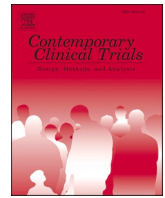




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## The link between vitamin D and COVID-19

To the Editor

A pragmatic design on the effect of vitamin D supplementation for early treatment and post-exposure prophylaxis of coronavirus disease 2019 (COVID-19) was published in the Contemporary Clinical Trials [1]. In this article, Wang et al. proposed a cluster-randomized, placebo-controlled, double-blind trial to evaluate the efficacy of vitamin D3 supplementation with 3200 IU/day for four weeks to reduce disease severity in persons with newly diagnosed COVID-19 and to prevent infection in closest householder members.

Previous data support that vitamin D could prevent respiratory tract infections (RTIs) [2], modulate both the innate and adaptive immune responses [3], or suppress the hyperinflammatory response during infection [4]. On the other hand, randomized controlled trials or meta-analysis have also shown that vitamin D supplementation did not reduce the risk of RTIs [5,6]. Reasons for the lack of agreement between observational studies and randomized controlled trials seem to be due to several factors, such as enrolling participants with relatively high 25(OH)D concentrations, using low vitamin D doses supplementation, and not measuring baseline and achieved 25(OH)D concentrations.

Concerning COVID-19, recent evidence also supported a protective role of vitamin D supplementation [7,8]. For instance, it is described that the risk of SARS-CoV-2 positivity is 54% higher in patients with 25(OH)D circulating levels <20 ng/mL when compared with those patients presenting a serum level of 30–34 ng/mL in multivariable analysis. Thus, the risk of SARS-CoV-2 positivity continued to decline until the serum levels of 25(OH)D reached 55 ng/mL [9]. In this scenario, Heaney [10] described that when the serum 25(OH)D level starting point is about 20 ng/mL, it takes 35 (85) days to reach 60 ng/mL with 10,000 IU/d (4000 IU/d). Conversely, serum 25(OH)D level can be increased to 40 ng/mL at five days after a single dose of 250,000 IU of vitamin D3 [11].

Therefore, we believe that to reduce COVID-19 severity in newly diagnosed patients and to prevent infection in closest householder members, Wang et al. [1] should consider to also test larger doses of vitamin D3 supplementation, mainly in patients presenting 25(OH)D deficiency (<20 ng/mL). In fact, a randomized placebo-controlled trial has shown that vitamin D oral supplementation (60,000 IU per day for at least seven days in asymptomatic or mildly symptomatic SARS-CoV-2 RNA positive vitamin D deficient, < 20 ng/mL, patients) increased the SARS-CoV-2 viral clearance and decrease fibrinogen levels [12].

In conclusion, there is a solid rationale to study whether vitamin D may prevent or reduce the severity of the symptoms of COVID-19 infection. However, the dose-response relationship between vitamin D and COVID-19 treatment or prevention and the safety of vitamin D supplementation should also be addressed.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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