METHODS. This was a randomized, double-blind, placebo-controlled trial. Both groups received open-label oral vitamin D₃ supplementation of 400 IU per day. The intervention group also received an intramuscular injection of 300 000 IU (<5 years of age) or 600 000 IUs (>5 years of age) (intramuscular + oral) of vitamin D₂.

RESULTS. A total of 256 patients were randomly assigned, with 127 assigned to treatment and 129 to placebo. Overall, there were no statistically significant between-group differences in asthma visit rates at the 3-, 6-, 9-, or 12-month time points when comparing rapid versus maintenance vitamin D supplementation. In the subgroup with the lowest vitamin D baseline values, there was a significant reduction in the rate of visits among those randomly assigned to more aggressive supplementation.

CONCLUSIONS. Although rapid vitamin D supplementation given to patients with vitamin D deficiency with asthma did not decrease overall unplanned asthma visits, there may be some early divergence of the group with the lowest level of vitamin D.

REVIEWER COMMENTS. The authors of this study attempted to examine the impact of rapid vitamin D supplementation on asthma exacerbations. Although there was no significant difference overall, those with the lowest levels of vitamin D may benefit from rapid supplementation.

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Joan H. Dunlop, MD
Corinne A. Keet, MD, PhD
Baltimore, MD

Oral Corticosteroid Exposure and Adverse Effects in Asthmatic Patients

PURPOSE OF THE STUDY. To examine the association between intermittent oral corticosteroid (OCS) use and adverse events (AEs) in patients with asthma.

STUDY POPULATION. The study included patients with asthma aged ≥18 years. The sample had a mean age of 38 years and was predominantly female (66%). Patients with chronic obstructive pulmonary disease, chronic bronchitis, emphysema, cystic fibrosis, or any of the selected AEs during the baseline period were excluded.

METHODS. Data were obtained from a retrospective review of an insurance claims data set (MarketScan Claims Database) from January 2000 to June 2014. The number of OCS prescriptions was reviewed. Patients were grouped into an OCS cohort and a no OCS cohort (no OCS prescription in the 12 months before baseline or during study follow-up). AEs were determined by International Classification of Diseases, Ninth Revision codes (osteoporosis, hypertension, diabetes, metabolic syndrome, dyslipidemia, obesity, cataracts, glaucoma, gastrointestinal bleeds and/or ulcers, tuberculosis, depression, herpes, and sepsis). Propensity matching was used to pair each patient in the OCS group with a similar patient in the control group. A regression analysis was used to compare the incidence of AEs between the OCS cohort and the no OCS cohort.

RESULTS. Before matching, there were 72 063 and 156 373 subjects in the OCS and no OCS cohorts, respectively. Subjects taking 1 to 3 or ≥4 OCS prescriptions within the year had increased odds of a new AE within the year (odds ratio: 1.04 and 1.29, respectively). Each year of exposure to ≥4 OCS prescriptions resulted in 1.20 times the odds of having an AE in the current year. Exposure to ≥4 OCS prescriptions in the current year was associated with a statistically significant increased odds (odds ratio of 1.21 to 1.44) of osteoporosis, hypertension, obesity, type 2 diabetes, gastrointestinal ulcers and/or bleeds, fractures, and cataracts.

CONCLUSIONS. The authors of this study found that the use of OCSs in patients with asthma was associated with greater odds of having an AE and that the number of prescriptions, regardless of dose or duration, was strongly associated with AEs.

REVIEWER COMMENTS. This study is a large retrospective data review of OCS prescriptions in patients with asthma. With this study, the authors suggest that OCS prescriptions have a cumulative impact on long-term health. This study reveals the importance of judicious use of OCSs, including consideration of alternative treatments when possible. The study was limited by reliance on claims data, which may have led to underreporting of AEs. It is also not possible to know if an OCS was actually taken or if a prescription was used for multiple exacerbations.

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Jennifer A. Dantzer, MD
Robert A. Wood, MD
Baltimore, MD

Association Between Inhaled Corticosteroid Use and Bone Fracture in Children With Asthma

PURPOSE OF THE STUDY. The authors aimed to determine whether inhaled corticosteroids increased risk of bone fracture in children with asthma.
STUDY POPULATION. The study included 19,420 children (61% boys) aged 2 to 18 years, with physician-diagnosed asthma who were eligible for public drug coverage and had filled at least 1 prescription during the previous year. Most were from low-income families or families with high drug costs relative to their income. Children were excluded if they had cancer, diabetes, or previous organ transplant.

