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EFFICACY OF LAMIVUDINE AS AN PRELIMINARY TREATMENT FOR CHRONIC HEPATITIS B

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Abstract:

Aim: *To understand the efficacy of lamivudine in the initial treatment of chronic hepatitis B and to understand the efficacy of lamivudine as envisaged in the National Hepatitis Treatment Program.*

Methodology: *The study was conducted under the National Hepatitis Program and Department of Gastroenterology at Services hospital Lahore for one-year duration from April 2019 to April 2020. HBsAg and HBV DNA was obtained. 76 consecutive patients 66 (86.84%) men and 10 (13.14%) women with chronic HBV infection were enrolled in the study and were treated with oral lamivudine 100 mg once daily for 6 months to 1 year. All patients were HBsAg positive, HBeAg positive / negative for at least 6 months prior to screening and had active liver disease. The ratio of men to women is very high. Most of the patients belonged to a very poor socioeconomic group and lower middle class, so treatment was free and the research was funded.*

Results: *The study included 76 patients, 66 (86.84%) men and 10 (13.14%) women. Early virologic response (EVR) (DNA not detected after 12 weeks of treatment) was achieved in 14 (21.21%) male patients and 5 (50%) female patients. In non-responders (HBV DNA detected after 3 months of treatment), 8 (12.12%) patients were male and 1 (10%) patient was female. 18 (27.27%) men and 3 (30%) women were non-runners. Treatment Response was 32 (48.48%) for males and 5 (50%) for females. 16 (24.24%) men and 2 (20%) women are under treatment. No adverse effect of lamivudine was observed or reported in any patient during this study.*

Conclusion: *The ratio of men to women in this study is very high. The response of hepatitis B to lamivudine in both genders is almost the same and the response is directly proportional to the duration of treatment, which is quite comparable to what has been shown in previous national and international studies. Therefore, to achieve full SVR, the duration of lamivudine may be extended to 3-5 years or life-long in some highly refractory cases.*

Key words: *lamivudine, hepatitis B, DNA*

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INTRODUCTION:

Chronic hepatitis B (CHB) infection causes a wide variety of diseases, ranging from clinically asymptomatic carriers to the development of complications associated with cirrhosis and hepatocellular carcinoma. The determinants of clinical outcome in CHB patients are still unknown[1-2]. Lamudine is widely used in the treatment of chronic hepatitis B. When administered to patients with hepatitis B, a reduction or loss of hepatitis B virus (HBV) DNA and serum HBeAg is observed, with decreased ALT levels. In previous studies, HBV DNA levels during treatment fell to undetectable levels at least once during treatment in> 89% of patients receiving lamudine[3-4]. Lamvudine, a strong nucleoside analogue, has been approved for the treatment of chronic hepatitis B for a very long time. lamivudine is highly effective in many patients and has an excellent safety profile[5-6]. Evidence suggests that a 12-month course of lamivudine treatment achieves normal transaminase levels and no detectable HBV DNA in 65% of patients with compensated HBeAg negative / HBV DNA positive liver disease. However, the high rates of biochemical and virological relapse soon after treatment discontinuation and the emergence of drug-resistant hepatitis B are the two major problems with lamivudine treatment. Lamivudine has been used for over ten years to treat chronic hepatitis B with proven efficacy[7-8]. Several factors, including genotype and cirrhosis, can predict the durability of the response to lamivudine; higher rates of resistance were reported for genotype A than for genotype D 54% compared to 8%[9]. This study was conducted to understand the hepatitis B virus response to lamivudine in our region and the efficacy of lamivudine presented in the prime minister's program.

PATIENTS AND METHODS:

The study was conducted under the National Hepatitis Program and Department of Gastroenterology at Services hospital Lahore for one-year duration from April 2019 to April 2020. HBsAg and HBV DNA were performed. 76 consecutive patients 66 men and 10 women with chronic HBV infection were enrolled in the study and were treated with oral lamivudine 100 mg once daily for 6 months to 1 year. Most of the patients belonged to a very poor socioeconomic group and lower middle class, so treatment was free and the research was funded by the Zakat Fund. All patients were HBsAg positive, HBeAg positive / negative for at least 6 months prior to screening and had active liver disease defined as (1) elevated or normal ALT levels, (2) detectable serum HBV DNA in the last month prior to initiation of treatment. Active alcohol consumption, hepatitis C and D virus and human immunodeficiency virus (HIV) positive, renal failure, serum creatinine greater than 1.5 mg / dL, Porto surgical systemic shunt or trans jugular intrahepatic shunt system Porto (TIPS); Liver transplant and hepatocellular carcinoma (HCC) by alpha-fetoprotein, ultrasound and CT scan were excluded.

