Kinetics of Hepatitis B Surface Antigen Level in Chronic Hepatitis B Patients who Achieved Hepatitis B Surface Antigen Loss during Pegylated Interferon Alpha-2a Treatment

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Abstract

Background: Hepatitis B surface antigen (HBsAg) loss/seroconversion is considered to be the ideal endpoint of antiviral therapy and the ultimate treatment goal in chronic hepatitis B (CHB). This study aimed to assess the patterns of HBsAg kinetics in CHB patients who achieved HBsAg loss during the treatment of pegylated interferon (PEG-IFN) α-2a.

Methods: A total of 150 patients were enrolled, composing of 83 hepatitis B envelope antigen (HBeAg)-positive and 67 HBeAg-negative patients. Patients were treated with PEG-IFN α-2a180 μg/week until HBsAg loss/seroconversion was achieved, which occurred within 96 weeks. Serum hepatitis B virus deoxyribonucleic acid and serological indicators (HBsAg, anti-HBs, HBeAg, and anti-HBe) were determined before and every 3 months during PEG-IFN α-2a treatment. Biochemical markers and peripheral blood neutrophil and platelet counts were tested every 1–3 months.

Results: Baseline HBsAg levels were 2.5 ± 1.3 log IU/ml, and decreased rapidly at 12 and 24 weeks by 48.3% and 88.3%, respectively. The mean time to HBsAg loss was 54.2 ± 30.4 weeks, though most patients needed extended treatment and 30.0% of HBsAg loss occurred during 72–96 weeks. Baseline HBsAg levels were significantly higher in HBeAg-positive patients (2.9 ± 1.1 log IU/ml) compared with HBeAg-negative patients (2.0 ± 1.3 log IU/ml; $t = 4.733$, $P < 0.001$), but the HBsAg kinetics were similar. Patients who achieved HBsAg loss within 48 weeks had significantly lower baseline HBsAg levels and had more rapid decline of HBsAg at 12 weeks compared to patients who needed extended treatment to achieve HBsAg loss.

Conclusions: Patients with lower baseline HBsAg levels and more rapid decline during early treatment with PEG-IFN are more likely to achieve HBsAg loss during 96 weeks of treatment, and extended therapy longer than 48 weeks may be required to achieve HBsAg loss.

Key words: Chronic Hepatitis B; Hepatitis B Surface Antigen; Kinetics; Pegylated Interferon Alfa-2a

INTRODUCTION

Chronic hepatitis B (CHB) is a serious liver disease worldwide and is the leading cause of cirrhosis and hepatocellular carcinoma (HCC).[1] Antiviral therapy is the most effective intervention to slow the disease progression and preventing the occurrence of hepatic cancer and cirrhosis. Hepatitis B envelope antigen (HBeAg) seroconversion may be a strong predictor of improved clinical outcome in HBeAg-positive patients after interferon (IFN) treatment.[2] However, a long-term follow-up study showed cumulative probabilities of hepatitis relapse in inactive HBsAg carriers of 10.2%, 17.4%, 19.3%, 20.2%, and 20.2% after 5, 10, 15, 20, and 25 years of follow-up, respectively, with an annual rate of 1.55%.[3] Another long-term longitudinal study (up to 23 years) showed that 1–17% of inactive carriers reverted back to HBeAg-positive chronic hepatitis.[4] Cirrhosis and HCC may still develop in some inactive hepatitis B surface

antigen (HBsAg) carriers.[3] Interestingly, no cirrhosis or HCC occurred in patients with HBsAg loss after IFN treatment, indicating that HBsAg clearance is currently the only parameter associated with an excellent long-term prognosis.[5] HBsAg loss/seroconversion is considered to be the ideal endpoint of antiviral therapy in both HBeAg-positive and -negative patients,[6] and the ultimate treatment goal in CHB.[7] However, HBsAg loss is rare in the natural course of CHB infection, with an annual rate of only 1.15%,[3] though treatment with pegylated (PEG)-IFN α-2a for 48 weeks can increase the incidence of HBsAg loss to 3%.[8]

