# A Comparison of Albuterol and Erythromycin for the Treatment of Acute Bronchitis

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*Background.* Based on observations that pulmonary function tests of patients with acute bronchitis resemble those of patients with asthma, it was hypothesized that a bronchodilator may be an effective form of treatment for patients with acute bronchitis.

*Methods.* Albuterol was compared with erythromycin in a prospective, randomized, double-blinded fashion. Participants were patients who presented to family physicians with a history of having a productive cough of less than 30 days' duration, no history or evidence of pneumonia, and no other pulmonary or cardiac disease. Patients completed a 7-day symptom diary and returned to their physician after 1 week of therapy for reexamination.

*Results.* Patients treated with albuterol were less likely to be coughing after 7 days of treatment than patients treated with erythromycin (41% vs 88%, $P < .05$). This was true for both smokers and nonsmokers and in patients with purulent-appearing sputum. Trends toward an earlier improvement in cough and an improved feeling of well-being also were observed in the albuterol group. No differences between groups were found as to the length of time before patients returned to work, the length of time until patients resumed normal activities, or the overall improvement in patient well-being. Minor side effects were equal in both groups.

*Conclusions.* Oral albuterol may be more effective than commonly used antibiotics in relieving the symptoms of acute bronchitis.

*Key words.* Bronchitis; albuterol; erythromycin; comparative study. *J Fam Pract 1991; 33:476-480.*

Acute bronchitis is one of the most common illnesses seen in ambulatory practice,[1–3] yet there is no clear effective treatment. Despite the opinion that acute bronchitis is a viral-mediated disease[4–6] and that antibiotics are not indicated for this disorder,[7,8] antibiotics are frequently prescribed for patients with acute bronchitis.[9,10] This may be based on observations that *Mycoplasma* may be recovered from patients with acute bronchitis.[11–14] However, other than two studies that showed a marginal benefit from erythromycin[15,16] and another study showing a small benefit of sulfamethoxazole with trimethoprim,[17] no antibiotic has been shown to be useful in treating acute bronchitis.

Other observations have shown that pulmonary function testing in patients with acute bronchitis resembles that of patients with acute asthma[18,19] and that patients with previous acute bronchitis are more likely to develop asthma in the future.[20] These reports suggest that acute bronchitis may respond to medications that are useful in treating acute reversible airway obstruction. In order to study this hypothesis, the effectiveness of an oral bronchodilator, albuterol, was tested in healthy adult patients who presented with an acute productive cough in the absence of pneumonia. Since over 90% of physicians use antibiotics for the treatment of acute bronchitis,[9,10] albuterol was compared with erythromycin, a commonly used antibiotic and one that has been demonstrated to have some small effect on the symptoms of acute bronchitis.[15,16]

## Methods

This study was conducted between September 1, 1989, and April 1, 1991, at three rural primary care centers and a suburban family practice residency program in northeastern Kentucky. Patients between the ages of 18 and 65 years who presented to their physician with a productive cough of less than 30 days' duration were considered for entry into the study. Patients were excluded for any of the following conditions: pregnancy, a history of chronic obstructive pulmonary disease or asthma, a history of cardiac disease, or an allergy to erythromycin or al-

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buterol. In addition, patients with clinical or radiographic evidence of pneumonia or who had a history of pneumonia in the past 6 months, or a temperature over 39.5°C, or who had taken antibiotics in the 14 days prior to the study were excluded from the study.

In order to compare albuterol with erythromycin in a double-blinded fashion, the liquid form of both medications was used. After informed consent, patients in the study were given a number-coded bottle that was tinted to prevent the physician from seeing the color of the contents and which contained either liquid albuterol in a concentration of 2 mg/5 mL or erythromycin ethylsuccinate at 400 mg/5 mL. Instructions on the bottle directed the patient to take one teaspoonful of medication every 6 hours for the next 7 days. Attached to the medication bottle was a patient symptom diary, which the patient was instructed to complete for each day of the study. The diary asked if the patient's cough had improved that day, if the patient had been kept awake by the cough, if the patient felt well enough to return to work, and if the patient had resumed normal activities by that day. In addition, patients were asked to rate their general feeling of well-being on a 5-point Likert scale and to indicate if they had taken any additional medications that day or had experienced any side effects from the study medication.

Following 7 days of medication, patients returned to their primary health care provider. The patient was reexamined, and the unused portion of medication and the symptoms diary were returned. Participating medical providers submitted to the principal investigator the patient symptoms diary and volume of unused medication along with preprinted number-coded forms containing the initial and follow-up patient history and physical examination findings.

Discrete data were analyzed using chi-square analysis with the Mantel-Haenszel correction or two-tailed Fisher's exact test in cases of comparisons with small cell sizes. Two-tailed *t* tests were used for continuous data. Statistical significance was defined as $P < .05$.

