INTRODUCTION:

Chronic hepatitis B affects an estimated 400 million people worldwide and causes more than 5 million deaths due to complications of chronic infection. Nearly 40 million people out of the global HBV infection pool are from India and every year over 100,000 Indians die due to complications associated with chronic infection. 

Chronically infected patients with prolonged elevated HBV DNA level, elevated ALT level, and presence of HBeAg are at increased risk of developing progressive liver disease, cirrhosis, hepatic decompensation, hepatocellular carcinoma (HCC) and death. HBV DNA level of more than 2000 IU/ml (10^6 copies/ml) is a strong predictor for development of complications like cirrhosis and HCC. Patients with chronic HBV infection who have ALT levels that are near the upper limit of the normal range are at a significantly higher risk for complications of cirrhosis and HCC than patients with ALT levels that are less than half the upper limit of the normal range. The highest risk of complication of cirrhosis and HCC occurs in patients with ALT levels that are one or two times the upper limit of the normal range.

Seroconversion for HBeAg and/or HBV-DNA>2,000 IU/ml are significant risk factors for cirrhosis and HCC development, even in asymptomatic subjects with chronic HBV infection. The goal of treatment is to suppress HBV replication and ensure the loss of HBeAg with ALT normalization at the end of the treatment, thus decreasing progression of the liver disease to cirrhosis and HCC. Drugs approved for HBV treatment include interferon, nucleoside or nucleotide analogs (lamivudine, adefovir, entecavir, tenofovir, and telbivudine) and lamivudine and telbivudine.

Interferon requires parental administration, and causes many side effects especially in cases of cirrhosis. A substantial percentage of patients particularly those with high levels of viral replication did not respond to treatment with interferon alfa alone or after a short course of corticosteroids. Nucleoside and nucleotide analogs are administered orally, they cause more profound HBV DNA suppression. However these drugs are associated with rebound increase of HBV DNA levels or reactivation of hepatitis if discontinued prematurely. In addition, long-term use of these drugs is compromised by the development of resistance.

ETV is a potent and selective inhibitor of HBV DNA polymerase. In preclinical studies performed in chronic woodchuck hepatitis virus infections, ETV showed potent and sustained suppression of viral DNA and an absence of both viral rebounds and emerging ETV resistance (ETVr). ETV reduced the covalently closed circular DNA viral reservoir to undetectable levels and extended the lives of treated woodchucks by preventing HCC. Therapy with ETV in HBeAg-positive CHB patients demonstrated superior histologic, virologic, and biochemical responses compared with lamivudine at 48 weeks.

In a study by Leung et al, comprehensive monitoring of genotypic and phenotypic antiviral resistance was performed on 673 ETV treated nucleoside naive HBV patients; only 3% of ETV treated patients exhibited virologic rebound by the end of 96th week. Therefore we conducted a prospective observational study to evaluate the efficacy of entecavir in seropositive chronic hepatitis B treatment naive Indian population in real life scenario.

MATERIALS & METHOD

Study design: This is an open label prospective observational study to evaluate the antiviral efficacy of ETV in treatment naive chronic hepatitis B patient. The study was conducted from January 2015 to December 2016 in the department of Hepatology, Pathology and Pharmacology at SCB Medical College & Hospital, Cuttack, Odisha after approval from Institutional Ethical Committee. Data were collected from patients with HBeAg positive chronic hepatitis B. Written informed consent was taken after explaining the details of the study protocol.

Patient selection: Patients were enrolled as per the following inclusion & exclusion criteria. HBeAg positive chronic hepatitis B men and women older than 16 years of age, patients with compensated liver disease document by elevated serum ALT levels, patients having HBV DNA levels greater than 2000 IU/ml, nucleoside naive patients, compliant patients were included in the study. Women of childbearing potential willing to use an acceptable method of contraception were included. Patients with ALT levels that are one to two times the upper limit of the normal range, elevated ALT level, and presence of HBeAg are at increased risk for complications of cirrhosis and HCC. Patients with ALT levels that are less than half the upper limit of the normal range are at a significantly higher risk for complications of cirrhosis and HCC than patients with ALT levels that are less than half the upper limit of the normal range.

