

Response to the letter of Morán et al. regarding our use of an inaccurate reference for the maximal dose of vitamin C in G6PD deficiency

Honore, Patrick M; Spapen, Herbert D; Marik, Paul; Boer, Willem; Oudemans-van Straaten, Heleen

Published in:
Annals of Intensive Care

DOI:
[10.1186/s13613-020-00712-5](https://doi.org/10.1186/s13613-020-00712-5)

Publication date:
2020

License:
CC BY

Document Version:
Final published version

[Link to publication](#)

Citation for published version (APA):

Honore, P. M., Spapen, H. D., Marik, P., Boer, W., & Oudemans-van Straaten, H. (2020). Response to the letter of Morán et al. regarding our use of an inaccurate reference for the maximal dose of vitamin C in G6PD deficiency. *Annals of Intensive Care*, 10(1), [93]. <https://doi.org/10.1186/s13613-020-00712-5>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LETTER TO THE EDITOR

Open Access



Response to the letter of Morán et al. regarding our use of an inaccurate reference for the maximal dose of vitamin C in G6PD deficiency

Patrick M. Honore^{1*}, Herbert D. Spapen², Paul Marik³, Willem Boer⁴ and Heleen Oudemans-van Straaten⁵

To the editor,

We thank Morán et al. [1] for their very attentive reading of our review on vitamin C dosing during renal replacement therapy [2], thereby noticing that one of the cited references [3] had been retracted. We used this retracted reference to support the assertion that a vitamin C dose up to 6 g/day was not contraindicated in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. In fact, the retraction notice appeared about 1 year after the original publication and unfortunately overlapped the first submission of our review. We sincerely apologize for missing this important item and completely agree with Morán et al. to eliminate the reference from our review.

Still, scarce data from the literature suggest that a vitamin C dose up to 6 g/day can be safely administered to patients with G6PD. Methemoglobinemia—the presence of methemoglobin in the blood—is most commonly treated with methylene blue [4]. However, methylene blue cannot be used in G6PD deficiency because it is ineffective and may even worsen G6PD deficiency-related hemolysis [4]. In vitro data going back to 1979 demonstrated that a vitamin C plasma concentration up to 5 mmol/L inhibited oxidation of oxyhemoglobin and Heinz body formation in G6PD-deficient red cells incubated with the strong oxidizing

drug acetylphenylhydrazine [5]. Applying a dosing regimen of 1.5 g IV q6h, vitamin C serum concentrations are typically situated between 200 and 600 $\mu\text{mol/L}$ [6]. Acute hemolytic anemia in a patient with severe methemoglobinemia and G6PD deficiency successfully resolved within 24 h following strictly monitored administration of 1 g vitamin C q6h [4]. However, a recent review reported that vitamin C doses of 4 to 6 g may propagate hemolysis [7]. This illustrates that vitamin C administration in G6PD patients requires caution. Alternative treatment [4] should be preferred if methemoglobinemia develops. In the absence of a valid alternative, a maximal IV dose of 4 to 6 g vitamin C could be considered, provided that strict monitoring is guaranteed. Meanwhile, it is wise to exclude patients with known or suspected G6PD deficiency from studies evaluating the use of 6 g vitamin C in populations that may benefit from this therapy such as septic shock or burn patients.

Abbreviation

G6PD: Glucose-6-phosphate dehydrogenase.

Acknowledgements

We would like to thank Dr. Melissa Jackson for critical review of the manuscript.

Authors' contributions

PMH, HDS, PM, WB and HOV designed the paper. All authors participated in drafting and reviewing. All authors read and approved the final manuscript.

Funding

None.

*Correspondence: Patrick.Honore@CHU-Brugmann.be

¹ ICU Dept, Centre Hospitalier Universitaire Brugmann-Brugmann University Hospital, Place Van Gehuchtenplein, 4, 1020 Brussels, Belgium
Full list of author information is available at the end of the article

Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare to have no competing interests.

Author details

¹ ICU Dept, Centre Hospitalier Universitaire Brugmann-Brugmann University Hospital, Place Van Gehuchtenplein, 4, 1020 Brussels, Belgium. ² Medicine, Development, Ageing & Pathology Research Department, Vrije Universiteit Brussel, Brussels, Belgium. ³ Division of Pulmonary and Critical Care Medicine, Eastern Virginia Medical School, 825 Fairfax Av, Suite 410, Norfolk, VA 23507, USA. ⁴ Dept of Anesthesiology, Intensive Care Medicine, Emergency Medicine & Pain Medicine, Ziekenhuis Oost-Limburg, Genk, Belgium. ⁵ Department of Intensive Care Medicine, Amsterdam UMC, Vrije Universiteit Amsterdam, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands.

Received: 25 June 2020 Accepted: 30 June 2020

Published online: 10 July 2020

References

1. Morán JM, Herrera-Peco I. Commentary to "Dosing vitamin C in critically ill patients with special attention to renal replacement therapy: a narrative review". *Ann Intensive Care*. 2020. <https://doi.org/10.1186/s13613-020-00710-7>.
2. Honore PM, Spapen HD, Marik P, Boer W, Oudemans-van Straaten H. Dosing vitamin C in critically ill patients with special attention to renal replacement therapy: a narrative review. *Ann Intensive Care*. 2020;10:23. <https://doi.org/10.1186/s13613-020-0640-6>.
3. Wu S, Wu G, Wu H. Hemolytic jaundice induced by pharmacological dose ascorbic acid in glucose-6-phosphate dehydrogenase deficiency: a case report: retraction. *Medicine (Baltimore)*. 2019;98(48):e18261. <https://doi.org/10.1097/MD.00000000000018261>.
4. Rehman A, Shehadeh M, Khirfan D, Jones A. Severe acute haemolytic anaemia associated with severe methaemoglobinemia in a G6PD-deficient man. *BMJ Case Rep*. 2018. <https://doi.org/10.1136/bcr-2017-223369>.
5. Winterbourn CC. Protection by ascorbate against acetylphenylhydrazine induced Heinz body formation in glucose-6-phosphate dehydrogenase deficient erythrocytes. *Br J Haematol*. 1979;41:245–52.
6. Marik PE. Is intravenous vitamin C contraindicated in patients with G6PD deficiency? *Crit Care*. 2019;23(1):109. <https://doi.org/10.1186/s13054-019-2397-6>.
7. Yanase F, Fujii T, Naorunroj T, et al. Harm of IV high-dose vitamin C therapy in adult patients: a scoping review. *Crit Care Med*. 2020. <https://doi.org/10.1097/CCM.0000000000004396>.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Submit your manuscript to a SpringerOpen[®] journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► [springeropen.com](https://www.springeropen.com)