

Comparison of HBV DNA Quantitative Log in Patients Hepatitis B with Telbivudine Therapy Compared with Tenofovir Therapy in Saiful Anwar General Hospital Malang: January 2016 - December 2017

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ABSTRACT

Background: Hepatitis B is a health problem with high endemic in Indonesia. Hepatitis B virus infection is transmitted parenterally, has a risk of liver cirrhosis and hepatocellular carcinoma. Detection and quantification of HBV DNA are markers of active HBV replication and determine treatment options for hepatitis B. **Methods:** compare log reduction of HBV DNA in patients treated with Telbivudine and Tenofovir. **Results:** There was no significant difference in HBV DNA levels between before and after Tenofovir treatment, namely 6 months follow-up (OR 95% CI = 5.41 [0.83 - 35.16], p = 0.0770) and 12 months (OR 95% CI = 5.39 [0.83 - 34.99], p = 0.0780). Telbivudine administration showed a significant difference in HBV DNA levels between before and after treatment at 6 months follow-up (OR 95% CI = 13.69 [4.53 - 41.40], p = 0.0001) and 12 months (OR 95% CI = 13.69 [4.53 - 41.41], p = 0.0001). Comparison of Tenofovir and Telbivudine therapy showed no significant difference at 6 months follow-up (OR 95% CI = 0.44 [0.10 - 1.88], p = 0.2690) but significant at 12 months follow-up (OR 95% CI = 6.23) [1.39 - 27.97], p = 0.0170). **Conclusion:** There was a significant difference between the administration of Telbivudine as a treatment for hepatitis B with lower serum HBV DNA levels compared with the administration of Tenofovir at 12-month follow-up therapy.

Keywords: Hepatitis B, Telbivudine, Tenofovir, HBV DNA levels

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INTRODUCTION

Hepatitis B threatens millions of people worldwide and has infected approximately 1.2 million people in the United States and 2 billion people in the world, with about 240 million people living with chronic hepatitis B. Most people do not realize they have been infected. Approximately one million people die every year from chronic hepatitis, cirrhosis, and hepatocellular carcinoma.^[1,2]

Hepatitis B is a health problem with high endemicity in Indonesia. Currently it is estimated that there are 28 million Indonesians infected with Hepatitis B and C, 14 million of whom have the potential to become chronic, and of these, 1.4 million people have the potential to suffer from hepatocellular malignancies which will have a huge impact on the quality of life of a patient.^[3]

Hepatitis B is a disease caused by infection with the hepatitis B virus (HBV), a double-stranded DNA virus from the hepadnaviridae family. HBV replicates in the liver and causes acute and chronic hepatitis. This disease is transmitted parenterally, can become chronic, and cause cirrhosis and hepatocellular carcinoma. HBV is primarily a blood-transmitted and sexually transmitted infection and is transmitted through percutaneous and mucosal exposure.^[4,5]

HBV DNA detection and quantification currently play an important role in the diagnosis of infection, making therapeutic decisions, and the assessment of response to therapy. The presence of HBV DNA in peripheral blood is a reliable marker for active HBV replication. HBV DNA levels also determine treatment options for hepatitis B, using either IFN- α , nucleoside analogues, or nucleotide analogues.^[6]

Therefore, this study will discuss the differences in Log HBV DNA after Telbivudin treatment compared with Tenofovir.

METHODS

This study is an analytical study with a prospective analytical observational approach conducted on patients undergoing treatment for hepatitis B infection using Telbivudine versus Tenofovir at the Gastroentero-hepatology Department, Internal Medicine Section of the Saiful Anwar Hospital Malang and followed for two years from January 2016 to December 2017. The sample in this study were adult patients according to the inclusion criteria who had hepatitis B and signed an informed consent. Data collection was carried out at follow-up by means of anamnesis on the family and study subjects, physical examination and vital signs of the patient when he arrived at the Gastroenterohepatology Clinic room, quantitative HBV DNA measurement, and recording the results of patient supporting examinations such as SGOT and SGPT.

Data analysis required in this study is multiple logistic regression analysis to assess the comparison of Log HBV DNA between the Telbivudine and Tenofovir treatment groups in patients with hepatitis B with p value (<0.05).

