ORIGINAL ARTICLE

Lamivudine as an Initial Treatment for Chronic Hepatitis B

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ABSTRACT

Objective: To know the efficacy of Lamivudine as an initial treatment of chronic hepatitis B and to know the efficacy of lamivudine provided in the National Program for Hepatitis.

Methods: This study was conducted in the National Program for hepatitis and The Department of Gastroenterology Bolan Medical Complex Hospital Quetta from 12-9-2009 to 15-1-2012. HBsAg and HBV DNA were done from Aga Khan University Hospital Karachi and Shoukat Khanum Memorial Hospital Lahore. 76 consecutive patients 66(86.84%) males and 10(13.14%) females with chronic HBV infection were included in the study and treated orally with Lamivudine100 mg once Daily for 6 months to 1 year. All patients were HBsAg positive, HBeAg positive / negative for at least 6months before screening and active liver disease. The male to female ratio is very high. The majority of the patients were belonging very poor socioeconomic group and lower middle class .this is why because the treatment was free and the investigations were funded by the Zakat Fund.

Results: 76 patients 66(86.84%) males and 10(13.14%) females were included in this study. Early virological Response (EVR) (DNA not detected after 12 weeks of therapy) was achieved in 14(21.21%) in male patients and 5(50%) in female patients. In Non Responders (HBV DNA detected after 3 months of treatment) the 8(12.12%) patients were males and 1(10%) patients were Female.18(27.27%) male patients and 3(30%) female patients were absconder End of the treatment Response was 32(48.48%) in male patients and 5(50%)in female patients.16(24.24%) male and 2 (20%) female patients are under treatment. No any side effect of lamivudine was observed or reported in any patient during this trial.

Conclusion: The male to female ratio in this trial is very high. The Response of hepatitis B to Lamivudine in both the gender is almost the same, and response is directly proportional to the duration of the therapy which is quite comparable to the fact proved in the previous trials conducted on National and Iternational level. So to achieve a complete SVR, the duration of lamivudine may be increased to 3-5years or life long in some very resistant cases.

Key words: Lamivudine, hepatitis B, DNA

INTRODUCTION

Chronic Hepatitis B (CHB) infection causes a spectrum of different diseases ranging from clinically asymptomatic carrier state to the development of cirrhosis related complications, and Hepatocellula Carcinoma. Factors determining the clinical outcome in CHB patients still remain unknown[1]. Lamudine has been widely used in the treatment of Chronic Hepatitis B. When it is administered to Hepatitis B Patients, a decrease or disappearance in serum Hepatitis B virus (HBV) DNA and HBeAg is observed and is associated with decrease in ALT. In the previous studies the HBV DNA level during treatment fell to un detectable level at least once during therapy in >89%of the patients receiving Lamudine[2-4].

Lamvudine a potent nucleoside analogue is approved for the treatment of Chronic Hepatitis B for a very long time. lamivudine is highly effective in a broad range of patients and has an excellent safety profile. Evidence suggests that that a twelve months course of Lamivudine achieves a normal transaminase level and no detectable HBV DNA in 65% of patients with compensated HBeAg negative/ HBV DNA positive Liver Disease[5]. How ever the high rates of biochemical and virological relapses soon after discontinuation of treatment and the emergence of drug resistant hepatitis B are the two major problems with Lamivudine treatment[6].

Lamivudine has been used for more than a decade for the treatment of chronic hepatitis B with proven efficacy. Several factors including genotype and the presence of cirrhosis may predict the durability of the response to Lamivudine; higher rates of resistance have been reported in genotype A than genotype D 54% vs 8%[7]. This study was done with the aim to know the response of hepatitis B to Lamivudine in our region and to know the efficacy of lamivudine provided in the Prime minister program.

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PATIENTS AND METHODS

This study was conducted in the; National Program for Prevention and Control of Hepatitis; and Department of Gastroenterology Bolan Medical Complex Hospital Quetta during the period from 12-09-2006 to 15-5-2008. HBsAg and HBV DNA was done Aga Khan University Hospital Karachi and Shoukat Khanum Memorial Hospital Lahore. 76 consecutive patients 66 males and 10 females with chronic HBV infection were included in the study and treated orally with Lamivudine100 mg once Daily for 6 months to 1year. The majority of the patients were belonging very poor socioeconomic group and lower middle class .this is why because the treatment was free and the investigations were funded by the Zakat Fund. All patients were HBsAg positive, HBeAg positive/negative for at least 6months before screening and active liver Disease as defined by (1) elevated ALT or normal ALT, (2) Detectable serum HBV DNA with in the last month before the initiation of treatment. Patients with active alcohol consumption ,positive serology for hepatitis C and D virus and human immunodeficiency virus (HIV), Renal insufficiency, with serum creatinine greater than1.5mg/dl, surgical Porto systemic shunt or transjuggular intrahepatic Porto systemic shunt (TIPS); Liver transplantation and evidence of hepatocellular carcinoma (HCC) by alpha fetoprotein, ultrasonography, and C.T Scan were excluded.

