

We thank the editors and the reviewers for considering our manuscript and advising changes to further improve it. We have incorporated all the changes as suggested by the reviewers. We hope, you will find it appropriate for publication now. However, we will be happy to make any further changes you may suggest.

No.	Reviewer's comments	Authors reply	Changes made
#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.	Thank you for your inputs. We agree that there were several shortcomings in the Marik trial, hence further studies were performed, which failed to replicate these results. Our article is also a reflection of the same.	No changes made.
	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.	As there is no current consensus regarding "high dose", different authors have defined it differently, hence the discrepancy. However, we have changed the reference in accordance to our manuscript.	Necessary changes made in the dosing.
	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.	Combination therapy mostly included corticosteroids, which have been shown to be beneficial in sepsis management. Hence, the benefits of combination regimens can not be attributed to vitamin C therapy and it can't be recommended based on these results.	No changes made.
	The proportion of rationale can be reduced and that of studies on high-dose vitamin C should be increased in this review.	We had included detailed tables to support the clinical evidence. Nevertheless, we have added more details as per the suggestion.	More details added in the clinical evidence.
#2	The paper mentioned that intravenous HDVC may be rarely associated with adverse reactions such as hemolysis,	Necessary text added.	Details added in the adverse effects.

	especially for vulnerable patients with G6PD deficiency or potential renal insufficiency, please describe that in detail in the main text.		
#3	Overall excellent manuscript and outlines all important evidence available on this topic and reads well. few suggestions that will make manuscript stronger. 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.	Thank you for your comments. Have added the recent Surviving Sepsis Guidelines	Changes made under in the "Discussion"
	Add a paragraph on author's practice at their institution	Necessary changes made	Changes made under in the "Discussion"
#4	Abstract: The reviewer suggests that the abstract should include the PRISMA method for systematic review reporting and should include a Results section and Conclusion	Thank you for your comments. We have written the abstract as per the Journal's recommendations which requires "Unstructured" abstract for "Mini-reviews"	No changes made
	Some syntax irregularities and English errors are present in the manuscript.	Necessary changes made	Necessary changes made through-out the manuscript.
	The reviewer suggests the revision of the statement in page 4 , lines 9-11. There are no clear international recommendations to the use of Vitamin C in the treatment of the specified diseases.	We agree that no current guidelines recommend use of Vitamin C. Have rephrased the lines and added specific "sepsis guidelines recommendations" under the clinical evidence	Necessary changes made in the introduction and clinical evidence
	The reviewer suggests that the statement in page 4, lines 16-18 should not be included considering its lack of relevance for the main topic of this mini review	Have removed the suggested lines	Necessary changes made in the introduction
	The reviewer suggests a revision in page 5, paragraph 1, lines 3-10. Considering that there is no statistically valid evidence to reliably prove the benefit of Vitamin C, the authors should consider to rephrase this section as "could potentially be"	Necessary changes made	Changes made in Rationale

	<p>The reviewer suggests that the authors should follow the PRISMA method for presenting systematic reviews in this manuscript. The definition of a methodology, even a succinct one, allows for the comprehension of the revision process and to determine the accuracy and bias of the submitted manuscript</p>	<p>This is a “mini-review” and hence, the PRISMA guidelines for “systematic review” do not apply. We have written the manuscript as per the Journal’s recommendations for “mini-review”</p>	<p>No changes made</p>
	<p>The reviewer suggest to exclude the terms " before and after" in page 7, line 8</p>	<p>Necessary changes made</p>	<p>Changes made in Clinical Evidence</p>
	<p>The reviewer suggests that, considering there was no statistical difference, a “hint” is not a valid statistical term and should prompt a revision of the statement (page 9, line 24-28).</p>	<p>Necessary changes made</p>	<p>Changes made in Clinical Evidence</p>
	<p>The reviewer suggests that an initial paragraph in the Results section should be considered establishing the organization of this section.</p>	<p>As this was a “mini-review” we had not followed the “IMRD” criteria and have discussed the results in detail under “Clinical evidence” and tables</p>	<p>No changes made</p>
	<p>The reviewer suggests that a Discussion section could be written. The interpretation of the article findings and the key points of the results should be added in this proposed section of the manuscript. No significance or relevance of the findings to the clinical practice were considered in the paper</p>	<p>As per the suggestion, “Discussion” section added</p>	<p>New section added</p>