METHODS. The authors used a nested-case control design in which cases were defined as having a bone fracture after an asthma diagnosis and matched with controls in a 1:4 ratio on the basis of date of birth or age, sex, and age at time of asthma diagnosis. Authors instituted a 1-year lookback to determine exposure status to inhaled steroids on the basis of prescription fill. Primary outcome was first emergency department visit for fracture after being diagnosed with asthma.

RESULTS. There was no significant association between first fracture after a diagnosis of asthma and inhaled corticosteroid use; results did not change on the basis of the number of inhaled corticosteroid prescriptions or with the daily dose of inhaled corticosteroids. Using systemic steroids, however, caused a 17% increase in the odds of fracture, with the effect greater in girls and best noted at the highest equivalent prednisone daily dose.

CONCLUSIONS. The use of inhaled corticosteroids in patients with asthma does not increase the risk of fracture, but the use of systemic steroids in the same population does in a dose-dependent manner.

REVIEWER COMMENTS. Physicians may be hesitant to prescribe and parents hesitant to administer inhaled corticosteroids because of a concern for systemic side effects, such as fracture risk; this study, however, reveals that the use of inhaled corticosteroids does not increase the risk of fracture. Poor asthma control due to medication non-adherence may lead to the increased need for systemic steroids, which were associated with an increased fracture risk. Even higher doses of inhaled corticosteroids are less likely than systemic steroids to increase the risk of fracture in this population. Several limitations to this study include the use of pharmacy fill data to judge medication use and the inability to assess patient-level risk factors such as asthma severity, family history, physical activity level, and calcium and/or vitamin D levels. Disease severity is particularly important because it may also be associated with other factors such as reduced physical activity or increased tobacco exposure that could independently contribute to fracture risk.

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Neelam A. Phadke, MD
Michael Pistiner, MD
Boston, MA

Immunology

Burden of Poor Health Conditions and Quality of Life in 656 Children With Primary Immunodeficiency

PURPOSE OF THE STUDY. To better understand the determinants of health status and quality of life in patients with primary immunodeficiency (PID).

STUDY POPULATION. The study required that patients be enrolled in the French Reference Center for Hereditary Immune Deficits registry, as a part of a national prospective cohort, the French Childhood Immune Deficiency Long-Term Cohort. Additional inclusion criteria were alive children <18 years old and living in France, resulting in 1047 eligible children, of which 656 were included in the study.

METHODS. The study was designed as a multicenter prospective follow-up in which patients completed 2 questionnaires used to evaluate health and health-related quality of life (HRQoL). Health conditions were assigned a severity score from grade 1 (mild) to grade 4 (life-threatening), which were reviewed and graded with specific criteria by a dedicated medical team. Children and parents’ perceived HRQoL of their children were assessed with 2 validated questionnaires, 1 for children 8 to 10 years old and 1 for children and adolescents 11 to 17 years old. Results were compared with age- and sex-matched controls from the general French population. Data were expressed as numbers and percentages or mean ± SEM.

RESULTS. Data for HRQoL were presented according to age group (ie, 8–10 years old and 11–17 years old). In the self- and parent reports for 8- to 10-year-old patients, PID had a statistically significant negative impact on both physical and mental dimensions compared with controls, with the exception of reinforced relations with family and teachers. There were similar findings in the 11- to 17-year-old group, except their summary score was not significant because of stronger scores in relationship with parents and teachers. HRQoL was not affected by PID diagnosis, the duration of the disease, or transplantation status (except physical well-being scored higher in adolescents with transplants). HRQoL was strongly associated with the burden of health conditions, with a higher likelihood of poor HRQoL in patients who had experienced at least 2 health conditions (grade 3–4 or 4). Of note, 83% of patients had at least 1 severe condition, 40% had at least 1 life-threatening condition, and 61% had 1 or more conditions, particularly in regard to respiratory; ears, nose, and throat conditions; gastrointestinal disorders; and conditions requiring surgery.

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Neelam A. Phadke and Michael Pistiner
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