PEG-IFN α-2a treatment is expensive and may be associated with adverse effects, and it is, therefore, crucial to identify those patients most likely to achieve HBsAg loss as a result of IFN-based therapy.[9]

We performed a retrospective study to assess the clinical characteristics and patterns of HBsAg kinetics in 150 CHB patients who achieved HBsAg loss/seroconversion during treatment with PEG-IFN α-2a. As a retrospective study, there were no shedding cases or dropouts in our entire study. In this study, only the data for clinical indicators were collected from the CHB patients during the IFN-treatment period, and all patients are currently being followed up. To the best of our knowledge and PubMed search results, this is the largest study enrolled 150 HBsAg loss/seroconversion patients during PEG-IFN α-2a treatment in the world.

METHODS

Patients

The study population comprised 150 consecutive patients with CHB who achieved HBsAg loss/seroconversion during 96 weeks of PEG-IFN α-2a therapy at the Department of Hepatology of Beijing Ditan Hospital from December 2008 to May 2016. All patients had no contraindication to PEG-IFN therapy, aged from 18 to 55 years. HBsAg loss is designated as HBsAg from positive to negative, and anti-HBs is still negative; whereas, HBsAg seroconversion is designated as HBsAg from positive to negative, and the anti-HBs from negative to positive. Participants included naïve patients, patients reached undetectable levels of serum hepatitis B virus deoxyribonucleic acid (HBV DNA) on nucleoside (acid) analogs (NA) treatment and those were HBV DNA-positive on NA treatment composing of relapse, resistance, or poor response.

All patients were positive for HBsAg and negative for anti-HBs before treatment of PEG-IFN α-2a. The exclusion criteria included active consumption of alcohol and/or drugs, coinfection with human immunodeficiency virus or hepatitis C virus, cirrhosis, autoimmune hepatitis, evidence of neoplastic liver disease, and contraindications to IFN.

Patients received PEG-IFN α-2a 180 μg/week by subcutaneous injection until HBsAg loss/seroconversion was achieved. Serum HBV DNA and serological indicators (HBsAg, anti-HBs, HBeAg, and anti-HBe) were determined before and every 3 months during PEG-IFN α-2a treatment. Biochemical markers and peripheral blood neutrophil and platelet counts were tested every 1–3 months. HBsAg loss was defined as HBsAg <0.05 IU/ml, and seroconversion was defined as HBsAg loss with anti-HBs level ≥10 mIU/ml. Undetectable serum HBV DNA after treatment was considered as a response. The study was conducted according to the guidelines of the *Declaration of Helsinki* and approved by the Ethics Committees of Beijing Ditan Hospital, Capital Medical University. All patients gave their written informed consent.

Laboratory measurements

HBsAg was quantified using the Architect HBsAg QT assay (Abbott Laboratories, Abbott Park, IL, USA; dynamic range, 0.05–250.00 IU/ml). If HBsAg levels were >250 IU/ml, samples were diluted 1:500 with Architect HBsAg diluents to obtain a reading within the range of the calibration curve. Anti-HBs (range 0–1000 mIU/ml), HBeAg, and anti-HBe were detected using Abbott Architect i2000 kits (Abbott Laboratories), based on an automated chemiluminescent microparticle immunoassay. Serum HBV DNA was quantitated using a commercially available real-time fluorescence quantitative polymerase chain reaction kit with a limit of detection of 500 copies/ml (Piji Company, Shenzhen, China). Liver function parameters, including serum alanine aminotransferase (ALT), aspartate aminotransferase, albumin, and total bilirubin levels, were measured using an automated biochemical analyzer (Hitachi 7600-11; Hitachi, Tokyo, Japan). Peripheral blood neutrophils and platelets were counted using an automatic blood cell analyzer (Beckman Coulter LH750, USA).

