Predictors of response to pegylated interferon treatment in HBeAg-negative patients with chronic hepatitis B

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Abstract

Introduction: Although pegylated interferons (pegIFNs) alpha-2a and alpha-2b have been used in chronic hepatitis B (CHB) treatment for many years, there are few studies concerning predictors of sustained virologic response (SVR) to pegIFN therapy. In this study, we aimed to investigate the predictors of response to pegIFN treatment in cases with HBeAg-negative CHB infection.

Methodology: Seventeen tertiary care hospitals in Turkey were included in this study. Data from consecutively treated HBeAg-negative CHB patients, who received either pegIFN alpha-2a or alpha-2b, were collected retrospectively. SVR is defined as an HBV DNA concentration of less than 2,000 IU/mL six months after the completion of therapy.

Results: SVR was achieved in 40 (25%) of the 160 HBeAg-negative CHB patients. Viral loads in patients with SVR were lower compared to those with no SVR, beginning in the third month of treatment (p < 0.05). The number of cases with a decline of 1 log_{10} IU/mL in viral load after the first month of treatment and with a serum HBV DNA level under 2,000 IU/mL after the third month of treatment was higher in cases with SVR (p < 0.05). The number of patients who had undetectable HBV DNA levels at week 48 among responders was significantly greater than among post-treatment virological relapers (p < 0.05).

Conclusions: Detection of a 1 log_{10} decline in serum HBV DNA level at the first month of treatment and a serum HBV DNA level < 2000 IU/mL at the third month of therapy may be predictors of SVR.

Key words: hepatitis B; interferon; sustained virological response; viral load.


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Introduction

Chronic hepatitis B (CHB) infection is a global health problem affecting approximately 400 million individuals all over the world. Cirrhosis, liver failure, or hepatocellular carcinoma (HCC) are long-term complications [1]. The main purpose in CHB treatment is to suppress virus replication [2]. By sustained suppression of viral replication, most long-term complications may be prevented. When hepatitis B virus deoxyribonucleic acid (HBV DNA) is > 10^6
copies/mL, the risk of HCC is increased, whereas the risk is decreased when HBV DNA is < 10^4 copies/mL [3,4]. Additionally, if serum HBV DNA level becomes undetectable, then hepatitis B surface antigen (HBsAg) clearance could be expected and liver fibrosis would be expected to regress [5].

Nucleos(t)ide analogues and pegylated interferons (s) are used in CHB treatment. The most significant advantage of pegIFNs is the induction of a sustained viral response with their use in a definite period of time. Moreover, more HBsAg loss may be observed in patients with virological response induced by pegIFN treatment. The most significant disadvantages of pegIFNs are parenteral administration, high annual costs, serious side effects, and the fact that therapeutic success is achieved in only a limited number of patients. [6-8].

Treatment of CHB should be considered: (1) when serum HBV DNA levels are above 2,000 IU/mL and serum alanine aminotransferase (ALT) levels are above the upper limit of normal (ULN), and (2) in patients over 35 years of age who have a serum HBV DNA level > 2,000 IU/mL and normal ALT levels. Treatment should be administered to patients who have a moderate to high histological activity index or a fibrosis score in liver biopsy according to Ishak score [9]. Meanwhile, the American Association for the Study of Liver Diseases (AASLD) guideline suggests treatment for patients who have ALT ≥ 2× ULN with serum HBV DNA levels greater than or equal to 20,000 IU/mL [10].

Pre-treatment serum HBV DNA level (HBV DNA < 10^5 IU/mL), ALT level (above 3×ULN), histological activity grade, and fibrosis stage (at least A2 by METAVIR scoring) are important factors for predicting treatment response in HBeAg-positive patients [11]. Additionally, better response is obtained in patients infected with genotypes A and B rather than genotypes C and D [12]. Therefore, pegIFN treatment is preferred only in selected patient groups with high response probabilities.

