Review: $\beta_2$ agonists are ineffective but increase adverse effects in acute bronchitis without underlying pulmonary disease


QUESTION: In patients who have acute bronchitis without underlying pulmonary disease, are $\beta_2$ agonists more effective than placebo or alternative treatments for improving symptoms?

Data sources
Studies were identified by searching Medline (1966 to 2000), EMBASE/Excerpta Medica (1974 to 2000), the Cochrane Library (August 2000), conference proceedings, the System for Information on Grey Literature in Europe (1980 to 2000), and Science Citation Index (1990 to 2000). Bibliographies of relevant articles were reviewed, and US manufacturers of brand-name $\beta_2$ agonists were contacted for unpublished studies.

Study selection
Studies in any language were selected if they were randomised controlled trials (RCTs) comparing $\beta_2$ agonists with placebo or an alternative treatment in patients ≥ 2 years of age who had acute bronchitis or acute cough without a clear cause (eg, pneumonia, pertussis, or sinusitis).

Data extraction
Data were extracted on sample size, patient inclusion and exclusion criteria, patient age, key components of the intervention, study quality, and outcomes. Outcomes included the duration, persistence, severity, or frequency of cough; productive cough; night cough; duration of activity limitations; and adverse effects.

Main results
7 RCTs (2 in children and 5 in adults) met the selection criteria. $\beta_2$ agonists assessed included albuterol and fenoterol. The 2 RCTs in children compared albuterol with placebo; the rate of adverse effects (shaking or tremor) was greater in the $\beta_2$ agonist group than the placebo group (table). Groups did not differ for improvement of symptoms (table). 4 RCTs of adults compared either albuterol (3 RCTs) or fenoterol (1 RCT) with placebo; the rate of adverse effects (tremor, shaking, or nervousness) was greater in the $\beta_2$ agonist group than the placebo group (table). Groups did not differ for improvement of symptoms (table). In 1 RCT of adults that compared albuterol with erythromycin, fewer patients in the albuterol group than the erythromycin group had a cough at the end of the trial ($p < 0.05$). Meta-analysis of the 5 RCTs in adults did not show any difference between groups for improvement of symptoms.

Conclusion
In patients who have acute bronchitis without underlying pulmonary disease, $\beta_2$ agonists are no more effective than placebo for improving symptoms, but they are associated with increased risk for adverse effects.

COMMENTARY
The systematic review by Smucny et al provides compelling evidence against the routine use of $\beta_2$ agonists for the treatment of cough associated with acute bronchitis in patients without underlying lung disease. The authors evaluated 7 RCTs that enrolled almost 500 patients. No overall benefit of $\beta_2$ agonist treatment was identified. However, as pointed out by Smucny et al, the 2 trials of children excluded patients with such abnormal lung findings as the presence of wheezing. Although trials of adults enrolled patients with abnormal results on lung examination, only the study by Melbye et al separately reported the results in this subgroup. In their study, patients who had wheezing on initial examination, FEV1 < 80% of predicted, or a positive result on the methacholine challenge test improved when treated with fenoterol (had a lower symptom score than the placebo group at day 2). Overall, treatment with $\beta_2$ agonists in patients with acute bronchitis should be limited to those with a history of airflow obstruction or asthma (or airway reactivity) or the presence of wheezing on physical examination.

However, in patients who have a persistent cough following acute bronchitis, inhaled ipratropium bromide may be of benefit. Holmes et al evaluated the effectiveness of inhaled ipratropium in a crossover trial of such patients after alternative explanations for persistent cough were excluded by radiography, pulmonary function tests (eg, bronchoprovocation challenge testing), and bronchoscopic evaluation; 12 of 14 patients improved, and 5 had a total resolution of cough while using inhaled ipratropium. Results of this trial suggest that cholinergic mechanisms may be important in mediating persistent cough following acute bronchitis. Given the trial’s small size, further studies are necessary to establish whether inhaled ipratropium bromide might be effective for treating the cough that occurs during the acute phase of bronchitis.

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