EBEM Commentators
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Are Bronchodilators Effective in Bronchiolitis?

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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: Kellner JD, Ohlsson A, Gadomski AM, Wang EEL. Bronchodilators for bronchiolitis (Cochrane Review). In: *The Cochrane Library.* Issue 3. Oxford, United Kingdom: Update Software; 2002.

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

OBJECTIVE

The objective of the systematic review was to assess the effects of various bronchodilators for bronchiolitis.

DATA SOURCES

Searches were performed of MEDLINE, EMBASE, Reference Update, and the reference lists of articles, in addition to the personal files of 2 of the authors in June 1998. The searches are updated to June 1998; the original search was performed in 1994.

STUDY SELECTION

Studies were included if they were randomized clinical trials of bronchodilators versus placebo. Included trials produced data related to symptoms or signs, not pulmonary function testing alone. Only complete manuscripts were considered. The articles were reviewed independently by 2 authors, and selection of articles was completely concordant.

DATA EXTRACTION

Two investigators extracted data independently. Unpublished data of interest were requested from authors. Data included clinical scores, pulse oximetry, and hospital admission rates and durations. Scores were reported in the studies as either dichotomous clinical improvement or average change in score with treatment.

MAIN RESULTS

Twenty studies met inclusion criteria. Thirteen included only first-time wheezers, whereas the remaining 7 included both patients with first-time and recurrent wheeze. Improvements could be demonstrated in clinical score (odds ratio [OR] 0.29; 95% confidence interval [CI] 0.19 to 0.45); however, the clinical significance of the difference in score was not identified in many studies, and 2 of those showing the most improvement included recurrent wheezers. No improvement in oxygenation could be identified (pooled difference 0.7; 95% CI 0.36 to 1.35), and the rate (OR 0.7; 95% CI 0.36 to 1.35) and duration of hospitalization (weighted mean difference 0.12 days; 95% CI –0.3 to 0.5 days) were not significantly different between study and control groups. Adverse effects that were found in significantly greater numbers in the treatment group included tachycardia, increased blood pressure, decreased oxygen saturation, flushing, hyperactivity, prolonged cough, and tremor.

CONCLUSIONS

Bronchodilators produce modest, short-term improvement in clinical scores when bronchiolitis is mild to moderately severe. Given the high cost and uncertain benefit of their use, routine use in management of first-time wheeze cannot be recommended. Further research is required into a validated measure of pulmonary status and the minimal clinically significant difference in this measure. Further trials should be conducted using placebo controls.

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COMMENTARY: CLINICAL IMPLICATION

Bronchiolitis is a common disease during winter months in children younger than 2 years. It is characterized by respiratory distress, wheezing, and crackles in the chest in association with a viral infection, most commonly respiratory syncytial virus. Generally, it is diagnosed in children younger than 2 years who have not had previous or recurrent wheezing; however, it is often difficult to differentiate from asthma. The emergency department (ED) management of this disease has been frustrating for emergency clinicians because there have been no curative therapies identified to date, and clinical and diagnostic tests to identify patients who will benefit from hospitalization are lacking. Because of the similar clinical presentation to asthma, therapies used for asthma have been applied to this disease in hopes of producing at least symptomatic benefit.

This systematic review examined all available evidence for ED and inhospital treatment of bronchiolitis with bronchodilator therapy (eg, albuterol, adrenergic agonists, ipratropium bromide). These agents are commonly available and are used frequently in all children with asthma, as well as for children younger than 24 months with wheezing. They form part of the mainstay of therapy for hospitalized patients with bronchiolitis, along with supplemental oxygen and intravenous fluids.[1] This study points out that, although bronchodilators produce a measurable benefit in terms of the child's appearance, there are no proven benefits with respect to important outcomes such as relapse to hospitalization for outpatients or duration of hospitalization and attendant costs for inpatients.

This treatment may continue to be used for the symptomatic benefit it appears to provide. However, the costs of using bronchodilators in outpatients are estimated within the review at approximately $37.5 million per year in the United States.[2-5] Moreover, this seems a high cost to pay for a therapy of limited efficacy. For example, side effects are also notable, including tachycardia, increased blood pressure, decreased oxygen saturation, flushing, hyperactivity, and tremor.

Although clinicians can be reassured that these agents will provide symptomatic relief for some patients, little direction is offered by these reviewers or this review. Further research is underway into therapies for bronchiolitis, including steroids for acute treatment[6] and vaccines for prevention.[7] Identification of subsets of patients in whom bronchodilators are more likely to be beneficial is also a goal of future research.

TAKE HOME MESSAGE

Although the use of bronchodilators may provide some symptomatic relief, this review finds that they should not be used routinely in bronchiolitis. The benefits of bronchodilators in selected children, and the effects of other therapies, remain the subjects for further research.

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EVIDENCE-BASED MEDICINE TEACHING POINTS

Assessing study quality. The methodologic quality of included studies is important to evaluate and report in any systematic review. The overall quality of included studies can be used to assess the validity of the conclusions of a systematic review,

in a quality sensitivity analysis, or as a method of weighting the analyses. Studies of lower quality may still be included in the review, but with the understanding that their data and conclusions may be less valid than the higher quality studies.

There is a wide variety of scoring approaches; however, few of these are valid. In addition, there are a limited number of quality criteria of clinical trials that have been shown empirically to be a clear reflection of quality. For example, quality of randomization, specifically blinding and concealment of allocation, has been shown to be an important marker of bias in trials.[8]

One valid method of assessing the quality of trials of therapy is the Jadad score.[9] In this scoring system, studies are evaluated on the quality of randomization, blinding, and reporting drop-outs and withdrawals. Studies receive points for being described as randomized and double-blinded and reporting their drop-outs and withdrawals. In addition, they receive additional points for their methods of randomization and blinding. Overall, a score of 0 to 5 is calculated, and studies with a Jadad score of 3 or greater are generally accepted as high-quality randomized controlled trials. The authors of this study did not report Jadad scores; however, they did examine component scores for double blinding of test subject and assessors, and concealment of allocation. Overall, 16 of the 20 included studies were described as double blinded, and concealment of allocation was adequate in 11 of the 20 studies. From these observations, one could conclude that the studies included in this review were of moderate quality. The authors of this review did not provide a sensitivity analysis of the primary outcome based on the highest quality studies.

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