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PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine
Manuscript NO: 36010
Title: Effects of mineralocorticoid receptor antagonists on responses to hemorrhagic shock in rats
Reviewer's code: 00505382
Reviewer's country: Italy
Science editor: Jin-Xin Kong
Date sent for review: 2017-10-30
Date reviewed: 2017-11-02
Review time: 3 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	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This study describes the effect of MR antagonist in a rat model of hemorragic shock, showing no benefit of pretreatment with MR antagonist. Article is well written and covers an interesting topic, with potential implication for clinical practice and future clinical studies. I would suggest some minor comments. - considering late deaths (e.g. one death after 7h in the control group), stretching the follow up from 8 to 12 or 24 hours somehow modify the results? - pH and HR figures would benefit from an adjustment of Y-axis scale - TNF-alfa figure is difficult to interpretate because of the overlap of the error bars, and could be rearranged

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PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine
Manuscript NO: 36010
Title: Effects of mineralocorticoid receptor antagonists on responses to hemorrhagic shock in rats
Reviewer's code: 02488399
Reviewer's country: Serbia
Science editor: Jin-Xin Kong
Date sent for review: 2017-11-02
Date reviewed: 2017-11-05
Review time: 3 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[Y] 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	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Excellent research with interesting study design, and results.

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PEER-REVIEW REPORT

Name of journal: World Journal of Critical Care Medicine
Manuscript NO: 36010
Title: Effects of mineralocorticoid receptor antagonists on responses to hemorrhagic shock in rats
Reviewer's code: 00506276
Reviewer's country: Poland
Science editor: Jin-Xin Kong
Date sent for review: 2017-11-02
Date reviewed: 2017-11-18
Review time: 16 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

In this study the authors examined the effect of mineralocorticoid receptor antagonists, spironolactone and eplerenone, in the preclinical model of hemorhagic shock in the rat. The MR antagonists were administered orally for 5 days and then hemorhagic shock was induced by blood removal followed by recovery after 40 minutes. It has been demonstrated that neither of the MR antagonists had any effect on survival rate, blood TNF-alpha concentration, liver TNF-alpha, IL-6 and IL-1beta and ICAM-1 mRNA expression or heart rate. However, eplerenone slightly improved blood pressure at the later stages of the recovery period.

The data are of interest. However, there are also some important concerns to be addressed.

Major comments:

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1) MR antagonists were administered in food. When food was withdrawn before the experiments? If the experiments were performed during the light period, is it possible that the activity of MR antagonists expired before exsanguination which could explain the negative results?
2) It should be specified how much blood was removed from the animal during the experiment.
3) Page 7: there is the discrepancy regarding time of blood collection for TNF measurement between line 4 and lines 5/6.
4) Results section (page 8): it should be clearly described how blood pressure changed in eplerenone-treated animals vs. other groups.
5) The method of lactate measurement should be described.
6) Why IL-1beta, IL-6 and ICAM-1 concentration were not measured in the blood? mRNA expression in the liver may not be representative for these inflammation markers. For example, IL-1beta level may be more dependent on inflammasome processing of its precursor rather than on mRNA expression.
7) That eplerenone improved blood pressure should be discussed. In addition, it should be discussed why EPL but not SPL had this effect on blood pressure.

Minor comments:

1) Page 3 Abstract/Conclusions: there is no evidence of anti-inflammatory effects of MR antagonists in this study.
2) The abbreviation “BGA” should be explained when used the first time.