

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 22519

Title: Hepatitis B and D viruses replication interference. Influence of hepatitis B genotype

Reviewer's code: 03257372

Reviewer's country: France

Science editor: Ze-Mao Gong

Date sent for review: 2015-09-28 13:43

Date reviewed: 2015-10-02 18:16

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The paper by Madejon et al is interesting but could be improved Major comments: 1) That the extent of suppression of HBV replication by HDV differs depending on the HBV genotype is something I have suspected for some time. However, I also think that the HDV genotype also plays an important role. In this respect, it is unfortunate that the HDV isolates were not genotyped. For the Caucasian patients these are almost certainly HDV 1, but the sub-Saharan patients may have "African" HDV genotypes. I think that this point of the potential role of HDV genotypes should be discussed 2) At the beginning of the Discussion the Authors make much of the fact that HDV-RNA titers are higher than HBV-DNA titers. I do not think that it is pertinent to compare the titers of two very different viruses. What is important is that HBV-DNA titers drop when there is HDV co-infection and the size of the drop seems to depend on the HBV genotype. 3) The Discussion is too long in any case and should be reduced. Minor comments: 1) In Figures 2A and 3A some of the box-plots are missing, being represented only by the thick bar that presumably represents the median value but this is not stated in the legends to the Figures. In Figure 2A, what is the meaning of the



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asterisk (*)? 2) There are several spelling and grammatical errors. This is especially the case for "titer" that at several places including in the Figures is spelled "titter". The paper should be reviewed by a competent English speaker.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 22519

Title: Hepatitis B and D viruses replication interference. Influence of hepatitis B genotype

Reviewer's code: 00012386

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2015-09-28 13:43

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

It looks acceptable.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 22519

Title: Hepatitis B and D viruses replication interference. Influence of hepatitis B genotype

Reviewer's code: 00504172

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2015-09-28 13:43

Date reviewed: 2015-10-13 01:05

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The study is really interesting and well conducted: there are only minor points to make and a few questions to ask. Questions: It is very difficult to know the duration of a HBV infection and in fact only for a few patients in the "longitudinal follow-up" these data are reported. For patients in the cross-sectional study is it possible to know something more? Can there be a bias due to a different duration of infection in patients with different genotypes? Is it known if HBV-HDV infections are co-infections or super-infections? Was the presence of HBV Mediterranean variant as a possible confounding factor evaluated? (Are the subjects with anti-HBe the result of a seroconversion from HBeAg or are Mediterranean variants?) It is likely that the present HDV genotype is genotype 1, given its ubiquity, but was the HDV genotype evaluated to check if HBV replication is HDV genotype dependent as well as HBV genotype dependent? Remarks: Materials and methods Since the term of chronic liver disease is a bit too concise, more detailed clinical descriptions of case studies would be desirable. Results Since in the Discussion there is the sentence: "different HBV genotypes seem to be not related with simultaneous infection with HCV...", the data and related statistics for



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both the cross-sectional study and for the longitudinal follow-up should be shown. Since In the discussion there is the sentence: "different HBV genotypes seem to be not related withthe previous treatment pressure", this has been described for the longitudinal follow-up but not for cross-sectional study. The term "tended" in the phrase " Similarly, the HDV-RNA titers tended to be higher in HIV-patients than in HIV-negatives...." gives rise to misunderstandings as $p = NS$. Discussion A short comment on the HBV Mediterranean variant and HDV genotypes in relation to this study may allow the reader to have a broader view of the problem.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 22519

Title: Hepatitis B and D viruses replication interference. Influence of hepatitis B genotype

Reviewer's code: 02861202

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2015-09-28 13:43

Date reviewed: 2015-10-13 01:35

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript by Dr. Madejon and co-workers refers to the influence of HBV genotype on HDV replication. The subject is of interest even though it is already known that HBV genotypes may affect a different HDV replication fitness. However, in order to draw solid conclusions, it is important to analyse HDV genotypes as well, since it is well known the existence of different replication fitness either inter genotypes and intra genotypes of HDV (European genotype 1 as compared to Asian genotype 1 of HDV).

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 22519

Title: Hepatitis B and D viruses replication interference. Influence of hepatitis B genotype

Reviewer's code: 00506552

Reviewer's country: South Korea

Science editor: Ze-Mao Gong

Date sent for review: 2015-09-28 13:43

Date reviewed: 2015-10-14 18:22

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Authors of this article (Madejón et al.) described that HBV-A genotype infection interfere viral replication than genotype D or E in HDV co-infected patients. Even though number of participated patients are not enough, it was worthwhile to investigate the genotype differences in CHB-CHD co-infected patients. If authors of this manuscript include the in vitro replication results with HBV-A only vs HBV-D only vs HBV-A and HDV vs HBV-D and HDV, it would be very interesting and certify the importance of HBV genotype in HDV co-infection. Generally, the importance of this trial is needed, but I have several suggestions. Since HBV-A DNA level was lower than HBV-D when HDV was co-infected, the authors of this manuscript should discuss the disease outcomes (HCC and/or cirrhosis) between these statues. Long term follow-up studies are needed, later. Throughout the manuscript, the authors described CHD (of course, it is no doubt), it was better to describe CHB-CHD co-infection all the time (Some readers are not from HBV research area). 16 CHD (+ CHB without HIV) patients were participated a longitudinal dynamic analysis, it would be better to include CHB (without HIV) for comparison. Results were very difficult to follow. In page 8 line 4

to 7, I cannot find where I can find in the table or Fig. In page 8, 'In all but one patient, ... (Table 2 and 3)', it must be Table 3 and 4. In page 8, 'In all but one patient, HDV-RNA was higher than HBV-DNA...', I think that without copy numbers, it cannot be said that HDV-RNA was higher than HBV-DNA. Author should calculate the exact copy number of HDV-RNA and HBV-DNA. In page 9, at first paragraph, was it Table 3? In page 9, at 3rd paragraph, where can I find the result? These types of confusions are throughout the manuscript. All of Figures need to add the numeral numbers (median numbers) at of the graphs since all of Fig. were very difficult to see the numeral numbers.