

CORRESPONDENCE

Open Access



Study claiming target in sepsis with erythromycin has no effect upon mortality and secondary outcomes includes patients with CRRT and RRT

Patrick M. Honore^{1*}, Sydney Blackman², Emily Perriens² and Ibrahim Bousbiat²

Reijnders et al. recently published an article concluding that, in their target trial emulation on critically ill patients with sepsis, they could not demonstrate an effect of treatment with low-dose erythromycin on mortality, secondary clinical outcomes, or host response biomarkers [1]. However, when carefully reviewing the baseline characteristics, we found that 49.8% of the patients in the treated group had acute kidney injury (AKI). Nearly half of critically ill patients—especially those with septic shock—have or developed AKI and 20–25% needed renal replacement therapy (RRT) within the first week of their stay [2]. So in Reijnders' study, since almost 50% had AKI, we could make the assumption that 20–25% needed RRT or continuous RRT (CRRT). As Reijnders' study did not provide numbers regarding RRT, this assumption may also overestimate any negative impact on effect estimates. Erythromycin has a molecular weight of 734 daltons making it in theory very easily removable by RRT and CRRT [3]. Although possible in theory, there are almost little to no published data on this issue. CRRT is performed using membranes that have a cut off value of

35–40 kDa; it is therefore logical to assume a considerable portion of erythromycin is eliminated by the CRRT [4]. New highly adsorptive membranes (HAM) are able to adsorb molecules with a molecular weight above 35 kDa, further increasing the removal of erythromycin [5]. Not taking the effect of RRT and CRRT on erythromycin into account can mislead evaluations and conclusions by artificially reducing the level of erythromycin and underestimating its effects in the treatment group [1]. We need to take into account that 75–80% of erythromycin is protein bound, leading to poor clearance by the kidney. Nevertheless, only a study looking into erythromycin clearance could precisely quantify the loss of erythromycin by RRT and the potential impact on the results of the study. If the findings of this new study show that erythromycin is significantly removed by RRT, excluding patients with AKI that may need RRT or CRRT is necessary to avoid potentially underestimating the effects of erythromycin in patients not undergoing RRT or CRRT in the future.

This comment refers to the article available online at <https://doi.org/10.1186/s13054-022-04016-x>.

*Correspondence:

Patrick M. Honore
patrick.honore@chuclouvain.be

¹ ICU Department, UCL Louvain Medical School, CHU UCL Godinne
Namur, Avenue G Thérèse 1, 5530 Yvoir, Belgium

² ICU Brugmann University Hospital, ULB University, Brussels, Belgium

Abbreviations

AKI	Acute kidney injury
RRT	Renal replacement therapy
CRRT	Continuous renal replacement therapy
HAM	Highly adsorptive membranes

Acknowledgements

None.



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Author contributions

PMH designed the paper. All authors read and approved the final manuscript.

Funding

None.

Availability of data and materials

Not applicable.

Declarations**Ethics approval and consent to participate**

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare to have no competing interests.

Received: 21 December 2022 Accepted: 24 January 2023

Published online: 07 February 2023

References

1. Reijnders TDY, Peters-Sengers H, van Vught LA, MARS consortium, et al. Effect of erythromycin on mortality and the host response in critically ill patients with sepsis: a target trial emulation. *Crit Care*. 2022;26(1):151. <https://doi.org/10.1186/s13054-022-04016-x>.
2. Ouattara M, Coulibaly S, N'Guessan Deto JP. Pharmacochemical aspects of the evolution from erythromycin to neomacrolides, ketolides and neoketolides. *Open J Med Chem*. 2020;10:57–112. <https://doi.org/10.4236/ojmc.2020.103005>.
3. Peters E, Antonelli M, Wittebole X, et al. A worldwide multicentre evaluation of the influence of deterioration or improvement of acute kidney injury on clinical outcome in critically ill patients with and without sepsis at ICU admission: results from The Intensive Care Over Nations audit. *Crit Care*. 2018;22(1):188. <https://doi.org/10.1186/s13054-018-2112-z>.
4. Honoré PM, Jacobs R, De Waele E, et al. Evaluating sepsis during continuous dialysis: are biomarkers still valid? *Blood Purif*. 2014;38(2):104–5. <https://doi.org/10.1159/000363497>.
5. Honoré PM, De Bels D, Spapen HD. An update on membranes and cartridges for extracorporeal blood purification in sepsis and septic shock. *Curr Opin Crit Care*. 2018;24(6):463–8. <https://doi.org/10.1097/MCC.0000000000000542>.

Publisher's Note

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

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

