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Q/ Does vitamin D supplementation reduce asthma exacerbations?

EVIDENCE-BASED ANSWER

A/ YES, to some extent it does, and primarily in patients with low vitamin D levels. Supplementation reduces asthma exacerbations requiring systemic steroids by 30% overall in adults and children with mild-to-moderate asthma (number needed to treat [NNT] = 7.7). The outcome is driven by the effect in patients with vitamin D levels < 25 nmol/L (NNT = 4.3), however; supplementation doesn't decrease exacerbations in patients with higher levels. Supplementation also reduces, by a smaller amount (NNT = 26.3), the odds of exacerbations requiring emer-

gency department care or hospitalization (strength of recommendation [SOR]: **A**, meta-analysis of randomized controlled trials [RCTs]).

In children, vitamin D supplementation may also reduce exacerbations and improve symptom scores (SOR: **C**, low-quality RCTs).

Vitamin D doesn't improve forced expiratory volume in 1 second (FEV₁) or standardized asthma control test scores. Also, it isn't associated with serious adverse effects (SOR: **A**, meta-analysis of RCTs).

Evidence summary

A Cochrane systematic review of vitamin D for managing asthma performed meta-analyses on RCTs that evaluated several outcomes.¹ The review found improvement in the primary outcome of asthma exacerbations requiring systemic steroids, mainly in adult patients, and in the secondary outcomes of emergency department visits or hospitalization, in a mix of adults and children (TABLE¹⁻⁶).

Most participants had mild-to-moderate asthma; trials lasted 4 to 12 months. Vitamin D dosage regimens varied, with a median daily dose of 900 IU/d (range, 400-4000 IU/d). Six RCTs were rated high-quality, and 1 had unclear risk of bias.

Supplementation reduced exacerbations in patients with low vitamin D levels

A subsequent (2017) systematic review and meta-analysis evaluating the primary out-

come of exacerbations requiring steroids⁷ included another study⁸ (in addition to the 6 RCTs in the Cochrane review).

When researchers reanalyzed individual participant data from the trials in the Cochrane review, plus the additional RCT, to include baseline vitamin D levels, they found that vitamin D supplementation reduced exacerbations overall (NNT = 7.7) and in patients with low baseline vitamin D levels (25[OH] vitamin D < 25 nmol/L; 92 participants in 3 RCTs; NNT = 4.3) but not in patients with higher baseline levels (764 participants in 6 RCTs). Vitamin D supplementation reduced the asthma exacerbation rate in patients with low baseline vitamin D levels (0.19 vs 0.42 events per participant-year; *P* = .046).

Smaller benefit found on ED visits and hospitalizations

The Cochrane review, with 2 RCTs with

TABLE

Effect of Vitamin D supplementation on frequency and severity of asthma exacerbations in patients with mild-to-moderate persistent asthma

Outcome measured	Studies	Population (mean ages)	Intervention vitamin D dose vs placebo ^a	Result (significant results in bold)	Comment
Asthma exacerbations requiring systemic steroids	658 Adults (2 RCTs ¹) 22 Children (1 RCT ¹)	Adults (40-48 y) Children (1-15 y)	Adults: 2000-4000 IU/d Children: 400-2000 IU/d	Overall: 0.28 vs 0.44 events/person-year	Low vitamin D = < 25 nmol/L
Asthma exacerbations requiring emergency department visit ± hospitalization	658 Adults (2 RCTs ¹) 305 Children (5 RCTs ²⁻⁶)	Adults (40-48 y) Children (1-18 y)	Adults: 2000-4000 IU/d Children: 400-1200 IU/d	25/1000 vs 63/1000 events in adults; NNT = 26.3	

NNT, number needed to treat.

^aAdditional Vitamin D dosing details: 400 IU/d,² 1000 IU/wk,³ 500 IU/d,⁴ 800 IU/d,⁵ 1200 IU/d.⁶

adults (n = 658)¹ and 5 RCTs with children (n = 305),²⁻⁶ evaluated whether Vitamin D reduced the need for emergency department visits and hospitalization with asthma exacerbations; they found a smaller benefit (NNT = 26.3).

Effects on FEV₁, daily asthma symptoms, and serious adverse effects

Several RCTs included in the 2017 meta-analysis found no effect of vitamin D supplementation on FEV₁, daily asthma symptoms (evaluated with the standardized Asthma Control Test Score), or reported serious adverse events.^{2-6,9,10} No deaths occurred in any trial.

Additional findings in children from lower-quality studies

A 2015 systematic review and meta-analysis of RCTs evaluating vitamin D supplementation for children with asthma found¹¹:

- moderate-quality evidence for decreased emergency department visits (1 RCT from India, 100 children ages 3 to 14 years, decrease not specified; *P* = .015);
- low-quality evidence for reduced exacerbations (6 RCTs [3 RCTs also in Cochrane review], 507 children ages 3 to 17 years; risk ratio = 0.41; 95% confidence interval, 0.27-0.63); and
- low-quality evidence for reduced standardized asthma symptom scores

(6 RCTs [2 RCTs also in Cochrane review], 231 children ages 3 to 17 years; amount of reduction not listed; *P* = .01).

Recommendations

No published guidelines discuss using vitamin D in managing asthma. An American Academy of Family Physicians (AAFP) summary of the Cochrane systematic review recommends that family physicians await further studies and updated guidelines before recommending vitamin D for patients with asthma.¹² The AAFP also points out that the Endocrine Society has recommended vitamin D supplementation for adults (1500-2000 IU/d) and children (at least 1000 IU/d) at risk for deficiency.

Editor's takeaway

In the meta-analyses highlighted here, researchers evaluated asthma patients with a wide range of ages, baseline vitamin D levels, and vitamin D supplementation protocols. Although vitamin D reduced asthma exacerbations requiring steroids overall, the effect was driven by 3 studies of patients with low baseline vitamin D levels. As a result, disentangling who might benefit the most remains a challenge. The conservative course for now is to manage asthma according to cur-

rent guidelines and supplement vitamin D in patients at risk for, or with known, deficiency. JFP

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