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Can vitamin D prevent acute respiratory infections?

A systematic review and meta-analysis says Yes, but the dosages used may not be what you'd expect.

PRACTICE CHANGER

Reduce acute respiratory tract infections in those with significant vitamin D deficiency (circulating 25-hydroxyvitamin D levels < 10 ng/mL) with daily or weekly vitamin D supplementation—not bolus vitamin D treatment.¹

STRENGTH OF RECOMMENDATION

A: Based on a systematic review and meta-analysis of 25 trials.

Martineau AR, Jolliffe DA, Hooper RL, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ*. 2017;356:16583.

ILLUSTRATIVE CASE

Ms. M is a 55-year-old woman who is generally healthy, but who was diagnosed recently with severe vitamin D deficiency (serum 25-hydroxyvitamin D level of 8 ng/mL). She is being seen for her second episode of acute viral bronchitis in the past 6 months. She has no significant smoking or exposure history, no history of asthma, and takes no respiratory medications. Standard treatment for her level of vitamin D deficiency is 50,000 IU/week in bolus dosing, but is that your best option in this case?

Acute respiratory tract infections (ARTIs) include nonspecific upper respiratory illnesses, otitis media, sinusitis (~70% viral), pharyngitis, acute bronchitis (also ~70% viral), influenza, respiratory syncytial virus, and pneumonia.^{1,2} In the United States, ARTIs strain the health care system and are the most common cause of ambulatory care visits, accounting for al-

most 120 million, or about 10% of all visits, per year.³ In addition, ARTIs account for almost 50% of antibiotic prescriptions for adults and almost 75% of antibiotic prescriptions for children—many of which are unnecessary.^{2,4}

While patient and parent education, antibiotic stewardship programs, and demand management may reduce inappropriate antibiotic use and the overall burden of ARTIs on the health care system, prevention of infections is a powerful tool within the overall approach to managing ARTIs.

STUDY SUMMARY

Vitamin D protects against ARTIs, but only in smaller doses

This 2017 systematic review and meta-analysis of 25 trials (N=10,933) evaluated vitamin D supplementation for the prevention of ARTIs in the primary care setting. Individual participant data were reevaluated to reduce risk of bias. The Cochrane risk of bias tool was used to address threats to validity.

The review and meta-analysis included institutional review board-approved, randomized, double-blind, placebo-controlled trials of vitamin D₃ or vitamin D₂ supplementation of any duration and in any language. The incidence of ARTI was a prespecified efficacy outcome. Duration of the included randomized controlled trials (RCTs) ranged from 7 weeks to 1.5 years.

Outcomes. The primary outcome was an incidence of at least 1 ARTI. Secondary outcomes included incidence of upper and lower ARTIs; incidence of adverse reactions

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to vitamin D; incidence of emergency department visits or hospital admission or both for ARTI; use of antimicrobials for ARTI; absence from work or school due to ARTI, and mortality (ARTI-related and all-cause).

■ **Findings.** Daily or weekly vitamin D supplementation (in doses ranging from < 20 to ≥ 50 µg/d) reduced the risk for ARTI (adjusted odds ratio [AOR] = 0.88; 95% confidence interval [CI], 0.81-0.96; number needed to treat [NNT] = 33). In subgroup analysis, daily or weekly vitamin D was protective (AOR = 0.81; 95% CI, 0.72-0.91), but bolus dosing (≥ 30,000 IU) was not (AOR = 0.97; 95% CI, 0.86-1.10).

In 2-step analysis, patients benefited who: had baseline circulating 25-hydroxyvitamin D concentrations < 10 ng/mL (AOR = 0.30; 95% CI, 0.17-0.53; NNT = 4); had baseline circulating 25-hydroxyvitamin D levels of 10 to 28 ng/mL (AOR = 0.75; 95% CI, 0.60-0.95; NNT = 15); were ages 1.1 to 15.9 years (AOR = 0.59; 95% CI, 0.45-0.79); were ages 16 to 65 years (AOR = 0.79; 95% CI, 0.63-0.99); or had a body mass index < 25 (AOR = 0.82; 95% CI, 0.71-0.95).

■ **Higher D levels are a different story.** Vitamin D supplementation in people with circulating levels of 25-hydroxyvitamin D ≥ 30 ng/mL did not appear to provide benefit (AOR = 0.96; 95% CI, 0.78-1.18). Supplementation in this population did not influence any of the secondary outcomes, including risk for all-cause serious adverse events (AOR = 0.98; 95% CI, 0.80-1.20).

WHAT'S NEW

A more accurate snapshot

Previous studies of vitamin D and respiratory tract infections were mostly observational in nature. Those that were RCTs used variable doses of vitamin D, had variable baseline 25-hydroxyvitamin D levels, and employed various methods to monitor ARTI symptoms/incidence.⁵⁻⁸ This is the first systematic review and meta-analysis of randomized, double-blind, placebo-controlled trials with supplementation using vitamin D₃ or vitamin D₂ that used individual participant-level data, which gives a more accurate estimate of outcomes when compared with traditional meta-analyses.

CAVEATS

Only the most deficient benefit?

Vitamin D supplementation was safe and protected against ARTIs overall, but the greatest effect of vitamin D supplementation on the prevention of ARTIs was noted in those who were most severely vitamin D deficient (those with circulating 25-hydroxyvitamin levels < 10 ng/mL, NNT = 4; 10-28 ng/mL, NNT = 15). There was no demonstrable effect once circulating 25-hydroxyvitamin D levels reached 30 ng/mL.

CHALLENGES TO IMPLEMENTATION

Breaking tradition

The study found that both daily and weekly doses of vitamin D were effective in reducing the incidence of ARTIs, but the doses used were much lower than the commonly used 10,000 to 50,000 IU bolus doses, which were ineffective in reducing ARTIs in the current meta-analysis. Since bolus dosing is an ingrained practice for many providers, changing this may prove challenging.

In addition, the authors of the study suggest that one of the ways to provide this level of vitamin D is through food fortification, but food fortification is often complicated by emotional and/or political issues that could thwart implementation.

JFP



This study found that low-dose daily or weekly vitamin D supplementation was protective against acute respiratory tract infections, but bolus dosing was not.

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