## Results

Forty-five patients were eligible for the study. Three patients declined to participate: two declined because they could not return in 7 days, and the third initially agreed and then changed his mind before signing the consent form. Of the 42 remaining patients, 22 began taking erythromycin and 20 began taking albuterol. Two patients in each group were withdrawn from the study because of medication side effects, and three patients (two in the erythromycin group and one in the albuterol group) failed to follow up after their 7-day course of treatment. Thirty-five patients completed the study, but one patient in the erythromycin group was excluded after completing the medication because she had a cough lasting more than 30 days and therefore did not meet the study entry criteria. Thus, data were analyzed for 34 patients, 17 in the albuterol group and 17 in the erythromycin group.

Table 1. Demographic Characteristics of Patients

| | Albuterol Group (n = 17) | Erythromycin Group (n = 17) | *P* Value |
|---|---|---|---|
| Sex | | | |
| Male | 8 | 6 | |
| Female | 9 | 11 | NS |
| Age, y (mean ± SD) | 44.1 (±15.9) | 33.3 (±9.2) | .02 |
| Smokers (%) | 11 (65) | 6 (35) | NS |
| Packs/day smoked (mean ± SD) | 1.2 ± 0.4 | 1.0 ± 0.4 | NS |
| Duration of cough, d (mean ± SD) | 5.2 ± 3.0 | 5.2 ± 3.3 | NS |
| Night cough present (%) | 10 (59) | 12 (71) | NS |
| Purulent sputum (%) | 13 (76) | 16 (94) | NS |
| Other symptoms present (%) | 16 (94) | 14 (82) | NS |
| Abnormal lung examination (%) | 8 (47) | 7 (41) | NS |

*SD denotes standard deviation; NS, not significant.*

Demographic information and characteristics of the patients' illnesses are shown in Table 1. The albuterol group had a greater proportion of male patients and an older mean age than the erythromycin group, although neither of these differences was statistically significant. The albuterol group also had a greater proportion of smokers than the erythromycin group (65% vs 35%, $P = .09$); the average number of packs per day smoked by those who did smoke, however, was similar in both groups.

The patients were also well matched in the severity and characteristics of their illness (Table 1). Patients in both groups had a similar duration of cough. Also, the number of patients with a night cough or purulent sputum (defined as yellow, green, brown, or bloody sputum that was thick in consistency) and the number of patients who reported other symptoms were comparable between groups. In addition, there was no difference in the percentage of patients who had abnormalities on initial physical examination.

After 7 days of therapy, it was found that 7 patients (41%) in the albuterol group were still coughing compared with 15 patients (88%) in the erythromycin group ($P = .004$) (Table 2). Furthermore, fewer patients in the albuterol group reported a productive cough (35% vs 71%, $P = .002$). The number of patients who still had purulent sputum or night cough, however, was similar

between the two groups. Also the number of patients with abnormal lung examinations after 7 days of medications was similar, although slightly higher in the albuterol group ($P = .61$).

Because the two groups differed in the percentage of patients who were smokers, a subanalysis was performed based on this variable. This analysis produced data similar to the results for the entire group. Among smokers, five patients (45%) in the albuterol group and six patients (100%) in the erythromycin group were still coughing after 7 days of therapy ($P = .03$); in nonsmokers, one patient (17%) in the albuterol group and nine patients (82%) in the erythromycin group were still coughing ($P = .02$). In comparing smokers and nonsmokers in the same treatment regimen, there was no significant difference between the percentage still coughing in either the albuterol group ($P = .25$) or the erythromycin group ($P = .28$).

Analysis of the patients' symptoms diaries showed that the coughing diminished and the general feeling of well-being in patients in the albuterol group tended to improve slightly sooner than in patients in the erythromycin group, although the results are not statistically significant (Table 3). Although patients in the albuterol group reported feeling better quicker, there was no difference between the albuterol and erythromycin groups in the overall improvement in their feeling of well-being during the course of therapy (+0.9 vs +1.4, respectively). There was also no difference between treatment groups in the mean number of days that patients missed work or limited their activity secondary to their illness. Patients in both groups were also equally likely to use over-the-counter medications.

According to patient diaries, 12 patients experienced mild side effects from their medications. Six patients (35%) in the albuterol group reported nervousness or tremulousness, while 6 patients (35%) in the erythromycin group reported gastrointestinal side effects. Despite side effects, compliance with therapy was very high, with patients in the albuterol group taking 95% of the doses prescribed for 7 days and patients in the erythromycin group taking 99% of the prescribed doses.