RESULTS

A total of 34 patients participated and were divided into the two treatment groups Tenofovir (n = 8, 48%) and Telbivudine (n = 26, 52%). Patients were followed for two years from January 2016 to December 2017. The mean age of the subjects was 45.91 ± 15.27 years, with male (34.7%) and female (65.3%) sex. The mean age for the Tenofovir group was 41 ± 15.0 years and the mean age for the Telbivudine group

was 45.0 ± 13.0 years. The mean baseline levels of Tenofovir SGOT were 146 ± 337 IU / L and Sebivo 86 ± 95 IU / L, baseline HBV DNA Tenofovir 5.05×10^7 IU / mL and Sebivo 5.59×10^6 IU / mL. With p-value (> 0.05) the entire study baseline was homogeneously distributed. It is shown at **Table 1** below.

Table 1. Subject Characteristic

Characteristic	Tenofovir (n = 8)	Telbivudine (n = 26)	p- value
Age (years)	41 ± 15	45 ± 13	0.4640
Men	7 [87.5]	18 [69.2]	0.3240
SGOT (IU/L)	146 ± 337	86 ± 95	0.4080
SGPT (IU/L)	182 ± 433	112 ± 121	0.4520
Baseline HBV DNA (IU/mL)	50512448 ± 76728588	55960938 ± 54853911	0.8230

Note: data were presented in mean \pm SD or n[%]; SGOT, serum glutamic oxaloacetic transaminase; SGPT, serum glutamate-pyruvate transaminase; HBV, hepatitis B virus; DNA, deoxyribonucleic acid

showed no significant difference between HBV DNA levels before and after Tenofovir treatment, both at 6-months follow-up (OR 95% CI = 5.41 [0.83 - 35.16], $p = 0.0770$) and 12 months (OR 95% CI = 5.39 [0.83 - 34.99], $p = 0.0780$). In contrast to Sebivo treatment, there was a significant difference between HBV DNA levels before and after Sebivo treatment, both at 6 months follow-up (OR 95% CI = 13.69 [4.53 - 41.40], $p = 0.0001$) and 12 months (OR 95 % CI = 13.69 [4.53 - 41.41], $p = 0.0001$).

The results of multiple logistic regression analysis of serum HBV DNA levels between Telbivudine and Tenofovir in **Table 3** and **Table 4** show that Telbivudine has a stronger association than Tenofovir. The mean \pm SD of Telbivudine at the 6-month follow-up treatment was 6912 ± 15176 and the 12-month follow-up was 2980 ± 7509 . Then the mean \pm SD of Tenofovir at the 6-month follow-up was 841 ± 2158 and the 12-month follow-up was 135508

Table 2. Comparison of serum HBV DNA levels between baseline and after therapy

Parameter	Baseline		N	Post-therapy		OR	95%CI	p-value	
	Mean	SD		Mean	SD				n
Tenofovir treatment 6 months	50512448	76728588	8	841	2158	8	5.41	0.83 - 35.16	0.0770
Tenofovir treatment 12 months	50512448	76728588	8	135508	280580	8	5.39	0.83 - 34.99	0.0780
Telbivudine treatment 6 months	55960938	54853911	26	6912	15176	26	13.69	4.53 - 41.40	0.0001
Telbivudine treatment 12 months	55960938	54853911	26	2980	7509	26	13.69	4.53 - 41.41	0.0001

Note: Data are presented in mean \pm SD; SD, standard deviation; n, sample size; OR, odd ratio; CI, confidence interval; HBV, hepatitis B virus; DNA, deoxyribonucleic acid.

± 280580 .

The results (**Table 2**) of the p-value at baseline comparison with after treatment

Table 3. Comparison of serum HBV DNA levels in patients with hepatitis B treated with Tenofovir and Telbivudine at 6 months and 12 months of therapy

Parameters	Tenofovir (n = 8)	Telbivudine (n = 26)	OR	95%CI	p-value
	Mean ± SD	Mean ± SD			
Treatment 6 month	841 ± 2158	6912 ± 15176	0.44	0.10 - 1.88	0.2690
Treatment 12 month	135508 ± 280580	2980 ± 7509	6.23	1.39 - 27.97	0.0170

Note: Data are presented in mean ± SD; SD, standard deviation; OR, odd ratio; CI, confidence interval; HBV, hepatitis B virus; DNA, deoxyribonucleic acid.

The results of the p-value on the comparison of Tenofovir and after administration of Telbivudine showed that there was no significant difference in the 6-months follow-up comparison of Tenofovir and Telbivudine treatment (OR 95% CI = 0.44 [0.10 - 1.88], p = 0.2690). However, striking results were seen after 12 months of follow-up, there was a significant difference in the 12-month follow-up comparison of the Tenofovir treatment with Telbivudine (OR 95% CI = 6.23 [1.39 - 27.97], p = 0.0170). It is shown at **Table 3**.

