

Review: β -agonists plus ipratropium bromide improve airflow obstruction in adults with acute asthma

Stoodley RG, Aaron SD, Dales RE. The role of ipratropium bromide in the emergency management of acute asthma exacerbation: a metaanalysis of randomized clinical trials. *Ann Emerg Med.* 1999 Jul;34:8-18.

QUESTION

Is the addition of inhaled ipratropium bromide to β -agonist therapy effective in the emergency treatment of adults with acute asthma?

DATA SOURCES

Studies were identified by searching MEDLINE (1966 to January 1997), EMBASE/Excerpta Medica (1980 to 1997), CINAHL (1982 to 1997), Biological Abstracts on CD (1990 to 1997), the Cochrane Library, *Current Contents* (1996 to August 1997), and bibliographies of relevant papers and by contacting the manufacturer of ipratropium.

STUDY SELECTION

Published and unpublished studies in English, French, and Italian were selected if they were randomized, placebo-controlled trials that assessed the use of ipratropium in addition to β -agonists (administered by inhaler or wet nebulizer) compared

with β -agonist therapy alone in adult patients with acute asthma presenting to a hospital emergency department (ED) or similar acute care setting. Exclusion criteria were patients < 18 years old or studies of patients who had chronic obstructive pulmonary disease alone.

DATA EXTRACTION

Trial design and methodologic quality; drug treatments, dosages, and time intervals; patient characteristics; mean percentage change from baseline in FEV₁ or peak expiratory flow rate (PEFR); hospitalization rate; and adverse effects.

MAIN RESULTS

10 studies (1377 patients, age range 30 to 53 y) met the selection criteria. Meta-analysis showed a greater improvement with β -agonists plus ipratropium bromide than with β -agonists alone: Improvement in FEV₁ was 7.3% (95% CI 3.8% to 10.9%), or 100 mL (CI 50 to 149 mL), at

assessment times ranging between 45 and 90 minutes (5 studies); improvement in PEFR was 22.1% (CI 11.0% to 33.2%), or 32 L/min (CI 16 to 47 L/min), at assessment times ranging between 30 and 60 minutes (5 studies). In 3 studies (1064 patients), β -agonists plus ipratropium bromide reduced the rate of hospitalization {11% vs 15%, $P = 0.04$ }* more than β -agonists alone. Neither combination therapy nor monotherapy was associated with adverse effects.

CONCLUSION

Ipratropium bromide added to β -agonist therapy improves airflow obstruction better than β -agonists alone in the emergency treatment of adults with acute asthma.

Source of funding: No external funding.

For correspondence: Dr. S.D. Aaron, Ottawa General Hospital, Room LM-17, 501 Smyth Road, Ottawa, Ontario K1H 8L6, Canada. FAX 613-737-8141. ■

*Data provided by author.

COMMENTARY

In the United States, 2 million ED visits for acute asthma occur annually (1), and the health care costs associated with this disease are enormous (2). Guidelines for acute asthma care have been developed, and treatments that improve outcomes in patients with acute asthma are an important contribution to health care.

Treatment involves the early use of inhaled β_2 -agonists. Systemic corticosteroid therapy is also recommended early in ED care (3). Both of these treatments are consistently used in North American EDs. However, the use of anticholinergic agents, such as ipratropium bromide, is rather limited. This reflects, in part, conflicting evidence in the published literature regarding efficacy.

By reducing the biases common to systematic reviews, Stoodley and colleagues have provided high-quality evidence that shows a beneficial effect of adding ipratropium bromide to inhaled β_2 -agonists in adult patients with acute asthma. Using accepted methods, the reviewers have shown improvements in pulmonary function; the effect appears greatest in patients with more severe asthma. Although the clinical significance of these effects is debated in the

review, it would be considered important in cases of severe airway obstruction. Moreover, the evidence suggests that ipratropium bromide is beneficial in reducing the hospitalization rate. In summary, although questions still need to be resolved about ipratropium bromide therapy in the ED setting (such as the dose-response relation), it seems prudent to use this agent in combination with β_2 -agonists for patients with severe acute asthma to improve pulmonary function and reduce hospitalizations.

Brian H. Rowe, MD, MSc
University of Alberta
Edmonton, Alberta, Canada

References

1. Camargo CA Jr, Richardson LD. Epidemiology of asthma. In: Brenner BE, ed. *Emergency Asthma*. New York: Marcel Dekker; 1999:80.
2. Weiss KB, Gergen PJ, Hodgson TA. An economic evaluation of asthma in the United States. *N Engl J Med.* 1992;326:862-6.
3. Rowe BH, Keller JL, Oxman AD. Effectiveness of steroid therapy in acute exacerbations of asthma: a meta-analysis. *Am J Emerg Med.* 1992;10:301-10.