Statistical analysis

Statistical analysis was performed using SPSS (version 11.5, SPSS Inc., Chicago, IL, USA). Serum HBV DNA levels and HBsAg concentrations were logarithmically transformed for analysis. Continuous variables were expressed as mean ± standard deviation (SD) or median (range), and categorical variables as absolute and relative frequencies. Characteristics were compared between groups using Mann-Whitney or two-sample Student's t-tests for analysis of continuous variables, and Chi-square or Fisher's exact tests for analysis of categorical variables and Mann-Whitney and two-sample Student's t-tests for analysis of continuous variables, as appropriate. A two-sided $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

Among a total of 1215 CHB patients, 680 HBeAg-positive and 535 HBeAg-negative, treated with PEG-IFN α-2a, 150 patients composing 83 HBeAg-positive and 67 HBeAg-negative patients who obtained HBsAg loss/seroconversion during PEG-IFN α-2a treatment were enrolled for analysis. One hundred and one patients

were naïve, and 49 patients experienced NA treatment (20 lamivudine, 18 entecavir, 8 adefovir dipivoxil, and 3 telbivudine) for a median of 24 months (range: 6–108 months), in which 38 patients with undetectable HBV DNA load and 12 patients with positive for serum HBV DNA load.

The baseline HBsAg level in all patients was 2.5 ± 1.3 log IU/ml, and the levels were significantly higher in HBeAg-positive (2.9 ± 1.1 log IU/ml) compared with HBeAg-negative patients (2.0 ± 1.3 log IU/ml; $t = 4.733$, $P < 0.001$). The overall baseline serum HBV DNA load was 5.3 ± 1.8 log copies/ml, and this was also significantly higher in HBeAg-positive (5.9 ± 1.6 log copies/ml) than in HBeAg-negative patients (4.3 ± 1.7 log copies/ml; $t = 4.249$, $P < 0.001$). Baseline HBsAg levels were significantly lower in patients with undetectable HBV DNA on NA treatment compared with patients who remained serum HBV DNA-positive (1.8 ± 1.3 log IU/ml vs. 2.7 ± 1.2 log IU/ml; $t = 4.010$, $P < 0.001$). The mean serum ALT level was 219.6 ± 355.0 U/L, and 25.3% of patients had ALT levels ≥5 upper limit of normal (ULN), including 15.3% of patients with ≥10 ULN [Table 1].

Virological response

Among 112 patients who were HBV DNA-positive before treatment, serum HBV DNA reached undetectable levels within 60 weeks (median: 15; Q1, Q3: 11–26), and cumulatively, 34.8%, 72.3%, and 91.1% of viral response occurred at 12, 24, and 48 weeks [Figure 1]. The time to viral response was significantly longer in HBeAg-positive patients compared to HBeAg-negative patients (18.5 weeks vs. 14.0 weeks; $t = 3.081$, $P = 0.003$) [Table 2].

Treatment time to hepatitis B surface antigen clearance

The study population comprised 150 consecutive patients with CHB who all achieved HBsAg loss during PEG-IFN α-2a therapy. Among 150 patients, there were 117 patients who achieved HBsAg seroconversion. The treatment time to HBsAg loss and seroconversion were 54.2 ± 30.3 weeks (median, 53.0; Q1, Q3, 25.0–80.0) and 56.5 ± 28.5 weeks (median, 55.5; Q1, Q3, 28.0–77.0), respectively. However, 55.3% of HBsAg loss/seroconversion occurred after extended treatment (longer than 48 weeks), and 30.0% occurred during weeks 72–96 of treatment [Figure 2]. The time to HBsAg loss was significantly longer in HBeAg-positive patients compared with HBeAg-negative patients (62.0 weeks vs. 41.0 weeks; $t = 2.905$, $P = 0.004$) [Table 2], and patients with higher HBsAg levels needed longer treatment than patients with lower HBsAg levels to achieve HBsAg loss ($F = 10.091$, $P < 0.001$) [Figure 3].

