

Measures to reduce maintenance therapy with oral corticosteroid in adults with severe asthma

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Background: Maintenance therapy with oral corticosteroid (OCS) is used, although not based on evidence, for patients with severe asthma, but OCS is associated with serious adverse effects; therefore, management strategies aimed at steroid sparing are important.

Objective: To provide an update on the evidence for OCS-sparing strategies in adults with severe asthma.

Methods: A systematic literature review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

Results: A total of 21 studies (which comprised 3060 subjects) were included. Of the nonbiologic oral steroid-sparing strategies ($n = 5$), the following lowered the OCS dose: Internet-based tapering strategy (44% reduction in OCS dose), inhaled corticosteroids (mometasone furoate [mean daily OCS dose reduction of 39% and 31% in patients treated with 800 mcg/day and 1600 mcg/day, respectively] and ciclesonide [OCS dose reduction of 47% and 63% in patients treated with 640 mcg/day and 1.280 mcg/day, respectively]), and methotrexate (OCS dose reduction of 55%). Of the biologic oral steroid-tapering strategies (16 studies) the following agents lowered the OCS dose: cyclosporin A (62% reduction in OCS dose), masitinib (78% reduction in OCS dose), mepolizumab (50%–83% reduction in OCS dose), and omalizumab (30%–64% of enrolled patients achieved a reduction in OCS dose, and one study reported a dose reduction of 45%).

Conclusions: In adults with severe asthma, several corticosteroid-sparing interventions were shown to be effective in reducing systemic steroid exposure, not least in studies of add-on biologic therapy. However, based on the available studies, ciclesonide, especially seems to be a good candidate for reducing steroid exposure in these patients before possible initiation of biologic therapy.

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Hygiene factors associated with childhood food allergy and asthma

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Background: Childhood food allergy and asthma rates are increasing. The hygiene hypothesis has been proposed as an explanation for the increased incidence of allergic disease.

Objective: To describe the association of childhood food allergy and asthma with hygiene factors, such as the number of siblings, antibiotic use, infection history, pet exposure, child care exposure, and maternal–child factors.

Methods: Children ages 0–21 years old ($N = 1359$) were recruited for a cross-sectional family-based study, including children with food

allergy and children without food allergy, and their siblings. We assessed the associations between childhood food allergy and asthma with hygiene factors.

Results: Of the 1359 children, 832 (61.2%) had food allergy, and 406 (30%) had asthma. In the adjusted analysis, the prevalence of food allergy was increased if there was a history of skin infection (prevalence ratio [RRR] 1.12 [95% confidence interval (CI), 1.01–1.24]) or eczema (RRR 1.89 [95% CI, 1.70–2.10]). The prevalence of asthma was increased with a history of respiratory syncytial virus infection (RRR 1.60 [95% CI, 1.34–1.90]) or eczema (RRR 1.54 [95% CI, 1.27–1.86]). A greater number of siblings were associated with a decreased prevalence of food allergy (RRR 0.79 [95% CI, 0.75–0.84]) and asthma (RRR 0.82 [95% CI, 0.74–0.91]).

Conclusion: Our findings supported the accumulating evidence of an association between skin infections and eczema with food allergy. Because these results could be subject to recall bias, additional prospective studies are needed to substantiate these findings.

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Effects of the addition of tiotropium on airway dimensions in symptomatic asthma

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Background: Tiotropium, a once-daily, long-acting anticholinergic bronchodilator, has shown efficacy and safety as an add-on to maintenance therapy in patients with symptomatic asthma.

Objective: The aim of the present study was to assess the effect of tiotropium on airway geometry and airway inflammation in patients with asthma who were symptomatic despite treatment with inhaled corticosteroid (ICS) plus a long-acting beta 2-agonist (LABA).

Methods: In total, 53 patients with symptomatic asthma who received ICS plus LABA and who had a prebronchodilator forced expiratory volume in 1 second of 60–90% of the predicted value were randomized to the addition of tiotropium 5 μ g once daily ($n = 25$) or no add-on ($n = 28$) to maintenance therapy for 48 weeks. Quantitative computed tomography, fractional exhaled nitric oxide, and pulmonary function were measured.

Results: Compared with maintenance therapy, the addition of tiotropium significantly decreased airway wall area (WA) corrected for body surface area (BSA) (WA/BSA) ($p < 0.05$) and wall thickness (T) ($T/\sqrt{BSA}$, $p < 0.05$), and improved airflow obstruction. No significant difference in the change of fractional exhaled nitric oxide was observed between the two treatment groups. Changes in WA/BSA and $T/\sqrt{BSA}$ were significantly correlated with the change in predicted forced expiratory volume in 1 second ($r = -0.87$, $p < 0.001$, and $r = -0.82$, $p < 0.001$, respectively).

Conclusion: The addition of once-daily tiotropium to maintenance therapy improved airflow limitation and reduced airway T. A triple combination of tiotropium and ICS plus LABA may have additive protective effects of bronchodilation and remodeling.

