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Evaluation of antiviral treatment response on liver histopathology in chronic hepatitis B infection patients

To the Editor,

We read with great interest the recent review article by Ormeci et al. (1). The authors investigated the effectiveness of tenofovir in terms of virological response. There are numerous surveys performed to define the changes in liver histology after antiviral therapy (2). We have also retrospectively researched histopathological changes owing to antiviral treatment in patients with chronic hepatitis B (CHB) infection. Subjects were allocated into three groups according to antiviral treatment regimen. Pre- and post-treatment liver biopsies were compared. In our study, 48 patients were enrolled. Of the 48 cases, all were men; the mean age of the subjects was 24.54+3.73 years, the mean duration of hepatitis B surface antigen status knowledge was 2.85+1.35 years, and 26 patients (54.2%) were positive for hepatitis B e antigen (HbeAg). A comparison between pre- and post-treatment histological activity index (HAI) and fibrosis (F) scores is shown in Table 1. Significant changes in HAI scores were revealed in all three treatment group. However, entecavir and tenofovir treatment did not exhibit good turn in terms of F scores. Antiviral agents could postpone the progression of fibrosis and forestall hepatic decompensation in patients with improved fibrosis and cirrhosis. Clinical researches have shown that lamivudine therapy can postpone the progression of fibrosis. Unfortunately, lamivudine has the high risk of viral breakthrough. The rate of virological resistance to lamivudine was reported to be at 30% in the first year and at 70% after 5 years (2). Chang et al. (3) revealed that 96% of patients (55/57) had histological recovery after long-term treatment with entecavir. Marcellin et al. (4) found that 87% of patients had histological recovery. They also showed that 51% of patients had fibrosis regression at 240th week after tenofovir treatment. Buti et al. (5) also reported performing a 5-year treatment with tenofovir and provided positive virologic, serologic, and histologic findings, regardless of the baseline cirrhosis status. Our results were different from those in the literature. Because of a limited number of patients, further studies are required to determine the effect of antiviral treatment on liver histology.

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Table 1. Duration of treatment and HBeAg status and comparison of pre- and post-treatment histological activity index and fibrosis scores

	(n, %)	HBeAg positive (n, %)	Duration of treatment (mean+SD)	Pre-treatment HAI (mean+SD)	Post-treatment HAI (mean+SD)	p	Pre-treatment F (mean+SD)	Post-treatment F (mean+SD)	p
Lamivudine	15 (31.3%)	10 (66.7%)	2.67+1.63	6.47+3.11	3.93+1.94	0.001	2.20+1.26	1.20+1.37	0.017
Entecavir	9 (18.8%)	6 (66.7%)	3.33+1.41	6.56+2.55	3.11+1.17	0.027	2.11+0.78	1.56+1.13	0.238
Tenofovir	24 (50%)	10 (41.7%)	2.79+1.14	6.13+2.49	3.92+1.89	0.001	1.92+0.97	1.42+1.18	0.102

HAI: histological activity index; F: fibrosis; HBeAg: hepatitis B e antigen; SD: standard deviation

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Author's Reply

We read your comments about our paper. We would like to discuss some points you have mentioned in your letter and about your study. We performed the study to assess the effectiveness of tenofovir in a retrospective manner. It was a multicenter study, and we have not planned on performing a second liver biopsy to assess the effectiveness of tenofovir on fibrosis. However, we agree with you that there are numerous studies about the effectivity of antivirals in treating chronic hepatitis B. These studies mostly have reported that antivirals are useful for decreasing the fibrosis stage; this issue has been proven in many studies. We read the results of your study with great interest. In your study, you could not show a decrease in the fibrosis stage. We think there are several reasons for obtaining such results. Firstly, the mean age of your patients is 24.5 years. The association between age and fibrosis progression in chronic hepatitis B remains controversial; however, age has been suggested to be an important factor that can predict the progression rate of fibrosis and developing cirrhosis in some studies (1). Fibrosis was found to be associated with increased age. The natural course of chronic HBV infection also changes with the age at which infection occurs. Your patients are at a young age; therefore, fibrosis stages related to that are supposed to be low.

Secondly, the follow-up period in your study is relatively short. Hence, you could not observe a significant improvement in the fibrosis stage. Histological improvement can be achieved in time. In a large cohort, Buti et al. reported that histological improvement was achieved in a 5-year follow-up with tenofovir treatment (2).

What are the factors predicting improvement in staging? In a study conducted by Papachrysos, the patients who have lower AST and ALT levels at the baseline showed a tendency to improve in fibrosis staging (3), but that result was not statistically significant. The other factors were not statistically significant. Therefore, it is difficult to predict improvements in fibrosis staging before the onset of treatment.

Finally, the small patient group in your study can be a limitation. We think a study involving larger patient groups with longer treatment durations can reveal histological improvements.

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