The Appearance of Hbeag Status in Patients with Chronic Hepatitis B Virus

Kartika Wensdi Renantriandani[1], Ummi Maimunah[2], Priyo Budi Purwono[3], Retno Handajani[4]

[1]Clinical Student at Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, [2]Lecturer at Department of Internal Medicine, Faculty of Medicine – General Hospital of Dr. Soetomo, Universitas Airlangga, Surabaya, Indonesia, [3]Lecturer at Department of Clinical Microbiology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, [4]Lecturer at Department of Medical Biochemistry, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

Abstract

Background: Chronic hepatitis B is a global burden disease with the mortality rate of over one million around the world because of the complication. In Indonesia the number of hepatitis B sufferers in a healthy population is estimated to reach 4-20.3%, where the figure is higher outside of Java. This study aims to analyze the description of HBeAg serological status in patients with chronic hepatitis B. **Method:** a descriptive study using medical records and sera of patients with chronic hepatitis B was used as primary data. The population of this study were patients with chronic hepatitis B in Gastroenterology and Hepatology Center of Dr. Soetomo General Hospital Surabaya in purposive sampling. The number of samples that fulfilled the inclusion and exclusion criteria was 82 people. **Result:** Most patients are between the ages of 50-59 (29,3%), males (67,1%), HbeAg loss (52,8%) receiving telbivudine (31,5%) and lamivudine (31,5%) as monotherapy for more than two years (42,1%) and have normal ALT (46,3%). **Discussion:** People with inactive (carriers) chronic HBsAg that are characterized by HBsAg last more than six months, also HBeAg negative, have serum ALT levels within normal limits. A temporary increase in ALT before remission can occur in some patients with chronic HBV infection after one year of treatment interruption. **Conclusion:** Telbivudine and lamivudine, separately as monotherapy, demonstrated greater HBeAg loss which reached within more than two years therapy.

Keywords: *chronic hepatitis B, HBeAg loss, ALT normalization, therapy*

Introduction

In the world, it is estimated that more than one million people die each year due to complications of chronic hepatitis B virus (HBV). In Indonesia, the number of hepatitis B sufferers in a healthy population is estimated to reach 4-20.3%.[1, 2]

HBV infection is characterized by the presence of Hepatitis B Surface Antigen (HBsAg) in the serum, which will stay for a long time as long as the virus is still in the body. HBV infection is classified as chronic if HBsAg is positive ≥6 months. Chronic HBV infection is a liver disease due to hepatitis B virus infection where inflammation and necrosis of the liver occur for at least 6 months, during which serum levels of Alanine aminotransferase (ALT) fluctuate fluctuate.[3]

The natural course of HBV infection is influenced by interactions from hosts, viruses, and the environment. HBV infection is transmitted through perinatal, sexual, percutaneous and close relationships between individuals through open wounds. Perinatal transmission is the transmission pathway that causes the most new infections in the world, contributing to 50% of people with positive HBsAg careers.[4] Hepatitis B seropositive Envelope Antigen (HBeAg) indicates active viral replication, and is a significant risk factor for hepatic cirrhosis and hepatocellular carcinoma.[5] HBeAg seroconversion is still considered an important endpoint

Corresponding Author:
Kartika Wensdi Renantriandani
Clinical Student at Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
Campus A, Jl. Mayjen Prof. Dr. Moestopo 47, Surabaya, Indonesia (Zip Code: 60131)
Email: kartikawrt@gmail.com

in the management of chronic HBeAg-positive HBV infection patients.[6]

Method

This study aims to analyze the description of HBeAg serological status in patients with chronic HBV infection. A cross-sectional study using isolates stored in the form of blood serum and the Health Medical Document (HMD) of chronic HBV infection patients was used.

Sample, Research Instrument and Data Analysis

The population were all patients with chronic HBV infection at the Center for Gastroenterology and Hepatology of Internal Medicine General Hospital of Dr. Soetomo Surabaya in 2017. Samples were obtained using a purposive sampling method that patients who met the criteria were 82 subjecs.

The data that has been collected was checked for completeness and carried out coding data (coding) using the McNemar test. The data was analysed using statistical software program Statistical Package for the Social Science (SPSS) version 17.0. (SPSS.Inc., Chicago, IL).