HBV genotype D is the predominant genotype in our country, and the response rate of patients infected with this genotype to interferon therapy is quite low [13]. In previously reported studies, sustained virological response (SVR) was detected in 21%–29% of HBeAg-negative patients infected with HBV genotype D [14,15]. The number of studies concerned with predictors of response to interferons is limited. In the present study, we aimed to investigate the response rates to pegIFN therapy in HBeAg-negative CHB cases and to determine the factors affecting the treatment response.

Methodology

Study design

The present retrospective study was conducted by assessing the clinical records of HBeAg-negative CHB patients. Ten consecutive HBeAg-negative CHB cases who were treated with pegIFNs between 2008 and 2010 from each center were to be involved. Twenty centers from different regions of the country were contacted. A total of 19 investigators from 17 centers agreed to participate in the study. A patient follow-up form (PFF) was prepared, containing questions regarding demographical data and laboratory parameters, which were completed by the participants in all of the centers between 1 January 2011 and 1 January 2012. However, fewer patient data were received than were required from some centers. Therefore, this trial involved 160 eligible patients.

The local ethics committee approval was provided from the Duzce University Medical School (26 August 2010/57).

Data recorded on PFF

Patients’ demographical characteristics (age, gender), serologic test results (HBeAg, AntiHBe, HBsAg), baseline serum HBV DNA levels, findings on liver biopsy (histologic activity index (HAI), fibrosis score), baseline biochemical tests (ALT and AST, gamma-glutamyl transferase [GGT]), baseline hematologic test (platelet, leukocyte, haemoglobin) values, and the results of serum HBV DNA level, biochemical and hematologic tests at the 4th, 12th, 24th, 36th, 48th, and 72nd weeks of pegIFN treatment were recorded.

Patients

Adult patients with chronic hepatitis B whose treatment was planned as 48-week pegIFN-alpha 2a 180 microgram/week or pegIFN-alpha 2b 1.5 microgram/kg/week were enrolled in the study after assessment of their eligibility at the trial coordinating center.

Inclusion criteria for the patients were hepatitis B surface antigen (HBsAg) positivity for at least six months, HBeAg negative and anti-HBe positive patients plus:

- age between 18 and 65 years,
- pre-treatment serum HBV DNA level > 2,000 IU/mL,
• histological activity index > 4 and/or fibrosis ≥ 2 graded according to modified Ishak scoring of the liver biopsy findings performed within the last 24 months (assessed by a local pathologist at each center), and
• antiviral and interferon therapy naïve patients. Exclusion criteria for the patients were:
• coinfection with hepatitis C virus, hepatitis D virus or human immunodeficiency virus,
• co-existing disease (Wilson disease, hemochromatosis, autoimmune diseases, hepatocellular carcinoma or other malignant diseases, uncontrollable diabetes, hyperthyroidism, advanced heart, lung or renal failure) or pregnancy,
• history of therapy with systemic corticosteroids, antineoplastic or immunomodulator drugs, and
• any abnormal laboratory findings such as a neutrophil count of less than 1,500/mm$^3$, a platelet count of less than 90,000/mm$^3$, and/or a serum creatinine level that was more than 1.5 times the upper limit of the normal range.

Laboratory tests
Serum HBV DNA levels and biochemical and hematological tests were performed at the participating centers by automated techniques. Serum HBV DNA levels in different units (some centers reported as copy/mL while some reported as IU/mL) were accepted. For standardization, copy/mL units were converted to IU/mL (assuming 1 U/mL = 5.82 copies) [16].

Cases that were scored according to the HAI (grade) and fibrosis (stage) of the modified Ishak method were included in the study [17].

Efficacy criteria
Efficacy analyses included all patients who received at least one dose of pegIFN. The criteria below were implemented in evaluating the effectiveness of the treatment [2]. The data of the patients with treatment failure were included until the end of each patient’s treatment.

Primary non-response is defined as less than 1 log$\text{}_{10}$ IU/mL decline in serum HBV DNA level from baseline at three months of therapy [9].

Virological non-response is defined as serum HBV DNA level > 2,000 IU/mL at the end of week 48. If patients discontinued the treatment due to adverse events, without achieving HBV DNA negativity, they were also regarded as having treatment failures [2].

