Hypertonic Saline and Acute Wheezing in Preschool Children

**PURPOSE OF THE STUDY.** To determine the effect of inhalation of hypertonic saline in children presenting to the emergency department (ED) with acute wheezing, on length of stay (LOS), admission rate (AR), and clinical severity score (CS).

**STUDY POPULATION.** Included in the study were 41 children presenting to 1 medical center in Israel.

**METHODS.** In a randomized, controlled, double-blinded study, 41 children aged 1 to 6 years old (mean age 31.9 months), presenting to the ED with acute wheezing and a CS ≥6, were randomly assigned to receive nebulized albuterol containing either hypertonic saline 5% (n = 16) or normal saline (n = 25) for the course of their treatment. While in the ED, induced sputum was obtained and tested via polymerase chain reactions for viral respiratory pathogens. Various statistical analyses were used to compare the LOS, AR, and CS between the 2 groups. Of note, patients admitted to the ICU were excluded from the study.

**RESULTS.** The LOS in the hypertonic saline group was a median of 2 days compared with the normal saline group median of 3 days (P = .027). The AR was 62.2% in the hypertonic saline group versus 92.0% in the normal saline group (P = .05). The CS greatly improved in both groups; however, no significant statistical difference was determined. Of the 29 sputum samples obtained and tested, 83% were positive for ≥1 respiratory virus, with the most common being rhinovirus. No adverse effects were observed in either group.

**CONCLUSIONS.** Administering nebulized hypertonic saline to wheezing children presenting to the ED significantly shortened the LOS and hospital AR, when compared with nebulized normal saline.

**REVIEWER COMMENTS.** Virus-induced wheezing episodes and asthma exacerbations are common in children’s EDs. The rationale for using hypertonic saline was that most acute wheezing episodes in preschool children are associated with rhinovirus, which decreases extracellular adenosine triphosphate levels, leading to airway surface liquid dehydration. This, along with submucosal edema, mucus plaques, and inflammation, causes failure of mucus clearance. Therefore, the authors evaluated this treatment to facilitate mucus clearance and hydration. This simple intervention appears to improve outcomes with minimal or no side effects. However, the small number of participants in this study limits the generalizability of conclusions.

The Effect of Montelukast on Respiratory Symptoms and Lung Function in Wheezy Infants

**PURPOSE OF THE STUDY.** Though montelukast therapy is an approved treatment for children, few studies have investigated its efficacy in young children who wheeze. This study aimed to determine the effectiveness, in terms of symptoms-free days and lung function, of montelukast as a monotherapy in the treatment of recurrent wheezing in children younger than 2 years.

**STUDY POPULATION.** A total of 113 full-term 6- to 24-month-old children (mean age 15.5 months), with at least 1 episode of physician-diagnosed wheezing episode, were included. All study participants must have successfully performed a methacholine challenge test for inclusion in the study. From the 367 patients screened, 254 (72%) did not meet the inclusion criteria. Notably, the study population was also 74% boys. Children who experienced an exacerbation that required steroid treatment or reasons for noncompliance were withdrawn.

**METHODS.** After the 2-week run-in period, participants were randomized to receive either montelukast (4-mg oral granule daily) or matching placebo. The treatment intervention was given for 8 weeks and symptoms of wheeze, dyspnea, and use of rescue medication were recorded daily using a visual analog scale ranging from 0 (no symptoms) to 10 (severe symptoms). Measurements of lung function, airway responsiveness to methacholine, and FeNO were collected on 77 (68%) of the 113 participants.

**RESULTS.** The primary outcome was symptom-free days, which was classified as a visual analog scale score ≤0.5 and no use of rescue albuterol. Mean changes in symptom-free days or use of rescue medication between the montelukast (3.1 to 3.7 days) and placebo (2.7 to 3.1 days) groups in response to treatment were not significant (P = .965).

**CONCLUSIONS.** Contradictory to previous studies, this study reveals that use of montelukast therapy has no effect on symptom-free days, use of rescue medication, exacerbations, or lung function.

