gender	Male	72.2
	Female	27.8
eAg	Positive	24.6
	Negative	75.4
Previous RX	Naïve	73.6
	Exposed	26.4
HCV co-inf		2.3
BMI		28.8 ± 6.4
Cirrhosis		32
	Compensated	73
	Decomp	27
HCC		14.6

Table 1: *Baseline characteristics.*

Disease	Subgroups	Frequency (%)
DM		27.9
HTN		26.3
Dyslipidemia		18.3
Cardiac Disease		7.4
Lung Disease		7.4
Thyroid Disorder	Hypo	8.3
	Hyper	0.9
Renal Disease		8.8
Organ Tx		4.8
Malignancy		5.2

Table 2: *Comorbidities.*

Parameter		%
Appearance	Normal	24.8
	Coarse/Hyperchoic	54.5
	Small/Nodular	20.7
Liver size		14.2 ± 2.0
Spleen Size		10.9 ± 2.6
Fatty Changes		39.5
Liver Lesion	Single	6.4
	Multiple	8.2

Table 3: *Radiological features.*

Parameter	Median (range)
Viral load (iu/ml)	30656 (34-1000000000)
Viral load (log)	4.6 (1.2-9)
DNA undetectable	12.3%
Parameter	Median (range)

Table 4: *Virological Features.*

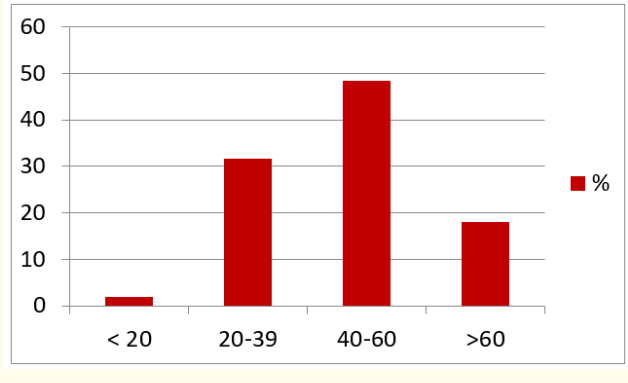

Figure 1: *Age distribution.*

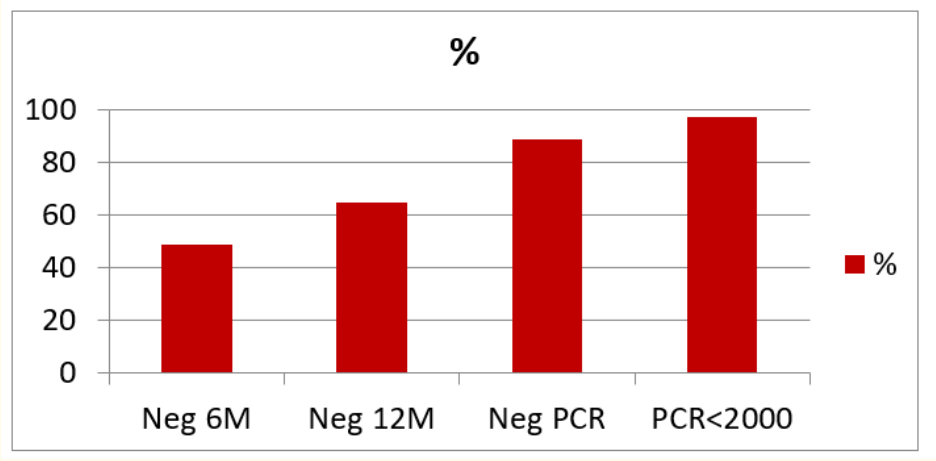

Figure 2: *Virological response.*

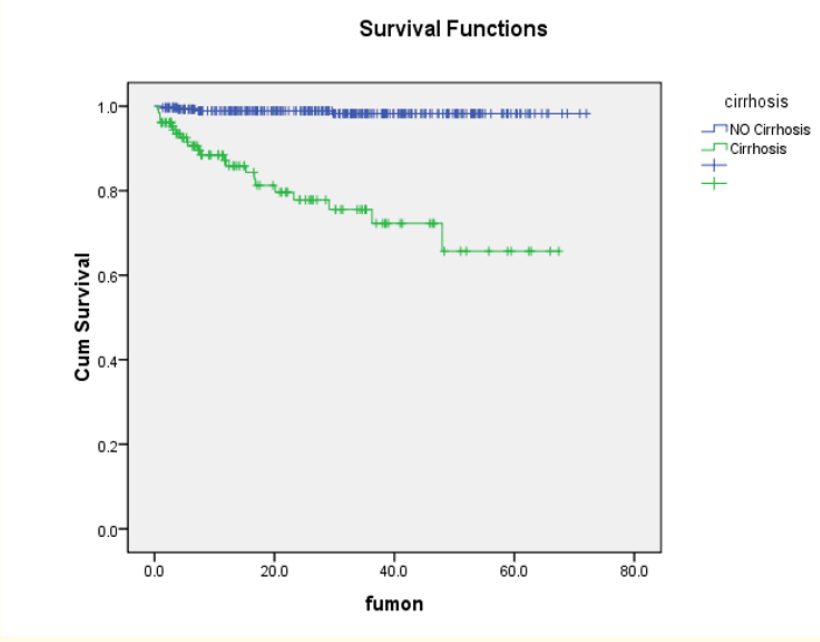

Figure 3: *Survival based on cirrhotic state.*

Discussion

Patients with chronic HBV in Saudi Arabia mostly are infected with D genotype [2]. The FDA has approved various drugs in order to manage patients with chronic HBV infection and avoid the progression to cirrhosis and hepatocellular carcinoma. Our aim in this study was to assess the efficacy of Entecavir in treatment of chronic HBV in Saudi Arabia where the predominant genotype is genotype D.