Virological response (VR) is defined as serum HBVDNA level < 2,000 IU/mL at the end of week 48 [2].

Sustained virological response (SVR) is defined as serum HBVDNA level < 2,000 IU/mL at week 72 [2].

Biochemical response (BR) is defined as ALT normalization at week 48 [2].

Sustained biochemical response (SBR) is defined as ALT normalization at week 72 [2].

Serological response is defined as HBsAg seroconversion (defined by HBsAg clearance and the development of anti-HBs antibody) [2].

Post-treatment virological relapse is defined as serum HBV DNA level of < 2,000 IU/mL at the end of treatment but > 2,000/mL at 24 weeks post-treatment (at week 72) [9].

Statistical methods
Frequency tables were presented for categorical variables and descriptive statistics (average, standard deviation, median, minimum, and maximum) were presented for continuous variables. Cross-table statistics were presented for inter-group categorical comparisons and their significance levels were tested with the Chi-square test and Fisher’s exact test. Continuous variables with normal distribution were compared by student’s t test, whereas those with abnormal distribution were compared by the Mann-Whitney U test. The statistical significance level was accepted as $p < 0.05$.

Results
The retrospective data of 160 HBeAg-negative CHB patients (42 females and 118 males) from 17 centers in Turkey were evaluated in this study. The mean age of the patients was 39.6 years. Mean ALT value was 124 U/L. While ALT levels of 12 (7.5%) patients were within the normal ranges, 64 (40%) patients had ALT levels > 3×ULN. Mean serum HBV DNA level of the study group was 16,220,516 IU/mL (min: 2471 IU/mL; max: 460,000,000 IU/mL). Among the patients, 28 (17.5%) had serum HBV DNA levels > 10,000,000 IU/mL, and 76 (47.5%) had HBV DNA levels < 1,000,000 IU/mL. Baseline demographic and other characteristics of patients are shown in Table 1.

Out of the 160 patients involved in this study, 132 completed the whole planned duration of 48-week therapy. Twenty-eight patients did not complete the treatment because of the side effects of pegIFN or because of primary non-response.
Table 1. Baseline characteristics of patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients</th>
<th>Responders* n = 40</th>
<th>Non-responders n = 120</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>39.64 ± 10.68</td>
<td>25-40.5-60 (40.1±10.51)</td>
<td>19-37-64</td>
<td>39.5 ± 10.8</td>
</tr>
<tr>
<td>Gender (F/M) (n)</td>
<td>42/118</td>
<td>8/32</td>
<td>34/86</td>
<td>0.29</td>
</tr>
<tr>
<td>ALT U/L</td>
<td>124 ± 87.27</td>
<td>33-87.5-451 (122.8 ± 93.4)</td>
<td>34-97.5-484 (125.2 ± 85.6)</td>
<td>0.55</td>
</tr>
<tr>
<td>AST U/L</td>
<td>77 ± 63.25</td>
<td>19-53-318 (82.1 ± 73.9)</td>
<td>12-59-412 (75.3 ± 59.5)</td>
<td>0.68</td>
</tr>
<tr>
<td>GGT U/L</td>
<td>38 ± 74.55</td>
<td>17-35-124 (44 ± 26.5)</td>
<td>6-30-129 (36.1 ± 21)</td>
<td>0.13</td>
</tr>
<tr>
<td>Normal ALT level, &lt;40 U/L (n)</td>
<td>13</td>
<td>5</td>
<td>8</td>
<td>0.19</td>
</tr>
<tr>
<td>Histologic activity index</td>
<td>1-7-17 (7.54 ± 3.01)</td>
<td>2-8-17 (8.36 ± 3.33)</td>
<td>1-7-15 (7.27 ± 2.86)</td>
<td>0.10</td>
</tr>
<tr>
<td>Fibrosis score**</td>
<td>1.91 (0-5)</td>
<td>0-1.5-4 (1.82 ± 1.03)</td>
<td>0-2-5 (1.95 ± 1.1)</td>
<td>0.46</td>
</tr>
<tr>
<td>HBV DNA log_{10} IU/mL</td>
<td>7.21 ± 1.15</td>
<td>3.39-5.65-8.35 (7.09 ± 1.24)</td>
<td>3.69-6.8-6.66</td>
<td>7.24 ± 1.12</td>
</tr>
</tbody>
</table>

