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## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 15531

**Title:** Metadoxine improves three and six-month survival rate in patients with severe alcoholic hepatitis: A randomized controlled trial

**Reviewer's code:** 00185965

**Reviewer's country:** Croatia

**Science editor:** Yuan Qi

**Date sent for review:** 2014-12-01 19:52

**Date reviewed:** 2014-12-11 03:53

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 checked="" type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

### COMMENTS TO AUTHORS

Dear Editor, With a great interest I read the paper Metadoxine improves three and six-month survival rate in patients with severe alcoholic hepatitis: A randomized controlled trial written by Fátima Higuera-de la Tijera. Although interested topic and results I can find important obstacles in this paper. 1. the sample is too small to draw any firm conclusion, there are no power analysis 2. authors did not provide the method of randomization

Minor comments 1. please explain abbreviations when first time used in text (the abstract, management of complications) 2. please explain the proposed mechanism how metadoxine can help in alcohol abstinence 3. SAH in the literature usually means Subarahnoid hemorrhage



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## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 15531

**Title:** Metadoxine improves three and six-month survival rate in patients with severe alcoholic hepatitis: A randomized controlled trial

**Reviewer's code:** 02936306

**Reviewer's country:** South Korea

**Science editor:** Yuan Qi

**Date sent for review:** 2014-12-01 19:52

**Date reviewed:** 2014-12-06 10:53

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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

Author groups reported a part of this study in Ann Hepatol. 2014 May-Jun;13(3):343-52, entitled as "Treatment with metadoxine and its impact on early mortality in patients with severe alcoholic hepatitis." In the current manuscript, they included pentoxifylline (PTX) treatment group for the analyses, but some data are redundant. Authors found that alcohol abstinence is an independent prognostic factor in the six-month mortality, and that patients with taking metadoxine (MTD) might be better to prevent re-consumption of alcohol than patients without. However, they did not state Acamprosate, which is a drug used for treating alcoholics. Authors should clarify whether the use of Acamprosate was excluded or not.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 15531

**Title:** Metadoxine improves three and six-month survival rate in patients with severe alcoholic hepatitis: A randomized controlled trial

**Reviewer's code:** 00034635

**Reviewer's country:** Spain

**Science editor:** Yuan Qi

**Date sent for review:** 2014-12-01 19:52

**Date reviewed:** 2014-12-06 19:04

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" 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 is a single-center open label clinical trial comparing pentoxifylline, prednisone or metadoxine alone or in combination to assess their efficacy in severe alcoholic hepatitis. Results showed that groups receiving metadoxine achieved better survival. As in other studies, maintenance of alcohol abstinence is the best predictor of survival. This is an interesting study focusing in a largely unmet need therapeutic area. However, intervention did not prevent complications associated to cirrhosis which may be explained either because the study was underpowered or that the effect of abstinence it-self rather than intervention was the main predictor for survival. I would like to make further comments. Major: 1.Randomization procedure was not described 2.Although the groups were well-balanced at baseline, only 33-35 patients were included in each group. How the sample size was calculated? 3.Benefit in survival was associated to abstinence which in turn occurred more frequently in those receiving MTD, the authors speculated about central effects of the drug in some cognitive items. Can you please further discuss on a potential causality or chance effect between MTD and abstinence? Minor: Recent results from the STOPAH trial should be discussed.