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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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LINKED CONTENT

This article is linked to Rhodes et al papers. To view these articles, visit https://doi.org/10.1111/apt.15777 and https://doi.org/10.1111/apt.15823.

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

EDITORS,

We thank Dr Mansur for his interest in our editorial in which we highlighted the association between northern latitude and increased COVID-19 mortality[1] and for his helpful comments about the potential importance of vitamin D effects on cathelicidin and on the renin-angiotensin system, which could be important in protecting against severe COVID-19.[2] Vitamin D is a secosteroid hormone, derived like cortisol and sex hormones from cholesterol, so not surprisingly it has a broad range of actions reflecting the several hundred or more genes that are vitamin D responsive.[3,4]

Thrombosis is another aspect of severe COVID-19 illness where vitamin D may be very important, as previously highlighted by Tian and Rong.[5] The lupus anti-coagulant abnormality, characterised by prolonged activated partial thromboplastin time, has recently been reported in COVID-19.[6] This is the coagulopathy associated with anti-phospholipid syndrome in which there is evidence of seasonality[7] and a strong association with vitamin D deficiency.[8] Kawasaki syndrome, currently being reported with increasing incidence while countries are in 'lockdown', also has a winter predominance and here too a causative role for vitamin D deficiency has been suggested.[9]

All the associations between vitamin D deficiency and COVID-19 severity are circumstantial but they are stacking up and obtaining more direct evidence will not be easy. If low serum vitamin D levels are found in patients with severe COVID-19 these could reasonably be attributed to the well-recognised negative acute phase reactant response of vitamin D to illness.[10] A controlled trial of vitamin D supplementation would be intellectually neatest but this too will be difficult. Giving vitamin D to patients who are already ill may be too late. A placebo-controlled trial of prophylactic vitamin D in the community might be best but it could be very hard to find people willing to take the chance of being randomised to placebo rather than to a vitamin that is known to be essential—the clue is in the name!

If the vitamin D hypothesis is correct, then we would hope to see some reduction of COVID-19 severity in the Northern Hemisphere as we move into summer—provided that people who are not taking supplements get sufficient sunlight. Meanwhile people in the Southern Hemisphere might be well advised to take vitamin D supplements as they move into winter.

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LINKED CONTENT

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