*Patients who had sustained virological response; **Scored according to the modified Ishak method [17]

Table 2. Hematological findings of responders and non-responders during treatment.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Responders* n = 40</th>
<th>Non-responders n = 120</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count K/uL (mean ± SD)</td>
<td>6475 ± 1600</td>
<td>6019 ± 1519</td>
<td>0.12</td>
</tr>
<tr>
<td>Hemoglobin K/uL (mean ± SD)</td>
<td>14.9 ± 1.63</td>
<td>14.7 ± 1.42</td>
<td>0.45</td>
</tr>
<tr>
<td>Platelet count K/uL (mean ± SD)</td>
<td>200.000 ± 65000</td>
<td>195.000 ± 49000</td>
<td>0.98</td>
</tr>
<tr>
<td>Platelet count &lt;10^3 K/uL at any time (n)</td>
<td>11</td>
<td>37</td>
<td>0.69</td>
</tr>
<tr>
<td>Dose alteration due to thrombocytopenia (n)</td>
<td>2</td>
<td>8</td>
<td>0.52</td>
</tr>
<tr>
<td>White blood cell count &lt;4,000 K/uL, at any time (n)</td>
<td>22</td>
<td>80</td>
<td>0.18</td>
</tr>
<tr>
<td>Dose alteration due to leukopenia (n)</td>
<td>2</td>
<td>2</td>
<td>0.26</td>
</tr>
</tbody>
</table>

*Patients who had sustained virological response

Table 3. Viral load patterns of patients who had and did not have sustained virological response parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Responders</th>
<th>Non-Responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV DNA IU/mL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1st month</td>
<td>&lt;2,000</td>
<td>&lt;2,000</td>
</tr>
<tr>
<td>n = 8 (%)</td>
<td>(62.5%)</td>
<td>(36.7%)</td>
</tr>
<tr>
<td>At 3rd month</td>
<td>&lt;2,000</td>
<td>&lt;2,000</td>
</tr>
<tr>
<td>n = 26 (%)</td>
<td>(84.6%)</td>
<td>(58.2%)</td>
</tr>
<tr>
<td>At 6th month</td>
<td>&lt;2,000</td>
<td>&lt;2,000</td>
</tr>
<tr>
<td>n = 37 (%)</td>
<td>(97.3%)</td>
<td>(62.2%)</td>
</tr>
<tr>
<td>At 9th month</td>
<td>&lt;2,000</td>
<td>&lt;2,000</td>
</tr>
<tr>
<td>n = 21 (%)</td>
<td>(100%)</td>
<td>(70.2%)</td>
</tr>
</tbody>
</table>

*P<0.05
At the end of treatment (week 48), 84 patients achieved VR, and 86 patients achieved BR. Also 40 (25%) patients achieved SVR, and 62 achieved SBR. Serological response was observed in one patient. Baseline demographic and laboratory results of sustained virological responders (Rs) and non-responders (NRs) were similar (p > 0.05). Also, hematological findings (platelet, hemoglobin, white blood count) and pegIFN dose alterations due to hematological side effects were not different between the two groups (p > 0.05) (Table 2).

Baseline serum HBV DNA levels and the number of patients with HBV DNA > $10^7$ IU/mL were similar in R and NR (p > 0.05). However, in the third month of treatment, while all Rs had HBV DNA levels of < 20,000 IU/mL, 23 (100%) NRs had HBV DNA levels higher than this limit (p < 0.001). In the sixth month of treatment, 36 (97.3%) of Rs and 74 (75.5%) of NRs had a serum HBV DNA level < 20,000 IU/mL (p < 0.01). In the ninth month of treatment, all of the Rs had serum HBV DNA levels of less than 20,000 IU/mL than those in the NR group. Twenty-two (84.6%) of Rs' and 39 (58.2%) of NRs' viral loads were observed to be below 2,000 IU/mL, which was statistically significant, with an odds ratio (OR) of 3.95 (CI: 1.11–15.29; p = 0.01). Also, the number of patients who had a 1 log$_{10}$ decline in HBV DNA levels in the R group was higher than in the NR, at the first, third, sixth, and ninth months of treatment (Table 3).

