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Putting Evidence into Practice

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This series is coordinated by Corey D. Fogleman, MD, Assistant Medical Editor.

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Beta$_2$ Agonists for Acute Cough or a Clinical Diagnosis of Acute Bronchitis

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Clinical Question

Are beta$_2$ agonists effective for improving symptoms of acute cough or a clinical diagnosis of acute bronchitis without wheeze?

Evidence-Based Answer

There is insufficient evidence to determine whether beta$_2$ agonists can improve symptoms for children with acute cough or bronchitis with wheeze. Beta$_2$ agonists are not likely to benefit and may cause adverse effects in adults who do not have evidence of airflow restriction (number needed to harm [NNH] = 2).[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Cough is a common reason patients seek acute ambulatory care, representing 2.8% of all U.S. office visits in 2012.[2] In clinical practice, physicians are most likely to document a diagnosis of acute bronchitis when a patient has lower respiratory tract symptoms, primarily a chest cough, but no clinical evidence suggestive of pneumonia.[3] Patients may receive inappropriate medications for acute bronchitis in part because of a discrepancy between patients' expectations of cough duration after an acute respiratory illness (five to nine days) and the typical duration of cough following a respiratory illness (18 days).[4]

This Cochrane review identified two trials of albuterol in children with acute cough.[1] Children with wheezing or other evidence of airflow restriction for which bronchodilator therapy might be clinically indicated were excluded. The trials found no difference between albuterol and placebo in clinical improvement, meaning no decrease in the daily cough impact or number of children with cough. There was also no significant difference in adverse effects between patients given placebo and those given albuterol.

The authors identified five trials of beta$_2$-agonist therapy in adults. When three of the trials were combined, they failed to show a significant difference between beta$_2$ agonists and placebo in cough reduction (in these trials, 19% to 52% of patients had wheezing on initial examination). In subgroup analyses, one trial found that fenoterol (not available in the United States) reduced symptoms by day 2 in patients with evidence of airflow restriction based on physical examination (e.g., wheezing) or testing (e.g., reduced forced expiratory volume in one second, a positive methacholine challenge). This trial also found that patients with a history of smoking or a history of antibiotic treatment had better symptom scores on day 7 if treated with fenoterol than placebo. However, these subgroup findings were not replicated in three other trials.

Adverse effects experienced by adults given beta$_2$ agonists included tremor, shaking, or nervousness (NNH = 2). There are several important limitations to the evidence identified by this Cochrane review. All of the included trials were of short duration (e.g., only three to seven days), raising the possibility that later symptomatic improvement could have been missed. Additionally, only two studies used inhaled beta$_2$ agonists, and participants were not given instructions on the use of spacers.

Guidelines do not recommend using bronchodilators in patients with acute illness who do not have wheezing or a history of chronic obstructive pulmonary disease.[5]

The practice recommendations in this activity are available at http://www.cochrane.org/CD001726.

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Citrate Salts for Preventing and Treating Calcium-Containing Kidney Stones in Adults

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Clinical Question

Do citrate salts treat and prevent calcium-containing kidney stones in adults?

Evidence-Based Answer

Citrate supplementation reduces stone size to less than 5 mm and prevents new stone formation when compared with placebo or no intervention. Citrate therapy also stabilizes existing stones and decreases the need for retreatment. These benefits come at the expense of upper gastrointestinal disturbances that lead to a higher dropout rate.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

In the United States, the prevalence of symptomatic kidney stones is 8.8% in the general population, and is higher in men (10.6%) and obese individuals (11.2%).[2] Without prevention, 10% of individuals will have a symptomatic recurrence of stones at one year, 33% at five years, 50% at 10 years, and 75% at 20 years.[3] Urinary tract stones represent an important health care expense with charges exceeding $10 billion annually in the United States.[3] Because citrate binds urinary calcium, it may inhibit the formation of calcium oxalate stones; therefore, the authors of this Cochrane review aimed to determine if the use of citrate salts can prevent and treat calcium-containing kidney stones.

This Cochrane review included seven randomized controlled trials with a total of 477 participants.[1] Three studies compared potassium citrate supplementation with placebo or no intervention, and three studies compared potassium-sodium citrate with no intervention. One study compared potassium-magnesium citrate with placebo. Primary outcomes included radiographic evidence (plain radiography, computed tomography, or intravenous urography) of reduced stone size to less than 5 mm, lack of new stone formation, or stone size stability over six months, one year, or two years. Secondary outcomes were the need for retreatment, adverse events, and dropout rates. Dosages of citrate therapy ranged from 30 to 60 mEq per day.

Citrate therapy increased the likelihood of stone size reduction to less than 5 mm (relative risk [RR] = 2.35; 95% confidence interval [CI], 1.36 to 4.05). The incidence of new stone formation over a period of 12 to 48 months was also significantly reduced (RR = 0.26; 95% CI, 0.10 to 0.68). Citrate therapy prevented growth of existing stones (RR = 1.97; 95% CI, 1.19 to 3.26). Only two studies reported the need for retreatment as an outcome; in these, citrate therapy significantly decreased the need for retreatment vs. control (RR = 0.22; 95% CI, 0.06 to 0.89) over a follow-up period of three to four years. In absolute terms, the need for retreatment was 3.6% vs. 41.4% in the first study[4] and 8% vs. 22% in the second.[5]

Adverse events and dropout rates were higher in the citrate treatment groups. The most commonly reported adverse events with citrate treatment were upper gastrointestinal disturbance and rash, but these differences were not significant between the citrate and placebo groups. Although rates of adverse events did not significantly differ between groups, dropout rates because of adverse events were significantly higher in patients receiving citrate therapy (RR = 4.45; 95% CI, 1.28 to 15.50). Overall, dropout rates because of noncompliance were similar between the groups. Risk

of bias was considered low. The individual studies did not provide enough information for the authors of this review to reach a conclusion regarding the most effective dose of citrate salts.

Current guidelines from the American College of Physicians recommend that patients with one or more previous kidney stone episodes increase their fluid intake to produce at least 2 L of urine per day.[6] If increased fluid intake fails to prevent recurrent episodes, treatment with a thiazide diuretic, allopurinol, or citrate is recommended. These recommendations are based on moderate-quality evidence.[6] The results of this Cochrane review support the recommendations in the American College of Physicians guidelines.

The practice recommendations in this activity are available at http://www.cochrane.org/CD010057.

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