Result

Distribution of Subjects

The most age group of Chronic HBV infection patients who were the subject of the study were aged 50 to 59 years, with the youngest age of 16 years, and the oldest age of 80 years. The mean age of the subjects of this study was 47.5 ± 13.4 years. Based on the data obtained, chronic HBV infection affects more men. The ratio between male and female patients is 2: 1. (Table 1)

Status of Serology Subjects: Status of HBeAg

Past HBeAg status obtained from HMD of study subjects, compared with current HBeAg status obtained from serum ELISA examination of study subjects. After being treated, about 17 (20.7%) HBeAg patients were positive and 65 (79.3%) HBeAg patients were negative. About 36 patients with initial HBeAg status positive, found 19 patients (52.8%) who later became negative. (Table 2)

Current HBeAg Status and Pain Diagnosis, HBeAg Status loss and Duration of Therapy, and HBeAg Status and Types of Therapy

The negative HBeAg status was more prevalent in the study subjects. Positive HBeAg status is most common in asymptomatic chronic hepatitis B cases. BeAg loss was found most in study subjects who had received therapy for more than two years. HBeAg loss was highest in the group receiving telbivudine and lamivudine therapy. HBeAg status that remained positive was found most in the group who had never received therapy. (Table 3)

Biochemical Response of Research Subjects

The mean ALT levels of the subjects of this study were 87.7IU/L with a median of 39.5IU/L. ALT obtained with the normal category at most in patients who have received therapy for one to two years. High ALT levels were highest in patients who have never received therapy. ALT with the normal category was highest in patients on telbivudine therapy. High ALT levels were also highest in patients on telbivudine therapy. (Table 4)

Table 1: Distribution of Respondances

Variable	Frequency	Percentage (%)
Age:		
≤19	4	4,9
20-29	2	2,4
30-39	18	22
40-49	18	22
50-59	24	29,3
60-69	13	15,9
70-79	2	2,4
≥80	1	1,2
Sexuality		
Male	55	67,1
Female	27	32,9

Table 2: Past and current HBeAg status of patients with Chronic Hepatitis B Virus infection

	Frequency	Percentage (%)
Past HBsAg status		
- Positive	36	43.9
- Negative	46	56.1
Current HBeAg Status		
- Positive	17	20.7
- Negative	65	79.3

Table 3: Current HBeAg Status and Pain Diagnosis, HBeAg loss and Duration of Therapy, HBeAg and Types of Therapy

Negative		**Current HBeAg Status**		**Total (%)**
		Positive		
Diagnostic	Chronic Hepatitis B	45 (78,9)	12 (21,1)	57 (100)
	Asymptomatic	16 (76,2)	5 (23,8)	21 (100)
	Cirrhosis Hepatis	4 (100)	0 (0)	4 (100)
	Hepatocellular Carcinoma	65 (79,3)	17 (20,7)	82 (100)
HBeAg loss and duration of therapy				
		Frequency	**Percentage (%)**	
Therapy Duration	<1 years	5	26,3	
	1-2 years	6	31,6	
	>2 years	8	42,1	
HBeAg and Types of Therapy				
		Loss (%)	Positive (%)	
Type of Therapy	Telbivudine	6 (31,5)	4 (23,5)	
	Lamivudine	6 (31,5)	1 (5,9)	
	Tenofovir	4 (21,1)	1 (5,9)	
	Lamivudine + Adefovir	0 (0)	2 (11,8)	
	Interferon	1 (5,3)	0 (0)	
	Telbivudine + Adefovir	1 (5,3)	1 (5,9)	
	Entecavir	0 (0)	0 (0)	
	Tenofovir + Entecavir	0 (0)	1 (5,9)	
	Telbivudine + Tenofovir	1 (5,3)	0 (0)	
	untreatment	0 (0)	6 (35,3)	
	None of data	0 (0)	1 (5,9)	

Table 4: Biochemical responses include the distribution of ALT, duration of therapy, type of therapy

		Frequency		**Percentage (%)**
ALT ≤1 X ULN >1 X ULN None of data		 38 36 8		 46,3 43,9 9,8
		ALT		
		≤1 X ULN (%)	>1 X ULN (%)	None of data (%)
Duration of Therapy	<1 Year	10 (26,3)	9 (25)	3 (37,5)
	1-2 Years	11 (29)	10 (27,8)	1 (12,5)
	>2 Years	7 (18,4)	4 (11,1)	1 (12,5)
	Untreatment	9 (23,7)	12 (33,3)	3 (37,5)
	None of data	1 (2,6)	1 (2,8)	0 (0)
Type of Therapy	Telbivudine	15(39,5)	15(41,6)	1 (12,5)
	Lamivudine	8 (21,1)	8 (21,1)	2 (25)
	Tenofovir	3 (8)	3(8,3)	1 (12,5)
	Lamivudine + Adefovir	1(2,6)	2(5,6)	0 (0)
	Interferon	1(2,6)	1(2,8)	0 (0)
	Telbivudine + Adefovir	1(2,6)	1(2,8)	0 (0)
	Entecavir	1(2,6)	0 (0)	1 (12,5)
	Tenofovir + Entecavir	1(2,6)	1(2,8)	0 (0)
	Telbivudine + Tenofovir	0 (0)	1(2,8)	0 (0)
	Untreatment	6 (15,8)	3(8,3)	3 (37,5)
	None of Data	1(2,6)	1(2,8)	0 (0)