Two log$_{10}$ decline in HBV DNA levels in the third month of treatment was observed in 23 (88.5%) and 45 (67.2%) patients in R and NR groups, respectively (p = 0.03). However, this difference was not observed in the sixth month of treatment (89.2 % vs. 76.5 %, p = 0.1).

Statistically significant response patterns were also reflected in the longitudinal change of serum HBV DNA concentrations, which showed greater reduction of viral load in the R group than in the NR group at week 12. The patterns of HBV DNA levels of the

**Table 4. Characteristics of responders and post-treatment virological relapsers**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Responders n = 40</th>
<th>Post-treatment virological relapsers n = 44</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>40.1</td>
<td>38.3</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>Gender (F/M) (n)</strong></td>
<td>8/32</td>
<td>14/30</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>Baseline ALT U/L (mean)</strong></td>
<td>121</td>
<td>115.2</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>Baseline ALT U/L (n)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3 x ULN</td>
<td>14</td>
<td>16</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>&lt; 3 x ULN</td>
<td>26</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td><strong>ALT level at week 48</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 1 x ULN</td>
<td>25</td>
<td>26</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>&gt; 1 x ULN</td>
<td>15</td>
<td>12</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>Histologic activity index</strong></td>
<td>8.35</td>
<td>7.09</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>Fibrosis score</strong></td>
<td>1.81</td>
<td>2.02</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>Baseline HBV DNA log$_{10}$IU/ml</strong></td>
<td>7.09</td>
<td>7.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td><strong>Baseline HBV DNA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 5 log$_{10}$ (n)</td>
<td>17</td>
<td>39</td>
<td>0.001</td>
</tr>
<tr>
<td>≤ 5 log$_{10}$ (n)</td>
<td>13</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>HBV DNA at week 48</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undetectable</td>
<td>35</td>
<td>18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Detectable</td>
<td>5</td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>

*Scored according to the modified Ishak method [17]
patients throughout the study are shown in Figure 1.

Post-treatment virological relapse was observed in 44 patients who achieved prior SVR. The number of patients who had a baseline HBV DNA level \( \leq 5 \log_{10} \) and undetectable HBV DNA at week 48 in the R group was significantly higher than in the patients with post-treatment virological relapse group (p < 0.05). However, no statistical difference was seen regarding the other parameters (Table 4).

**Discussion**

In the present study, predictors of pegIFN treatment response in HBeAg-negative CHB patients were investigated. The most significant finding of our study was that HBV DNA values obtained in the first and third months of treatment had critical threshold values for predicting SVR. In the third treatment month, SVR probability was 3.95 times higher in patients with HBV DNA levels lower than 2,000 IU/mL, namely patients who entered the inactive phase (CI: 1.11 < OR < 15.29). In agreement with the literature, if HBV DNA level is not below 2,000 IU/mL in the third treatment month, then pegIFN treatment should be discontinued and antiviral treatment should be started, since SVR cannot be obtained in 88% of those patients [2,18].

The probability of SVR was 50% in HBeAg-negative CHB cases with HBV DNA levels < 20,000 IU/mL at week 12 of treatment [2]. In our study, SVR was achieved in 36.1% of patients who had HBV DNA levels below 2,000 IU/mL in the third month of therapy. In contrast, SVR was not achieved in 87.5% of cases who did not have HBV DNA levels below that number (p = 0.01). It is currently recommended that treatment should be started in HBeAg-negative CHB cases with HBV DNA levels > 2,000 IU/mL [2,19]. Thus, considering an HBV DNA level of 20,000 IU/mL as the threshold value for predicting SVR at week 12 is not rational. Based to our results, HBV DNA levels under 2,000 IU/mL at week 12 should be accepted as a marker for predicting SVR.