Analysis:

The mean HBV DNA at baseline was 5.99 log [on a base-10 scale] IU/mL which decreased to 2.12 log IU/mL at the end of 40 weeks. Thus there was a mean change of 3.87 log IU/mL which was statistically significant (P<0.0001). Out of 140 HBeAg positive subjects, 90 (64.29 %) had become negative at the end of 40 weeks. Only 10.71 % of the patients had normal ALT levels, 35.71% of the patients had normal ALT levels, and 35.71% of the patients had normal ALT levels, and 35.71% of the patients had normal ALT levels, and 35.71% of the patients had normal ALT levels.
HBV DNA (Viral Load):

**Baseline**

- **Efficacy analysis:**
  - Table 1: The mean age of subjects was 37.6 years, with a minimum of 22 years and a maximum of 65 years. There were more male subjects (N=100, 71.43%) than female subjects (N=40, 28.57%). The mean (SD) weight was 60.1 kgs, with a minimum of 46 kgs and maximum of 75 kgs. All patients were HBeAg positive.
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**Data Collection**

Data collection was done at baseline (visit 1) and at visits 2, 3 and 4 at initiation i.e. at 12, 24, 40 weeks of treatment. The data collected at baseline were demographics, laboratory investigation, concomitant medications and drug allergies. At subsequent visits data useful to evaluate the efficacy of ETV i.e. HBV DNA load, serum ALT and HBeAg were collected.

**Assay Methodology**

Serum HBV DNA was quantified using the qRT-PCR technology. The lower limit of detection was (<20 IU/ml). Serum ALT level was quantified by local laboratory, normal value range 0-40 IU/L.

**Efficacy Analysis**

The efficacy of antiviral therapy of chronic hepatitis B is measured using surrogate markers. These include undetectable levels of HBV DNA, normalization of ALT, and HBeAg seroconversion at the end of 40 weeks.

**Statistical methods & analysis**

The software package used for statistical analysis was SAS software version 9.1.3. Pairwise t-test was used for finding changes from any two visits when the data followed normality assumption and Wilcoxon signed rank test was used when data did not follow normality assumption. McNemar’s test was used for paired categorical data for finding change between visits.

**OBSERVATION**

Demographic summary: Demographics for all the subjects are shown in Table 1. The mean age of subjects was 37.6 years, with 22 years as minimum and 65 years as maximum. There were more male subjects (N=100, 71.43%) than female subjects (N=40, 28.57%). The mean (SD) weight was 60.1 kgs, with a minimum of 46 kgs and maximum of 75 kgs. All patients were HBeAg positive.

**Table 1: Demographic and disease characteristics at the baseline**

<table>
<thead>
<tr>
<th>Demography</th>
<th>N=140</th>
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<tbody>
<tr>
<td>Male/Female (n %)</td>
<td>90 (64.29%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.5±8.43</td>
</tr>
<tr>
<td>Weight (Kgs)</td>
<td>60.1±10.86</td>
</tr>
<tr>
<td>DISEASE CHARACTERISTICS</td>
<td></td>
</tr>
<tr>
<td>Mean HBVDNA</td>
<td>Log 5.99±1.116 IU/mL</td>
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<tr>
<td>Mean Serum ALT</td>
<td>69.7±25.88 IU/L</td>
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<tr>
<td>HBeAg positive</td>
<td>N=140 (100%)</td>
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</tbody>
</table>

**Efficacy analysis:**

HBV DNA (Viral Load):

**LIMITATIONS OF THE STUDY**

The limitation of our study were that safety parameters were not
CONCLUSION:
Our study cohort was small and patients had no other co-morbid conditions or any concurrent drug therapy. Thus further studies evaluating the efficacy in such complex settings. We conclude that entecavir significantly improves viral biochemical and serological markers of HBeAg positive chronic hepatitis treatment naive patients who have not received nucleoside analogs for their condition.

CONFLICT OF INTEREST: NIL

REFERENCES