

Response to reviewers

2 Peer-review report

Reviewer #1: This is a succinct yet comprehensive overview of the manifold effects and possible clinical uses of vitamin C in critically ill patients. Well-written and supported with literature.

Reviewer #2: Nabzyk et al have summarized about increasing body of evidence in favor of high dose vitamin c administration which improves hemodynamics, end-organ function, and may improve survival in critically patients. Amongst its functions it serves as potent anti-oxidant, co-factor in the collagen and catecholamine synthesis, and modulator of immune cell biology. Furthermore, an increasing body of evidence suggests that high dose vitamin c administration improves hemodynamics, end-organ function, and may improve survival in critically patients. This article "Vitamin C in the critically ill – indications and controversies" reviews studies that evaluate vitamin c in pre-clinical models and clinical trials with regards to its therapeutic potential. The paper is well written in a narrative format in easy to understand language. It would be more interesting to see a sytemic review and meta-analysis to have a more scientific aspect of the topic as well.

Reviewer #3: The manuscript summarizes broadly and succinctly, with good organization, the complex literature on vitamin C in the critically ill. While some of the topics are not conventionally considered critical illness (eg., complex regional pain syndrome, malignancy), yet the overall picture is enhanced by inclusion of these topics. Minor language polishing - grammar, capitalization of the C in vitamin C - needs to be done. Well written, overall, and a worthy contribution to the critical care literature.

Reviewer #4: This is an interesting an well-written mini-review for the intensivists. I found no major comments. Maybe the authors could comment on the potential role of vitamin C in ischemic-reperfusion injury and inflammation after hemorrhagic shock

Authors' response to reviewers

Reviewer #1: We thank the reviewer for the careful evaluation of the manuscript. Reviewer #1 made no specific requests to change the manuscript.

Reviewer #2: We thank the reviewer for the careful evaluation of the manuscript. We agree with reviewer #2 that a systematic review and meta-analysis of this topic would be very interesting and may help in the debate about the appropriate clinical indications for the use of vitamin C in the critically ill. We are

hopeful that in the near future more high quality clinical data will be available that justifies a systematic review and meta-analysis.

Reviewer #3: We thank the reviewer for the careful evaluation of the manuscript. We addressed spelling and grammar issues that were raised by reviewer #3 and believe that the manuscript quality has improved because of that.

Reviewer #4: We thank the reviewer for the careful evaluation of the manuscript and for suggesting to add a section about the role of vitamin C in the setting of hemorrhagic shock. As requested, a separate section was added that summarizes the most relevant findings pertaining to this subject.