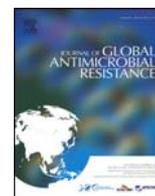




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Short Communication

Vitamin D deficiency and the COVID-19 pandemic

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The COVID-19 (coronavirus disease 2019) pandemic is having a colossal human, societal and economic cost that is encouraging individuals, physicians, collectives and authorities to re-evaluate the benefit/cost ratio of the various resources that could help us to better address the crisis—and limit the risk of its recurrence. In this context, we cannot ignore evidence in a recent ‘individual patient data’ meta-analysis that vitamin D supplementation protects against acute respiratory infections (ARIs) [1]. In this meta-analysis of 25 randomised controlled trials (RCTs) for which the full data of almost 11 000 individual patients were available, subgroup analyses revealed that the benefit was observed in those who received frequent (e.g. daily) doses of vitamin D but not in those who received bolus doses, and that the effect was largest when

vitamin D was given to individuals with vitamin D deficiency. Since then, several new RCTs have been published with mixed results, with some studies showing beneficial effects of vitamin D on ARIs while other did not. It is known that vitamin D stimulates innate immunity and modulates acquired immunity [2], explaining at least in part how vitamin D may fight against ARIs. Given that vitamin D deficiency is very common [3], especially during the ‘cold’ season owing to a lack of sunlight exposure, and given that containment at home will prevent sunlight exposure for many people worldwide, even in spring/summer, we believe that vitamin D supplementation should be encouraged, at least in any individual with risk factors of vitamin D deficiency (e.g. obesity, old age, dark skin, wearing covering clothes, no sunshine exposure). We acknowledge that while COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a type of ARI, we have no data enabling us to assert that vitamin D supplementation will reduce the incidence of COVID-19 infection.

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However, except for certain rare situations of vitamin D hypersensitivity (e.g. mutation in the CYP24A1 gene or sarcoidosis), daily supplementation with moderate doses of vitamin D₃ is safe. Specifically, there was no increased occurrence of renal stones in recent mega-trials that tested vitamin D₃ doses of 2000 IU/day [4] or 4000 IU/day [5]. In conclusion, despite a lack of direct evidence of an effect of vitamin D status on COVID-19 infection, we believe that vitamin D deficiency is an easily modifiable risk factor of ARIs and should be actively corrected through inexpensive, safe and readily-available vitamin D supplements. Even a small decrease in COVID-19 infections would easily justify this intervention. Nevertheless, we acknowledge that specific high-quality data are needed to demonstrate the efficacy of vitamin D supplementation in the prevention of COVID-19.

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Competing interests

None declared.

Ethical approval

Not required.

References

- [1] Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 2017;356:i6583, doi:<http://dx.doi.org/10.1136/bmj.i6583>.
- [2] Brighenti S, Bergman P, Martineau AR. Vitamin D and tuberculosis: where next? *J Intern Med* 2018;284:145–62, doi:<http://dx.doi.org/10.1111/joim.12777>.
- [3] Cashman KD, Dowling KG, Škrabáková Z, Gonzalez-Gross M, Valtueña J, De Henauw S, et al. Vitamin D deficiency in Europe: pandemic? *Am J Clin Nutr* 2016;103:1033–44, doi:<http://dx.doi.org/10.3945/ajcn.115.120873>.
- [4] Manson JE, Cook NR, Lee IM, Christen W, Bassuk SS, Mora S, et al. Vitamin D supplements and prevention of cancer and cardiovascular disease. *N Engl J Med* 2019;380:33–44, doi:<http://dx.doi.org/10.1056/NEJMoa1809944>.
- [5] Pittas AG, Dawson-Hughes B, Sheehan P, Ware JH, Knowler WC, Aroda VR, et al. Vitamin D supplementation and prevention of type 2 diabetes. *N Engl J Med* 2019;381:520–30, doi:<http://dx.doi.org/10.1056/NEJMoa1900906>.