Vitamin D and covid-19

Article

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Can current guidelines on vitamin D supplementation prevent or treat SARS-CoV-2 infection?

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SARS-CoV-2 infection-related health crisis has led to unfounded or exaggerated claims on treatments. One area of controversy has been the role and dose of vitamin D supplementation in COVID-19[1 2]. Given the potential importance but prevailing uncertainty, the joint National Institute for Health and Care Excellence (NICE), Public Health England and Scientific Advisory Committee on Nutrition rapid guideline was recently published. It concluded that there was little evidence, highlighted the need for further research, and supported the existing government advice predicated on musculoskeletal health on vitamin D supplementation of 400IU/day for adults and children between October and March, when people in the UK do not make sufficient vitamin D from sunlight. It also stressed that certain populations such as minority ethnic groups, should consider taking this dose throughout the year[3]. The guidance is timely, but questions remain.

What is the evidence for a link between vitamin D and COVID-19?

Vitamin D supplementation of 400-1000IU/day has a modest protective effect for acute respiratory infections[4], providing indirect evidence for SARS-CoV-2 infection. There is, however, sparse research on a direct link.

The NICE review included one small randomised controlled trial (RCT) for COVID-19 treatment[5], no RCTs for COVID-19 prevention, and 12 observational studies of associations between vitamin D status and COVID-19 incidence or treatment. Among 76 Spanish patients hospitalised with COVID-19, high-dose supplementation equivalent to 21,280IU cholecalciferol on admission day and 10,640IU on day 3 and 7, then weekly until discharge reduced disease severity[5]. We found two further RCTs with conflicting findings. Among 240 Brazilian hospitalised patients with COVID-19, a single oral vitamin D_3 dose of 200,000IU versus placebo did not reduce the hospital length of stay[6]. In contrast, in 40 Indian SARS-CoV-2 positive Indians, infection vitamin D 60,000IU daily for 7 days, followed by the same dose either weekly or daily led to greater negative tests at 21 days[7]. These discrepancies highlight

the challenges of RCT design, with varying selection criteria, initial vitamin D status, the type, dose, and duration of supplementation, the endpoints studied, and risk of bias and study quality.

The observational evidence is inconsistent with some, but not all, studies reporting an association between vitamin D insufficiency and SARS-CoV-2 infection[3 8]. However, the observed link could be attributed to several confounding factors including age[9], ethnicity[10], genetic heterogeneity[11], and obesity[12 13] which are incompletely or not accounted for in different studies.

High-quality evidence is currently lacking, but there is suggestive evidence for an immunomodulatory role of vitamin D for respiratory infections and contextual evidence of the shared risk factors between vitamin D deficiency and COVID-19 severity: older age, obesity, and minority ethnicity. There is also a correlation between seasonal decline of vitamin D and higher COVID-19 burden in high-latitude countries[14]. The available evidence cannot be ignored and makes a compelling case for further research.

What next with the UK guidance on use of vitamin D supplementation?

The recommendation of 400IU seems justifiable to maintain 25(OH)D levels >25nmol/l in 97.5% of the UK population, but it is unclear whether this level is appropriate for immunomodulatory actions for COVID-19. Guidance recommending 400IU/day vitamin D supplementation in the UK has been in existence for a while, but its implementation has not been ensured. Raising awareness of the relevance of vitamin D is therefore appropriate for musculoskeletal health, particularly during lockdowns. It may also be relevant for COVID-19, given the suggestive though not conclusive evidence of its potential role and the precautionary principle. We also need clear guidance on how to obtain vitamin D for vulnerable groups. Health care professionals can point people to the free NHS vitamin D supplement provisions for people at high risk[15] and for women and children who qualify for the Healthy Start scheme.

Clinicians also need to be aware that vegetarians or vegans would need guidance on appropriate sources of vitamin D supplements.

The public health emergency posed by COVID-19 demands the use of all promising solutions, therefore vitamin D remains a plausible candidate. However, policy recommendations need to ensure that the public are not falsely reassured regarding the role of vitamin D for COVID-19. These guidelines therefore must be accompanied with continued messaging on hand hygiene, face coverings, physical distancing, and the importance of vaccine uptake in culturally and linguistically adapted campaigns through local community groups.

The published guidelines have clearly articulated the currently unconvincing evidence of vitamin D for COVID-19; therefore, it is vital that ongoing and future trials evaluate the effect of vitamin D supplementation with improved design including attention to comparing different dosing regimens, initial vitamin D status, inclusion of different population subgroups, older participants and those with morbidities, and in settings including hospitalised patients and population-based samples. Ongoing trials such as COVIT-TRIAL[16] and CORONAVIT (NCT04579640), which is comparing the national recommendation with higher dosage (800IU/day and 3200IU/day), will be important to inform future guidance.

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Duality of Interest

NGF is an honorary consultant public health physician with Public Health England. The views expressed are her own. KK is Director of the University of Leicester Centre for Black Minority Ethnic Health, Trustee of the South Asian Health Foundation, Chair of the Ethnicity Subgroup of SAGE and Member of Independent SAGE**.**

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