Serum hepatitis B surface antigen kinetics

Among all patients, HBsAg levels decreased significantly at 12 and 24 weeks, with declines of 1.6 ± 1.5 log IU/ml and 2.3 ± 1.4 log IU/ml (48.3% and 88.3% of baseline), respectively [Table 2]. HBsAg levels at 48 weeks reached <100 IU/ml in 93.3% (140/150) of patients and only one patient had HBsAg levels >1000 IU/ml. The kinetics of HBsAg decline was similar in HBeAg-positive and -negative patients [Figure 4]. In HBeAg-positive

Table 1: Demographic and baseline characteristics of study population

Characteristics	All patients (n = 150)	HBeAg-positive patients (n = 83)	HBeAg-negative patients (n = 67)	Statistical values	P
Age (years), mean ± SD	32.3 ± 10.9	29.8 ± 10.3	35.4 ± 11.0	3.198*	0.002
Gender (male/female), n	106/44	54/29	52/15		0.107
NA-naïve, n (%)	101 (67.3)	53 (63.9)	48 (71.7)		0.382
Patients reached viral response on-NAs, n (%)	37 (24.7)	21 (25.3)	16 (23.9)	0.040†	0.841
Baseline HBV DNA load (log copies/ml), mean ± SD	5.3 ± 1.8	5.9 ± 1.6	4.3 ± 1.7	4.249*	<0.001
ALT levels					
Values (U/L), mean ± SD	219.6 ± 355.0	259.4 ± 363.6	170.3 ± 340.3	1.535*	0.127
Values (U/L), median (Q1–Q3)	66 (28−201)	105 (42−223)	41 (21−98)		
<1 ULN, n (%)	51 (34.0)	18 (21.7)	33 (49.3)		
1 ULN ≤values <2 ULN, n (%)	29 (19.3)	15 (18.1)	14 (20.9)		
2 ULN ≤values <5 ULN, n (%)	32 (21.3)	24 (28.9)	8 (11.9)		
5 ULN ≤values <10 ULN, n (%)	15 (10.0)	11 (13.3)	4 (6.0)		
≥10 ULN, n (%)	23 (15.3)	15 (18.1)	8 (11.9)		
Baseline HBsAg level					
Values (log IU/ml), mean ± SD	2.5 ± 1.3	2.9 ± 1.1	2.0 ± 1.3	4.733*	<0.001
<1 log IU/ml, n (%)	15 (10.0)	4 (4.8)	11 (16.4)	23.797†	<0.001
1 log IU/ml ≤values <2 log IU/ml, n (%)	28 (18.7)	10 (12.0)	18 (26.9)		
2 log IU/ml ≤values <3 log IU/ml, n (%)	48 (32.0)	24 (28.9)	24 (35.8)		
3 log IU/ml ≤values <4 log IU/ml, n (%)	47 (31.3)	33 (39.8)	14 (20.9)		
≥4 log IU/ml, n (%)	12 (0.8)	12 (14.5)	0		

