Is vitamin D effective in decreasing asthma exacerbations in children and adults with asthma?

EVIDENCE-BASED ANSWER

Vitamin D supplementation in children and adults with asthma modestly decreases the number of asthma exacerbations requiring systemic corticosteroids by 0.13 to 0.16 attacks per person per year and reduces asthma-related emergency department visits, hospitalizations, or both, with a number needed to treat of 27 to 33 (SOR: **A**, based on meta-analyses of randomized control trials [RCTs] with patient-oriented outcomes). The beneficial effect of vitamin D on asthma exacerbations does not appear to be dependent on baseline serum 25-hydroxyvitamin D level, age, gender, ethnic origin, body mass index, use of bolus-dose vitamin D, or concomitant use of inhaled corticosteroids (SOR: **A**, based on meta-analysis of individual participant data from RCTs).

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A meta-analysis of seven randomized control trials (N=963) examined the effectiveness of vitamin D supplementation in reducing exacerbations in patients with primarily mild-to-moderate asthma.[1] Participants included children (five trials, N=305; age range 1–18 years old) and adults (two trials, N=658; mean age range 39.7–47.9 years old) seen in primary care clinics, specialty practices, and hospitals across five countries. Vitamin D dosing included 500 to 1,200 IU daily, 1,000 IU weekly, 120,000 IU bolus every two months, or a 100,000 IU single bolus followed by 400 or 4,000 IU daily. The control groups received placebo in six studies and 400 IU vitamin D daily in one study. In nearly all the trials, vitamin D was administered for the duration of the study, which ranged from 4 to 12 months. The primary outcome was the rate of asthma exacerbations, defined as use of systemic corticosteroids. Vitamin D supplementation modestly decreased the rate of asthma exacerbations requiring systemic corticosteroids (three trials; N=680; 0.28 vs 0.44 events per person per year; absolute difference 0.16 events per person per year; rate ratio [RR] 0.64; 95% CI, 0.46–0.90) as well as exacerbations requiring emergency department visits, hospitalizations, or both (seven trials, N=963; odds ratio [OR] 0.39; 95% CI, 0.19–0.78; number needed to treat [NNT]=27) compared to control. No difference was noted in serious adverse events of any cause (five trials; N=879; OR 1.01; 95% CI, 0.54–1.89). Reviewers rated the evidence as high quality. Limitations included heterogeneity of vitamin D dosing. The authors prespecified their intent to carry out subgroup analyses but were unable to follow through because of an inability to disaggregate data.

To determine if the rate of asthma exacerbations differed by subgroup, including baseline serum 25-hydroxyvitamin D (25[OH]D) level, a second meta-analysis[2] (conducted by many of the same authors as the above meta-analysis) obtained individual participant data from seven trials, including six trials from the above meta-analysis. This second meta-analysis included 297 children and 658 adults (mean age ranges 2.9–47.9 years old) with asthma seen in primary care clinics, specialty practices, and hospitals across six countries. The vitamin D dose, control intervention, and primary outcome were similar to the first meta-analysis. This meta-analysis confirmed that vitamin D supplementation modestly decreased the rate of asthma exacerbations requiring systemic corticosteroids (seven trials, N=955; 0.30 vs 0.43 events per person per year; absolute difference 0.13 events per person per year; adjusted incidence rate ratio [aIRR] 0.74; 95% CI, 0.56–0.97) as well as exacerbations resulting in emergency visits, hospitalizations, or both (seven trials, N=955; adjusted odds ratio [aOR] 0.46; 95% CI, 0.24–0.91; NNT=33) compared to control. Post-hoc subgroup analyses showed that participants with baseline serum 25[OH]D levels <25 nmol/L who received the vitamin D treatment had fewer asthma exacerbations per year as compared with control (three trials, N=92; aIRR 0.33; 95% CI, 0.11–0.98), whereas those with baseline serum 25[OH]D levels of 25 nmol/L or more saw no significant difference between intervention and control groups in asthma exacerbations per year (six trials, N=764; aIRR 0.77; 95% CI, 0.58–1.03). However, interaction testing was not statistically significant (P=.25), indicating the authors were not able to demonstrate that the protective effects of vitamin D were stronger in the low serum 25[OH]D group than the other. Similarly, P values for interaction for other subgroups (ie, age, gender, ethnic origin, body mass index, use of bolus-dose vitamin D, and concomitant use of inhaled corticosteroids) were all >.05, suggesting no subgroup effect. No difference in serious adverse events was noted between the control and the intervention groups (seven trials, N=955; aOR 0.87; 95% CI, 0.46–1.63); no participants were found to have hypercalcemia or renal

stones. Reviewers rated the evidence as high quality, limited by the heterogeneity of vitamin D dosing. EBP

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AU1 The authors declare no conflicts of interest.

References

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2. Jolliffe DA, Greenberg L, Hooper RL, et al. Vitamin D supplementation to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data. *Lancet Respir Med.* 2017; 5(11):881–890. [STEP 1]