

Vitamin D Tied to Airway Hyperresponsiveness

BY BRUCE JANCIN

KEYSTONE, COLO. — Low vitamin D levels in adults with asthma are associated with impaired lung function, increased airway hyperresponsiveness, and diminished in vitro response to glucocorticoids, according to a cross-sectional study.

The inference from this study is that vitamin D deficiency—a common finding in adults with asthma—may be one of the mechanisms underlying suboptimal clinical response to inhaled corticosteroids. This raises the testable hypothesis that vitamin D supplementation may improve asthma severity and treatment response, Dr. E. Rand Sutherland said at a meeting on allergy and respiratory diseases.

A multicenter prospective clinical trial of vitamin D supplementation in asthma is forthcoming to see whether it improves asthma control. Results are probably 4 years away, said Dr. Sutherland, who is chief of the division of pulmonary and critical care medicine at Na-

VITALS

Major Finding: There was a 22.7-mL increase in forced expiratory volume in 1 second (FEV₁) for each 1 ng/mL increase in serum vitamin D. In subjects with reduced vitamin D levels below 30 ng/mL, 1.03-mg/mL provocative concentration of methacholine was required to induce a 20% fall in FEV₁, whereas 1.92 mg/mL was required in those with a serum vitamin D level of 30 ng/mL or more.

Data Source: A cross-sectional study included 54 nonsmoking adults with persistent asthma.

Disclosures: The current study was supported by the National Institutes of Health. Dr. Sutherland disclosed that he serves on advisory boards for Dey and GlaxoSmithKline and as a consultant to Schering-Plough.

tional Jewish Health, Denver.

"I don't know that we have actionable data here in terms of what to do with asthmatics, but there is probably very little harm in giving 1,000-4,000 IU/day of cholecalciferol. If you're up against the wall in terms of what to do with a patient, this is one thing that's cheap, relatively easy, and may not be harmful," he said in response to an audience question.

The cross-sectional study included 54 nonsmoking adults with persistent asthma. Their mean serum vitamin D con-

centration was 28 ng/mL; most experts consider levels below 30 ng/mL insufficient, he noted at the meeting, sponsored by the National Jewish Medical and Research Center.

The higher a study participant's serum vitamin D concentration, the greater the lung function. In a multivariate regression analysis, there was a 22.7-mL increase in forced expiratory volume in 1 second (FEV₁) for each 1 ng/mL increase in vitamin D (*Am. J. Respir. Crit. Care Med.* 2010;181:699-704).

Airway hyperresponsiveness was also more pronounced in subjects with reduced vitamin D levels. They had a 1.03-mg/mL provocative concentration of methacholine to induce a 20% fall in FEV₁, whereas 1.92 mg/mL was required in those with a serum vitamin D level of 30 ng/mL or more.

Among the 30 subjects not on inhaled corticosteroid therapy, higher serum vitamin D concentrations were associated with greater dexamethasone-induced expression of mitogen-activated protein kinase phosphatase-1 by peripheral blood mononuclear cells.

"We feel pretty good about these data as a potential biologic underpinning to some of the population data that suggested higher vitamin D concentrations are a biomarker of steroid responsiveness," he said. He cited a study of 616 school-age children with asthma, in which higher vitamin D concentrations were associated with decreased need for inhaled corticosteroids (*Am. J. Respir. Crit. Care Med.* 2009;179:765-71). ■

Vitamin D Insufficiency May Be Linked to Allergies, Asthma

BY HEIDI SPLETE

NEW ORLEANS — Approximately half of children with asthma were deficient in vitamin D in a study of 99 children aged 18 and younger.

Previous published studies in the literature have suggested that vitamin D insufficiency contributes to the pathophysiology of allergic disease.

However, data on vitamin D's impact on children with allergies and asthma are limited, Dr. Daniel Searing said in a poster presentation at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

In his investigation, Dr. Searing and colleagues at National Jewish Health in Denver, Colo., identified 99 children who had asthma, atopic dermatitis, and/or a food allergy.

The researchers assessed vitamin D by measuring serum 25-hydroxyvitamin D levels.

Overall, 47% of the patients had insufficient levels of vitamin D (less than 30 ng/mL). The median vitamin D level was 31 ng/mL.

