Critical Care

MATTERS ARISING

Open Access

Thiamine supplementation in septic shock patients: still looking for the target population

Amanda Gomes Pereira[1*], Nara A. Costa[2], Mariana B. de Moraes[1], Marina P. Okoshi[1], Leonardo A. M. Zornoff[1], Paula S. Azevedo[1], Marcos F. Minicucci[1], Sérgio A. R. de Paiva[1] and Bertha F. Polegato[1]

Dear editor,

In recent years, there has been a growing interest in thiamine as a potential adjunctive therapy in septic shock, given its key role in the maintenance of cellular metabolism and energy production, being involved in various biological processes [1]. It is supposed that treatment of thiamine deficiency could mitigate alterations associated with organ dysfunction and lead to better outcomes in this critical population.

In light of this, Donnino and colleagues have been at the forefront of the efforts to provide clinical data regarding the efficacy of thiamine administration across different outcomes after sepsis [2–7]. We read with great interest the recent study published by his group, in which the authors conducted a post hoc analysis focusing on the effects of thiamine versus placebo on kidney protection. Vine et al. [8] included a cohort of 158 patients with septic shock from their two previous phase II clinical trials. The primary outcome of the study was the patients' condition at the time of hospital discharge, which was defined as being alive and RRT (Renal Replacement Therapy)-free at the time of hospital discharge. They reported that thiamine administration was associated with higher odds of being alive and RRT-free (adjusted odds ratio [aOR] 2.05 [95% confidence interval (CI) 1.08–3.90]) and not needing RRT (aOR 2.59 [95% CI 1.01–6.62]). Importantly, the effect was more pronounced in the thiamine-deficient patients (considered as < 8 nmol/L).

Similarly, we performed a sub-analysis of our previous randomized pilot trial [9] to explore the effects of thiamine on renal outcomes. The cohort included a total of 108 patients with septic shock at Intensive Care Unit (ICU) admission who were not receiving RRT at the time of enrolment (51 in the thiamine group and 57 in the placebo group). In contrast to the findings of Vine et al. [8], our analysis revealed no difference between the thiamine and placebo groups in the need for RRT, even after adjusting for age, sex, creatinine, and APACHE II (Table 1). Additionally, we performed other analyses excluding patients with acute kidney injury (AKI) at ICU admission. In this analysis, we had only 27 patients in the placebo group and 19 in thiamine group. Despite that, thiamine administration was not able to reduce AKI or RRT (Tables 2 and 3, respectively).

However, some points are important to be highlighted. In our analysis, the thiamine group showed a higher incidence of AKI at baseline compared to the placebo group (87% vs 64%, $p = 0.068$), although this difference was not statistically significant. Interestingly, creatinine was positively correlated with thiamine levels on baseline ($r = 0.646$, $p < 0.001$). The reduced glomerular filtration capacity, as indicated by the elevated creatinine concentration, may have led to a decreased urinary excretion of thiamine, resulting in a thiamine deficiency rate of only 8.6% (n = 9) in our sample. This is notably lower than the 29% reported by Vine et al. [8], who suggested that

This comment refers to the article available online at https://doi.org/10.1186/s13054-024-04818-1.

*Correspondence:
Amanda Gomes Pereira
ag.pereira@unesp.br
[1] Department of Internal Medicine, Botucatu Medical School, São Paulo State University (UNESP), Av. Prof. Mario Rubens Guimaraes Montenegro, S/N, UNESP - Campus de Botucatu, Botucatu, SP 18618 687, Brazil
[2] Faculty of Nutrition, Federal University of Goiás (UFG), Goiânia, Brazil

© The Author(s) 2024. **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.

Table 1 Logistic regression model for the prediction of RRT in 108 patients with septic shock

Variable	OR	CI 95%	*p*
RRT*	1.923	0.884–4.184	0.099
RRT**	1.916	0.667–5.506	0.227
RRT***	1.861	0.688–5.037	0.221

*Unadjusted **Adjusted by age, sex, creatinine and APACHE II ***Adjusted by creatinine

Table 2 Logistic regression model for the prediction of AKI in 43 patients with septic shock

Variable	OR	CI 95%	*p*
AKI*	2.222	0.600–8.237	0.232
AKI**	2.128	0.544–8.319	0.278

*Unadjusted **Adjusted by age, sex and APACHE II

Table 3 Logistic regression model for the prediction of RRT in 43 patients with septic shock

Variable	OR	CI 95%	*p*
RRT*	8.667	0.873–86.062	0.065
RRT**	5.495	0.482–62.682	0.170

*Unadjusted **Adjusted by age, sex and APACHE II

thiamine deficiency-patients would benefit most from thiamine administration. It is important to note that our relatively small sample size could increase the risk of a type II error and may have influenced the results.