*Student's ttest; †Chi-square test; others using Fisher's exact test. NAs: Nucleoside (acids) analogues. SD: Standard deviation; HBsAg: Hepatitis B surface antigen; ALT: Alanine aminotransferase; ULN: Upper limit of normal; HBV DNA: Hepatitis B virus deoxyribonucleic acid.
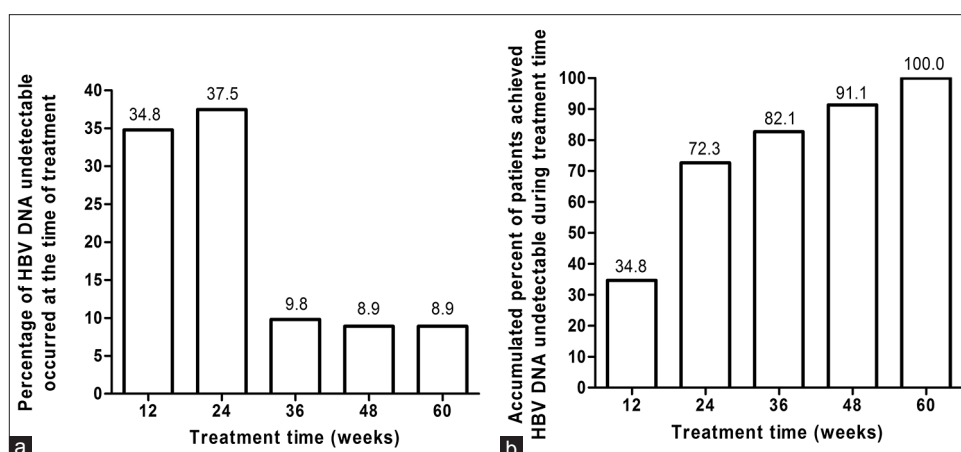
Figure 1: Viral response during treatment. Most patients achieved hepatitis B virus deoxyribonucleic acid response after 24 weeks treatment (a), and all patients reached serum hepatitis B virus deoxyribonucleic acid undetectable within 60 weeks of treatment (b).

Table 2: Viral and HBsAg responses during treatment

Variables	All patients (n = 150)	HBeAg-positive patients (n = 83)	HBeAg-negative patients (n = 67)	t	P
Time to viral response (weeks)				3.081	0.003
Mean ± SD	21.7 ± 13.4	24.8 ± 15.1	17.2 ± 9.0		
Median (Q1–Q3)	15.0 (11.0–26.0)	18.5 (11.0–37.0)	14.0 (11.0–20.0)		
HBsAg decrease at 12 weeks (log IU/ml)				0.899	0.370
Mean ± SD	1.6 ± 1.5	1.7 ± 1.6	1.5 ± 1.3		
Median (Q1–Q3)	1.1 (0.2–2.7)	1.3 (0.2–2.7)	1.0 (0.3–2.7)		
Percentage of HBsAg decline at 12 weeks (%), median (Q1–Q3)	48.3 (47.2–99.7)	40.7 (34.0–99.4)	56.3 (47.2–99.7)	1.379	0.171
HBsAg decline at 24 weeks (log IU/ml)				0.286	0.775
Mean ± SD	2.3 ± 1.4	2.3 ± 1.6	2.3 ± 1.2		
Median (Q1–Q3)	2.2 (1.1–3.4)	1.9 (0.9–3.6)	2.3 (1.2–3.3)		
Percentage of HBsAg decline at 24 weeks (%), median (Q1–Q3)	88.3 (60.9–100.0)	85.9 (53.5–100.0)	92.3 (70.4–100.0)	0.066	0.948
Time HBsAg loss (weeks)				2.905	0.004
Mean ± SD	54.2 ± 30.3	60.6 ± 29.8	46.5 ± 29.3		
Median (Q1–Q3)	53.0 (25.0–80.0)	62.0 (38.0–85.0)	41.0 (21.0–71.0)		
Patients with seroconversion, n (%)	117 (78.0)	67 (80.7)	50 (74.6)		0.430*
Time to HBsAg seroconversion (weeks)				2.420	0.017
Mean ± SD	56.5 ± 28.5	61.9 ± 28.2	49.3 ± 27.5		
Median (Q1–Q3)	55.5 (28.0–77.0)	62.5 (39.0–85.0)	49.5 (24.0–70.0)		

*Fisher's exact test. SD: Standard deviation; HBsAg: Hepatitis B surface antigen.

patients, HBsAg levels decreased by 40.7% and 85.9% of baseline, at 12 and 24 weeks, and those in HBeAg-negative patients were 56.3% and 92.3% [Table 2].

