

ANSWER LETTER



Nov. 12, 2013

Dear Editor,

Thank you for the very cordial review.

Title: What physicians should know about the management of chronic hepatitis B in children? -East Side Story-

Author: Hun-Jee Choe, ¹Byung-Ho Choe

Name of Journal: *World Journal of Gastroenterology*

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We thank the reviewer for the positive comment.

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Major issues

General comments

- 1) It is not clear to whom the paper is directed to, since some of the topics are treated in depth in an extremely accurate and specialistic way, while other basic issues are poorly addressed or not even mentioned.
 - Since the review article is focused on the special issue of 'chronic hepatitis B' for World Journal of Gastroenterology on 2014, the authors have reviewed the published articles comparing Asian children to adults as well as western children as mentioned in introduction. This review is directed to Western hepatologists (or Eastern adult hepatologists) interested in the management of chronic hepatitis B in Asian children. I'm pretty sure that the basic issues must be addressed on the other review articles on same special issue for 'chronic hepatitis B'.
- 2) Topics discussed in detail should be better summarized in tables and/or flow charts to render the material more available and practical for the reading physician.
 - I think the management plan must be well summarized by flow charts on the other review articles on same special issue for 'chronic hepatitis B'. I'm focusing on telling the similarity and differences between children and adults as well as Eastern and Western. The figure of natural course is added for the readers.

Detailed issues

Methods:

There are no methods paragraphs in the paper. Search strategies, consequent study selection, and methods of data extraction should be provided and detailed.

- Since this review does not compass the whole children's data published before, I have not applied the whole database search as you might have asked.
- Please understand that this review article is not a meta-analysis, but acceptance for the invitation to contribute an article like as book chapter for the WJG special issue for 'chronic hepatitis B'.

Contents:

In the introduction there are neither data about the actual prevalence of HBV worldwide nor in East Asia. Thus, if the review was issued for medical education purposes, we believe that these data should have been provided to define the burden of HBV among children in this area.

- It was provided as your comments. The introduction looks much better thanks to your request.

As the Authors correctly point out in the introduction section, the reduction of HBV prevalence obtained with the introduction of universal vaccination. However, data on vaccine response, need for HBV status checking after having completed vaccine schedule, or management of non responders have not been provided.

- I have prepared the vaccine story at the first time. However, its amount is as much as the management story, so that I had to remove it from this review. Please understand my indecisive answer.

As indicated by the authors the main modality of HBV infection transmission in Asia is the vertical, and few data about perinatal transmission prevention program are given in the introduction.

- The data of perinatal transmission prevention program is limited in Asia, except Taiwan and Korea. The data of Taiwan was added in introduction.

Regarding the natural history of HBV infection, I believe that the Authors should have provided the rates of chronic infection development after infection in the different ages ranges, and define in detail the concept of chronic hepatitis. In addition, in the "natural history of chronic hepatitis B" paragraph data on the rate of evolution from chronic hepatitis to cirrhosis and on the risk of hepatocarcinoma development, the two major complication of hepatitis in terms of morbidity and mortality, should be provided.

- It was provided in [The natural course of chronic hepatitis B] and the first sentence in introduction as your comments.
data on the rate of evolution from chronic hepatitis to cirrhosis and on the risk of hepatocarcinoma development: The data of Taiwan was added, but not in detail because LC and HCC data are absolutely present but very limited in Eastern Asia.

In the "liver biopsy" paragraph indications on who and when to perform liver biopsy should be provided. Comments on the possible role of non invasive testing (e.g.Fibroscan) should be addressed to complete this paragraph.

- It was provided as your comments. The indication for liver biopsy is not widely accepted as consensus, so that it is not very clearly described. Please understand my indecisive answer.

Interferon, and preliminary phase III data on peg-interferon treatments have not been addressed. Even with limited results in terms of percentages, this class provides a true chance of cure, offering

a limited but interesting opportunity of HBsAg loss. Thus, the possible benefits and limits of this class of medications should be provided and discussed. Comparative comments on other antivirals should be addressed. A flow chart with the possible therapeutic choices in the different setting might help in the understanding and practical application of data regarding drug management.

- Interferon story was added at [6. Treating chronic hepatitis B with Nucleos(t)ide analogue]. I think interferon, other antivirals and treatment strategy would be discussed in detail in other articles of same issue. Other antivirals were also addressed in this article.

Management of nucleos(t)ide therapy on the basis of laboratory results should be preferably discussed in a separate paragraph instead of including it in the diagnosis paragraph.

- It was moved to [How long to use] subparagraphs.

What is discussed in the paragraph “missing treatment and liver complication” should be included in the “natural history of hepatitis B” chapter, since these are the natural evolution of chronic HBV infection.

- I agree with your comment. It was revised as recommended.

Structure

Main paragraphs have been numbered with progressive arabic numerals as subparagraphs. This modality of presentation renders difficult to follow the logical structure of the paper. I suggest that the fragmentation in subparagraphs should be reduced to the minimum, and that these should be better defined, for example using roman numerals.

- The structure was improved as your suggestion. Thank you for your comment.

Language

English style should be strongly improved and should be revised by an English speaking person. The language could be ranked as grade C.

- I apologize for missing English edition for the first draft. It was done at this revised draft. Please understand it requests cost at every revision.

To render the paper more suitable for publication, we suggest the authors to analyze and confront the recently published paper by EASL on the management of HBV in childhood.

- I'm sorry if this review was not very organized for your expect. Please understand that the main readers would be the general physicians in China as well as the Western adult hepatologists who may have chance to manage and treat Asian children with chronic hepatitis B. Some pearls from the recently published paper by EASL were referenced as your recommendation.

Thank you again and we do hope that our revised version will be evaluated acceptable in the *World Journal of Gastroenterology*.

Sincerely yours,

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