We have observed that about 88% of patients included in the study had undetectable HBV DNA after 24 months of treatment while 95% of them had HBV DNA below 2000 iu/ml. Hamad Al-Ashqar., *et al*. reported that treatment response to Entecavir at 12 months with an undetectable HBV DNA was 46.5%. When the treatment was extended beyond 48 weeks, with a median of 24 months, the undetectable HBV DNA escalated to 67.4%. The low response rate was reported to previous exposure to antiviral agents, low compliance and high number of HBeAg positive patients included in the study [8]. In compare to Ashqar., *et al.* the high response rate can be attributed to low number of HBeAg positive patients enrolled in our study.

A large clinical study was done by the European Association for the Study of the Liver (2009), aimed to update recommendations for the optimal management of chronic hepatitis B, reported that undetectable HBV DNA after 12 months of Entecavir was seen in 67% of HBeAg positive patients and in 90% of HBeAg- negative patients [9]. When we compared our data to such results, we found that the response to Entecavir at 12 months is almost the same (65%). Pol S., *et al.* reported that the response rate in chronic HBV patients managed with Entecavir at 48 weeks, was 66% in HBeAg-positive and 90% of HBeAg-negative patients achieved undetectable HBV [10].

Our study found that HBeAg loss and seroconversion was achieved in 20% of the patients. Ma H., *et al*. enrolled 33 patients with a chronic HBV refractory to lamivudine to receive Entecavir and reported that HBeAG seroconversion was achieved in 33.3% [11]. Additionally, Gish RG., *et al.* reported 11% seroconversion in their study. A total of 354 patients were enrolled in order to evaluate the HBeAg seroconversion after Entecavir treatment [12].

We found that the overall survival rate at 5 years was 90% with significant difference between cirrhotics and non cirrhotics patients. Xiaoguo Zhang., *et al.* evaluated the rescuing efficacy and safety of Entecavir in patients with CHB and reported that Entecavir improved survival rate at 4 weeks after treatment [13].

Conclusion

Entecavir is found to have a significant effect in reducing the viral load in patients with chronic HBV infection, and increasing the survival rate. Further studies are needed to compare Entecavir with other management options in patients with HBeAg positive patients.

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Bibliography

1. McMahon BJ. "Epidemiology and natural history of hepatitis B". *Seminars in Liver Disease* 25.1 (2005): 3-8.
2. Al Ashgar Hi., *et al.* ". Prevalence of hepatitis B virus genotype in Saudi Arabia: a preliminary report". *Indian Journal of Gastroenterology* 27 (2008): 81-82.
3. Iloeje UH., *et al.* "Predicting cirrhosis risk based on the level of circulating hepatitis B viral load". *Gastroenterology* 130 (2006): 678-686.
4. Chen cJ., *et al.* "Risk of hepatocellular carcinoma across a biological gradient of serum hepatitis B virus DnA level". *The Journal of the American Medical Association* 295 (2006): 65-73.
5. European Association for the Study of the Liver. "EASL Clinical Practice Guidelines: management of chronic hepatitis B". *Journal of Hepatology* 50 (2009): 227-242.
6. Liaw YF and Chu CM. "Hepatitis B virus infection". *Lancet* 373 (2009): 582-592.

7. Buster eH., *et al.* "Treatment of chronic hepatitis B virus infection - Dutch national guidelines". *The Netherlands Journal of Medicine* 66 (2008): 292-306.

8. Hamad Ibrahim Al-Ashqar., *et al.* "Entecavir for the treatment of real-life chronic hepatitis B patients: a study from Saudi Arabia". *Annals of Saudi Medicine* 33.2 (2013): 119-123.

9. EASL clinical Practice Guidelines: management of chronic hepatitis B". *Journal of Hepatology* 50 (2009): 227-242.

10. Pol S and Lampertico P. "First-line treatment of chronic hepatitis B with entecavir or tenofovir in 'real-life' settings: from clinical trials to clinical practice". *The Journal of Viral Hepatitis* 19 (2012): 377-386.

11. Ma H., *et al.* "[Week 24 suppression of HBvin entecavir-treated chronic hepatitis B patients in whom lamivudine treatment failed is associated with efficacy at week 48]". *Zhonghua Shi Yan He Lin chuang Bing Du Xue Za Zhi* 21 (2007): 102-104.

12. Gish rG., *et al.* "Entecavir therapy for up to 96 weeks in patients with HBeAg positive chronic hepatitis B". *Gastroenterology* 133 (2007): 1437-1444.

13. Xiaoguo Zhang., *et al.* "He efficacy and safety of entecavir in patientswith chronic hepatitis B- associated liver failure: a meta-analysis". *Annals of Hepatolog* 14.2 (2015): 150-160.

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