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Circulating follicular T-helper cell subset distribution in patients with asthma

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Background: The pathogenesis of allergic asthma is primarily characterized by abnormality in the immunoglobulin E (IgE) pathway, suggesting a possible role for follicular T-helper cells (Tfh) in the genesis of excessive IgE accumulation. The blood chemokine (C-X-C motif) receptor 5 (CXCR5)⁺CD4⁺ T cells, known as "circulating" Tfh, share common functional characteristics with Tfh cells from germinal centers. There are three subsets of circulating Tfh cells: Tfh1 (CXCR3⁺CC chemokine receptor [CCR] 6⁻), Tfh2 (CXCR3⁻CCR6⁻) and Tfh17 (CXCR3⁻CCR6⁺). However, data on circulating Tfh cell subsets distribution in patients with asthma are not available.

Objective: To investigate the circulating Tfh cell subsets distribution in patients with asthma and to assess the relationship between Tfh cell subsets distribution and the serum IgE level.

Methods: Thirty patients with severe allergic asthma and 30 age- and sex-matched healthy controls were enrolled in this study. The percentages and phenotypic assays of circulating Tfh cell subsets were assessed by flow cytometry. The total IgE levels were also measured. The correlation between the percentage of circulating Tfh cell subsets and the levels of serum total IgE was analyzed.

Results: Our results showed polarization of Tfh2 cells within circulating Tfh cell subsets in the patients with asthma. Phenotypic assays showed that activated Tfh2 subtypes displayed the features of Tfh cells, including invariably coexpressed programmed cell death 1 (PD-1), and inducible costimulator (ICOS). Furthermore, not only the frequency of Tfh2 cells but also the ratio (%Tfh2/%Tfh1) positively correlated with the total IgE level in the blood.

Conclusion: Results of our data described an altered circulating Tfh subset distribution, which implied that this cell subset might play an important role in the pathogenesis of asthma.

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Pulmonologist perspectives regarding diagnosis and management of primary immunodeficiency diseases

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Background: The time from symptom onset to diagnosis for patients with primary immunodeficiency diseases (PID) is an average of 12 years, but prompt diagnosis and treatment can promote best outcomes.

Objective: Because the manifestations of PID are often sinopulmonary in nature, patients with undiagnosed PID are frequently referred to pulmonologists. This study sought to identify opportunities among these specialists to improve diagnosis and clinical management of patients with PID.

Methods: A survey was sent to American Medical Association and American Osteopathic Association members whose specialty was

pulmonology. Responses were compared with those from a historical survey of 71 subspecialist immunologists (American Academy of Allergy, Asthma & Immunology members who devoted >10% of their practice to patients with PID).

Results: The surveys were returned by 485 pulmonologists, 49% of whom had diagnosed at least one patient with PID. In comparison with subspecialist immunologists, fewer pulmonologists were aware of the professional PID diagnosis and management guidelines and fewer followed up patients with various PIDs. Pulmonologists and subspecialist immunologists also differed in the practice of prescribing prophylactic antibiotics and immunoglobulin replacement and in avoiding live viral vaccines.

Conclusion: Differences in the diagnosis and treatment of patients with PID between these two groups of specialists revealed areas in which PID-focused educational initiatives may be helpful for pulmonologists.

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Long-term outcome after pediatric intensive care unit asthma admissions

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Background: Patients with asthma admitted to the pediatric intensive care unit (PICU) are often found to have had previous severe asthma exacerbations.

Objective: To prospectively evaluate the outcome of children after PICU admission.

Methods: Patients, ages 2–18 years, admitted to the PICU at Assaf Harofeh Medical Center over a 10-year period were assessed at a mean of 10 years after their admission and compared with matched patients admitted to the pediatric ward. Each patient filled out a questionnaire on subsequent hospitalizations and current asthma treatment and control. Pulmonary function studies and allergy skin tests were performed.

Results: Compared with patients admitted to the pediatric ward, those admitted to the PICU had more hospitalization and ICU admissions after their index admission ($p = 0.022$ and $p = 0.021$, respectively). Most patients in both groups (60–70%) had uncontrolled asthma, and 47% of those (PICU) and 33% (ward) were not receiving controller therapy. Patients in the PICU group had more recent asthma exacerbations ($p = 0.014$), weekly wheezing ($p = 0.017$), and bronchodilator use ($p = 0.007$). Lung function tests were comparable between the two groups, but 30–45% in each group had airflow obstruction. No significant differences were found between preschool and school-age children in any of the parameters.

Conclusion: Compared with patients admitted to the pediatric ward, those admitted to the PICU with asthma exacerbations, experienced more asthma-related hospitalizations and their asthma was less controlled even years later. The lack of regular follow-up and controller therapy in most patients after asthma hospitalization indicated that this increased morbidity might be prevented.

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