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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 31005

Title: Serum 25-hydroxy vitamin D deficiency is associated with hepatic encephalopathy in patients with chronic liver disease
Short running title: 25-OHD deficiency and hepatic encephalopathy

Reviewer's code: 00037028

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2016-10-28 19:27

Date reviewed: 2016-10-29 05:07

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

Very nice paper.



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Name of journal: World Journal of Hepatology

ESPS manuscript NO: 31005

Title: Serum 25-hydroxy vitamin D deficiency is associated with hepatic encephalopathy in patients with chronic liver disease
Short running title: 25-OHD deficiency and hepatic encephalopathy

Reviewer's code: 02942755

Reviewer's country: China

Science editor: Ze-Mao Gong

Date sent for review: 2016-10-28 19:27

Date reviewed: 2016-10-30 17:43

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 checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This article indicated that patients with chronic liver disease have low levels of 25-OHD, which are associated with the presence of HE. Supplementation with vitamin D and monitoring of vitamin D levels can prevent the development of HE.

My comments are following:

- Figure 5 showed that Vitamin D deficiency correlates with MELD score in both patients with and without HE. This figure was confusing, and I suggest that the correlation between MELD score and levels of Vitamin D deficiency should be described respectively (Figure 5A and Figure 5B).
- According to the updated 2014 practice guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver, HE is classified into three types: type A is due to acute liver failure, type B is predominantly caused by portosystemic bypass or shunting without intrinsic liver disease, and type C occurs in patients with underlying cirrhosis. The



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type B and type C HE are similar, they are subdivided into overt and covert HE, according to the severity of the manifestations. In this context, patients with overt HE may develop varying degrees of confusion, stupor and coma. In contrast, patients with covert HE (including minimal HE and grade I HE) have none of the neurologic symptoms that are associated with overt HE, although they do have several quantifiable cognitive defects, which primarily lead to impairments in selective attention, response inhibition and working memory.

This paper indicated that lower levels of 25-OHD are associated with the presence of overt HE. However, the correlation between lower levels of 25-OHD and the presence of covert HE is not clear. I suggest that the correlation between 25-OHD and covert HE should be discussed.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 31005

Title: Serum 25-hydroxy vitamin D deficiency is associated with hepatic encephalopathy in patients with chronic liver disease
Short running title: 25-OHD deficiency and hepatic encephalopathy

Reviewer's code: 00182114

Reviewer's country: Japan

Science editor: Ze-Mao Gong

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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

Dear author This is very interesting paper about the relationship between 25-OH deficiency and hepatic encephalopathy. Author concluded that there is a significant association between low-25-OHD levels and the development of HE. I think the liver plays a central role in the vitamin D metabolism by hydroxylation of cholecalciferol to its bioactive form, namely 25(OH)D3. Therefore, it is obvious that in patients with severe liver insufficiency, the metabolism leading to 25(OH)D3 generation is disturbed. I ask some questions. 1. Please tell me the reason why 25-OHD levels is predictor of chronic liver disease. 2. How about the relationship between 25-OHD and Child A,B,C. 3. From the point of predictor of hepatic encephalopathy, which is more sensitive predictor of hepatic encephalopathy,NH3 or 25-OHD?