

Effect of montelukast on markers of airway remodeling in children with asthma

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Background: Asthma is a pathology characterized by chronic inflammation and remodeling of the airways.

Objectives: To evaluate the effect of montelukast treatment on markers of airway inflammation and remodeling in children with mild asthma and to evaluate if the administration of montelukast to children with mild asthma could inhibit the release of matrix metalloproteinase 9, matrix metalloproteinase 12, tissue inhibitor of metalloproteinase 1, transforming growth factor beta 1, C-peptide terminal procollagen type (PICP), and eosinophils count, which are markers of inflammation and remodeling in induced sputum.

Methods: Thirty children with mild asthma were recruited. They were randomized into two groups: group A received montelukast and as needed beta-2-agonist for 8 weeks (T0-T1), whereas group B received placebo and as needed beta-2-agonist for 8 weeks. After 2 weeks of washout (T1-T2), they were reallocated for treatment according a crossover design (T2-T3). Tests for lung function, oral exhaled nitric oxide, and hypertonic saline solution-induced sputum level were performed at T0-T1-T2-T3.

Results: In the placebo group, the PICP mean (standard deviation [SD]) value at baseline was 2279.42 ± 2530.77 pg/mL and 1916.00 ± 2178.75 pg/mL after treatment. Patients treated with montelukast, in contrast, showed a baseline mean (SD) value of 2439.29 ± 2834.51 pg/mL and 1406.72 ± 1508.65 pg/mL after treatment. The difference between the mean pre- and posttreatment decrease of PICP in the two groups was statistically significant (delta -690.21 pg/mL [95% confidence interval, -1220.83 to -159.5844 pg/mL]; $p = 0.011$). The mean (SD) percentage of the eosinophil count in the placebo group was $3.11 \pm 4.03\%$ at baseline and $4.86 \pm 5.83\%$ after treatment. Patients treated with montelukast, in contrast, showed a percentage mean (SD) value at baseline of $4.51 \pm 5.48\%$ and, after treatment, of $3.06 \pm 3.29\%$. The difference between the mean pre- and posttreatment decrease of the percentage eosinophil count in the two groups was statistically significant (delta -2.76% [95% confidence interval, -4.65 to -0.87%]; $p = 0.004$).

Conclusion: This study investigated *in vivo* effects of montelukast on remodeling markers. The reduction of PICP levels and eosinophil count supported the hypothesis that montelukast can modulate collagen deposition in airways and reduce eosinophilic airway inflammation. Clinical Trials database clinicaltrials.gov (NCT00875082).

(Allergy Asthma Proc 37:e77–e83, 2016; doi: 10.2500/aap.2016.37.3978)

Serum tryptase level and inflammatory markers in exhaled breath condensate of children with exercise-induced symptoms

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Background: The pathogenesis of exercise-induced bronchoconstriction (EIB) is poorly understood.

Objective: To evaluate the biomarkers concentration in exhaled breath condensate (EBC) in schoolchildren with postexercise symptoms. We also evaluated changes in fractional exhaled nitric oxide (FeNO) value and the serum tryptase level after exercise.

Methods: One hundred children with postexercise symptoms were included. Methacholine challenge testing (MCT) was performed at visit 2, and exercise challenge testing (ECT) was performed at visit 3. Before and after ECT serum tryptase levels and FeNO values were measured. EBC was collected after ECT from 10 randomly selected children from each group. The children were assigned to the following groups: ECT⁺ MCT⁺, ECT⁺ MCT⁻, ECT⁻ MCT⁺, ECT⁻ MCT⁻. We measured the following molecules: eotaxin, interleukin (IL) 8, IL-1ra, IL-1 beta, IL-6, IL-1 alpha, IL-12(p40), IL-5, AQ:3:4 granulocyte-macrophage colony-stimulating factor, IL-7, IL-15, IL-4, IL-2, IL-10, tumor necrosis factor alpha, interferon gamma, IL-13, tumor necrosis factor beta, monocyte chemoattractant protein-1, IL-17A, macrophage inflammatory proteins-1 alpha, macrophage inflammatory proteins-1 beta, IL-12(p70), and regulated on activation, normal T-cell expressed and secreted by using a multiplex immunoassay. Prostaglandin E2 (PGE2), leukotriene B4, and cysteinyl leukotriene were analyzed by using separate enzyme-linked immunosorbent assay kits.

