

## Nebulizers Versus Inhalers With Spacers for Acute Asthma

### EBEM Commentator

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### SYSTEMATIC REVIEW SOURCE

This is a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the Cochrane Database of Systematic Reviews and a commentary by an emergency physician knowledgeable in the subject area.

The source for this systematic review abstract is: Cates CJ, Bara A, Crilly JA, Rowe BH. Holding chambers versus nebulisers for beta-agonist treatment of acute asthma (Cochrane Review). In: *The Cochrane Library*. Issue 4. Oxford, United Kingdom: Update Software; 2003.

The *Annals'* EBEM editors helped prepare the abstract of this Cochrane systematic review as well as the Evidence-Based Medicine Teaching Points.

### OBJECTIVE

To assess the effects of holding chambers compared with nebulizers for the delivery of  $\beta_2$ -agonists for acute asthma.

### DATA SOURCES

An initial search was performed using the Cochrane Airways Group trials register (composed of MEDLINE, EMBASE, CINAHL, and United Kingdom Research Register standardized searches) and other relevant electronic databases. The reviewers searched the bibliographies, contacted trialists, and searched conference proceedings for additional published and unpublished

studies. The review is considered updated to November 2002.

### STUDY SELECTION

Randomized controlled trials in adults and/or children (aged  $\geq 2$  years) with acute asthma, where holding chamber  $\beta_2$ -agonist delivery was compared with wet nebulization, were selected. This report will focus on the results from adult studies only.

### DATA EXTRACTION AND ANALYSES

Two reviewers independently selected articles for inclusion, evaluated methodological quality of the studies, and abstracted the data. Continuous variables were reported as weighted mean difference, and dichotomous variables were reported as relative risk (RR), both with associated 95% confidence intervals (CIs).

### MAIN RESULTS

This review has been updated in 2003 and has now analyzed 1,076 children and 444 adults included in 22 trials from emergency department (ED) and community settings. In addition, 5 trials on inpatients with acute asthma (184 children and 28 adults) have been added to the review. Method of delivery of  $\beta_2$ -agonist did not appear to affect hospital admission rates. In adults, the relative risk of admission for holding chamber versus nebulizer was 0.88 (95% CI 0.56 to 1.38). Length of stay in the ED for adults was similar for the 2 delivery methods (weighted mean difference 0.02 hours; 95% CI -0.04 to 0.44 hours). Peak flow and forced expiratory volume were also similar for the 2 delivery methods.

### CONCLUSION

Metered-dose inhalers with holding chambers produced outcomes that were at least equivalent to nebulizer delivery in adults treated for acute asthma.

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## COMMENTARY: CLINICAL IMPLICATION

Asthma is a common chronic disease with a prevalence of 4% to 8%, important morbidity, and occasional mortality.<sup>1</sup> Acute asthma accounts for almost 2 million ED visits per year in the United States.<sup>2</sup> Asthma is a common disorder with immense medical and economic consequences to the patient and the health care system. It is estimated that the disease affects 10 to 12 million people in the United States. In 1998, the indirect and direct expenditures for asthma exceeded US\$12 billion in the United States.<sup>3</sup> In Canada, the cost reached Can\$600 million; 25% of these costs were expended on acute care of asthma (ED visits and hospitalization).<sup>4</sup> Although asthma affects more children than adults, the burden of illness is high in both groups. Despite repeated national attempts to standardize and improve asthma care, wide gaps still remain between what is known to be effective treatment and what is practiced.<sup>5</sup> It is widely accepted that the pathophysiology of asthma exacerbations is an inflammatory process that leads to increased mucus production and secondary bronchoconstriction. These changes lead to obstruction of both the large and small airways. The treatment of acute asthma can be divided into 2 components. The first component consists of the use of quick relief or "rescue" medication to treat bronchospasm. These medications consist of short-acting  $\beta$ -agonists (albuterol), anticholinergics (ipratropium bromide), and magnesium sulfate.<sup>6,7</sup> The second component consists of the use of agents to control the underlying inflammation (ie, inhaled and systemic corticosteroids).

