Review: β_2-agonists are ineffective but increase adverse effects in acute bronchitis without underlying pulmonary disease

Smucny JJ, Flynn CA, Becker LA, Glazier RH. **Are β_2-agonists effective treatment for acute bronchitis or acute cough in patients without underlying pulmonary disease? A systematic review.** J Fam Pract. 2001 Nov;50:945-51.

QUESTION

In patients who have acute bronchitis without underlying pulmonary disease, are β_2-agonists more effective than placebo or alternative treatments for improving symptoms?

DATA SOURCES

Studies were identified by searching 5 databases, reviewing conference proceedings and bibliographies of relevant articles, and contacting U.S. manufacturers of β_2-agonists for unpublished studies.

STUDY SELECTION

Studies in any language were selected if they were randomized controlled trials (RCTs) comparing β_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 (e.g., 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. β_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 β_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 β_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, β_2-agonists are no more effective than placebo for improving symptoms, but they are associated with increased risk for adverse effects.

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For correspondence: Dr. J.J. Smucny, State University of New York Upstate Medical University, Syracuse, NY, USA. E-mail smucnyj@upstate.edu.

β_2-agonists vs placebo for acute bronchitis without underlying pulmonary disease*

Outcomes	Patient group	Weighted event rates		RRI (95% CI)	NNH (CI)
		β_2-agonists	Placebo		
Shaking or tremor at 3 to 7 d	Children	11%	0%	576% (–14 to 5218)	9 (5 to 100)
Shaking, tremor, or nervousness at 3 to 7 d	Adults†	55%	11%	388% (185 to 758)	3 (2 to 3)
				RRR (CI)	NNT
Cough at > 7 d	Adults	64%	71%	14% (–18 to 37)	Not significant
Night cough at > 7 d	Adults	24%	29%	16% (–33 to 46)	Not significant
		Standardized mean differences (CI)			
DCSSs at 3 d	Children	0.36 (–0.05 to 0.77)			
DCSSs at 4 d	Adults	–0.14 (–0.38 to 0.11)			

*DCSSs = daily cough symptom scores. Other abbreviations defined in Glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article using random effects.
†Event rates provided by author.

COMMENTARY

The systematic review by Smucny and colleagues provides compelling evidence against the routine use of β_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 β_2-agonist therapy was identified. However, as pointed out by Smucny and colleagues, 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 and colleagues (1) separately reported the results in this subgroup. In their study, patients who had wheezing on initial examination, $FEV_1 < 80\%$ of predicted value, 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 β_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 (2). Holmes and colleagues (2) 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 (e.g., 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.

Herbert Wiedemann, MD
Cleveland Clinic Foundation
Cleveland, Ohio, USA

References

1. **Melbye H, Aasebo U, Straume B.** Fam Pract. 1991;8:216-22.
2. **Holmes PW, Barter CE, Pierce RJ.** Respir Med. 1992;86:425-9.