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315-321 Lockhart Road,
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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 1208

Title: Effects of propranolol and propranolol plus isosorbide-5-mononitrate on the variceal pressure in schistosomiasis presinusoidal portal hypertension

Reviewer code: 00009152

Science editor: Huang, Xin-Zhen

Date sent for review: 2012-12-24 10:50

Date reviewed: 2013-02-28 06:55

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The authors have compared the effect of propranolol alone with the combination of propranolol and isosorbide-5-mononitrate on variceal pressure in patients with portal hypertension due to schistosomiasis. They found that the combination led to a more pronounced decrease of variceal pressure than propranolol did. The manuscript is fairly well written; the design of the study is clinically relevant and scientifically sound. I have some minor questions and comments: 1. The main response variable was the percentage decrease in variceal pressure. This variable should be included in Table 2. It is NOT the VP at 6 months that is significantly lower in PR+ISMN compared to PR, but the percentage difference from baseline. 2. I am uncertain if the authors have miscalculated the average decrease in VP in the PR+ISMN group. From the mean pressures at baseline and at 6 months I would expect the mean difference to be $(25.69-20.48)/25.69$ which is about 20.3% but the authors state that this difference was 15.9% in Results. Please explain or correct. 3. A statistical significance should be $p < 0.05$ NOT $p \leq 0.05$, i.e. a p-value of exactly 0.05 should not be considered statistically significant. 4. The authors state that Spearman's rank correlation was used for testing correlations but I couldn't find any results for correlations. 5. The discussion can be condensed and concentrate on discussing the findings of the study. I think it would be interesting to discuss if the increase in side effects from hypotension and headache might outweigh the marginal increase in effect on variceal pressure. Is it worth pushing variceal pressure further down? I do acknowledge that this should be studied in a larger cohort of patients but I am also convinced that there is a border when side effects will outweigh the benefits.



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Title: Effects of propranolol and propranolol plus isosorbide-5-mononitrate on the variceal pressure in schistosomiasis presinusoidal portal hypertension

Reviewer code: 00053634

Science editor: Huang, Xin-Zhen

Date sent for review: 2012-12-24 10:50

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

General Comment The authors aimed at evaluating the effects on variceal pressure of propranolol compared to the association of propranolol + ISMN in 40 patients with schistosomiasis-related portal hypertension in a randomized controlled trial. At 6 months, reduction in variceal pressure was more marked in schistosomiasis patients receiving PR plus ISMN than PR alone ($p < 0.05$). The topic is interesting. However there are several weak methodological issues that need to be corrected. Major issues 1) No detail is provided about randomization procedure, power of the study, primary and secondary endpoints, etc. This information is relevant to evaluate the quality of the study and finally the reliability of the results. 2) The authors should acknowledge that the higher reduction of variceal pressure observed in patients who received the combination treatment does not imply a superiority of this strategy. This may be assessed only using the bleeding rate or the mortality as the endpoint 3) Statistical analysis must be rewritten. For example the authors used a parametric test such as the t-test and a non-parametric one (Spearman test). It is not clear whether the quantitative variables are distributed in Gaussian or non-Gaussian fashion. Moreover I cannot find no use of correlation test. In addition, in the table 1 the authors compared qualitative variables, but no test to compare them in cited in the section of Statistical analysis. Finally it seems that they used paired and non-paired t-test, but this is again never mentioned. 4) The authors used guidelines at the time of trial beginning. However they should specify this and also quote current literature. For examples it is currently not recommended to titrate the betablockers using the 25% decrease in heart rate, etc. Indeed the following relevant references must be cited by the authors: a. Bari K, Garcia-Tsao G. Treatment of portal hypertension. World J Gastroenterol. 2012 Mar 21;18(11):1166-75 b. Gentile I, Thabut D. Noninvasive



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prediction of oesophageal varices: as simple as blood count? *Liver Int.* 2010 Sep;30(8):1091-3. c. White CM, Kilgore ML. PillCam ESO versus esophagogastroduodenoscopy in esophageal variceal screening: A decision analysis. *J Clin Gastroenterol.* 2009;43(10):975-81. d. de Franchis R. Non-invasive (and minimally invasive) diagnosis of oesophageal varices. *J Hepatol.* 2008 Oct;49(4):520-7. Minor points: 1) In results section the authors state: "25 patients were randomized to receive PR plus ISMN and 23 were randomized to receive PR alone", while in the abstract they write: "Forty schistosomiasis patients without previous variceal bleeding were randomly assigned to treatment with PR plus ISMN or PR alone". Indeed, 48 patients were randomized and data on change in variceal pressure were available for 40 patients. 2) English language level should be improved in the whole manuscript



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Reviewer code: 00058672

Science editor: Huang, Xin-Zhen

Date sent for review: 2012-12-24 10:50

Date reviewed: 2013-03-13 09:30

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
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		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The authors aim to compare the effects on variceal pressure with PR to that with PR plus ISMN in patients with schistosomiasis presinusoidal portal hypertension. The document is well-written with outstanding illustrations. I found the results to be compelling and proper for publication. I recommend that a minor revision is needed, to add the limitation in the discussion section.