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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36631
Title: Beneficial long term effect of a phosphodiesterase 5 inhibitor in cirrhotic portal hypertension. A case report with 8 years follow-up
Reviewer's code: 03029329
Reviewer's country: Japan
Science editor: Ke Chen
Date sent for review: 2017-10-28
Date reviewed: 2017-10-29
Review time: 1 Day

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

COMMENTS TO AUTHORS

The authors presented a case with portal hypertension due to AIH/PBC overlap syndrome, who had recurrently bled from esophageal varices and had been successfully treated by a PDE-5-inhibitor. HVPG decreased by 14% at the initial hemodynamic test and by 15% a few months later. Portal venous flow increased by 28% as measured by Doppler ultrasound and by 16% as measured by four-dimensional flow MRI. They showed that these measurements persisted for more than eight years and were accompanied by a beneficial clinical effect without any adverse effects. This manuscript appears nearly acceptable for publication, but several revisions would be considered as follows. In this paper, the authors have not taken up the ethical point of view, including informed consent. There were a few descriptions of the mechanism of a PDE-5-inhibitor how lower portal hypertension in patients with liver cirrhosis. Furthermore, they should

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mention the limitation of this technique.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36631
Title: Beneficial long term effect of a phosphodiesterase 5 inhibitor in cirrhotic portal hypertension. A case report with 8 years follow-up
Reviewer's code: 02942549
Reviewer's country: Greece
Science editor: Ke Chen
Date sent for review: 2017-10-28
Date reviewed: 2017-10-31
Review time: 2 Days

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

COMMENTS TO AUTHORS

It is an interesting case report about the role of PDE 5 inhibitors on the reduction of portal pressure in a patient with liver cirrhosis. I have only one comment to make. There is no doubt about the effect of the drug on the acute setting, as the authors showed direct reduction of HVPG after the administration of the drug. However, I have some concerns about the role of the drug on the long term. We do not have any information about liver histology. We do not know if autoimmune hepatitis was under control at the beginning or if this happened later, during the follow up. Thus, we can't be sure if the portal pressure became stable during the long term because of the drug, or because of the regression of liver damage. So it would be very important to give us some information about liver histology, or liver stiffness at the beginning of the study and during the follow up.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36631
Title: Beneficial long term effect of a phosphodiesterase 5 inhibitor in cirrhotic portal hypertension. A case report with 8 years follow-up
Reviewer's code: 03258338
Reviewer's country: Italy
Science editor: Ke Chen
Date sent for review: 2017-10-28
Date reviewed: 2017-11-07
Review time: 10 Days

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

COMMENTS TO AUTHORS

Dear Editor, In the manuscript authors shed light in the complex pathophysiological substrate of portal hypertension adding data on therapeutic approach. Therefore, I think that Manuscript can be accepted, with the following concerns. 1) If patient was diagnosed with overlap syndrome, why UDCA was not administered? Explain better. 2) No relevant effect was observed on systemic blood pressure with use of the drug. This in an important item: results should be report in text (not only " no relevant effect"). 3) Case report describe a patient with a cirrhosis in Child A class. In discussion, literature debating the role of NO inhibition in different stage of liver disease should be report (cfr. angelico et al, Long-acting nitrates in portal hypertension: to be or not to be? Dig Liver Dis. 2001). Finally, I suggest authors to remark this concept also in the last sentence of abstract.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36631
Title: Beneficial long term effect of a phosphodiesterase 5 inhibitor in cirrhotic portal hypertension. A case report with 8 years follow-up
Reviewer's code: 02861189
Reviewer's country: Italy
Science editor: Ke Chen
Date sent for review: 2017-10-28
Date reviewed: 2017-11-10
Review time: 13 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
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[ ] Grade E: Poor		[Y] No	[Y] Major revision
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		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This case report is an appreciable attempt of exploring new potential approaches to portal hypertension-related bleeding prophylaxis in cirrhotic patients, especially considering the increasing amount of paper highlighting potential pitfalls of chronic beta-blockers administration in advanced cirrhosis. In the described case, clinical and endoscopic goals of the treatment with PDE-5-inhibitors were reached, and the Authors were even able to show a clear decrease in HVPG during follow-up (although the standard decrease of > 20% was not reached). Despite this, after carefully reading the paper, I think that there are some major issue that need to be examined before any conclusion about the potential use of these drugs in this setting. 1) Which was the systemic heamodynamic effects of these drugs? Patient with cirrhotic portal hypertension usually present alteration in systemic haemodynamic (low SVR, high CO

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and CI…) and using a vasoactive drug (such as PDE-5-inhibitors, beta-blockers…) could lead to an heamodynamic derangement. Therefore, monitoring of systemic haemodynamics should be done while testing drugs with such vasoactive effects in this setting. If performed, data about right heart catheterization at baseline and during follow-up are very valuable. If not, data about heart rate, blood pressure and ecocardiographic findings could be an acceptable surrogate 2) Related to point 1, cirrhotic patients with portal hypertension with worsening of systemic heamodynamic alterations usually present an increase or a de novo appearance of ascites, not even predictable using only HVPG value: data about clinical and ecographic findings are therefore crucial 3) The patient described presented (despite a long history of bleedings) with a quite-compensated cirrhosis, as evidenced by Child-Pugh score A. For reason mainly related to Point 2, I'm not sure that patients at a more decompensated stage of cirrhosis could tolerate these drugs as well. I think that this should be underlined in the text and lead to more cautious and single patients-oriented conclusions