COVID-19 and Vitamin D: Partners in Crime, or Simply Associates?

Clinical Question: Does Vitamin D help prevent or treat COVID-19?

Bottom Line: While observational evidence suggests an association between low vitamin D levels and COVID-19 infection, it is unclear if this is simply reflective of overall health status. There are no randomized, controlled trials (RCTs) assessing vitamin D for prevention of COVID-19 infections. The highest quality RCT of vitamin D treatment during hospitalization did not demonstrate benefit for clinical outcomes.

Evidence:
- 3 RCTs assessed treatment in hospitalized patients with COVID-19, all received standard care in addition to oral:
  - Cholecalciferol 200,000 IU once versus placebo (240 patients, unpublished preprint).\(^1\)
    - No difference in length of stay (both 7 days).
    - No difference mortality, ICU admission or ventilation.
  - Calcifediol (~21,000 IU) on day 1, (~10,000 IU) days 3 and 7, then once weekly versus usual care (76 patients, pilot study). Study length not reported.\(^2\)
    - Vitamin D group showed:
      - Significant reduction ICU admission 1/50 (2%) versus 13/26 (50%).
      - Mortality 0/50 versus 2/26 (8%), not statistically different.
    - Limitations: Unbalanced randomization (more diabetes and hypertension in control), patients and physicians not blinded.
  - Cholecalciferol 60,000 IU daily x 7 days versus placebo in 40 patients with mild or no COVID-19 symptoms and Vitamin D deficient \([25(OH) D <20ng/ml]\).\(^3\)
    - Significantly more patients tested negative for COVID-19 within 21 days with vitamin D supplementation.
    - Limitations: Unclear randomization concealment and blinding, clinical outcomes not reported.
- There are no published RCTs evaluating the use of Vitamin D for prevention of COVID-19.
Systematic reviews of observational studies generally demonstrate an association of low Vitamin D levels with COVID-19 infection and severity of infection, although included studies are often at high risk of bias.⁴⁻⁶

**Context:**
- Low vitamin D is associated with poor health⁷ and it is unclear if low vitamin D levels are causative or simply reflect health status.
- Additional confounders linked to COVID-19 severity and low vitamin D levels⁷ include higher body mass index, diabetes, older age, and Black race/ethnicity (versus non-Hispanic white).⁸
- Current guidelines recommend against Vitamin D supplementation solely for prevention or treatment of COVID-19.⁹

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**Disclosures:**
Authors do not have any conflicts of interest to declare.

**References:**