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OPEN PEER REVIEW

# Effects of Entecavir on Serum Hepatitis B Virus-DNA, Interferon-γ, and Pregenomic RNA in Patients with Chronic Hepatitis B Virus Infection

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## About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

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## 1 Original submission

2 comments · 9 Nov 2022 – 17 Nov 2022

**Fatemeh Faraji** Reviewer

MINOR REVISION 9 Nov 2022

Comments to the Author
- Here are some suggestions that have been made to improve the manuscript:

1. The English writing needs to be improved and checked.
2. In the method section, please mention the name of the hospital where the patients were admitted.
3. Please add the thermocycling temperature program and reaction mixture component to the method section.
4. In the discussion section, the reason for decreased levels of IFN-γ following treatment with ETV needs to be checked.

**Editor-in-Chief**

MAJOR REVISION 17 Nov 2022

Dear Authors,

Please follow the peer-review comments and submit a revision.

Regards,
EIC

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# Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

**Manuscript ID: 132684**
**Manuscript Title: Effects of entecavir on serum hepatitis B virus, interferon-γ and pregenomic RNA in patients with infection**

**Reviewer 1:**
- here are some suggestions that have been made to improve the manuscript:

***1. English writing needs to be improved and checked.***
Response: We have asked a native speaker to revise the English language throughout the manuscript.

***2. In the method section please mention the name of the hospital where the patients were admitted.***
Response: Thank you very much for your valuable comment. However, we are required to remove all the identification information in the manuscript.

***3. Please add the thermocycling temperature program and reaction mixture component to the method section.***
Response: We have added the required descriptions.

***4. In the discussion section the reason for decreased levels of IFN-γ following treatment with ETV needs to be checked.***
Response: We have added the required discussion in the last but one paragraph of Discussion.

**Reviewer 2:**
Dear editorial office,
In the current study, authors try to provide evidence for the importance of entecavir therapy in HBV infection and its benefits in decrees pgRNA of HBV.
Before any further steps, there are some points that I ask authors to consider:
***1. Background in the abstract should be informative and include the aim of the study. The objective of the study by itself could not be considered as a background.***
Response: We have revised the background in the abstract according to your requirement.

***2. In title of manuscript: it will be better to mention what variable about the HBV instated of "… on serum hepatitis B virus (HBV)…", for instance: serum HBV viral load and pgRNA? serological markers? Markers?***
Response: We have revised the title for clarification.

***3. running title does not reflect the Major title.***
Response: We have revised the running title.

***4. I highly suggest you provide more information about the diagnostic or prognostic role of pgRNA of HBV in the introduction section.***
Response: We have added the required descriptions and supporting references in the introduction section.

***5. rewrite this "patients complicated with hepatitis C/D," in a more descriptive form. In method section 3.2***
Response: We have clarified the description.

***6. Please provide method section 3.4 part in two separate sections for HBV-DNA and pgRNA evaluation.***
Response: We have made the required revision.

***7. Why do you use miRNA RT kit, instate of any other cDNA synthesize kit? (method 3.4)***
Response: We are really sorry for the mistake, and revised corresponding description.

***8. While you use COBAS TaqMan you will get the results for viral load. So why do you use HBV nucleic acid kit and mention primers? (method 3.4)***
Response: We are really sorry for the mistake, and revised corresponding description.

***9. provide the manufacturer information for SPSS.***
Response: We have added the manufacturer information for SPSS.

***10. use SD or standard deviation for reporting the results instead of S (method section 3.6)***
Response: We have made the required revision.

***11. All the provided p-values in Table 3 are p<0.05, while in the result section is not like this, is there any explanation? (result section 4.3)***
Response: We are really sorry for the mistake, and have revised related descriptions.

**Associate Editor 1:**
Dear author
Your manuscript has undergone review by reviewers with expertise in this subject. In addition to the comments of our reviewers, I have some comments. It is requested to provide a point-by-point response to reviewers' comments and submit a revised version of the manuscript. The manuscript needs a major revision to clarify several issues:

***1. In the title of the manuscript, "Effects of entecavir on serum hepatitis B virus…." Which marker of HBV? HBV DNA, HBV antigens? If HBV antigen, which of them?***
Response: We have revised the title according to your requirement.

