Cochrane for Clinicians

Putting Evidence into Practice

Effectiveness of Bronchodilators for Bronchiolitis Treatment

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The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Drs. Seehusen and Yancey present a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at http://www.cochrane.org/reviews/en/ab001266.html.

EB CME

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A collection of Cochrane for Clinicians published in *AFP* is available at http://www.aafp.org/afp/cochrane.

Clinical Scenario

An eight-month-old male infant presents with a one-day history of cough, fever, congestion, and a visible increase in respiratory effort, but has no prior history of such symptoms. On examination, the child has tachypnea, diffuse wheezing, and a mildly decreased pulse oximetry reading. His physician diagnoses bronchiolitis and wonders if a nebulized bronchodilator treatment might improve his oxygen saturation and keep him out of the hospital.

Clinical Question

Do bronchodilators improve outcomes in infants with a new diagnosis of bronchiolitis who do not have a history of wheezing?

Evidence-Based Answer

Bronchodilators may transiently improve the clinical status of infants with bronchiolitis and no prior history of wheezing. However, moderately strong evidence shows that key outcomes such as oxygen saturation, need for hospitalization, length of hospitalization, and duration of symptoms are not changed by the use of bronchodilators.[1] (Strength of Recommendation = A, based on consistent, good-quality patient-oriented evidence)

Practice Pointers

Bronchiolitis is an acute infectious illness that starts as an upper respiratory tract infection. It can progress to respiratory distress with signs of bronchiolar obstruction, including wheezing and air trapping.[2] This wheezing has resulted in bronchiolitis being treated with interventions known to work in asthma, including bronchodilators and steroids.[3] However, unlike asthma, the wheezing of bronchiolitis is caused by inflammation and debris within the airways rather than bronchoconstriction.[1]

This Cochrane review included a total of 28 randomized controlled trials examining the use of bronchodilators for bronchiolitis in children younger than two years.[1] The bronchodilators reviewed included albuterol, salmeterol (Serevent), ipratropium (Atrovent), terbutaline, and adrenergic agents. Studies examining epinephrine or inhaled steroids were excluded from the review. A previous Cochrane review found inadequate evidence to recommend epinephrine therapy for bronchiolitis.[4]

The primary outcome for the review was oxygen saturation, a physiologic endpoint.[1] Secondary patient-oriented outcomes included improvement in clinical score, hospital admission, time to illness resolution, and duration of hospitalization. Inpatient and outpatient studies were included. The authors included 20 studies measuring pulse oximetry. They found no significant improvement in oxygen saturation with use of bronchodilators (mean difference = –0.45; 95% confidence interval [CI], –0.96 to 0.05).

There was a statistically significant difference in the number of infants showing improved clinical scores (odds ratio for no improvement = 0.18; 95% CI, 0.06 to 0.50) and in the magnitude of the improvement (standardized mean difference = –0.37; 95% CI, –0.62 to –0.13) with the use of bronchodilators. The authors noted that the clinical significance of this improvement was highly questionable. Potential bias was introduced by interrater variability within individual trials and by variability among the different clinical scores used in different trials. In addition, there is no evidence that any of the

Cochrane Abstract

Background: Bronchiolitis is an acute, viral lower respiratory tract infection affecting infants and often treated with bronchodilators.

Objectives: To assess the effects of bronchodilators on clinical outcomes in infants with acute bronchiolitis.

Search Strategy: The authors searched the Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* 2010, Issue 1), which contains the Acute Respiratory Infections Group's Specialized Register, Medline (1966 to March 2010), and EMBASE (2003 to March 2010).

Selection Criteria: Randomized controlled trials comparing bronchodilators (other than epinephrine) with placebo for bronchiolitis.

Data Collection and Analysis: Two authors assessed trial quality and extracted data. Unpublished data were obtained from trial authors.

Main Results: The review included 28 trials (n = 1,912) of infants with bronchiolitis. In 10 inpatient and 10 outpatient studies, oxygen saturation did not improve with bronchodilators (mean difference [MD] = −0.45; 95% confidence interval [CI], −0.96 to 0.05; n = 1,182). Outpatient bronchodilator treatment did not reduce the rate of hospitalization (12 percent in bronchodilator group versus 16 percent in placebo; odds ratio = 0.78; 95% CI, 0.47 to 1.29; n = 650). Inpatient bronchodilator treatment did not reduce the duration of hospitalization (MD = 0.06; 95% CI, −0.27 to 0.39; n = 349). In seven inpatient and eight outpatient studies, average clinical score decreased slightly with bronchodilators (standardized mean difference [SMD] = −0.37; 95% CI, −0.62 to −0.13; n = 1,006).

Oximetry and clinical score outcomes showed significant heterogeneity. Including only studies at low risk of bias significantly reduced heterogeneity measures for oximetry (I^2 statistic = 17 percent) and average clinical score (I^2 statistic = 26 percent), but had little impact on the overall effect size of oximetry (MD = −0.38; 95% CI, −0.75 to 0.00; $P = .05$) and average clinical score (SMD = −0.26; 95% CI, −0.44 to −0.08; $P = .005$). Effect estimates for outpatients were slightly larger than for inpatients for oximetry (outpatients MD = −0.57; 95% CI, −1.13 to 0.00; versus inpatients MD = −0.29; 95% CI, −1.10 to 0.51) and average clinical score (outpatients SMD = −0.49; 95% CI, −0.86 to −0.11; versus inpatients SMD = −0.20; 95% CI, −0.43 to 0.03). Adverse effects included tachycardia and tremors.