RESULTS

A total of 76 patients were enrolled 66(86.84%) were males and 10(13.15%) were Females. Early Virological Response (EVR) (DNA not detected after 12 weeks of therapy) was achieved in 14(21.21%) male patients and 5(50%) in female patients. In Non Responders (HBV DNA detected after 3 months of treatment) 8(12.12%) patients were males and 1(10%) patient was female. 18(27.27%) male patients and 3(30%) female patients were absconder End of the treatment Response was 32(48.48%) in male patients and 5(50%)in female patients.16(24.24%) male and 2(20%) female patients are under treatment (Table 1&2).

No side effect of the drug was observed or reported in this trial. The majority of the patients had no idea about vaccination, causative factors, investigations treatment, complications, and preventing measures, especially females are ignored for investigations and treatment by their male gender in a male dominant society of Balochistan which shows a very pathetic situation of the patients of hepatitis in Balochistan.

Table 1: Response of Chronic HBV infection to lamivudine according to Gender. n=76

Description	HBV		Total
	Male	Female	
Total no HBV +ve	66(86.84 %)	10(13.15 %)	76
Responders. Early Virological Response (EVR)	14(21.21 %)	5(50%)	19(25%)
Non Responders (RNA detected at 3 months during therapy.	8(12.12%)	1(10%)	9(11.84%)
Absconders	18(27.27 %)	3(30%)	21(27.63 %)
Under Treatment	16(24.24 %)	2(20%)	18(23.68 %)
End of the treatment response(ETR)	32(48.48 %)	5(50%)	37(48.68 %)

Table 2: Response of HBV infection to Lamivudine according to age.

15-24 Years		25-44 Years		45-64 Years		64 & above		Total		Total
Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
26 (36.61%)	2 (2.82%)	31 (43.61%)	5 (7.04%)	6 (8.45%)	1 (1.41%)	0	0	64 (90.42%)	7 (9.85%)	71
28(39.43%)		36(50.07%)		7(9.85%)		0		71		71

DISCUSSION

Hepatitis B is a leading cause of death through out the world by development of Hepatocellular carcinoma in chronic hepatitis B Patients8.Studies suggest that infection with HBeAg variants is associated with more severe Liver Disease, characterized by intermittent flares in disease activity, and a greater life time risk of hepatocellular carcinoma[9,10]. The initial response to 12 months of

Lamivudine therapy appears to be similar in patients with HBeAg –ve and HBeAg +ve liver disease .However the majority of HBeAg –ve patients relapse following cessation of Lamivudine . Patients with both HBsAg –ve and HBsAg+ve liver disease are at risk of developing resistance to lamivudine with prolonged therapy[11,12,13]. The durability of HBeAg seroconversion beyond 52 weeks was evaluated in several studies with sufficient follow up (up to 3 years) all showed relapse rate of36 to 57% with the highest percentage in Asian patients[14,15,16,17,18]. We have carried out our study on patients with both HBsAg +ve and HBsAg-ve liver disease, the response is still very good in both groups of patients, as the patient are still under treatment and the study is continue. There fore we can not comment on the relapse rate.

Results of lamivudine trials in Asia , how ever, have shown response rate of only 15% with emergence of YMDD mutations in 6-9 months, with resistance increasing with duration of therapy.19 The appearance of YMDD mutant was significantly lower with combination of peg interferon and lamivudine therapy than with lamivudine alone.20.In our study the early virological response is 21.21% in males 50% in females which is quite good than the studies done previously in other parts of the world .End of the treatment response (ETR) is 48.48% in male patients and 48.68% in female patients which shows that as the duration of the therapy increases, the response rate is also increasing proportionately, Which is quite opposite to the response rate shown in other studies, which may be due to the fact that the genotype prevalent in our region is responsive to lmivudine therapy. As we have not done genotype in our patients, because this Facility was not provided in the Prime Minister program, and the patients were non affording on self Finance bases.

Analysis of large series of patients with chronic hepatitis B treated for one year revealed, that pre treatment ALT level was significant predictor of HBeAg loss secondary to Lamivudine treatment. As pre treatment ALT level increased, HBeAg loss became more frequent and the rate of HBeAg loss was markedly higher among patients with pre treatment level greater than 5 times the ULN. The rates of HBeAg loss appeared similar for Asians and Caucasians treated with Lamivudine across all ALT groups[21]. We included in our study the patients across all ALT groups, but the response to lamivudine is still very good and is encouraging. This proves the fact that that in Asians HBeAg loss is similar for Asians treated with lamivudine across all ALT groups as mentioned above. So further separate studies are needed on patients normal and abnormal ALT level and known genotype for a prolonged period of more than 3 years.

CONCLUSION

The male to female ratio in this trial is very high.The Response of hepatitis B to Lamivudine in both the gender is almost the same, and response is directly proportional to the duration of the therapy which is quite comparable to the fact proved in the previous trials conducted on National and International level. So to achieve a complete SVR, the duration of lamivudine may be increased to 3-5years or life long in some very resistant cases.

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