***2. In the title of the manuscript "…in patients with infection". Which infection? Please specify type of infection.***
Response: Thank you very much for your valuable comment. We actually mean "hepatitis B virus" infection, but have omitted it to avoid repetition of words in the title.

***3. The running title written in the present form in not representative of the current work. Please rewrite it.***
Response: We have revised the running title.

***4. The below sentence in the Abstract:***
***"ETV can inhibit the replication of serum HBV-DNA".***
***"Replication of serum HBV-DNA" is not a correct phrase. HBV DNA does not replicate in the sera to inhibit by ETV.***
Response: We are really sorry for the mistake, and have revised the descriptions.

***5. Please mention the novelty of the current work in the last paragraph of the Background***

***section.***
Response: We have mentioned the novelty of the current work according to your requirement.

***6. In the Objective section, "the effects of ETV on serum HBV":***
***Specify which markers of HBV.***
Response: We have revised the description for clarification.

***7. Please mention locations where specimens were collected in the methods section.***
Response: The specimens were collected from our hospital. The hospital's name was eliminated due to the anonymous requirement.

***8. What do you mean from "t" and "F" in tables 1 and 2? Define in in the table footnote.***
Response: As we have mentioned in the "Statistical analysis" subsection, the measurement data were compared by the t-test between two groups and by the F test at different time points.

***9. Please write limitations of the current study before the conclusion section at the bottom of the discussion section.***
Response: We have added the study limitations at the bottom of the discussion section.

***10. There is no description about extraction of viral nucleic acids, PCR temperature condition and reactions for HBD DNA and pgRNA detection.***
Response: We have added the required descriptions.

***11. Please mention limit of detection (LOD) of Roche COBAS AmpliPrep/COBAS TaqMan.***
Response: The detection range of Roche COBAS AmpliPrep/COBAS TaqMan for HBV-DNA was $2.293\times10^{3}$-$7.566\times10^{9}$ copies/ml.

## 2 Revision 1

2 comments · 5 Jan 2023 – 5 Jan 2023

### Associate Editor

MINOR REVISION 5 Jan 2023

Dear Author
Thank you for your responses to the previous comments raised by our reviewers. I agree with your responses and revisions to the manuscript, except in one case:
The title of the manuscript includes “...in patients with infection”.
Please mention "Hepatitis B virus infection".
Also, clarify the type of Hepatitis B virus infection: acute Hepatitis B virus infection or chronic Hepatitis B virus infection?
After this minor revision to the title, the manuscript will be suitable for publication in Hepatitis Monthly journal.

Regards

### Editor-in-Chief

MINOR REVISION 5 Jan 2023

Dear Authors,

Please follow the peer-review comment and submit a revision.

Regards,
EIC

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# Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

**Manuscript ID: 132684**
**Manuscript Title: Effects of entecavir on serum hepatitis B virus-DNA, interferon-γ and pregenomic RNA in patients with infection**
**Revision: [1]**

**Reviewer 1:**
***Thanks for the reply.***
Response: Thank you very much for your positive comment.

**Associate Editor 1:**
***Dear Author***
***Thank you for your responses to the previous comments raised by our reviewers. I agree with your responses and revisions on the manuscript. Except in one case:***
***In the title of the manuscript "…in patients with infection".***
***Please mention "Hepatitis B virus infection".***
***Also clarify which kind of Hepatitis B virus infection? acute Hepatitis B virus infection or chronic Hepatitis B virus infection"?***
***After this minor revision in the title, the manuscript will be suitable for publication in Hepatitis Monthly journal.***
Response: Thank you very much for your positive comment. We have revised the title according to your requirement.

**EIC Decision:**
***Dear Authors,***
***Please follow the peer-review comment and submit a revision.***
Response: We have further revised the manuscript according to all the valuable comments.

## 3 Revision 2

1 comment · 9 Jan 2023

### Editor-in-Chief

ACCEPT 9 Jan 2023

Dear Authors,

I am delighted to inform you that your manuscript is accepted for publication in Hepatitis Monthly.

Regards,
EIC