

PEER-REVIEW REPORT

Name of journal: *World Journal of Critical Care Medicine*

Manuscript NO: 78878

Title: Current role of high dose vitamin C in sepsis management: A concise review

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02498841

Position: Editor-in-Chief

Academic degree: MD, PhD

Professional title: Dean, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: India

Manuscript submission date: 2022-07-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-20 08:53

Reviewer performed review: 2022-07-25 08:30

Review time: 4 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This review summarized the research progress of vitamin C in the treatment of sepsis. Juneja D et al demonstrated that the use of high concentration of vitamin C in patients with sepsis and septic shock may be harmful, while the use of vitamin C cocktail therapy (HAT), may be beneficial. The manuscript has a good concept and is well drafted. Only several scientific concern/questions need to be answered: 1. In Marik's study mentioned in the review, the experimental group was used cocktail therapy including hydrocortisone, thiamine, and ascorbic acid, the control group was only used thiamine, and ascorbic acid. The variable is not ascorbic acid, which can only show the effect of hydrocortisone in cocktail therapy, but cannot actually highlight the effect of vitamin C. 2. The review mentioned that currently there was no precise definition of the specific concentration of high-dose vitamin, and it was generally considered a dose of more than 10 gm/day in adults as a high dose. However, doses of vitamin C used in the listed combination therapy studies were 1.5g every 6 hours, or 50mg/kg every 12 hours, which I suppose whether it is against the title of the review. 3. The conclusions section briefly summarized that routine use of HDVC was not recommended in the management of sepsis, while few studies on the adverse effects of high-dose vitamin C on patients with sepsis was listed in the review. Moreover, the combination therapy even showed potential benefits to the patients, so I consider that the summary lacks comprehensiveness. 4. The proportion of rationale can be reduced and that of studies on high-dose vitamin C should be increased in this review.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04913291

Position: Peer Reviewer

Academic degree: MD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: India

Manuscript submission date: 2022-07-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-20 03:14

Reviewer performed review: 2022-07-27 06:01

Review time: 7 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statementsConflicts-of-Interest: [☐] Yes [☒] No**SPECIFIC COMMENTS TO AUTHORS**

This article reviews the rationale and current clinical evidence for use of high-dose vitamin C in the management of patients with sepsis and septic shock. The manuscript was well organized. However, there are some (major) issues should be addressed. 1. The paper mentioned that intravenous HDVC may be rarely associated with adverse reactions such as hemolysis, especially for vulnerable patients with G6PD deficiency or potential renal insufficiency, please describe that in detail in the main text.

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05427157

Position: Peer Reviewer

Academic degree: MD

Professional title: Director, Staff Physician

Reviewer's Country/Territory: United States

Author's Country/Territory: India

Manuscript submission date: 2022-07-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-19 21:18

Reviewer performed review: 2022-07-28 02:49

Review time: 8 Days and 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Overall excellent manuscript and outlines all important evidence available on this topic and reads well. few suggestions that will make manuscript stronger 1) add a paragraph on major professional critical care society guidelines on use of high dose vitamin C in sepsis/septic shock or if they don't address mention that they don't. 2) add a paragraph on author's practice at their institution

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05405005

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Portugal

Author's Country/Territory: India

Manuscript submission date: 2022-07-19

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-21 19:54

Reviewer performed review: 2022-07-29 18:10

Review time: 7 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Dear author, This reviewer presents his appreciation for the submitted article and the work developed in it. This reviewer also considers that it is based on a solid clinical issue which have remained questionable in the management of patients with sepsis and septic shock and it potentially could add a small contribution to the field. However, I also consider that the manuscript needs a major revision in order to add valid clinical conclusions. The PRISMA method for reporting the clinical findings of systematic revisions should be used and it should prompt a rearrangement of the submitted manuscript in order to be valid for publication. Furthermore, an initial paragraph in the Results section should be considered establishing the organization of this section. A Discussion section with the interpretation of your findings and highlighting concisely the key points of your results should also be added to thsi manuscript. No significance or relevance of your findings to the clinical pratice were considered in your paper. In that regard, the reviewer has included a document with some questions and revisions to you in an attempt to improve the manuscript and increase its interest and publication value. Best regards,

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Peer-review model: Single blind

Reviewer's code: 05405005

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Portugal

Author's Country/Territory: India

Manuscript submission date: 2022-07-19

Reviewer chosen by: Yun-Xiaojuan Wu

Reviewer accepted review: 2022-08-12 10:48

Reviewer performed review: 2022-08-14 12:13

Review time: 2 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear author, This reviewer presents his appreciation for the submitted article and the work developed in it. This reviewer also considers that the manuscript has been greatly improved by the reviewer's suggestions, and that its interest and scientific accuracy has increased. Well done. Best regards,