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Research Paper

A Study on the efficacy of Adefovir dipivoxil in the treatment of HBe antigen Positive Chronic Hepatitis B

Medical Science

KEYWORDS :

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ABSTRACT

In patients with HBeAg positive Chronic Hepatitis B 48 weeks of 10 mg Adefovir dipiovoxil per day resulted in reduced serum HBV DNA and alanine transaminases levels and increased rates of HBeAg seroconversion. Adefovir treatment lead to virological and serological improvement in patients with chronic hepatitis B.

Introduction:-

Hepatitis B virus infection is a global health problem and it is estimated by the World Health Organisation (WHO), that approximately one third of the world population has been infected with HBV with serological evidence of past or present infection with HBV. Of the approximately 2 billion people who have been infected world wide, more than 350 million (5 -7 % of the world's population) suffer from chronic hepatitis B infection. Approximately 15 – 40 % of the patients infected with HBV will develop life threatening liver consequences (including cirrhosis, liver failure and hepatocellular carcinoma) resulting in 600,000 to 1.2 million deaths per year due to HBV.

India has over 40 million HBV carriers and accounts for 10 – 15 % of the entire pool of HBV carriers of the world. Of the 25 million infants born every year in India, it is estimated that that over 1 million run the life time risk of developing chronic HBV infection. Every year over 100,000 Indians die due to illness related to HBV infection.

There are varying reports of overall rate of HbsAg positivity in India ranging between 2 – 4.7%.(1) Spread of HBV infection in many South Asian countries is attributed to unsafe blood supply, reuse of contaminated syringes, lack of maternal screening to prevent perinatal transmission and delay in introduction of hepatitis B vaccine. (2) The predominant mode of transmission is horizontal rather than vertical in India. (3)

Various guidelines including the AASLD, EASL and APASL guidelines have been published for the management of HBV. The ultimate goal of management is to prevent progression of the disease to cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma.

Adefovir is a potent nucleotide analogue and has a potent antiviral effect when given in chronic hepatitis B cases. In a trial by Mercellin P , Chang TT and et al 2003 it was found that daily doses of 10 mg of Adefovir dipivoxil inhibited HBV replication , reducing serum HBV DNA by approximately 4 log copies per milliliter , normalized alanine transferases and induced HBeAg loss and seroconversion in a diverse population.

On the basis of above clinical trials , Adefovir dipivoxil will be used in patients of chronic hepatitis B with E antigen positive to evaluate its efficacy after a period of 48 weeks.

Material and Methods:-

In the present study 20 cases of Chronic Hepatitis B were selected from the OPD medical wards of Katihar medical college Katihar Bihar.They were given 10 mg Adefovir for 48 weeks.The primary end point was suppression of DNA viral load and normalization of liver enzymes.

INCLUSION CRITERIA-

1-HBs Ag Positive
2-Hepatitis B e Antigen Positive
3- ALT greater than 2 times normal
4-High DNA Viral load (>20000 IU / ml)

EXCLUSION CRITERIA-

1. Treated previously with interferon or had received antiviral or immunosuppressive medication.
2. Tested positive for antibody to Hepatitis C virus.
3. Chronic liver disease and other viral hepatitis.
4. Alchol or drug abuse within 1 year of study entry.
5. Obstructitve jaundice.

EVALUATION- Serial clinical examination, lab investigation including DNA Viral load,trans aminases(AST,ALT) and serum alkaline phosphatase were evaluated at 3 monthly interval.USG abdomen was done to look for liver size and echotexture,spleen size and portal vein to look for cirrhosis of liver and hepatocelular carcinoma.

Discussion:-

A total of 400 patients were screened during the study period of whom 40 patients were selected and randomized for Adefovir after fulfillinf the inclusion and exclusion criteria.

20 patients were selected for study group and 20 were selected for the control group. Both the treatment groups were compared with respect to demographic and disease characteristics. Overall there were 31 males and 9 females. The two groups were compareble with respect to age and sex distribution. All the patients in both groups completed 48 weeks of therapy.

The mean serum bilirubin level in the study group at the time of admission was 0.77± 0.25, median ALT was 115, and median serum HBV was 9.88, SD 0.22 log10 copies / ml, where as in the control group the mean serum bilirubin at the time of admission was 0.76 ± 0.24, mean ALT 417.5 ± 236.91 SD and mean serum HBV DNA 8.3 log10.

In the study group 4 weeks after admission mean ALT was 67.5, range 32- 236 and mean viral load reduction was -4.42 log10 copies / ml (0.35 SE) where as in the control group median ALT at

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4 weeks was 189.50, range 40 -600.

12 weeks after treatment median ALT in the study group was 54, range 32- 128 and mean viral load reduction was 4.42 (0.35 SE) where as in the control group median ALT after 12 weeks was 96.21, range 32- 200 and mean reduction in the viral load was 2.09.

24 weeks after treatment median ALT reduction in the study group was 43.3, range 30 – 78 and median reduction in the viral load was 4.84, SE 0.35 whereas in the control group median ALT was 66.31, range 30-90 and mean reduction in the viral load was 2.58.

48 weeks after treatment median ALT in the study group was 36, range 31- 56 and mean reduction in the viral load was 5.08, SE 0.46 where as in the control group median ALT was 54.42, range 30- 100 and mean viral load reduction was 2.9.

In the study group 155 of the patients seroconverted to Anti HBe, there was normalization of serum TLT in 100% of the patients but there was no loss of serum HbsAg. Where as in the control group no patient seroconverted from HBeAg and ALT remain elevated in around 80 % of the patients.

There was no significant difference in the total serum bilirubin before and after treatment in both groups. Blood urea and serum creatnine remained normal at the end of treatment in both the groups.

The drug Adefovir is well tolerated with no adverse events during the 48 weeks of treatment period. There were no deaths or instances of hepatic decompensation.

RESULT-
After 48 weeks of treatment there was reduction in HBV DNA by a median of 3.52 (p< 0.001) and 0.55 log copies per milliliter, HBeAg seroconversion in 2 patients, normalization of alanine transferases in 10 patients (48 %).

CONCLUSION :
HBe Ag positive chronic hepatitis B infection can result in progressive liver disease and affect about 350 million people worldwide . The goal of antiviral therapy is to arrest or delay the progressive liver disease. The present study showed that Adefovir brought about early normalization of serum ALT levels with reduction in serum HBV DNA load.

Adefovir was given to 20 patients of chronic hepatitis B with E antigen positive for 48 weeks. There was normalization of serum ALT levels in all patients (100 % improvement) with a median reduction of 79 IU/ l. Other studies have reported mean reduction of 59 IU/l in serum ALT at 96 weeks and normalization in 48 - 73 percent, mean reduction of 64 IU/ l at 24 weeks. (113-117).

In our study HBeAg was negative in 15% of the patients where as other studies have reported HBeAg seroconversion in 12% of the patients . (113 –117) HBV DNA was negative in 19% of the patients after therapy. Other studies have reported that at the end of 24 weeks and 52 weeks mean HBV reduction was 4.97 log copies/ml and 4 log copies / ml respectively (118) and 3.47 log copies/ ml at 96 weeks (119).

In a study by Pradeep Kumar S and et al, mean reduction in HBV DNA was 1.92 log copies /ml after 24 weeks of therapy.(120)

In our study there was a median reduction of 5.08 log10 copies/ ml after 48 weeks of therapy.

To summarize Adefovir treatment lead to virological and serological improvement in patients with chronic hepatitis B.

On the basis of these observations in the present series of work, Adefovir may be recommended for the treatment of chronic hepatitis B.

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