Results: In the MCT⁺ group, a detectable level of IL4 in EBC and detectable levels of eicosanoids were seen in the ECT⁺ group. We observed the opposite direction of ECT-induced changes in FeNO and serum tryptase concentrations in patients with detectable compared with patients without detectable levels of cytokines in EBC. We showed ECT-induced reduction in the tryptase level in patients with a nondetectable PGE2 level in EBC and an increase in tryptase levels in patients who had detectable levels of PGE2 in EBC.

Conclusions: EBC was a useful method to estimate inflammation but only in children with symptoms and with EIB shown by a positive ECT. Children with a positive ECT had detectable levels of eicosanoids in EBC; the opposite direction of ECT-induced changes in FeNO and serum tryptase concentrations was observed. The results of above study confirm the role of mast cells and eicosanoids in the pathogenesis of EIB in children.

(Allergy Asthma Proc 37:e84–e92, 2016; doi: 10.2500/aap.2016.37.3974)

Comparison of pain during skin-prick testing, immunizations, and phlebotomy

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Background: Allergy skin prick testing is a medical procedure that is very useful for assessing a patient's sensitization to specific allergens. Some patients are worried about pain associated with prick skin testing.

Objective: To compare pain among different age groups, to look at pain during skin prick testing in younger children, and to compare the pain during skin prick testing to procedures including routine immunizations and phlebotomy.

Methods: A survey was provided to patients undergoing allergy skin testing, immunizations or phlebotomy at the Wilford Hall Medical Center.

Results: There were 197 patients and 26 parents of patients aged 3–8 years who completed surveys during allergy skin testing. The average anticipated (pre procedure) pain score was 4.3 for the patients aged 3–8 years, 4.6 for the patients aged 9–17 years and 3.2 for the patients older than 17 years. The average actual pain score of the patients during skin testing was 3.1 for the patients aged 3–8 years, 2.2 for the patients aged 9–17 years and 1.4 for the patients older than 17 years. For the parents of patients aged 3–8 years, the average anticipated average pain score was 3.0 and the average actual pain score was 1.7.

Conclusions: The actual pain experienced from skin prick testing is perceived to be much less than the anticipated pain. Patients and referring physicians should not have a fear of pain from allergy skin prick testing.

(Allergy Asthma Proc 37:e93–e97, 2016; doi: 10.2500/aap.2016.37.3961)

Effect of training by a physician on dynamics of the use of inhaler devices to improve technique in patients with obstructive lung diseases

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Background: Pharmacotherapies for obstructive lung diseases are dependent on agents delivered *via* inhaler devices, and the correct technique is essential for efficiency of these drugs.

Objective: To determine the rate of incorrect inhaler techniques among patients with pulmonary diseases and the efficacy of delivering physician-provided training to patients by letting them practice with their inhaler devices.

Methods: Patients ages ≥ 18 years with asthma, chronic obstructive pulmonary disease, or asthma chronic obstructive pulmonary disease overlap syndrome were enrolled. At the first visit, the patients were requested to use their own inhalers that they were currently on for initial evaluation of their inhalation technique. Correct and incorrect techniques were determined according to steps previously described in the literature. At the same visit, the physician provided practical training on faulty techniques detected, and a control visit was scheduled.

Results: The study involved 108 patients, and 158 different inhalation techniques were assessed. Types of inhaler devices included in the study were metered-dose inhaler and five types of dry-powder inhalers. Fifty-six incorrect practices (35.4%) were noted. Although 64 patients (59.3%) used all of their inhaler devices with the correct technique, 44 (40.7%) used one or more inhalers inappropriately. At the control visit, the patients who misused their inhalers decreased significantly, to 8.3% ($p < 0.001$). The faulty technique ratio was decreased to 7.0%, which yielded the success of practical training as 80.4%.

