Indian Pediatrics (2025) 62:349–350
https://doi.org/10.1007/s13312-025-00033-5

INVITED COMMENTARY

Does Selenium Supplementation have Any Benefit in Children with Lower Respiratory Infection?

Joseph L. Mathew[1]

Received: 26 January 2025 / Accepted: 21 February 2025 / Published online: 22 April 2025

Selenium supplementation has been explored in diverse health conditions [1–8]. It follows a long list of 'once promising' nutritional supplements, that have now been shown to have little value. These include vitamin C, zinc, vitamin A, and more recently vitamin D. Does selenium- the new kid on the block- meet the same fate, or fare better as a therapeutic intervention?

In this issue of *Indian Pediatrics*, Shaikh et al. present a randomized controlled trial comparing oral selenium versus placebo in young children with acute lower respiratory tract infection (ALRTI) [9]. They suggested that although selenium did not influence the time required for clinical recovery or the length of hospitalization, it somehow reduced the need for ventilation support. However, before examining their trial results, it is worth evaluating the methodology.

The trial enrolled 120 young children (6 mo- 5y) with ALRTI defined as the combination of four clinical features viz. fever, cough, age-specific tachypnea, plus one of the following additional signs viz. use of accessory muscles, wheeze or crackles, feeding difficulty, or lethargy [9]. Although no literature reference was cited for this definition, it appears reasonable and fits the general understanding of ALRTI. However, the major flaw in this study is that somehow only 76/120 (63.3%) enrolled participants actually had tachypnea (this startling information is presented in the table of baseline characteristics) [9]. This raises two problems. First, if the inclusion criteria were not properly followed, the credibility of the trial is questionable. Second, if one-third of the children did not have tachypnea, they probably had other illnesses such as upper respiratory infection, middle ear infection, or even non-respiratory conditions- making the study invalid for ALRTI.

Half the enrolled children were randomized to receive oral selenium whereas the other half received distilled water. The allocation sequence was created using a computer program that developed equal-sized blocks. The authors stated that allocation concealment was achieved using serially numbered opaque sealed envelopes (SNOSE) [9] without specifying what the envelopes contained or whether they actually used these envelopes when participants were enrolled. This is important because they later mentioned that the hospital pharmacy prepared identical bottles containing either selenium or placebo, that were coded. If this is true, then it is unclear why they required SNOSE for allocation concealment as the bottles should simply have been serially numbered and dispended as per the allocation sequence. The investigators also stated that the dispensation of identical bottles resulted in the trial participants and investigator being blinded, but they also mentioned that 'blinding was done by a researcher not involved in the management' of the participants. These discrepancies lead one to wonder whether the various trial procedures dutifully reported were actually performed. The dosage of selenium supplementation chosen for this trial is interesting. A previous systematic review suggested that in sepsis, selenium supplementation at dosages higher than the daily requirement could be associated with reduced mortality [10]. In that context, it is intriguing why the investigators of this trial decided to administer the recommended daily intake, especially when there was no clinical or laboratory documentation of baseline selenium levels [9].

In terms of clinical care, the monitoring frequency of the enrolled children leaves a lot to be desired. The authors reported that the ward nursing officers recorded vital signs every twelve hours. This is very inadequate considering that the children were fairly sick with a quarter of them receiving mechanical ventilation.

Giving these methodological limitations that seriously comprise the internal validity of the trial [9], should the results be examined? The answer is an emphatic no, because

✉ Joseph L. Mathew
dr.joseph.l.mathew@gmail.com

[1] Advanced Pediatrics Centre, PGIMER Chandigarh, Chandigarh 160012, India

results are trustworthy only if the methods are appropriate. Nevertheless, a couple of points are worth exploring. In this trial, the majority of children appear to have recovered very quickly. In fact, most were free from all the presenting symptoms (fever, respiratory distress, feeding difficulty, etc.) within 2–3 days. This is quite remarkable considering that over 25% were receiving ventilation. Interestingly, despite clinical recovery within 3–4 days, the median duration of hospitalization was 6 days, suggesting that 'clinically recovered' children continued to stay in hospital for another 2–3 days. As the criteria for clinical recovery used in this study [9] correspond to the criteria for discharge in most settings, this interval between recovery and discharge is inexplicable. Unfortunately, the matter cannot be explored further as the investigators did not specify the discharge criteria.