The promising potential of using thiamine to manage septic shock is primarily grounded in the physiological plausibility of treating the deficiency of this essential vitamin. However, the clinical evidence is currently insufficient and inconclusive both in the general and target septic shock population. Further research is still needed to refine methods for accurately measuring thiamine levels and to identify which patient subpopulations might benefit most from thiamine administration.

Therefore, we can conclude that, to date, taken together, study results have not consistently demonstrated benefits with thiamine supplementation in patients with septic shock, including decreased mortality and renal protection. However, in patients with thiamine deficiency, supplementation could induce beneficial effects.

Author contributions

Conceptualization: A.G.P., B.F.P., M.F.M., and S.A.R.d.P. Methodology: A.G.P., N.A.C., and M.B.M. Formal analysis and investigation: A.G.P., S.A.R.d.P., and B.F.P. Writing—original draft preparation: A.G.P. and B.F.P. Writing—review and editing: A.G.P., B.F.P., M.F.M., S.A.R.d.P., M.P.O., L.A.M.Z., P.S.A., and N.A.C. Funding acquisition: A.G.P. and B.F.P. Resources: B.F.P. Supervision: B.F.P. All authors read and approved the final manuscript.

Funding

Supported by São Paulo Research Foundation (FAPESP), grant #2017/21554-5; The National Council for Scientific and Technological Development (CNPq), grant #309180/2021; and Pró-Reitoria de Pesquisa (PROPe) of São Paulo State University.

Availability of data and materials

The datasets utilized and/or analyzed during this study can be obtained from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The prospective, single-center, randomized, double-blind pilot study (RBR-M6BNY) were approved by local Institutional Review Boards. All study participants or their legal representatives were asked for written informed consent.

Consent for publication

Not Applicable.

Competing interests

The authors did not receive support from any organization for the submitted work.

Received: 10 June 2024 Accepted: 29 June 2024
Published online: 08 July 2024

References

1. Costa NA, Pereira AG, Sugizaki CSA, Vieira NM, Garcia LR, de Paiva SAR, et al. Insights into thiamine supplementation in patients with septic shock. Front Med. 2022;8:805199.
2. Donnino MW, Andersen LW, Chase M, Berg KM, Tidswell M, Giberson T, et al. Randomized, double-blind, placebo-controlled trial of thiamine as a metabolic resuscitator in septic shock: a pilot study. Crit Care Med. 2016;44:360–7.
3. Moskowitz A, Donnino MW. Thiamine (vitamin B1) in septic shock: a targeted therapy. J Thorac Dis. 2020;12:S78-83.
4. Moskowitz A, Donnino MW. Reply to Mumin et al.: the challenges of using and measuring thiamine in critical care. Am J Respir Crit Care Med. 2024;209:607–8.
5. Moskowitz A, Berg KM, Grossestreuer AV, Balaji L, Liu X, Cocchi MN, et al. Thiamine for renal protection in septic shock (TRPSS): a randomized, placebo-controlled, clinical trial. Am J Respir Crit Care Med. 2023;208:570–8.
6. Donnino MW, Carney E, Cocchi MN, Barbash I, Chase M, Joyce N, et al. Thiamine deficiency in critically ill patients with sepsis. J Crit Care. 2010;25:576–81.
7. Moskowitz A, Andersen LW, Cocchi MN, Karlsson M, Patel PV, Donnino MW. Thiamine as a renal protective agent in septic shock. A secondary analysis of a randomized double-blind, placebo-controlled Trial. Ann Am Thorac Soc. 2017;14:737–41.
8. Vine J, Lee JH, Kravitz MS, Grossestreuer AV, Balaji L, Leland SB, et al. Thiamine administration in septic shock: a post hoc analysis of two randomized trials. Crit Care Lond Engl. 2024;28:41.
9. Pereira AG, Costa NA, Amancio SC, Okoshi MP, Zornoff LA, Azevedo PS, et al. Effect of thiamine on clinical outcomes in septic shock patients: a randomized, double-blinded pilot study. Am J Respir Crit Care Med. 2023. https://doi.org/10.1164/rccm.202208-1583LE.

Publisher's Note

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