Early treatment of acute asthma has focused on the symptoms related to bronchospasm and the use of short-acting bronchodilators (ie, albuterol), which can be administered through nebulization, or metered-dose inhalers with holding chamber or spacer devices. Choosing the appropriate route of administration (nebulization versus metered-dose inhalers/spacers) could impact the effectiveness, convenience, and cost of caring for patients with acute asthma. The methods described above also pose different risks of potential cross-infection. Generally, nebulized treatment is associated with greater cost and higher rates of cross-infection and maintenance.<sup>8</sup> In patients with severe asthma, continuous nebulization might be the preferred route because of its reported effectiveness and ease of administering bronchodilators compared with metered-dose inhalers/spacers.<sup>9</sup>

Although this review combines pediatric and adult studies, this commentary focuses on the evidence from adult patients only. The main question for emergency physicians is: What is the evidence for using metered-dose inhalers/spacers rather than nebulization in adults

with acute asthma in the ED? From 22 studies examining 444 patients, hospital admissions were similar using either method for the delivery of  $\beta$ -agonists in acute asthma (RR 0.65; 95% CI 0.4 to 1.06). These results were consistent even when excluding studies of lower quality. The time spent in the ED was not altered by the route of administration (weighted mean difference 0.02 hours; 95% CI -0.04 to 0.44 hours); however, these results only take into account 64 patients in the holding chamber group and 68 patients in the nebulization group. There were no significant differences between the 2 delivery systems 30 minutes after the initiation of treatment or at the end of the study with respect to peak expiratory flow rate (weighted mean difference -1.07% predicted; 95% CI -4.35 to 2.21) or the forced expiratory volume in 1 second (weighted mean difference 0.72% predicted; 95% CI -2.92 to 4.37). These results were consistent even when performing a subgroup analysis on patients with severe asthma (eg, forced expiratory volume in 1 second <30%; weighted mean difference -1.6 predicted; 95% CI -7.69% to 4.49%). Overall, there was no significant difference in any physiologic parameters, such as pulse or respiratory rate, between the 2 groups. Only 4 out of 6 studies included in the analysis of admissions used systemic corticosteroids as a standard of care in the treatment of asthma.

The traditional approach whereby adult patients seen in the ED need to be treated with nebulized bronchodilators is not substantiated by this review. This first-line therapy can be administered by either nebulization or metered-dose inhaler/spacer. The subsequent admission, length of stay, pulmonary functions, and other physiologic parameters, such as respiratory and pulse rate, are not significantly different between the 2 methods of bronchodilator administration for acute asthma. Moreover, no outcomes studied were worse with holding chamber even when subgroup analysis was performed on patients with severe asthma. All studies that included patients with life-threatening asthma (considered for ventilation: peak expiratory flow rate 30%), however, were excluded. Consequently, these results should not be applied to patients with life-threatening asthma. Finally, the benefit of metered-dose inhalers/spacers is maximized by titrating treatments to individual patient response. For example, clinicians are encouraged to use 4 to 6 puffs via a holding chamber and to titrate at frequent intervals, mirroring the techniques used by trialists in this group of studies.

## TAKE HOME MESSAGE

Given the similar effectiveness, higher costs, and greater risk for cross-contamination resulting from nebulized

delivery of bronchodilators in acute asthma, emergency physicians should work toward increasing the proportion of patients with mild-to-moderate asthma who receive metered-dose inhaler/spacer bronchodilator delivery in the ED.

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#### EBEM TEACHING POINT

**Cochrane Review Group.** The authors of this Cochrane Review belong to a review group called the Cochrane Airways Group (<http://www.cochrane-airways.ac.uk>). Review groups within the Cochrane Review are responsible for producing and updating reviews in specific topic areas. In the case of the Airways Group, they are responsible for producing reviews in asthma, chronic obstructive pulmonary disease, bronchiectasis, sleep apnea, interstitial lung disease, and pulmonary embolism. Other review groups that may be of interest to emergency physicians include acute respiratory infections (eg, croup, bronchitis, bronchiolitis, pneumonia), heart (eg, myocardial infarction, unstable angina, atrial fibrillation), muscu-

loskeletal injuries (eg, ankle injuries, fluid resuscitation), and stroke (eg, transient ischemic attack, stroke, intracerebral bleeds). A review group is generally led by a respected clinician and/or scientist in the field, has a Review Group Coordinator, a central office, and often a central database for searching purposes. Review group members contribute to the Cochrane Review through hand searching, methods work, and completion of systematic reviews. Emergency physicians interested in contributing to a Cochrane Review Group should contact the Review Group Coordinator; contact details are found at the end of each review.

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