

**Response to Letter to the Editor from Viola Viola: “Calcifediol treatment and COVID-19-related outcomes”**

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We thank Dr. Viola and colleagues for their letter to our article (1). We agree with the authors' point that 25(OH)D levels should be assayed during the hospital stay and even after discharge. Unfortunately, because of the harsh working conditions during the first wave of the pandemic, data were obtained in only a few patients. However, a rapid rise in 25(OH)D levels was expected after acute oral calcifediol intake, according to previous studies (2), and was confirmed in in-house controls (data not shown). Vitamin D's role in immune response mechanisms appears to be regulated primarily by availability of 25(OH)D, induction of CYP27B1 in the antigen-presenting cells by the invading pathogens and, ultimately, by stimulation of 1,25(OH)<sub>2</sub>D in the immune system (3). Potential effects of 1,25(OH)<sub>2</sub>D by inducing antimicrobial peptides, recruitment of neutrophils, monocytes/macrophages, and dendritic cells, as well as by modulating the adaptive immune response would help to overcome the COVID-19. Importantly, vitamin D may suppress the cytokine storm by simultaneously enhancing the innate immune system and reducing the overactivation of the adaptive immune system (3). Hence, treatment with calcifediol at higher doses is recommended to prevent worse COVID-19 outcomes as an adjuvant therapy in the hospital. Anyhow, further studies in an RCT setting are being carried out to corroborate this calcifediol effect.

Overall, there is well-established agreement that an adequate vitamin D status is necessary to maintain both musculoskeletal and general health (4, 5), thus regular monitoring of 25(OH)D levels should be considered at the population level and, in particular, in osteoporotic patients and the elderly. Accordingly, calcifediol or vitamin D supplementation should be strongly recommended to maintain adequate serum 25(OH)D levels in the general population.

## References

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