Conclusion: Incorrect inhaler technique is still a problem for patients with obstructive lung diseases even in urbanized areas. Physician-provided practical training on the use of inhaler devices was an effective tool in the correction of inhaler techniques.

(Allergy Asthma Proc 37:e98–e102, 2016; doi: 10.2500/aap.2016.37.3969)

Health care resource use and associated costs among patients with seasonal versus perennial allergic rhinitis

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Background: Health care resource use (HRU) and costs among patients with seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR) have not been widely studied.

Objective: To develop an algorithm to classify patients with SAR and patients with PAR, and to evaluate treatment patterns, HRU, and costs among them.

Methods: Patients with allergic rhinitis (AR) were identified retrospectively by using electronic medical records and administrative claims data, with an index date as the earlier of the date of AR diagnosis or allergy medication use. Patients with AR were followed-up from 12 months before the index date through 12 months after the index date (follow-up) and were classified as SAR or PAR based on medication patterns during follow-up. AR-related HRU, allergy immunotherapy administration, and costs per patient per year during follow-up were compared between patients with SAR and those with PAR, with analyses stratified by asthma diagnosis before the index date and by physician specialty (primary care physician versus specialist).

Results: Approximately 23% of patients with AR were classified as having PAR and 77% as having SAR. During follow-up, the patients with PAR had more allergy medication prescriptions versus the patients with SAR (8.0 versus 2.4 prescriptions), higher prescription medication costs (\$1551 versus \$313), higher allergy immunotherapy cost (\$180 versus \$118), and higher total AR-related costs (\$1944 versus \$643); all with $p < 0.001$. Patients with asthma, and those seen by a specialist had higher costs than patients without asthma and patients treated by primary care.

Conclusion: Patients with PAR experienced more AR-related prescription drug use and higher health care costs than patients with SAR, with prescription drug costs being the main cost driver. Treatments that reduce the need for ongoing prescription medication use have the potential to be cost saving.

(Allergy Asthma Proc 37:e103–e111, 2016; doi: 10.2500/aap.2016.37.3984)

American Academy of Allergy, Asthma & Immunology membership experience with allergen immunotherapy safety in patients with specific medical conditions

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Background: Little data in the literature exist concerning patients with certain underlying medical conditions who receive allergen subcutaneous immunotherapy (SCIT).

Objective: To survey allergists' experience with SCIT in patients with medical conditions considered to impose an elevated risk for untoward outcomes.

Methods: A Web-based survey was conducted among members of the American Academy of Allergy, Asthma & Immunology to query about their experience with SCIT in patients with certain medical conditions.

Results: There were 1085 replies (21% response), of whom, 86% were U.S. based, 51% were suburban, 31% were academic, 42% were medium-sized practices, and 54% had >15 years' experience. In responders' opinion, SCIT was "contraindicated" in patients with the following: acquired immune deficiency syndrome (AIDS) (48%), cancer (and still receiving active treatment) (33%), severe asthma (32%), and a history of transplantation (30%). Even so, survey responders collectively gave SCIT to >2400 patients for each of these conditions: severe asthma, coronary artery disease, cancer in remission, and autoimmune disorders; and to $\geq$ 5400 patients with hypertension and $\geq$ 4100 women who became pregnant. The experience of colleagues with these patients rarely resulted in major problems (*i.e.*, activation

of underlying disease, systemic reactions to SCIT, or SCIT discontinuation), with the exception of severe asthma (12.5%), initiation of SCIT during pregnancy (5.4%), and AIDS (4.2%). For most other conditions, it was $\leq$ 1.5% (*e.g.*, continue during pregnancy, cancer in remission, history of transplantation, positive human immunodeficiency virus and no AIDS).

Conclusion: According to the experience of a large group of practicing allergists, the American Academy of Allergy, Asthma & Immunology members, few medical conditions seemed to pose an elevated risk for untoward outcomes from SCIT. Because these are survey results, prospective research might yield even more solid data.

(Allergy Asthma Proc 37:e112–e122, 2016; doi: 10.2500/aap.2016.37.3981)

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