Nebulised ipratropium combined with albuterol led to improved pulmonary function in children with severe asthma

Qureshi F, Zaritsky A, Lakkis H. **Efficacy of nebulized ipratropium in severely asthmatic children.** Ann Emerg Med. 1997 Feb;29:205-11.

Objective
To compare the effectiveness of ipratropium bromide plus standard therapy with standard therapy alone in improving pulmonary function in children with severe asthma presenting to the emergency department.

Design
Randomised, double-blind, placebo-controlled trial with 120-minute follow-up.

Setting
Emergency department of a children's hospital in Virginia, USA.

Patients
90 children who were 6 to 18 years of age (mean age 12 y, 61% boys) and who had a history of asthma, presented with an acute asthma exacerbation and a peak expiratory flow rate (PEFR) < 50% of the predicted normal value, and showed the ability to undergo reliable pulmonary function testing. Exclusion criteria were alternative or concurrent illness, contraindication to β-adrenergic or anticholinergic medications, or need for immediate resuscitation.

Intervention
All children received nebulised 0.5% albuterol solution (0.15 mg/kg of body weight to a maximum of 5 mg) every 30 minutes for 3 doses and oral steroids with the second dose of albuterol. 45 children also received 2.5 mL (500 μg) of ipratropium bromide (the other 45 children were allocated to 2.5 mL of saline) with the first and third doses of albuterol. After the third dose, all children were given nebulised albuterol every 30 minutes.

Main outcome measures
PEFR and forced expiratory volume at 1 second (FEV_1) before each 30-minute dose.

Main results
After adjustment for baseline PEFR and FEV_1 values, children in the ipratropium group had greater improvement in PEFR than did children in the placebo group at 60 minutes ($P = 0.02$), 90 minutes ($P = 0.002$), and 120 minutes ($P < 0.001$) and a greater improvement in FEV_1 at 120 minutes ($P = 0.013$). The increase in PEFR and FEV_1 between 30 and 120 minutes was 22.7% and 19.5%, respectively, in the ipratropium group compared with 15.4% and 14.3%, respectively, in the placebo group ($P < 0.001$). No differences existed for rates of hospitalisation or for changes in pulse, blood pressure, or oxygen saturation.

Conclusion
Nebulised ipratropium combined with albuterol and oral steroids led to greater improvement in pulmonary function over 120 minutes than did standard therapy alone in children with severe asthma presenting to the emergency department.

Source of funding: No external funding.

For article reprint: Dr. F. Qureshi, Pediatric Emergency Medicine, Children's Hospital of the King's Daughters, 601 Children's Lane, Norfolk, VA 23507, USA. FAX 757-668-7568.

Commentary

The results of this well-conducted clinical trial are consistent with a recently published systematic review of the benefits of additional nebulised ipratropium bromide in the management of acute severe asthma in adults and children (1). This issue is important because of the frequency of the condition in children.

The results of this study showed short-term physiological benefits from adding ipratropium to albuterol. However, these benefits are of little value in themselves. Additionally, despite randomisation, lung function was better at baseline in patients in the ipratropium group compared with those in the saline control group. The factors that determine the distribution of a nebulised aerosol in the lungs are complex, but lung function is important. Thus, the patients with better lung function may have received a higher dose than did those with poorer lung function. Adjusting for baseline differences would not overcome what is in effect a higher dose to those with less severe disease. However, the authors have provided me with an additional, unpublished analysis that shows to my satisfaction that ipratropium has a real additional effect over and above albuterol alone.

If the additional time and cost involved in adding ipratropium to albuterol in a nebuliser is minimal, then even the modest benefits described in this study would be worthwhile. With this starting point, we still need answers to the following question: Were the duration of stay in the emergency department and the need for hospital admission reduced?

Michael Silverman, MD
University of Leicester
Leicester, England, UK

Reference

1. **Ducharme F.** The Cochrane Collaboration; Issue 1. Oxford: Update Software; 1997.

Authors' response

Although not reported in the article, we separately analysed the change in pulmonary function from baseline over time for 3 cohorts of 15 patients from each group: the lowest, middle, and highest one third in terms of pulmonary function. The PEFR and FEV_1 values in children with the lowest baseline pulmonary function in the ipratropium group crossed over the response of children in the middle pulmonary function group in the saline group. This effect was also seen for PEFR values between the middle group and the highest group. These observations suggest that the difference in response to ipratropium was because of the severity of lung disease.

Arno Zaritsky, MD
Faiqa Qureshi, MD