

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

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**CME** This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 286. Author disclosure: No relevant financial affiliations.

## Vitamin D for the Management of Asthma

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### Clinical Question

Does the use of vitamin D improve asthma symptoms and reduce asthma exacerbations requiring corticosteroid treatment?

### Evidence-Based Answer

Despite the authors' caution that further data are needed to clarify the role of vitamin D in care, this Cochrane review found that its use reduces the average number of asthma exacerbations requiring corticosteroid treatment from 0.44 to 0.28 per person per year. It also decreases the risk of emergency department visits and hospitalizations due to asthma exacerbation from 6% per year to around 3% per year.<sup>1</sup> (Strength of Recommendation: A, based on high-quality evidence.) Vitamin D has no effect on asthma symptom control as measured by the Asthma Control Test or on lung function as measured by predicted forced expiratory volume in one second (FEV<sub>1</sub>).<sup>1</sup> (Strength of Recommendation: A, based on high-quality evidence.) Family physicians should await further studies and updated guidelines before recommending the use of vitamin D for this indication.

### Practice Pointers

Asthma is a chronic inflammatory small airway disease characterized by recurrent episodes of dyspnea, wheezing, cough, and chest tightness (commonly known as asthma exacerbations). Asthma affects all age groups, with a prevalence of 8.4% in children and 7.6% in adults in the United States.<sup>2</sup> Exacerbation is a major cause of morbidity and mortality in persons with asthma. An exacerbation is classified as severe when the treatment includes systemic corticosteroids, emergency department visits, or hospitalization.<sup>3</sup> Vitamin D levels are often low in patients with asthma, and this has been linked to an increased

risk of exacerbation.<sup>4,5</sup> Vitamin D has been shown to induce antimicrobial activity<sup>6</sup> and anti-inflammatory activities.<sup>7</sup> It also enhances responsiveness to inhaled corticosteroids in patients with asthma.<sup>8</sup> The authors of this review sought to determine if use of vitamin D prevents asthma exacerbations and improves asthma symptoms.

This Cochrane review included nine double-blind, placebo-controlled trials that lasted at least 12 weeks.<sup>1</sup> Seven studies involved 435 children and two studies involved 658 adults for a total of 1,093 participants. Most of the participants had mild or moderate persistent asthma, and a minority had severe asthma.

Oral administration of vitamin D<sub>3</sub> (cholecalciferol) significantly decreased asthma exacerbations requiring systemic corticosteroid treatment. The average number of exacerbations per person per year decreased from 0.44 to 0.28 with vitamin D; in other words, a patient treated with vitamin D gained more than one year (from one event every 2.2 years to one event every 3.5 years) between exacerbations (relative risk = 0.63; 95% confidence interval [CI], 0.45 to 0.88). Vitamin D also significantly decreased emergency department visits and hospitalizations due to asthma exacerbation (absolute risk reduction = 3.8%; 95% CI, 1.3% to 5%; number needed to treat = 27 [95% CI, 20 to 76]).

Vitamin D had no effect on daily asthma symptom control, the use of inhaled beta agonists, predicted FEV<sub>1</sub>, peak expiratory flow rate, or the incidence of serious adverse events. Given that there were no fatalities in the trial, mortality data were not calculated.

Trials conducted in adults contributed disproportionately to this analysis. There was considerable heterogeneity in the vitamin D<sub>3</sub> regimens used in the studies, with dosages ranging from 400 to 4,000 IU daily (median dosage = 900 IU daily) with or without an additional 100,000 IU bolus dose in several studies. Formulations of 1,000 IU taken weekly, 60,000 IU monthly, or 120,000 IU bimonthly were used in other studies.

Further research is needed in children and to determine whether baseline and circulating 25-hydroxyvitamin D concentrations influence the effect of this therapy.

The Endocrine Society clinical guideline suggests that infants and children at risk of vitamin D deficiency may require a daily vitamin D supplement of at least 1,000 IU, and adults may need at least 1,500 to 2,000 IU.<sup>9</sup> Currently, no published guidelines discuss the use of vitamin D in the management of asthma.