To assess the impact of vitamin D on inflammation, the researchers cultured peripheral blood mononuclear cells (PBMC) from 11 patients using either 10 nM vitamin D or a placebo medium for 24 hours, and supplemented them with either 10 or 100 nM of dexamethasone for the last 3 hours of culturing.

Next, they measured mitogen-activated protein kinase phosphatase-1 (MKP-1) and interleukin-10 (IL-10).

"Vitamin D enhances glucocorticoid induction of MKP-1 and IL-10 in asthmatic

PBMC in vitro," the researchers explained.

In turn, the addition of supplemental vitamin D can enhance the activity of dexamethasone more than 10-fold, they added.

However, "the relationship between vitamin D and corticosteroid pathways, as well as its effect on the inflammatory response, is not fully understood," the researchers emphasized.

VITALS

Major Finding: In this sample, 47% of children with allergies also were deficient in vitamin D.

Data Source: Researchers assess vitamin D levels in 99 children who had asthma, atopic dermatitis, and/or a food allergy.

Disclosures: Researchers had no financial conflicts to disclose. The study was supported in part by a grant from the National Institutes of Health.

But the results suggest that vitamin D supplementation may enhance the anti-inflammatory function of corticosteroids in asthma patients, they noted.

Median vitamin D levels were significantly lower in children taking inhaled corticosteroids (29 ng/mL), oral corticosteroids (25 ng/mL), and long-acting beta-agonists (25 ng/mL), compared with children who were not taking inhaled corticosteroids, oral corticosteroids, or long-acting beta-agonists (35 ng/mL, 32 ng/mL, and 34 ng/mL, respectively).

In addition, median vitamin D levels were significantly lower in children with positive vs. negative aeroallergen sensitivity to dog dander (29 ng/mL vs. 35 ng/mL) and house dust mites (27 ng/mL vs. 31 ng/mL). ■

To watch an interview of Dr. Searing, go to www.youtube.com/user/ElsGlobalMedicalNews.

Biomarkers Suggest Asthma Differs in Children, Adults

BY HEIDI SPLETE

NEW ORLEANS — Children with severe asthma have significantly higher levels of serum IgE and exhaled nitric oxide than adults, based on data from 47 consecutive patients with severe asthma.

Severe asthma affects fewer than 10% of all asthma patients, but it accounts for a disproportionate number of all asthma-related hospitalizations and emergency department visits, said Dr. Jonathan Malka of National Jewish Health in Denver.

Few studies have examined the phenotypic differences in severe asthma based on age, and recognizing the differences and similarities could help clinicians identify severe asthmatics, Dr. Malka said.

To compare levels of impairment and inflammation in children and adults, Dr. Malka and his colleagues evaluated 23 children and 24 adults with severe asthma who presented to National Jewish Health. The average age of the children was 12 years, and the average age of the adults was 47 years. The mean asthma durations were 9 years in children and 27 years in adults. The results were presented in a poster at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

Serum IgE was significantly higher in children than in adults (about 600 IU/mL vs. about 200 IU/mL). Similarly, exhaled nitric

oxide levels were significantly higher in children than in adults (about 54 parts per billion vs. about 27 parts per billion).

Children with severe asthma had significantly less lung function impairment than did adults, based on two measures of lung function. Forced vital capacity (FVC) in children was 94% of the predicted value vs. 72% in adults. Forced expiratory volume in 1 second (FEV₁) in children was 73% of the predicted value vs. 56% in adults. Children also fared better than adults in terms of the FEV₁/FVC ratio and in changes in FEV₁ after using albuterol, but those differences were not significant.

Children and adults showed no significant differences in three measures of asthma morbidity: weekly albuterol use, annual asthma exacerbations, and lifetime hospitalizations.

The study was limited by the small sample size, but the biomarker findings suggest pathophysiologic differences in asthma based on age—although adults and children alike were equally compromised, Dr. Malka said. Additional research may help clinicians adjust management of their severe asthma patients based on age, he said in an interview.

Dr. Malka had no financial conflicts to disclose. ■

To watch an interview of Dr. Malka, go to www.youtube.com/user/ElsGlobalMedicalNews.