Authors' Conclusions: Bronchodilators do not improve oxygen saturation, do not reduce hospital admission after outpatient treatment, do not shorten the duration of hospitalization, and do not reduce the time to resolution of illness at home. The small improvements in clinical scores for outpatients must be weighed against the costs and adverse effects of bronchodilators.

clinical scores used are valid indicators of pulmonary or overall clinical status.

Seven studies with a total of 344 participants evaluated whether nebulized bronchodilators administered to outpatients reduced the rate of hospitalization. There was no significant difference between the bronchodilator and placebo groups in admission rates (12 versus 16 percent, respectively; odds ratio = 0.78; 95% CI, 0.47 to 1.29). Three studies also found no reduction in hospitalization rates in infants treated with oral bronchodilators in the emergency department or at home.

The use of bronchodilators in hospitalized infants with a diagnosis of bronchiolitis did not change the length of stay. The mean difference between bronchodilator and placebo groups was a statistically nonsignificant 0.06 days (95% CI, −0.27 to 0.39). Similarly, the use of bronchodilators did not change infants' duration of illness. Two studies with a total of 269 participants compared oral bronchodilators used at home with placebo. The mean difference between groups was a nonsignificant 0.29 days (95% CI, −0.43 to 1.00). None of the studies using nebulized bronchodilators looked at time to resolution of illness.

Many studies included in this meta-analysis did not evaluate or report adverse effects. Studies that reported adverse effects found them almost exclusively among the participants receiving bronchodilators. Tachycardia, tremor, and jitteriness are commonly described adverse effects of bronchodilators. Additionally, mild hypertension, flushing, cough, and sometimes even decreased oxygen saturation were described in participants receiving bronchodilators.

Although a small, short-term improvement in subjective clinical scores may occur with the use of bronchodilators in infants with bronchiolitis, important outcomes such as hospitalization, oxygen saturation, and duration of illness are not changed. These facts, when combined with the high frequency of adverse effects, make bronchodilators a poor treatment option for infants with a new diagnosis of bronchiolitis and no prior history of wheezing. Bronchodilators continue to be a reasonable option in those infants with a prior history of wheezing.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army Medical Department or the U.S. Army Service at large.

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Author disclosure: Nothing to disclose.

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Cochrane Briefs

Screening for the Early Detection and Prevention of Oral Cancer

Clinical Question

Should family physicians routinely examine the oral cavity to detect pre-cancers and cancers?

Evidence-Based Answer

Screening by visual inspection of the oral cavity does not appear to reduce deaths from oral cancer in the general population, although there is some evidence that it could be effective in high-risk patients who use tobacco and alcohol. (Strength of Recommendation = B, based on inconsistent or limited-quality patient-oriented evidence)

Practice Pointers

An estimated one in 98 persons born in the United States will be diagnosed with a cancer of the oral cavity and pharynx during his or her lifetime, and nearly 8,000 persons died from oral cancer in 2010.[1] At the time of diagnosis, about 50 to 60 percent of oral cancer cases have regional or distant metastases and are associated with poor survival. Approximately 80 percent of patients with oral squamous cell cancers have used tobacco products.[2]

In this Cochrane review, the authors searched multiple electronic databases for randomized controlled trials of screening for oral cancer and potentially malignant oral lesions that used visual examination or adjunctive screening aids (toluidine blue, fluorescence imaging, or brush biopsy) and that reported mortality outcomes.

Only one cluster randomized trial of visual screening met inclusion criteria. This trial, conducted in an area of India with a very high incidence of oral cancer compared with the United States, showed no statistical difference (relative risk = 0.79; 95% confidence interval, 0.51 to 1.22) in oral cancer mortality rates between the screened and the control groups. However, a post hoc subgroup analysis of participants who reported using tobacco and/or alcohol found a statistically significant reduced risk of death (relative risk = 0.66; 95% confidence interval, 0.45 to 0.95) in the screened group. The authors assessed this study as having a high risk of bias caused by lack of blinding in outcome assessment and failure to account for the effect of clustering on the results.

In 2004, the U.S. Preventive Services Task Force found insufficient evidence to recommend for or against screening adults for oral cancer.[3] Despite inconclusive data that screening for oral cancer detects clinically significant lesions or improves health outcomes in U.S. populations, experts have suggested screening on other grounds: the test is noninvasive, takes relatively little time to perform, and may provide an opportunity to intervene at premalignant disease stages.[4] However, as with screening tests for breast and prostate cancers, false-positive results and overdiagnosis (i.e., identification of premalignant lesions or indolent cancer that would not have affected a patient's health) may lead to anxiety and unnecessary treatment, potentially outweighing any small benefits. The examination also takes time that could be spent on other, potentially more useful interventions that improve patient outcomes.

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Author disclosure: Dr. Lin is an associate editor of *Essential Evidence*, published by John Wiley & Sons, Inc., who also publish *The Cochrane Library*.

SOURCE: Brocklehurst P, Kujan O, Glenny AM, et al. Screening programmes for the early detection and prevention of oral cancer. *Cochrane Database Syst Rev*. 2010;(11):CD004150.

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