The practice recommendations in this activity are available at <http://www.cochrane.org/CD011511>.

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## Pregabalin for Fibromyalgia Pain in Adults

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### Clinical Question

Does pregabalin (Lyrica) reduce the pain associated with fibromyalgia in adults?

### Evidence-Based Answer

There is high-quality evidence that pregabalin in daily dosages of 300 mg, 450 mg, and 600 mg reduces pain associated with fibromyalgia. The most effective dosage seems to be 450 mg daily; this dosage is more effective than placebo at reducing pain by at least 50% (number needed to treat [NNT] = 9.7). Compared with patients taking placebo, those taking pregabalin who tolerate titration to an effective dosage are more likely to maintain at least a 30% pain reduction for 13 weeks (NNT = 5.3).

Discontinuation of therapy occurs more often in patients taking pregabalin than in those taking placebo. For example, patients often quit taking pregabalin (450 mg daily) because of adverse effects (number needed to harm [NNH] = 11).<sup>1</sup> (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

### Practice Pointers

Fibromyalgia is the second most common rheumatologic condition in the United States, occurring in 2.4% of the population.<sup>2,3</sup> Fibromyalgia negatively affects quality of life, with 35% of patients reporting difficulty with activities of daily living.<sup>4</sup> The authors of this review sought to evaluate the effect of pregabalin on fibromyalgia pain in adults.

This Cochrane review included five randomized trials with 3,283 patients who had pain from fibromyalgia.<sup>1</sup> Studies lasted two to three months. Two additional studies followed patients for 13 to 26 weeks after titration of pregabalin to monitor maintenance of benefit.

The most effective daily dosage of pregabalin was 450 mg, which reduced pain by at least 50% vs. placebo (NNT = 9.7; 95% confidence interval [CI], 7.2 to 15), although with more discontinuation for adverse effects (NNH = 11; 95% CI, 8.4 to 17). Patients treated with 150 mg of pregabalin had no more pain relief than those taking placebo. Patients who took 300 mg of pregabalin also experienced at least a 50% pain reduction over baseline compared with patients taking placebo (NNT = 14; 95% CI, 8.9 to 32). Of note, the patients taking 300 mg of pregabalin daily were less likely to discontinue treatment because of adverse

effects (NNH = 17; 95% CI, 10 to 41) when compared with patients taking 450 mg daily.

Patients taking 600 mg of pregabalin daily were less likely to see at least a 50% reduction in their level of pain (NNT = 11; 95% CI, 7.1 to 21) than patients taking 450 mg; they were also more likely to discontinue treatment due to adverse effects (NNH = 5.9; 95% CI, 4.6 to 8) vs. patients taking 450 mg daily. Common adverse effects in patients taking pregabalin included somnolence, dizziness, weight gain, and peripheral edema. Meta-analysis demonstrated that approximately 10% of patients with fibromyalgia were able to tolerate the medication at doses that provided moderate or greater pain relief compared with placebo.

The authors evaluated two trials involving 687 patients who were monitored for at least 13 weeks after titration of pregabalin or placebo. Compared with patients taking placebo, those taking pregabalin were more likely to maintain at least 30% pain reduction over baseline at the study conclusion (NNT = 5.3; 95% CI, 3.9 to 8.2). In another recent meta-analysis, duloxetine (Cymbalta) at a dosage of 60 mg daily was more effective than pregabalin at a dosage of 300 mg daily at reducing fibromyalgia pain.<sup>5</sup> Guidelines on the management of fibromyalgia from the European League Against Rheumatism give a weak recommendation for the use of pregabalin, the

same recommendation given to other U.S. Food and Drug Administration–approved medications such as duloxetine.<sup>6</sup>

The practice recommendations in this activity are available at <http://www.cochrane.org/CD011790>.

The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, or the U.S. government.

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