Reviewed by 00073008

The authors of this article try to explain an interesting medical problem – the correlation between liver fibrosis and response to antiviral therapy in chronic hepatitis B (CHB). The advantage of this study is a large group of studied patients. Unfortunately, a retrospective analysis in this study forces some limitations. In the CHB the activity of liver inflammation is an important factor responsible for the final effect of antiviral therapy, except HBV viral load. In this study, an activity of liver inflammation was not presented, unfortunately. The fazes of HBV infection in treated patients groups were not analyzed, we have no information about the proportion of immunotolerant and immunoactive patients in the studied populations. In my opinion, presented study results support a commonly known observation – a better response in immunoactive faze of CHB (lower viral load, more rare HBe positive status, higher FIB-4 index). Each table should be sent on a separated page

Qusetion 1:

Unfortunately, a retrospective analysis in this study forces some limitations. In the CHB the activity of liver inflammation is an important factor responsible for the final effect of antiviral therapy, except HBV viral load. In this study, an activity of liver inflammation was not presented, unfortunately.

Answer 1:

Thank you for the suggestion.We agree with you very much,we have mentioned the limitations on our paper, such as the study was a retrospective study and the dynamic changes of liver inflammation in the study,we will observe the changes of liver inflammation in our later study.

Qusetion 2:

The fazes of HBV infection in treated patients groups were not analyzed, we have no information about the proportion of immunotolerant and immunoactive patients in the studied populations.

Answer 2:

Thank you for the suggestion.We will observe the dynamic changes of FIB-4 index and liver inflammation in the proportion of immunotolerant and immunoactive patients.

Qusetion 3:Each table should be sent on a separated page.

Answer 3::Thank you for the suggestion , I have followed the suggestion and each table have been sent on a separated page.

Reviewed by 00053786

The authors have presented a retrospective study to investigate the predictor variables for complete or partial virological responses in 231 chronic hepatitis B patients receiving entecavir therapy for three years. The study was well designed and the manuscript clearly explains the results. Congratulations!

The paper is well-written, but there are several points to be addressed.
1.I can't understand the Figure 2B. By definition, the partial responder should have positive HBV DNA at week 48. But, in this figure, 80% of HBeAg negative partial responders already had negative HBV DNA at week 48. Likewise, 100% of HBeAg positive complete responder should have negative HBV DNA at week 48 in Figure 2A.
Answer:Thanks for your question very much.
The results were the genuine(if it is necessary ,we can provide the initial data).

2.Figure 4 is also somewhat confusing. In the 'Histologic liver assessment' session, 76 patients have a follow up biopsy at week 48. Then, does the X-axis in Figure 4B represent the degree of fibrosis at week 48? If it is true, FIB-4 index is no longer valid in anti-viral treated patients. Maybe, normalization of AST/ALT affected the performance. And please insert the number of patients according to the degree of fibrosis
Answer:Thanks for your question very much.
Yes, the X-axis in Figure 4B represent the degree of fibrosis at week 48.I have inserted the number of patients according to the degree of fibrosis.

3. Question 2:If it is true, FIB-4 index is no longer valid in anti-viral treated patients. Maybe, normalization of AST/ALT affected the performance.
Question 3:For the same reason, it is natural that FIB-4 index improved with ETV treatment, because AST and ALT are important parameters in the equation. Therefore, I think it is not appropriate to use FIB-4 index during antiviral treatment. At least, we cannot say that the fibrosis was improved by FIB-4 index because the value in Fibrosis 5 and 6 was lowered even though they still have significant fibrosis.
Answer:Thanks for your question very much.
According to the ALT level at week 48,we have divided the patients into sub--group patients : In CVR (or PVR) group ,the FIB-4 index did not show significant difference between ALT≤40IU/L and ALT＞40IU/L patients (P=0.31 or P=0.98)When ALT≤40IU/L at week 48,FIB-4 index at week 144 show significant difference between CVR and PVR group (1.31±0.86 vs 0.98 ±0.55, P=0.003). ALT＞40IU/L at week 48,FIB-4 index in CVR group is higher than PVR group at week 144(1.54±1.02 vs 1.12±1.00, P=0.021).

4.In Figure 5, the number of patients was 152, but liver biopsy was performed in 76 patients. I think it is not appropriate to assess the performance of FIB-4 index by combining pre- and post-treatment biopsies. It should be analyzed separately for the reason mentioned above.

Answer: Thanks for your question very much.
we agree with you very much. We have analyzed pre- and post-treatment biopsies separately(data have not been provided) ,but because of the number of the patients were too small,the ROC curve were unsatisfactory.In our later study,we will increase the sample size of the patients .

5. It is advisable to insert the definition of group A and B in the footnote of Table 1.
Answer: Thanks for your question very much.
I have inserted the definition of group A and B in the footnote of Table 1.

6. Generally, the complete responders at week 48 had higher ALT and AST levels and the age was older. Therefore, it is not certain whether the difference of FIB-4 index truly resulted from the difference of fibrosis degree. I do recommend to compare the degree of fibrosis in biopsied patients between the two groups, although the sample size may be small.
Answer:Thanks for your question very much.

The complete responders at week 48 had higher ALT and AST levels and the age was older,but after adjusting for covariates by multivariate logistic regression analysis, age and the level of ALT and AST did not differ between the groups.

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