Why do we give ipratropium to kids with asthma exacerbations in the emergency room?

Qureshi F et al. Effect of nebulized ipratropium on the hospitalization rates of children with asthma. N Engl J Med 1998; 339: 1030-5.

Take Home Message: Adding ipratropium to albuterol and corticosteroids for children with acute asthma exacerbations in the emergency room significantly decreased the hospitalization rate for those with *severe* asthma.

Highlights: The inhaled anticholinergic, ipratropium, is known to be an effective bronchodilator for patients with acute asthma exacerbations. Qureshi et al.[i] sought to determine if adding ipratropium in the emergency room would have effects on hospitalization rates, as there were no prior large randomized controlled trials investigating this. Published in 1998, this trial randomized 434 children having acute asthma exacerbations in an emergency room to receive either ipratropium or normal saline with standard ER care of albuterol and steroids. Adding ipratropium significantly decreased the hospitalization rate for those with severe asthma; however, it did not reduce hospitalization rates for children with moderate asthma. Adding ipratropium to albuterol and corticosteroids is now the standard of care in many emergency rooms for children presenting with moderate to severe asthma exacerbations.

A 2013 Cochrane Review[ii] reviewed 20 trials, including Quereshi's, and confirmed that the addition of an anticholinergic to a short-acting beta-2-agonist significantly reduced the rate of hospital admission by 27%. Trends toward a greater effect with increased asthma severity were noted but not significant.

Despite the decrease in hospitalization rate with ipratropium use, two studies have shown that ipratropium does not seem to improve clinical outcome once patients are hospitalized. [iii][iv]

The Nitty-Gritty:

- **Design**:
    - Randomized, double blind, placebo-controlled study, single center
    - N=434
        - Control/placebo group (n=219)
        - Ipratropium group (n=215)
    - Setting: 1 tertiary care urban medical in the US
    - Enrollment: 1996-1997
    - Primary Outcome: rate of hospitalization
- **Population:**
    - **Inclusion Criteria:**
        - 2-18 years old
        - Known history of asthma

- § Presenting to ED with acute asthma exacerbation

- o **Exclusion Criteria:**

  - § < 2 years old
  - § treatment with ipratropium < 6 hours before visit to ED
  - § disease known to have chronic effect on respiratory function
  - § stridor
  - § possible foreign body
  - § medical condition that would contraindicate B2-adrenergic or anticholinergic medications
  - § need for immediate resuscitation or airway intervention

- o **Baseline Characterstics -** from the ipratropium group, no significant differences between groups except for sex which is ipratropium vs. control

  - § Male: 52% vs. 62% (greater proportion of girls in ipratropium group, p=0.04)
  - § Race: White 16.3%, Black 80%
  - § Age: 8.4 +- 4.1 years
  - § Peak expiratory flow rate (% predicted value) 40.0 +- 7.5

- Severity of asthma: 36.7% moderate, 63.3% severe

- **Intervention:**
  - Randomized to received either 500ug (2.5 mL of ipratropium) with the second and third dose of albuterol or receive 2.5 mL of normal saline, in addition to standard therapy of albuterol and corticosteroids

- **Outcomes:** Comparisons are ipratropium vs. control
  - **Primary Outcome:** Rate of hospitalization (for all patients and stratified by asthma severity)
    - Rate of hospitalization for all patients: 27.4% vs. 36.5% (p=0.05)
    - Rate of hospitalization for patients with moderate asthma: 10.1% vs. 10.7% (NS)
    - Rate of hospitalization for patients with severe asthma: 37.5% vs. 52.6% (p=0.02)
  - **Secondary Outcomes**: only change in asthma score and change in oxygen saturation with severe asthma were significant; comparisons are ipratropium vs. control
    - Time to disposition:
      - Moderate asthma: 2.22 vs. 2.23 hours
      - Severe asthma: 3.03 vs. 2.44 hours
    - No of nebulizer treatments before disposition

- Moderate asthma: 3 in both groups
- Severe asthma: 4 in both groups

§ Change in peak expiratory flow rate (% predicted)

- Moderate asthma: 26+-12% vs. 29+- 12%
- Severe asthma: 32+-15% vs. 31+-17%

§ Change in oxygen saturation (%)

- Moderate asthma: 1.9% vs. 1.2%
- Severe asthma: 2.3% vs. 1.9% (p=0.02 but not clinically significant)

§ No. of patients seeking medical care within 72 hours after discharge

- Moderate asthma: 1 vs. 2 patients
- Severe asthma: 7 vs. 4 patients

§ Change in severity according to asthma score (asthma score improved to a greater extent in the treatment group (p=0.05), and the effect was even greater in children with severe asthma (p=0.01)).

- Moderate -> mild: 94.9% vs. 90.5%
- Severe -> moderate: 31.6% vs. 44.4%

- Severe -> mild: 56.6% vs. 41.5% (p=0.01)
- Moderate -> moderate: 9.5% vs. 5%
- Severe-> severe: 14% vs. 12%

[i] Qureshi F et al. Effect of nebulized ipratropium on the hospitalization rates of children with asthma. N Engl J Med 1998; 339: 1030-5.

[ii] Griffiths B & Ducharme FM. Combined inhaled anticholinergics and short-acting beta2-agonists for initial treatment of acute asthma in children. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No.: CD000060.

[iii] Craven et al. Ipratropium bromide plus nebulized albuterol for the treatment of hospitalized children with acute asthma. J Pediatr 2001; 138:51-8.

[iv] Goggin et al. Randomized trial of the addition of ipratropium bromide to albuterol and corticosteroid therapy in children hospitalized becsuse of an acute asthma exacerbation. Arch Pediatr Adolesc Med. 2001;155 (12):1329.