Considering all these concerns, can we learn anything from this study? First, investigators should focus on appropriate methods that are associated with low(er) risk of bias in order for results to be valid. Second, it is more important to "do things right" than "report things right". In this context, it is pertinent that a recent systematic review evaluating the efficacy of selenium supplementation administered to pregnant women (for various maternal and infant outcomes), excluded 11 potentially eligible studies due to concerns about research integrity [2]. Third, given that this methodologically weak study has been published, its results will find their way to systematic reviews (and meta-analyses) on the subject, resulting in flawed analyses and data interpretation. Previously also, a systematic review of two trials reported that selenium supplementation impressively prevented late onset neonatal sepsis, but not mortality [3]. Last, but not the least, inappropriately designed and/or conducted research studies also create ethical concerns by exposing participants to study procedures lacking value (as the results cannot be interpreted).

Funding None.

Data Availability None.

Declarations

Conflict of interest None.

References

1. Li S, Tang T, Guo P, Zou Q, Ao X, Hu L, Tan L. A meta-analysis of randomized controlled trials: efficacy of selenium treatment for sepsis. Medicine (Baltimore). 2019;98: e14733.
2. McDougall AR, Dore G, Aboud L, et al. The effect of selenium supplementation in pregnant women on maternal, fetal, and newborn outcomes: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2023;5: 101160.
3. Garg BD, Bansal A, Kabra NS. Role of selenium supplementation in prevention of late onset sepsis among very low birth weight neonates: a systematic review of randomized controlled trials. J Matern Fetal Neonatal Med. 2019;32:4159–65.
4. Monangi N, Xu H, Khanam R, et al. Association of maternal prenatal selenium concentration and preterm birth: a multicountry meta-analysis. BMJ Glob Health. 2021;6: e005856.
5. Lacour M, Zunder T, Restle A, Schwarzer G. No evidence for an impact of selenium supplementation on environment associated health disorders–a systematic review. Int J Hyg Environ Health. 2004;207:1–13.
6. Fakhrolmobasheri M, Mazaheri-Tehrani S, Kieliszek M, Zeinalian M, Abbasi M, Karimi F, Mozafari AM. COVID-19 and selenium deficiency: a systematic review. Biol Trace Elem Res. 2022;200:3945–56.
7. Roldán-Bretón NR, Capuchino-Suárez AG, Mejía-León ME, Olvera-Sandoval C, Lima-Sánchez DN. Selenium serum levels in patients with SARS-CoV-2 infection: a systematic review and meta-analysis. J Nutr Sci. 2023;12: e86.
8. Jaff S, Zeraattalab-Motlagh S, Amiri Khosroshahi R, Gubari M, Mohammadi H, Djafarian K. The effect of selenium therapy in critically ill patients: an umbrella review of systematic reviews and meta-analysis of randomized controlled trials. Eur J Med Res. 2023;28:104.
9. Shaikh RJ, Joshi TA, Mundada SM, Pawar SY, Khaire PB. Oral selenium as an adjunct in the treatment of acute lower respiratory tract infections in children: a double-blind randomized controlled trial. Indian Pediatr 2025
10. Alhazzani W, Jacobi J, Sindi A, Hartog C, Reinhart K, Kokkoris S, et al. The effect of selenium therapy on mortality in patients with sepsis syndrome: a systematic review and meta-analysis of randomized controlled trials. Crit Care Med. 2013;41(6):1555–64.