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## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 26904

**Title:** THE ROLE OF NITRIC OXIDE IN LIVER TRANSPLANTATION: SHOULD IT BE ROUTINELY USED?

**Reviewer's code:** 03536011

**Reviewer's country:** Japan

**Science editor:** Jing Yu

**Date sent for review:** 2016-05-04 12:33

**Date reviewed:** 2016-05-15 14:43

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" 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 checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" 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 checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

This review article is well written with a wide area of experimental and clinical results involved in NO and NOS of liver IR injury. In inflamed liver, iNOS is expressed in Kupffer cells and hepatocytes, followed by high levels of NO production. Proinflammatory cytokines including TNF- $\alpha$  and IL-1 $\beta$  and NO produced by iNOS have been implicated as factors in liver injury [Inflammation & Allergy- Drug Targets, 2015;14:77-83]. In general, NO produced by eNOS in liver sinusoidal endothelial cells protects against injury, whereas NO produced by iNOS contributes to pathological processes. However, NO produced during various types of liver injury may have either detrimental or beneficial effects depending on the insults and cell types involved. Reviewer agree authors' conclusion; Accumulated evidence indicates that inhaled NO may have protective-effects on the donor liver graft against IR injury in patients undergoing liver transplantation.



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**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 26904

**Title:** THE ROLE OF NITRIC OXIDE IN LIVER TRANSPLANTATION: SHOULD IT BE ROUTINELY USED?

**Reviewer's code:** 00502871

**Reviewer's country:** United States

**Science editor:** Jing Yu

**Date sent for review:** 2016-05-04 12:33

**Date reviewed:** 2016-06-04 00:01

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 checked="" type="checkbox"/> Grade C: Good	<input checked="" 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 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

The manuscript is a well performed literature review of studies of nitric oxide. It would be an appropriate introduction for a grant proposal for a randomized control trial of use of nitric oxide in liver transplantation. Such a study would be useful, but until it is performed, it is premature to recommend this as a change in standard of care. Revision of the manuscript may be possible.



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 26904

**Title:** THE ROLE OF NITRIC OXIDE IN LIVER TRANSPLANTATION: SHOULD IT BE ROUTINELY USED?

**Reviewer’s code:** 03042420

**Reviewer’s country:** China

**Science editor:** Jing Yu

**Date sent for review:** 2016-05-04 12:33

**Date reviewed:** 2016-06-15 11:45

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 checked="" 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 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 checked="" 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**

In this review, authors recapitulated biological characteristics and therapeutic application of nitric oxide (NO) in liver transplantation. In general, this manuscript is well prepared although there are several revisions that need to be addressed. Major points: As shown previously and discussed by the authors, the exact role of NO in organ repair/regeneration is quite controversial. The main determinants of the effects of NO on liver protection are its concentration, dosage, and duration. In this regard, the authors should address the potential risk on the therapeutic use of NO for liver transplantation in the animal experiments and clinical translation. Minor points: Grammar and typo errors: “These pulmonary effects include decrease pulmonary and systemic vascular resistance with resultant improvements in tissue oxygenation, ...”



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## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**ESPS manuscript NO:** 26904

**Title:** THE ROLE OF NITRIC OXIDE IN LIVER TRANSPLANTATION: SHOULD IT BE ROUTINELY USED?

**Reviewer's code:** 03051573

**Reviewer's country:** Spain

**Science editor:** Jing Yu

**Date sent for review:** 2016-05-04 12:33

**Date reviewed:** 2016-06-16 19:07

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 checked="" 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 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 very interesting manuscript that reviews the role of nitric oxide administration during ischemia/reperfusion injury in patients undergoing liver transplantation. The manuscript is well written although the text needs some improvement. A list of potential modifications to the manuscript has been attached for author's evaluation to be included.