However, baseline HBsAg levels were significantly lower and HBsAg decrease at 12 weeks was more rapid in patients who achieved HBsAg loss within 48 weeks, compared to those who needed extended treatment longer than 48 weeks to achieve HBsAg loss (2.0 ± 1.4 log IU/ml vs. 3.0 ± 0.9 log IU/ml; $t = 5.171$, $P < 0.001$) and (77.2% vs. 29.2%; $t = 2.461$, $P = 0.015$), respectively [Figure 5].

DISCUSSION

HBsAg is the most important serological marker of HBV infection, and serum HBsAg level correlates with the intrahepatic amount and transcriptional activity of covalently closed circular DNA (cccDNA), the main replicative template of HBV.[10] HBsAg loss and seroconversion to anti-HBs is generally considered to be the ultimate goal of therapy, indicating a complete response to treatment and the resolution of the disease. It reflects immunological control of the infection and confers an excellent prognosis in the absence of preexisting cirrhosis or concurrent infections with other viruses.[11]

IFN has antiviral and immunomodulatory properties that result in direct inhibition of viral replication and enhancement of the cell-mediated immune response in the process of virus clearance. Reportedly, PEG-IFN therapy can only achieve 30–40% HBeAg seroconversion in HBeAg-positive patients, 19.2–40.0% sustained viral response (SVR) after cessation
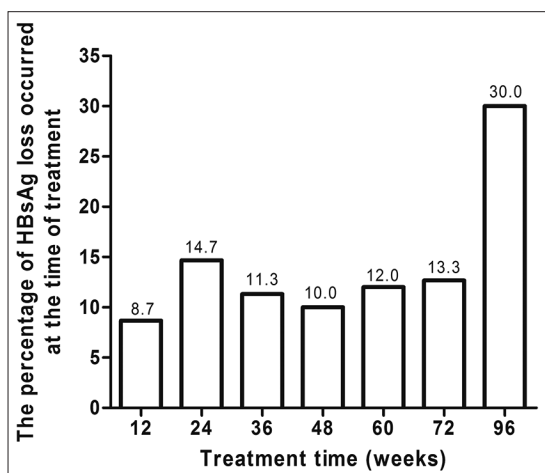
Figure 2: Proportion of and time to hepatitis B surface antigen loss during pegylated interferon α-2a treatment. More than half of hepatitis B surface antigen loss occurred after extended treatment and one-third of patients needed 96 weeks of treatment to achieving hepatitis B surface antigen loss.
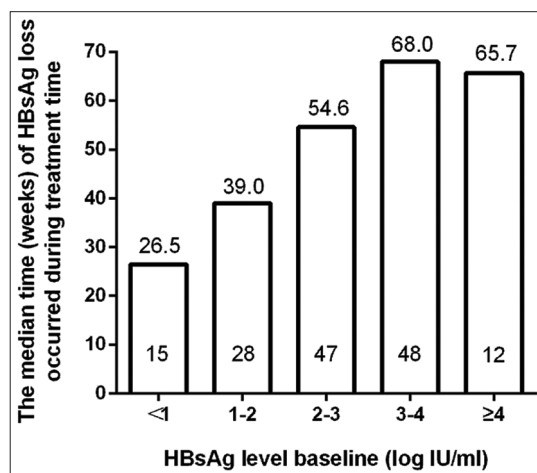

Figure 3: Time to hepatitis B surface antigen loss on the basis of baseline hepatitis B surface antigen levels. The longer treatment time was needed in patients with higher baseline of hepatitis B surface antigen level for hepatitis B surface antigen loss.
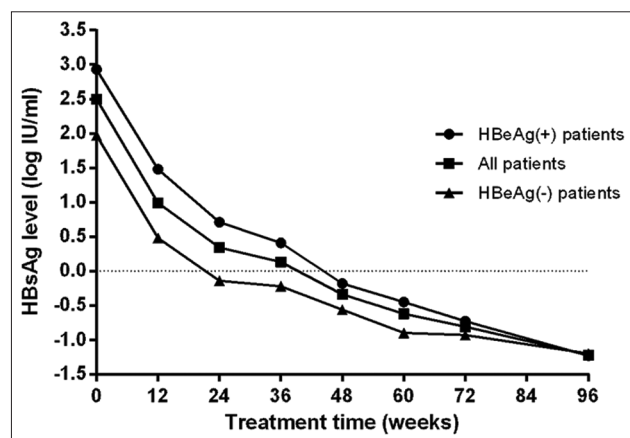