RESULTS:

A total of 76 patients were enrolled, 66 (86.84%) were male and 10 (13.15%) were female. Early virologic response (EVR) (DNA not detected after 12 weeks of treatment) was achieved in 14 (21.21%) men and 5 (50%) women. In non-responders (HBV DNA detected after 3 months of treatment), 8 (12.12%) patients are male and 1 (10%) patient is female. 18 (27.27%) men and 3 (30%) women escaped at the end of treatment.

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%)

The responses were 32 (48.48%) men and 5 (50%) women. 16 (24.24%) men and 2 (20%) patients are under treatment (Tables 1 and 2).

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

No adverse drug reaction was observed or reported in this study. Most patients had no idea of vaccination, causative agents, diagnostic treatment, complications and preventive measures, especially women are overlooked in research and treatment due to male gender in the dominant male.

DISCUSSION:

Hepatitis B is the leading cause of death worldwide from the development of hepatocellular carcinoma in patients with chronic hepatitis B8 Studies suggest that infection with HBeAg variants is associated with more severe liver disease, characterized by intermittent exacerbations in disease activity and longer life expectancy the risk of hepatocellular carcinoma over time. The initial response to treatment with lamivudine for 12 months appears to be similar in patients with HBeAg –ve and HBeAg + ve liver disease, but most patients with HBeAg –ve recur after discontinuation of lamivudine. Patients with both HBsAg -ve and HBsAg + ve liver disease are at risk of developing lamivudine resistance with long-term treatment. The persistence of HBeAg seroconversion beyond 52 weeks has been assessed in several sufficiently followed-up studies (up to 3 years), all of which reported a relapse rate of 36–57%, with Asian patients being the highest proportion[10-11]. We conducted our study in patients with both HBsAg + ve and HBsAg-ve liver disease, the response is still very good in both patient groups as the patient is still on treatment and the study continues[12]. Therefore, we cannot comment on the relapse rate. However, results from studies with lamivudine in Asia showed only a 15% response rate to the emergence of the YMDD mutation within 6-9 months, with resistance increasing with the duration of treatment.19 The emergence of the YMDD mutant was significantly lower with the combination of peg interferon and lamivudine therapy compared to lamivudine alone. In our study, the early virological response was 21.21% in males, 50% in females, which is quite a good result compared with previous studies elsewhere in the world.) is 48.48% in men and 48.68% in women, which shows that as the duration of therapy increases, the response rate also increases proportionally, in contrast to the response rate shown in other studies, which may be due to the fact that the genotype dominant in our region responds to lmiivudine therapy[13-14]. Because we did not make a genotype in our patients, because this Facility was not provided for in the Prime Minister's program, and patients did not benefit from self-financing. An analysis of a large number of patients with chronic hepatitis B treated for one year showed that pre-treatment ALT was a significant predictor of HBeAg decline after lamivudine treatment. As pre-treatment ALT increased, the loss of HBeAg became more frequent and the rate of HBeAg loss was significantly higher among patients with pre-treatment levels greater than 5 times UNL. HBeAg loss rates appeared to be similar in Asians and Caucasians treated with lamivudine in all ALT groups. We included patients from all ALT groups in our study, but the response to lamivudine is still very good and encouraging. This proves that in Asians the loss of HBeAg is similar in Asians treated with lamivudine in all ALT groups, as mentioned above. Therefore, further separate studies are needed on patients with normal and abnormal ALT levels and known genotypes over an extended period of over 3 years[15].

CONCLUSION:

The male-to-female ratio in this study is very high, the response of hepatitis B to lamivudine in both genders is nearly the same and the response is directly proportional to the duration of treatment, which is fairly comparable to what has been proven in a previous nationally conducted study and internationally. Therefore, to achieve full SVR, the duration of lamivudine may be extended to 3-5 years or life-long in some highly refractory cases.

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