



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: <http://www.clinicalnutritionespen.com>

Letter to the Editor

## Micronutrient supplementation before COVID-19 vaccination can protect against adverse effects



To the editor,

We read with interest recent “Dietary supplements and herbal medicine for COVID-19: A systematic review of randomized control trials” Feng Z et al. [1]. They have highlighted the importance of micronutrients in maintaining good immune function and protecting against COVID-19 infection.

Recent reports have brought to light 2 adverse effects after COVID vaccinations, namely thrombosis mainly cerebral vein thrombosis and exacerbation of autoimmune conditions [2,3]. We wish to bring to attention that micronutrient supplementation and maintenance will also help to protect against the adverse effects of the vaccination. This is especially important as booster doses are now being recommended in the elderly and immunosuppressed individuals. Micronutrient deficiency is a major global public health problem, the prevalence being higher in elderly individuals and middle and low-income countries.

All the class 2 micronutrients: vitamin D, selenium and zinc have the potential to boost humoral immunity and may help to boost the immune response to the vaccination [4].

Moreover, besides boosting humoral immunity these micronutrients have the potential to protect against thrombosis. Vitamin D and its metabolites through activation of VDR play an important role in thrombosis-related pathways and vitamin D deficiency has been seen in pregnant women with cerebral vein thrombosis [5]. Selenium supplementation is also associated with activation of anti-thrombotic pathways and downregulation of thrombosis, such as increased levels of prostacyclin  $I_2$  and decreased  $TxA_2$  [6]. Zinc, is also known to be an important regulator of haemostasis and thrombosis and deficiency has been implicated in haemorrhagic strokes [7].

Finally, all these micronutrients have the potential to protect against activation or relapse of autoimmune conditions. Vitamin D supplementation protects against aberrant autoimmune response through modulation of the dendritic cells and other antigen presenting cells, to keep them tolerogenic, and inhibition of Th1-type immune activity and suppression of B cells (key players in autoimmune conditions) [8]. Selenium supplementation has been shown to protect against autoimmune responses through a decrease in B cell activating factor (BAFF), increase in expression of IL-10 in end-organ tissues and upregulation of B cell regulation and upsurges of T cell regulation. Supplementation of both vitamin D and selenium is known to reduce and modulate disease activity in autoimmune thyroid diseases [8,9]. Zinc is known to play an important role in protection

against autoimmunity and low concentrations have been seen in autoimmune conditions [10].

Micronutrients exert an important role in the immune system and consequently could have a positive impact on SARS-CoV-2 infection. We present an argument for addition of vitamin D, zinc and selenium, relatively cheap and non-invasive supplements to prevent aberrant autoimmune reactions and to prevent thrombosis. The target population will include individuals with nutritional deficiencies, individuals with autoimmune conditions or individuals with a higher propensity towards developing thrombosis.

### Declaration of competing interest

The author declares no potential conflict of interest.

### Acknowledgement

RD is supported in part by the Ministry of Health, Clinician Scientist Award [MOH-000014]; and National Medical Research Council Centre Grant [NMRC/CG/017/2013]. All authors attest they meet the ICMJE criteria for authorship.

### References

- [1] Feng Z, Yang J, Xu M, Lin R, Yang H, Lai L, et al. Dietary supplements, and herbal medicine for COVID-19: a systematic review of randomized control trials. *Clin Nutr ESPEN* 2021;44:50–60.
- [2] Siegler JE, Klein P, Yaghi S, Vigilante N, Abdalkader M, Coutinho JM, et al. Cerebral vein thrombosis with vaccine-induced immune thrombotic thrombocytopenia. *Stroke* 2021 Jul 26. <https://doi.org/10.1161/STROKEAHA.121.035613>. STROKEAHA121035613.
- [3] Vuille-Lessard É, Montani M, Bosch J, Semmo N. Autoimmune hepatitis triggered by SARS-CoV-2 vaccination. *J Autoimmun* 2021;123:102710.
- [4] Zimmermann P, Curtis N. Factors that influence the immune response to vaccination. *Clin Microbiol Rev* 2019;32(2):e00084. 18.
- [5] Yevgi R, Bilge N, Simsek F, Eren A, Cimilli Senocak GN. Vitamin D levels and C-reactive protein/albumin ratio in pregnant women with cerebral venous sinus thrombosis. *J Thromb Thrombolysis* 2021 Aug 3. <https://doi.org/10.1007/s11239-021-02541-0> [Epub ahead of print].
- [6] Abdulah R, Katsuya Y, Kobayashi K, Nakazawa M, Nara M, Murakami M, et al. Effect of sodium selenite supplementation on the levels of prostacyclin I (2) and thromboxane A (2) in human. *Thromb Res* 2007;119:305–10.
- [7] Grüngreiff K, Gottstein T, Reinhold D. Zinc deficiency—an independent risk factor in the pathogenesis of haemorrhagic stroke? *Nutrients* 2020;12:3548.
- [8] Mele C, Caputo M, Bisceglia A, Samà MT, Zavattaro M, Aimaretti G, et al. Immunomodulatory effects of vitamin D in thyroid diseases. *Nutrients* 2020;12:1444.
- [9] Gärtner R, Gasnier BC, Dietrich JW, Krebs B, Angstwurm MW. Selenium supplementation in patients with autoimmune thyroiditis decreases

thyroid peroxidase antibodies concentrations. *J Clin Endocrinol Metab* 2002;87:1687–91.

- [10] Sanna A, Firinu D, Zavattari P, Valera P. Zinc status and autoimmunity: a systematic review and meta-analysis. *Nutrients* 2018;10:68.

Rinkoo Dalan\*

*Department of Endocrinology, Tan Tock Seng Hospital, Singapore*

*Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore*

Bernhard O. Boehm  
*Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore*

\* Corresponding author. Department of Endocrinology, Tan Tock Seng Hospital, Singapore.

E-mail address: [rinkoo\\_dalan@ttsh.com.sg](mailto:rinkoo_dalan@ttsh.com.sg) (R. Dalan).

12 September 2021