**REVIEWER COMMENTS.** The results of the study reported conflicting data to current publications on the efficacy of montelukast treatment in young asthmatic patients to alleviate symptoms and reduce exacerbations. Although current asthma management guidelines (National Asthma Education and Prevention Program and PRACTical
Mepolizumab for Severe Eosinophilic Asthma (DREAM): A Multicentre, Double-Blind, Placebo-Controlled Trial

PURPOSE OF THE STUDY. To elucidate the efficacy, safety, and patient characteristics of responsiveness to mepolizumab (a humanized monoclonal antibody against interleukin 5). Previous small, proof-of-concept studies in subjects with severe, eosinophilic asthma revealed that mepolizumab decreased exacerbation rates.

STUDY POPULATION. From 81 multinational centers, 621 patients were enrolled. Major inclusion criteria included: age 12 to 74 years, asthma diagnosis with objective measures, ≥2 asthma exacerbations requiring oral corticosteroids in the last year, refractory asthma as defined by the American Thoracic Society criteria, and signs of eosinophilic inflammation (sputum eosinophil count ≥3%, an exhaled nitric oxide concentration ≥50 ppb, peripheral blood eosinophil count ≥0.3 × 10^9/L, or prompt deterioration of asthma control with inhaled or oral steroid weaning). Smokers, present or former (≥10 pack-years), were excluded.

METHODS. Subjects were randomized to receive placebo or 1 of 3 doses of mepolizumab (75, 250, or 750 mg). Every 4 weeks for 13 cycles, patients received infusions. Asthma symptom scores, objective lung testing results, and blood eosinophil counts were collected at baseline and follow-up visits. The primary outcome of verified, clinically significant exacerbations during treatment and 4 weeks thereafter was defined a priori.

RESULTS. All mepolizumab-treated groups demonstrated a significant decrease in clinically significant exacerbations (75 mg: −48% [P < .0001]; 250 mg: −39% [P = .005]; 750 mg: −52% [P < .0001]). Visits to emergency departments and admissions also decreased; however, no significant changes in spirometry or asthma control scores were noted. No treatment-associated deaths occurred, and other potential adverse events were equivocal in the placebo and treatment groups.

CONCLUSIONS. Mepolizumab is generally safe and reduces exacerbation rates in select patients with asthma who have the severe, refractory, eosinophilic subtype.

REVIEWER COMMENTS. Using more clinically available inclusion criteria and a larger cohort, mepolizumab provides another tool in select patients with severe, eosinophilic asthma. The study supports the clinical importance of asthma phenotyping in effectively treating asthma subjects but provides no insight for efficacy in other asthma phenotypes. The equivalent responses from the 75- and 750-mg dose might improve the cost to benefit ratio of mepolizumab depending on the manufacturer’s pricing strategy. Despite seemingly optimized design and execution, all results must be viewed through a scrutinizing lens because the manufacturer participated in all aspects ranging from design to writing.

IMMUNOTHERAPY
Efficacy of Subcutaneous and Sublingual Immunotherapy With Grass Allergens for Seasonal Allergic Rhinitis: A Meta-Analysis-Based Comparison

PURPOSE OF THE STUDY. To compare the efficacy of subcutaneous (SCIT) and sublingual immunotherapy (SLIT) to grass by meta-analysis of double-blind, placebo-controlled trials.

STUDY POPULATION. Among 36 studies selected for this meta-analysis, 14 included children.

METHODS. An electronic literature search identified 36 randomized controlled trials (RCTs) comparing SCIT and SLIT to placebo for grass pollinosis. All the studies assessed symptom scores and 31 assessed medication scores as outcome measures. To standardized comparative studies, the authors used the “standard mean difference” method (SMD) to compare SCIT or SLIT versus placebo. A “fail-safe” number (the number of insignificant or missing studies that would need to be added to a meta-analysis to reduce a significant result to insignificance) calculation was performed.

RESULTS. The 36 RCTs (22 SLIT [10 drops, 12 tablets], 14 SCIT) included 3014 treated patients and 2768 patients given placebo. Nine SLIT studies and 5 SCIT studies included children. There was great variation in the
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