Optimising vitamin D levels in patients with COVID-19

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As the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues, the focus on establishing a comprehensive treatment strategy is greater than ever. Coronavirus disease 2019 (COVID-19) places an immense burden on public health and limited hospital capacity; thus, it comes as no surprise that an effective therapeutic option has become a dire necessity. Although many drugs are currently undergoing clinical trials to test their efficacy and safety for treating patients with COVID-19, no specific medicine has been confirmed as truly beneficial to date.

The pathogenesis of SARS-CoV-2 is considered a two-phase viral response: the first immune defence-mediated protective phase and the second inflammation-driven destructive phase. Clinicians need immune boosters to manage phase one of COVID-19, and immune suppressors to manage phase two.

Recently, tocilizumab, an immunosuppressive drug, has gained considerable attention as a potential treatment option for patients with COVID-19. Tocilizumab, a synthetic monoclonal antibody, competitively inhibits the binding of interleukin (IL)-6 to its receptor, making it incapable of inducing immune damage, and relieving the inflammatory reactions.[1] Therefore, tocilizumab provides hope for treating critically ill patients with COVID-19; however, it can be used to manage only phase two, the inflammatory phase of COVID-19. Moreover, tocilizumab is expensive and requires intravenous administration, and it is associated with complications including gastrointestinal perforation and elevated pancreatic biomarkers.[1] Thus, there is a growing need for a cheaper and more readily available alternative treatment that can be used in both phases of COVID-19.

Several studies have demonstrated a potential link between vitamin D and various respiratory illnesses.[2] The role of vitamin D against viral infections is twofold. First, vitamin D induces the production of antiviral peptides such as cathelicidin in the respiratory epithelium, which strengthens mucosal defenses.[3] Second, vitamin D reduces cytokine production by enhancing the innate immune system and suppressing the overactivation of the adaptive immune system secondary to viral load.[4] Recent evidence also suggests an association of increased levels of IL-6 with vitamin D deficiency in HIV infection.[5] Vitamin D may mitigate the production of pro-inflammatory and anti-inflammatory cytokines, such as tumour necrosis factor α and IL-6, generated by the innate immune system in response to SARS-CoV-2 infection.

There is little evidence on the role of vitamin D deficiency in COVID-19 severity and mortality. The SARS-CoV-2 outbreak emerged during winter in the Northern Hemisphere; influenza virus also happens to peak in winter.[6] Because supplementation with vitamin D lowers the risk of influenza A,[7] insufficient levels of vitamin D due to reduced sunlight exposure in Northern regions may have contributed to the increased incidence of COVID-19.

Another indirect connection between poorer outcomes of COVID-19 and low vitamin D levels arises from the observation that some ethnicities are differentially affected by ongoing pandemic. Darker skin tone raises the risk of vitamin D deficiency, and estimates from the Office for National Statistics, United Kingdom, indicate a fourfold risk of COVID-19-related deaths in dark-skinned individuals from England and Wales relative to lighter-skinned individuals.[8]

We extracted data on the number of COVID-19 cases and deaths up to 6 August 2020 from the worldwide COVID-19 pandemic database[9] and data on about the prevalence of vitamin D deficiency from previous studies (Table).[10-14] We found that people residing in regions that are severely affected by COVID-19 also often had vitamin D deficiency, further reinforcing the potential correlation of vitamin D with seriousness of the disease.

Although low vitamin D levels are implicated in severity and mortality of COVID-19, there is no evidence to date supporting supplementation

TABLE. Burden of coronavirus disease 2019 (COVID-19) and prevalence of vitamin D deficiency in selected countries

Authors	Country	Sample size	Age, y	Prevalence of vitamin D deficiency (<50 nmol/L)	COVID-19 cases and deaths from worldwide COVID-19 pandemic data portal up to 6 August 2020[9]			
					Total cases	Total deaths	Cases/1 M population	Deaths/1 M population
Zhang et al[10]	China	322	60-75	71.7%	84 491	4634	59	3
Jolliffe et al[11]	United Kingdom	278	41-92	61.5%	307 184	46 364	6093	850
Tabrizi et al[12]	Iran	1911 (men) 3683 (women)	>18	Pooled prevalence: 55.21% (men) 64.71% (women)	317 483	17 802	3775	212
Liu et al[13]	United States	26 010	≥18	28.9%	4 947 715	161 088	14 939	486
Lelli et al[14]	Italy and Spain	420	≥65	94.3%	248 803 (Italy); 352 847 (Spain)	35 181 (Italy); 28 499 (Spain)	4116 (Italy); 7546 (Spain)	582 (Italy); 610 (Spain)

with vitamin D as a therapy with dose-response curve. However, several randomised open-label and blinded clinical trials are currently in progress of investigating vitamin D as a treatment option for COVID-19, rather than a preventive measure.[15-17]

Considering the expensiveness, limited availability, and adverse effects of tocilizumab, we believe that vitamin D is safe and offers a viable therapeutic option. The twofold mechanism of vitamin D in countering SARS-CoV-2 infection reinforces our confidence in its preventive and therapeutic adequacy. Further research is required to elucidate the exact mechanism of vitamin D in SARS-CoV-2 pathogenesis. We recommend that patients with COVID-19 have blood vitamin D levels tested on hospitalisation; these data would be invaluable in investigating any links between COVID-19 mortality and vitamin D. In the meantime, we recommend following the vitamin D supplementation guidelines set out by public health authorities.

Author contributions

Conflicts of interest

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