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INVITED COMMENTARY

Oral Selenium as an Adjunct in the Treatment of Acute Lower Respiratory Tract Infections in Children

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Selenium is an essential trace mineral that is vital in maintaining human health and exists primarily as selenoproteins; around 25 selenoprotein genes have been characterized in humans. Some of these play a pivotal role in maintaining the redox homeostasis, modulating immune response, and regulating the inflammatory cascade [1]. In particular, glutathione peroxidase (G-Px), a selenoprotein, and thioredoxin reductase contribute to antioxidant defence, safeguarding the body against the damaging effects of reactive oxygen and nitrogen species. Another significant selenium-dependent function involves iodothyronine deiodinases, which facilitate the conversion of inactive thyroxine or tetraiodothyronine (T4) into the active thyroid hormone triiodothyronine (T3) [2].

The intake of selenium varies significantly in different geographic locations; due to variable content of the soil. Dietary selenium deficiency occurs in certain places, such as some parts of China where the soil is low in selenium [3] manifestaing as Keshan disease an endemic cardiomyopathy.

There has been an interest in exploring the therapeutic status of selenium in respiratory diseases over the past few decades with most studies not displaying a clinical benefit. The study by Shaikh et al. published in this issue of *Indian Pediatrics* is a double-blind, randomized controlled trial that included children aged 6 months to 5 years hospitalized with acute lower respiratory tract infection (ALRTI) at a tertiary care hospital in Aurangabad, Maharashtra, India [4]. Participants were randomly allocated (1:1) to receive oral selenium (20–30 mcg) or matching placebo in a once daily dose until discharge, along with standard treatment as per the unit protocol. The primary outcome was the time required for clinical recovery. The secondary outcomes were duration of hospital stay, modes of oxygen support required and side effects of selenium. The authors concluded that oral selenium, administered as an adjunct in a daily dose of 20–30 mcg orally for a short duration, does not reduce the time needed for clinical recovery or the duration of hospitalization but reduces the requirement for mechanical ventilation in under-five children with ALRTI. This is one of the well-conducted randomized controlled trials from India on the use of selenium in respiratory illnesses in children and is performed at a setup where all cases of varying severity are treated; however, children with very severe disease were excluded from the analysis. The results of the study may have been affected by the status of deficiency in the study group, severity of illness, etiological agents, duration of illness, and comorbid conditions. Selenium levels of the patients enrolled in this study were not known at baseline, but it is unlikely that these children were deficient in the mineral as Indian soils are not known to be selenium depleted. Some reports from India suggest disease due to selenium toxicity [5]. As selenium is routinely added to fertilizers and therefore agricultural soil is usually not deficient in the same. Since baseline selenium levels in the study participants were not measured or considered to decide dosing, deficiency cannot be ruled out with certainty and the given dose could have been inadequate to achieve the desired effect. As per guidelines of the National Institute of Health (NIH), the recommended daily allowance (RDA) of selenium is 15–20 mcg for a child aged 1–3 years, and 30–40 mcg for 4–13-year-olds. For older children and adults, the daily dose is 55–70 mcg. In the study by Shaikh et al. the doses of 20–30 mcg per day were administered which would cover the RDA but would possibly not be adequate to cover a deficiency of selenium if present [4].

The severity of illness seems to be similar in the two groups. The authors mention that there was a faster clinical recovery in children with bacterial pneumonia in the selenium group than in the control group. The precise definition of viral or bacterial pneumonia is not included nor it can be concluded from the available information. The day of administration of intervention cannot be assessed from the

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available data, however, it is less likely that it can affect the outcome. The authors tried to exclude children with comorbidities. Overall, the present study suggests no benefit of selenium as an adjunct treatment in a group of children with ALRTI, however, they observed a trend of faster recovery in children with bacterial pneumonia and reduced need for mechanical ventilation.

Two studies from China had shown benefit of selenium in high doses [6, 7]. Another study from Iraq explored the use of magnesium (200 mg) plus selenium (200 mcg) in asthmatic children with viral pneumonia [8]. Patients who received magnesium plus selenium in a single daily dose for 7 days showed better clinical and radiological response than controls. However, whether the effect was due to selenium or magnesium was not established. The intra-venous preparation of magnesium has a definite role in the management of acute severe asthma, and it cannot be ruled out if the effect was an extrapolation of the same. Again, the baseline levels of selenium in the study population were not known.

Majeed et al. documented a lower selenium levels in blood of COVID-19 patients as compared to healthy individuals in South India [9].

Majeed et al. in 2021 documented better outcome of administration of selenium (40 mcg/day) along with other ingredients in a randomized, placebo-controlled, trial Compared to the placebo group, the patients receiving selenium had a better therapeutic response with reduced COVID-19 symptoms [10].

The available scientific evidence as well as the results of the current study do not support any beneficial effect of selenium as an adjunct treatment of all ALRTI in under-five children. The current study generates a hypothesis that selenium helps in faster recovery and reduces the need for mechanical ventilation. The research question remains open to test the hypothesis in uniform groups (bacterial pneumonia and those needing mechanical ventilation) with adequate sample size.

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Declarations

Conflict of Interest None.

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