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Letter: does vitamin D have a potential role against COVID-19? Authors' reply

EDITORS,

We thank Kumar et al for their comments on our review article and the letter connected with that by Panarese and Shahini.[1,2] We agree that there is a complicated effect of vitamin D in preventing the severity of COVID-19, while this mechanism is not exactly the same as that of influenza.

Vascular injuries have become a focus of attention in COVID-19, especially in its severity and mortality; major risk factors include hypertension, diabetes and age. ACE2 is widely expressed in arterial and venous endothelial cells and arterial smooth muscle cells.[3] This provides the possibility for the virus to attack and damage blood vessels followed by increased blood clotting and platelet aggregation, which will eventually lead to thrombus formation.

Accumulating evidence suggests that coagulopathy is an important pathological process in COVID-19. Extensive coagulopathy can explain phenomena like ischemic skin lesions, increased risk of stroke and hypoxaemia in some severely ill patients even without breathing problems.[4] Several studies have shown that vitamin D deficiency was related to endothelial dysfunction and pathological changes to the vascular system.[5] $1,25(OH)_2D$ has been reported to promote vascular endothelial repair by inducing vascular smooth muscle cells to produce vascular endothelial growth factor (VEGF).[6] Vitamin D receptor knockout mice have coagulation disorders with injury.[7] Therefore, we speculate that the possible role of vitamin D in SARS-CoV-2 infection is not only from its impact on innate and adaptive immune responses (as in influenza), but also from effects on the cardiovascular system.

A recent retrospective study showed that 11 of 13 ICU patients had vitamin D insufficiency, compared to four of seven non-ICU patients. The mean serum 25(OH)D levels were 19.2 ± 10.8 ng/mL in ICU patients and 29.8 ± 13.3 ng/mL in non-ICU patients.[8] Based on evidence from the current literature, we propose that patients with low vitamin D levels might be at increased risk of severe COVID-19, but no evidence supports that vitamin D has any benefit as COVID-19 treatment. We suggest that groups at high risk for vitamin D deficiency, including the elderly, pregnant women, those exposed to insufficient UV radiation, and medical staff performing shift work should, if infected with COVID-19, take an appropriate dose of vitamin D, which may reduce the possibility of aggravation.

However, the recommended dosage of vitamin D supplementation remains unclear. Guidelines for many countries recommend 600-4000 IU/d and consider that a 25(OH)D concentration of 20 ng/mL is sufficient. Grant et al[9] have argued that a concentration of 40-60 ng/mL might be beneficial to high-risk groups for virus infection and have suggested taking 5000 IU/d after an initial 10 000 IU/d to raise the concentration rapidly. Since the safety of high serum 25(OH)D levels is uncertain, a serum concentration of 20-30 ng/mL seems appropriate. The actual supplementary dose should be determined according to the baseline level of vitamin D, an individual's general condition and risk of COVID-19 infection.

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LINKED CONTENT

This article is linked to Tian et al and Kumar et al papers. To view these articles, visit https://doi.org/10.1111/apt.15731 and https://doi.org/10.1111/apt.15801.

Yuan Tian
Long Rong

Department of Endoscopy Center, Peking University First Hospital, Beijing, China
Email: drronglong@foxmail.com

ORCID
Yuan Tian https://orcid.org/0000-0003-0192-3037
Long Rong https://orcid.org/0000-0001-5450-0535

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Letter: low population mortality from COVID-19 in countries south of latitude 35 degrees North supports vitamin D as a factor determining severity

EDITORS,

The recent editorial by Rhodes et al considered latitude and mentioned one mechanism that vitamin D is important in regulating and suppressing the inflammatory response of cytokines of respiratory epithelial cells and macrophages to various pathogens, including respiratory viruses and preventing cytokine storm and the subsequent acute respiratory distress syndrome (RDS).[1]

It is appropriate to add the induction of the antimicrobial peptide cathelicidin with anti-viral action,[2,3] and other beneficial mechanism of vitamin D including inhibition of the renin-angiotensin system (RAS) with inhibition of AT1R receptor, and stimulation of ACE2, the enzyme to which coronavirus binds and inhibits. This enzyme transforms angiotensin II into angiotensin (1-7), which is vasodilatory and hypotensive. This step, beneficial in these circumstances, is inhibited by SARS-CoV-2 and stimulated by vitamin D.

Lin reported that the renoprotective effect of calcitriol was due to the action on ACE, ACE2 and the ratio between both.[4] Xu demonstrated in rats with RDS that calcitriol pre-treatment inhibited renin, ACE and angiotensin II, but induced ACE2, and resulted in clinical improvement.[5] Gatera reviewed available evidence on vitamin D supplementation in animals and humans with RDS, and concluded that it was effective.[6]

In conclusion, both mechanisms may play a beneficial role in the action of vitamin D in COVID-19 infection—stimulation of the immune system and inhibition of RAS by stimulating ACE2.

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Jose L. Mansur

Center of Endocrinology and Osteoporosis, La Plata, Universidad Nacional de la Plata Facultad de Ciencias Medicas, Buenos Aires, Argentina
Email: joseluismansur@yahoo.com.ar