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Letter to the Editor

Selenium supplementation may improve COVID-19 survival in sickle cell disease

Abstract

Sickle cell disease is associated with lower selenium levels, and the serum selenium level is inversely associated with haemolysis in SCD. The SCD population is more vulnerable to adverse COVID-19 outcomes. SARS-CoV-2 infection lowers the serum selenium level and this is associated with severity of COVID-19. Selenium supplementation is proposed to improve COVID-19 outcomes in the sickle cell disease population.

Further to Ulfberg & Stehlik's letter of September 29th, further evidence supports the role of Se in COVID-19 virulence[1]. In their pre-print analysis by machine learning of Medicare patients, Dun et al. found that the leading comorbidity associated with COVID-19 mortality, adjusted for age and race, was sickle cell disease (aOR, 1·73; (95 % CI 1·21, 2·47)), followed by chronic kidney disease (aOR, 1·32; (95 % CI 1·29, 1·36))[2].

Both SCD and kidney disease can lower Se levels by decreasing tubular Se resorption and are associated with deficient Se status[3,4].

Se status or intake has been correlated with COVID-19 outcomes, including mortality and recovery rates, in four patient groups in China, Germany, South Korea and southern India[5–8]. SARS-CoV-2, like other RNA viruses, sequesters Se causing Se levels to drop during infection[6,9]. SARS-CoV-2 may infect cells in bone marrow, supressing red blood cell formation[10]. Se status is inversely associated with haemolysis in SCD and may both inhibit haemolysis and enhance erythropoiesis in SCD[3,11].

Se is required for the actions of both vitamin D and dexamethasone[12,13]. Se infusion is safe, including in critically ill and dialysis patients, and Se supplementation has had favourable effects in other RNA virus infections[14–16].

It should be noted that vitamin C and Mg are also commonly deficient nutrients and are required for the activation of vitamin D_3 by hydroxylation[17–19]. Deficiency of ascorbate has been associated with COVID-19 and COVID-19 outcomes in hospital populations[20].

Se, supplemented if necessary with its cofactors in vitamin D metabolism, is proposed to be an important protective factor in the general population, but has the potential to reduce mortality from SARS CoV-2 infection in the sickle cell disease population to an even greater extent.

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doi:10.1017/S0007114521003718

Acknowledgements

George Henderson reports that he has no conflict of interest to report in regard to this letter.

References

1. Ulfberg J & Stehlik R (2020) Finland's handling of selenium is a model in these times of coronavirus infections. *Br J Nutr*, 1–2.
2. Dun C, Walsh CM, Bae S, *et al.* (2020) A machine learning study of 534,023 Medicare beneficiaries with COVID-19: implications for personalized risk prediction. *medRxiv*.
3. Delesderrier E, Cople-Rodrigues CS, Omena J, *et al.* (2019) Selenium status and hemolysis in sickle cell disease patients. *Nutrients* **11**, 2211.
4. Iglesias P, Selgas R, Romero S, *et al.* (2013) Selenium and kidney disease. *J Nephrol* **26**, 266–272.
5. Zhang J, Taylor EW, Bennett K, *et al.* (2020) Association between regional selenium status and reported outcome of COVID-19 cases in China. *Am J Clin Nutr* **111**, 1297–1299.
6. Moghaddam A, Heller RA, Sun Q, *et al.* (2020) Selenium deficiency is associated with mortality risk from COVID-19. *Nutrients* **12**, 2098.
7. Im JH, Je YS, Baek J, *et al.* (2020) Nutritional status of patients with coronavirus disease 2019 (COVID-19). *Int J Infect Dis* **100**, 390–393.
8. Majeed M, Nagabhushanam K, Gowda S, *et al.* (2020) An exploratory study of selenium status in normal subjects and COVID-19 patients in south Indian population: case for adequate selenium status: selenium status in COVID-19 patients. *Nutrition* **82**, 111053.
9. Wang Y, Huang J, Sun Y, *et al.* (2020) SARS-CoV-2 suppresses mRNA expression of selenoproteins associated with ferroptosis, ER stress and DNA synthesis. *BioRxiv*.
10. Reva I, Yamamoto T, Rasskazova M, *et al.* (2020) Erythrocytes as a target of SARS CoV-2 in pathogenesis of covid-19. *Archiv EuroMedica* **10**.
11. Jagadeeswaran R, Lenny H, Zhang H, *et al.* (2018) The impact of selenium deficiency on a sickle cell disease mouse model. *Blood* **132**, Suppl. 1, 3645.
12. Schütze N, Fritsche J, Ebert-Dümig R, *et al.* (1999) The selenoprotein thioredoxin reductase is expressed in peripheral blood monocytes and THP1 human myeloid leukemia cells – regulation by 1,25-dihydroxyvitamin D_3 and selenite. *Biofactors* **10**, 329–338.
13. Rock C & Moos PJ (2009) Selenoprotein P regulation by the glucocorticoid receptor. *Biometals* **22**, 995–1009.

14. Zhao Y, Yang M, Mao Z, *et al.* (2019) The clinical outcomes of selenium supplementation on critically ill patients: a meta-analysis of randomized controlled trials. *Medicine* **98**, e15473.
15. Manzanares W, Lemieux M, Elke G, *et al.* (2016) High-dose intravenous selenium does not improve clinical outcomes in the critically ill: a systematic review and meta-analysis. *Crit Care* **20**, 356.
16. Steinbrenner H, Al-Quraishy S, Dkhil MA, *et al.* (2015) Dietary selenium in adjuvant therapy of viral and bacterial infections. *Adv Nutr* **6**, 73–82.
17. Cantatore FP, Loperfido MC, Magli DM, *et al.* (1991) The importance of vitamin C for hydroxylation of vitamin D_3 to 1,25(OH) $2D_3$ in man. *Clin Rheumatol* **10**, 162–167.
18. Dai Q, Zhu X, Manson JE, *et al.* (2018) Magnesium status and supplementation influence vitamin D status and metabolism: results from a randomized trial. *Am J Clin Nutr* **108**, 1249–1258.
19. Cooper ID, Crofts CAP, DiNicolantonio JJ, *et al.* (2020) Relationships between hyperinsulinaemia, magnesium, vitamin D, thrombosis and COVID-19: rationale for clinical management. *Open Heart* **7**, e001356.
20. Carr AC & Rowe S (2020) The emerging role of vitamin C in the prevention and treatment of COVID-19. *Nutrients* **12**, 3286.

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