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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 28003
Title: Prolonged feeding with guanidinoacetate, a methyl group consumer, exacerbates ethanol-induced liver injury
Reviewer's code: 03644873
Reviewer's country: Germany
Science editor: Jing Yu
Date sent for review: 2016-06-24 15:29
Date reviewed: 2016-07-02 18:46

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	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In the paper "Prolonged Feeding with Guanidinoacetate, a Methyl Group Consumer, Exacerbates Ethanol-Induced Liver Injury" Osna and colleges investigated whether exposure to GAA either alone or in combination with ethanol intake for a prolonged period of time (6 weeks) would cause more liver damage that the acute one that they had previously reported (2 weeks). Methods: Adult male Wistar rats were fed the control or ethanol Lieber DeCarli diet in the absence or presence of GAA supplementation. At the end of 6 weeks of the feeding regimen, various biochemical and histological analyses were conducted.Interestingly, rats were fed the GAA-supplemented ethanol diet, displayed similar histological and biochemical changes as observed after 2 weeks of combined treatment, including inflammation, macro- and micro-vesicular steatosis and a marked decrease in the methylation potential were noted. In addition, rats on the combined treatment exhibited increased liver toxicity and fibrosis. The authors speculate that this could be due to the increased accumulation of GAA in the liver and the inability of creatine generated to exert its hepato-protective effects. Whereas the paper clearly shows the synergism between GAA and ethanol, a need to investigate the

mechanisms by which this synergy exerts and increase in TG and cholesterol metabolism resulting in hepatosteatosis is still missing. An important point is to know whether prolonged administration of both GAA and ethanol would lead to hepatocellular carcinoma development and whether the observations are species-specific (rats, mice..). Thus, these novel synergy could replace the current experimental models of ASH lacking the NASH component as observed after Lieber de Carli feeding and represent an alternative to this diet alone. Moreover, if HCC development exists in the chronic situation this would a very valuable experimental tool for the study of ASH.