Discussion

The most age group in this study is between 50 to 59 years, amounting to 29.3%. The results of this study were not much different from other studies which stated the most age group of chronic HBV infection patients is between 46 to 55 years or in a similar study found an average age of 56.8 ± 15.8 years with the youngest age 21 years and the oldest age 84 years.[7, 8] The age factor contributes to the incidence of chronic HBV infection, this can be attributed to an increase in the prevalence of HBsAg which is quite large.[9]

Patients with chronic HBV infection are predominantly male, with a ratio of male and female patients of 2: 1.[8, 10, 11] 12 14 This is related to sex hormones which play a role in increasing risk factors for hepatocellular carcinoma. The risk of hepatocellular carcinoma increases due to the active pathway that androgen receptors have in men. In women the process of hepatocarcinogenesis in necrotic hepatocytes is inhibited by Kupffer cells with the role of the hormone estrogen.[12]

All chronic HBV infections have positive HBsAg status. Hepatitis B surface antigen (HBsAg) is the earliest serological sign of HBV infection.[8] A positive HBsAg test result indicates someone has been infected by the hepatitis B virus.[13]

After comparing past and present HBeAg status, it was found that 52.8% of patients experienced HBeAg loss, ie HBeAg was not detected in patients who were initially HBeAg positive. The occurrence of HBeAg loss, with or without anti-HBe seroconversion, in patients with chronic HBV infection is positive HBeAg is an important end result, as it often illustrates immune control in chronic HBV infection.[14]

In the past HBeAg status, the percentage of HBeAg patients was negative at 56.1% and 79.3% in the current HBeAg status. There were more HBeAg negative groups than HBeAg positive.[7] The HBeAg negative group was always more abundant, both in cases of asymptomatic chronic hepatitis B, hepatic cirrhosis, and hepatocellular carcinoma.[15]

Acute exacerbations occur together with high viral replication, ALT increases to five times more than the upper limit of normal and twice more than the baseline, and histological development is a common feature of negative HBeAg groups developing into hepatic cirrhosis faster than in the group HBeAg positive.[16, 17] Persistent cirrhosis and persistently high levels of viremia are the two main risk factors for hepatocellular carcinoma in chronic HBV infection.[18]

HBeAg loss occurred most in the group with a duration of therapy of more than two years and the least occurred with a duration of therapy of less than one year, namely in the order of 42.1% and 26.3%. In the group that had received therapy for one to two years, HBeAg loss was 31.6%.[19]

In this study, the highest HBeAg loss occurred in the group receiving telbivudine and lamivudine therapy, each at 31.5%. HBeAg status that remained positive was found most in the group who had never received therapy. From other studies it can be concluded that telbivudine gives better results compared to entecavir and lamivudine to achieve HBeAg loss during one year of therapy.[19, 20] The occurrence of high HBeAg seroconversion in telbivudine shows that telbivudine not only inhibits viral replication, but also stimulates the patient's immune response. This can be attributed to HBV DNA that depends on the immune system of patients compared to pharmacological suppression.[21]

Patients with chronic HBV infection had an average ALT level of 87.7 IU/L and a median of 39.5 IU/L with the lowest levels of 6 IU/L and the highest 882 IU/L. The most common group was patients with normal ALT levels, which was 46.3 %.[8, 22] People with chronic HBsAg carriers that are characterized by persistent HBsAg for more than six months, as well as negative HBeAg, have serum ALT levels within normal limits.[1, 14]

Normal ALT levels are most common in patients who have been receiving therapy for one to two years. High ALT levels are highest in patients who have never received therapy.[19, 23, 24] Post-therapy monitoring continues, at least for one year every three months to confirm ongoing biochemical responses that are sometimes difficult to evaluate. A temporary increase in ALT before remission can occur in some patients with chronic HBV infection after one year of treatment interruption.[1, 14]

In this study, normal ALT levels were highest in patients on telbivudine therapy. High ALT levels are also highest in patients on telbivudine therapy. In randomized controlled trials (RCTs), it was concluded that telbivudine was better than lamivudine in normalizing ALT.[20]

Conclusion

Telbivudine and lamivudine, separately as monotherapy, demonstrated greater HBeAg loss. Greater HBeAg loss reached within more than two years therapy.

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