Figure 4: Kinetics of hepatitis B surface antigen levels during pegylated interferon treatment. HBeAg-positive patients had higher hepatitis B surface antigen level baseline than HBeAg-negative patients, however, their kinetics during treatment were similar.
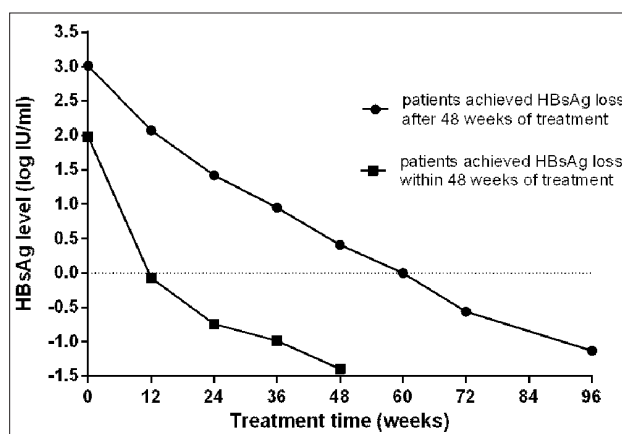

Figure 5: Kinetics of hepatitis B surface antigen levels in patients who achieved hepatitis B surface antigen loss within and after 48 weeks. Patients achieved hepatitis B surface antigen loss within 48 weeks of treatment had a lower hepatitis B surface antigen level baseline and sharp hepatitis B surface antigen decline during treatment compared with patients obtained hepatitis B surface antigen loss by extended treatment.

of therapy in HBeAg-negative patients,[12] and 2.0–7.0% HBsAg loss/seroclearance,[8,13] which remains far from satisfactory. Even if HBeAg seroconversion and SVR are well-recognized, continuous long-term viral suppression does not ensure HBsAg clearance when treatment is discontinued. Therefore, it is important to identify pretreatment and on-treatment parameters for predicting patient response and nonresponse to IFN, especially with the aim of identifying patients likely to achieve HBsAg loss.

Well-known predictors of an SVR include low baseline HBV DNA, high ALT levels, younger age, female gender, and HBV genotype. Sustained responders tend to have lower baseline HBsAg and HBV DNA than nonsustained responders.[14] Low baseline HBsAg was shown to be more reliable than serum HBV DNA levels for predicting good response to PEG-IFN and lamivudine treatment in HBeAg-positive patients.[15,16] An important clinical characteristic of patients

in the present study was low baseline HBsAg levels; 2.9 ± 1.1 log IU/ml and 2.0 ± 1.3 log IU/ml in HBeAg-positive and- negative patients, respectively. However, HBsAg levels of 3.0–4.4 log IU/ml and 2.5–4.0 log IU/ml have been previously reported in HBeAg-positive and -negative patients in similar studies.[17] Although there were no control groups involving patients without HBsAg loss during PEG-IFN treatment in the current study, others demonstrated that low baseline HBsAg level was the only significant prognostic predictor of HBsAg seroconversion following conventional IFN treatment.[18,19] These results suggest that CHB patients with low HBsAg levels should be considered PEG-IFN therapy to achieve HBsAg loss.