Detection of HBV DNA level < 2.5 \( \log_{10} \) copy/mL at week 12 of treatment had a positive predictive value of 64% for SVR [20]. In our study, mean viral loads of Rs and NRs in the third month of therapy were 2.97 \( \log_{10} \) IU/mL and 6.8 \( \log_{10} \) IU/mL, respectively (p < 0.01). In the sixth month of treatment, these values were 3.36 \( \log_{10} \) IU/mL and 7.17 \( \log_{10} \) IU/mL (p < 0.01). In the twelfth month of treatment, the difference was very significant; 1.53 \( \log_{10} \) IU/mL in Rs, and 6.57 \( \log_{10} \) IU/mL in NRs (p < 0.01).

According to the guidelines, response probability to interferon treatment in the third month should be evaluated using HBV DNA level measurements, and treatment should be discontinued in cases without any decrease in HBsAg levels and with a decrease in HBV DNA levels less than 2 \( \log_{10} \) IU/mL [2]. In our study, the number of cases with a decrease in viral load of 2 \( \log_{10} \) in the third month of therapy was higher in Rs (p = 0.03). However, this was not true in the sixth month of therapy (p > 0.05). This condition indicates that SVR probability is higher if the virological response is achieved at the beginning of the treatment, but the probability of SVR would be lower if virological response was achieved in later months of treatment. As a result, if HBV DNA level is above the 2,000 IU/mL threshold in the third month of therapy, the treatment should be discontinued and antiviral agents should be considered alternatively.

HBeAg-negative CHB patients with good immunoreactivity (high basal ALT level, low basal HBV DNA level, and high necroinflammatory activity in histopathological examinations) have responded better to pegIFN treatment [11,21]. Young age and female gender are the other important predictors for SVR [22]. In contrast, age, gender, baseline ALT and HBV DNA levels were not statistically significant in our study. HAI was also not statistically significant. However, HAI was slightly higher in Rs (8.35 vs. 7.27). This condition might be related to being infected with only genotype D.

Post-treatment virological relapse was observed in 52.4% (44/84) of virological responders. Predictive factors for post-treatment virological relapse were a basal HBV DNA level > 5 \( \log_{10} \) IU/mL, and inability to decrease HBV DNA to an undetectable level in the 48th week of treatment. Hence, pegIFN treatment should be preferred in patients with a basal HBV DNA level < 5 \( \log_{10} \) IU/mL. If HBV DNA level is not under the current detection limits of PCR methods at the end of treatment (treatment week 48) (in other words, if it is even lower than the SVR criteria), patients should be very closely followed after treatment is completed. Age, gender, pre-treatment ALT level, inflammation grade, and hepatic fibrosis stage were not related to relapse after treatment in our study. Similar to our results, Liu et al. [23] found that gender, pre-treatment ALT level, inflammation grade, and hepatic fibrosis stage were not related to relapse. In their trial, relapsers were older and the relapse rates in the HBeAg-negative group (55.8%) were significantly higher than that in the HBeAg-positive group (33.8%). Our study has some limitations. First, as our study was
designed as a retrospective one, all of the required information could not be obtained from patients’ records; for example, HBV DNA levels at the critical weeks could not be obtained for some of the enrolled patients. The other limitation of our study was the absence of HBsAg titration and genotyping. However, as nearly all of the CHB cases in our country are infected with genotype D, we can estimate that all of our cases also were infected with HBV genotype D [13,24]. The last limitation of our study was that treatment efficacy was evaluated according to data of post-treatment week 24. If treatment efficacy had been evaluated 48 weeks after the study had been completed, then our results would have been more useful.

Conclusions

HBV DNA levels of HBeAg-negative CHB patients should be closely followed starting from the first month of treatment. Detection of a 1 log₁₀ decline in serum HBV DNA level starting at the first month of therapy, and HBV DNA levels < 2,000 IU/mL in the third month of therapy may be accepted as SVR predictors. Also, another potent predictor for SVR is the presence of undetectable HBV DNA level at the end of treatment.

References


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