Vitamin D

**Recommendation**

- There is insufficient evidence to recommend either for or against the use of vitamin D for the prevention or treatment of COVID-19.

**Rationale**

Vitamin D is critical for bone and mineral metabolism. Because the vitamin D receptor is expressed on immune cells such as B cells, T cells, and antigen-presenting cells, and because these cells can synthesize the active vitamin D metabolite, vitamin D also has the potential to modulate innate and adaptive immune responses.\(^1\)

Vitamin D deficiency (defined as a serum concentration of 25-hydroxyvitamin D ≤20 ng/mL) is common in the United States, particularly among persons of Hispanic ethnicity and Black race. These groups are also overrepresented among cases of COVID-19 in the United States.\(^2\) Vitamin D deficiency is also more common in older patients and patients with obesity and hypertension; these factors have been associated with worse outcomes in patients with COVID-19. In observational studies, low vitamin D levels have been associated with an increased risk of community-acquired pneumonia in older adults\(^3\) and children.\(^4\)

Vitamin D supplements may increase the levels of T regulatory cells in healthy individuals and patients with autoimmune diseases; vitamin D supplements may also increase T regulatory cell activity.\(^5\) In a meta-analysis of randomized clinical trials, vitamin D supplementation was shown to protect against acute respiratory tract infection.\(^6\) However, in two double-blind, placebo-controlled, randomized clinical trials, administering high doses of vitamin D to critically ill patients with vitamin D deficiency (but not COVID-19) did not reduce the length of the hospital stay or the mortality rate when compared to placebo.\(^7,8\) High levels of vitamin D may cause hypercalcemia and nephrocalcinosis.\(^9\)

The rationale for using vitamin D is based largely on immunomodulatory effects that could potentially protect against COVID-19 infection or decrease the severity of illness. Ongoing observational studies are evaluating the role of vitamin D in preventing and treating COVID-19. Some investigational trials on the use of vitamin D in people with COVID-19 are being planned or are already accruing participants. These trials will administer vitamin D alone or in combination with other agents to participants with and without vitamin D deficiency. The latest information on these clinical trials can be found on ClinicalTrials.gov.

**Clinical Data**

**Randomized Clinical Trial of Vitamin D Versus Placebo in Patients With Moderate to Severe COVID-19**

In a double-blind, placebo-controlled randomized trial that was conducted at two sites in Brazil, 240 hospitalized patients with moderate to severe COVID-19 received either a single dose of 200,000 international units of vitamin D\(_3\) or placebo.\(^10\) Moderate to severe COVID-19 was defined as patients with a positive result on a SARS-CoV-2 polymerase chain reaction test (or compatible computed tomography scan findings) and a respiratory rate >24 breaths/min, oxygen saturation <93% on room air,
or risk factors for complications. The primary outcome in this study was the length of the hospital stay. The median length of stay was not significantly different between the vitamin D₃ arm (7.0 days [IQR 4.0–10.0 days]) and the placebo arm (7.0 days [IQR 5.0–13.0 days]; \( P = 0.59 \), log-rank test). No significant differences were observed between the arms in the percentages of patients who were admitted to the intensive care unit, who required mechanical ventilation, or who died during hospitalization.

It should be noted that this study had a small sample size and enrolled participants with a variety of comorbidities and concomitant medications. The time between symptom onset and randomization was relatively long, with patients randomized at a mean of 10.3 days after symptom onset. In this study, a single, high dose of vitamin D₃ did not significantly reduce the length of stay for hospitalized patients with COVID-19.

References