DISCUSSIONS

Hepatitis B is a liver infection caused by the hepatitis B virus. HBV DNA logs are said to have an association with treatment response, prognosis, and progression to malignancy in hepatitis B infection. HBV DNA level > 10,000 copies / mL was a strong predictor of risk for developing hepatitis to HCC, and was an independent factor of HBeAg, serum ALT levels, and cirrhosis. Previous studies have suggested that Telbivudine and Tenofovir can lower the HBV DNA log in patients with Hepatitis B. [7]

The incidence of hepatitis B according to national surveillance data in Indonesia is quite high. Approximately 240 million individuals are chronically infected by Hepatitis B, and 75% are in Asia. The endemicity of Hepatitis B in Indonesia ranges from 2.5% to 10% for hepatitis B surface antigen, and men

are more infected than women, and the peak age of infection in adults is 19-45 years with increased risk factors for transmission in pregnant women, blood transfusion, and same-sex. [8,9]

Tenofovir, a nucleotide analogue (nucleoside monophosphate), has strong activity against retroviruses and hepadnaviruses. The effect of Tenofovir treatment causes DNA chain breakdown, thereby preventing viral replication. [10,11]

Whereas Telbivudine is a synthetic thymidine nucleoside analogue with very specific antiviral activity for the treatment of hepatitis B virus (HBV), both for use alone or in combination with other agents in hepatitis B therapy. Di-deoxy telbivudine triphosphate competes with thymidine for insertion into viral DNA, thus leading to termination of the DNA chain and inhibiting the function of DNA polymerase from HBV (reverse transcriptase), thereby causing blockade of HBV DNA replication and virus propagation. [12]

One of the assessments of disease progression, choice of treatment, treatment response and prognosis of hepatitis B is quantitative HBV DNA examination. The presence of HBV-DNA in serum or plasma indicates active HBV infection and, depending on viral load, correlates with patient infectivity. The tests vary in terms of sensitivity and

standardization. These tests can be used to assess prognosis and guide HBV treatment.^[13]

Mild ALT levels and low HBV DNA levels (eg <20,000 IU / mL for HBeAg-positive and <2,000 IU / mL for HBeAg-negative patients) can be predictors of the long-term benefit and safety profile of anti-HBV therapy.^[14]

In this study, the results of multiple logistic regression analysis showed a significant difference between the administration of Telbivudine as a hepatitis B treatment with lower serum HBV DNA levels compared to the administration of Tenofovir at the 12-month follow-up therapy.

Telbivudine is a synthetic thymidine nucleoside analogue with very specific antiviral activity for the treatment of hepatitis B virus (HBV), both for use alone or in combination with other agents in hepatitis B therapy. Di-deoxy telbivudine triphosphate competes with thymidine for insertion into viral DNA, thus causing DNA chain termination and inhibiting the function of DNA polymerase from HBV (reverse transcriptase). This causes a blockade of HBV DNA replication and virus propagation.^[15]

Telbivudine inhibits HBV DNA polymerase (reverse transcriptase) by competing with a natural substrate, thymidine 5'-triphosphate. This results in the termination of the DNA synthesis chain, thereby inhibiting viral replication. Telbivudine also inhibits the anticomplement or second-strand DNA. Telbivudine is an inhibitor of the synthesis of the HBV first and second chains, and shows a different preference for inhibiting the production of the second chain.^[16,17]

Telbivudine is an effective antiviral treatment, and is of particular interest because

it has higher levels of HBeAg and HBeAb seroconversion and potentially good effects on glomerular filtration levels. Seroconversion of HBeAg to HBeAb is considered to be a good prognostic predictor for HBV-GN cases. Then Telbivudine also exerts a protective effect on renal function, the serum creatinine level decreases and almost reaches normal, followed by an increase in eGFR. Even in the case of HBV-GN, the patient's HBV DNA can decline well. At week 52, serum ALT levels became normal in patients receiving Telbivudine 400 mg, and Telbivudine 600 mg.^[18,19]

Telbivudine provides lower HBV DNA levels followed by ALT repair reaching normal and improved clinical conditions with Telbivudine. Telbivudine is also effective for use in patients with kidney problems, pregnant women, and chronic hepatitis B.^[20]

CONCLUSION

Telbivudine was more effective in lowering quantitative HBV DNA serum levels in patients with hepatitis B than Tenofovir with 12 months of treatment and follow-up compared to 6 months of treatment.

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All authors declare no competing interest.

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