A 48-week course of PEG-IFN is recommended for CHB;[6] however, only 3% of patients obtained HBsAg loss after this recommended course. Long-term follow-up of PEG-IFN

trials showed continuing HBsAg loss up to 11% at 3 and 4 years after stopping treatment,[20] but only 63% of HBeAg-negative patients had HBV DNA ≤400 copies/ml 3 years after treatment, despite HBsAg levels ≤19 IU/ml at the end of 48 weeks of treatment.[21] This suggests that individualized treatment programs may be needed to consider extending the duration of therapy for CHB. Extended duration of therapy can increase the rate of SVR in HBeAg-negative patients treated with either standard or PEG-IFN therapies,[22] and can enhance the rate of HBeAg seroconversion after treatment in HBeAg-positive patients,[23] and the rate of HBsAg clearance after or during treatment.[23-25] In the present study, more than half of the HBsAg clearance occurred after extended treatment, with 30.0% of patients needing treatment for 72–96 weeks to achieve HBsAg loss. This indicates that extended treatment was essential for HBsAg clearance during PEG-IFN-based therapy.

Treatment should be optimized by careful patient selection and individualized treatment decisions in order to increase the success rate of IFN treatment and to minimize the risk of adverse events. Many studies have demonstrated that decrease of HBsAg during treatment was predictor of response and indicator for stopping IFN. HBsAg <1500 IU/ml at 12 weeks[26,27] and at 24 weeks[28,29] were associated with and predictive of HBeAg seroconversion after IFN treatment in HBeAg-positive patients. A decrease in HBsAg levels compared to baseline predicted SVR in HBeAg-negative patients.[18] Moreover, a decline in HBsAg was also significantly associated with HBsAg clearance after IFN treatment.[21] However, the pattern of HBsAg decline in patients who achieved HBsAg clearance during IFN treatment remains unclear.

The present study showed that HBsAg levels decreased by 48.3% and 88.3% at 12 and 24 weeks, respectively, while 93.3% of patients achieved HBsAg <100 IU/ml and nearly all patients achieved HBsAg <1000 IU/ml. Although HBsAg levels in HBeAg-positive patients were higher than those in HBeAg-negative patients, the patterns of decline during treatment were similar in both groups. These results suggest that a rapid decline in HBsAg levels, regardless of baseline, is essential for HBsAg clearance during PEG-IFN treatment in both HBeAg-positive and -negative patients. Notably, baseline HBsAg levels were significantly lower and the degree of HBsAg decline at 12 weeks was significantly greater in patients who achieved HBsAg loss within 48 weeks, compared with those who needed extended treatment to achieve HBsAg loss. Thus, patients who achieve HBsAg loss within 48 weeks should have characteristics of lower baseline levels, sharp and rapid decline at early treatment time.

A decline in serum HBV DNA reflects a reduction in viral replication while a decline in serum HBsAg represents a reduction in the translation of mRNAs produced from transcriptionally-active cccDNA or integrated sequences.[30] The viral response during treatment alone may not represent a reliable indicator of SVR to antiviral therapy, and the kinetics of HBV DNA and HBsAg level are dissociated in NA-treated patients and relapsers to PEG-IFN. Several studies have shown that combining cutoff levels for HBsAg and HBV DNA can reliably identify patients with inactive disease,[31,32] and that HBsAg and HBV DNA kinetics are parallel in sustained responders to PEG-IFN.[13,21,33]

In the present study, all patients who were HBV DNA-positive before IFN treatment achieved viral response within 60 weeks, most within 48 weeks. However, most patients needed extended treatment for HBsAg clearance, suggesting that a strong immune response stimulated by IFN treatment could efficiently control viral replication and clear HBV-infected hepatocytes. Viral response was the essential condition for HBsAg clearance during IFN-based therapy.

In summary, the results of this study demonstrate that patients with lower baseline HBsAg sustained and rapid decline of HBsAg during treatment, and early viral response are more likely to achieve HBsAg clearance[34] during IFN-based therapy. However, most patients needed extended treatment longer than 48 weeks to achieve HBsAg loss during treatment.

Conflicts of interest

There are no conflicts of interest.

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