Table 2. Results of Treatment of Patients with Bronchitis After 7 Days of Therapy

| | Albuterol Group No. (%) | Erythromycin Group No. (%) | *P* Value |
|---|---|---|---|
| Cough still present | 7 (41) | 15 (82) | .004 |
| Cough still productive | 5 (35) | 13 (71) | .005 |
| Producing purulent sputum | 2 (16) | 6 (38) | .24 |
| Night cough present | 5 (50) | 7 (58) | 1.0 |
| Abnormal lung examination | 4 (50) | 2 (29) | .61 |

*NOTE: Data are expressed as the number of patients with symptoms after 7 days (% of patients who presented with symptoms initially).*

Table 3. Summary of Patient Symptoms Diaries After 7 Days of Treatment for Bronchitis

| | Albuterol Group (mean ± SD) | Erythromycin Group (mean ± SD) | *P* Value |
|---|---|---|---|
| Days until improvement in well-being | 2.8 ± 2.3 | 3.4 ± 1.7 | .60 |
| Days until improvement in cough | 2.8 ± 1.7 | 3.4 ± 2.0 | .52 |
| Days until night cough gone | 2.4 ± 2.7 | 3.1 ± 2.2 | .60 |
| Days until return to work | 2.1 ± 1.8 | 2.1 ± 1.9 | .92 |
| Days until return to normal activity | 2.8 ± 2.2 | 2.7 ± 2.1 | .80 |
| Improvement in well-being | 0.9 ± 0.9 | 1.4 ± 1.1 | .15 |

*NOTE: Data are expressed in the number of days until first improvement in symptoms. For improvement of well-being, results are expressed as the total number of points improved on a 5-point Likert scale.*
*SD denotes standard deviation.*

## Discussion

This randomized, double-blinded study showed that patients with acute bronchitis who were treated with oral albuterol were more likely to resolve their cough within 7 days than patients treated with erythromycin. In addition, there was a trend favoring a quicker reduction in coughs and more rapid improvement in general feeling of well-being in the patients taking albuterol as compared with those taking erythromycin, but neither of these differences proved to be statistically significant. The incidence of major side effects that prompted patients to drop out of the study and the incidence of minor side effects that patients were able to tolerate were similar in both groups. Thus, these data suggest that treatment with albuterol is more effective at relieving some of the symptoms of acute bronchitis than erythromycin, with no increase in untoward side effects.

The results of this study are consistent with the findings that patients with acute bronchitis have reversible airway obstruction and suggest that many of the symptoms of acute bronchitis are secondary to this bronchospasm.[19,20] It is clear that infectious organisms play a role in the development of acute bronchitis,[4–6] but therapy directed against causative agents may not be as efficacious as treating the bronchial reaction to infection. These results suggest that antibiotics may not be the best therapy for acute bronchitis even for patients who produce so-called purulent sputum. If physicians insist on employing medications to treat self-limited conditions

such as acute bronchitis, it appears that a bronchodilator such as albuterol would be a better choice than an antibiotic.

Although the patients taking albuterol reported that their cough decreased sooner and that they started to feel better sooner, it was disappointing to note that there was no advantage of albuterol over erythromycin in the duration that patients were unable to work or perform their usual activities. This implies that whereas a cough is a predominant symptom of acute bronchitis, other symptoms may have a greater effect on patients' perceptions of their health and ability to return to normal activities. It can be inferred that the disappearance of cough is only one of several clinical developments in the course of acute bronchitis and that studies examining this disease need to consider multiple functional and symptomatic endpoints to determine if a true clinical benefit is attained. In this study, it is unclear whether the resolution of cough observed in the group treated with albuterol offered any clinical benefit over the group treated with erythromycin.

These data demonstrate superiority of albuterol to erythromycin in reducing the cough of acute bronchitis, but two limitations of this study must be addressed. The first is the small sample size. The small number of subjects limits the power of the study to detect small differences between the two medications. Those factors that showed a trend favoring one medication over the other might have reached statistical significance with a larger sample size. Additionally, a larger study group might also have allowed a comparison of the patients with purulent sputum with those with nonpurulent sputum. The small number of patients in this study with nonpurulent sputum makes such a comparison unreliable. Thus, if more subjects had been included in this trial, additional conclusions might have been possible that would have been helpful in selecting certain populations of patients who might have benefited from antibiotic treatment.

A second limitation of this study is the route by which albuterol was administered. In order to facilitate the blinding of the study participants, albuterol was used in the oral dosing form rather than by the more commonly used metered-dose-inhaler delivery system. The nervousness and tremulousness reported as side effects in the albuterol group are more prevalent with orally administered medication as compared with a metered-dose-inhaler route. If the metered-dose-inhaler delivery of bronchodilators produced results similar to those of the oral form with a reduction in the side effects, then therapy with bronchodilators would not only be more effective, it also would be accompanied by fewer side effects than erythromycin. Additionally, since the mechanisms of action of bronchodilators and antibiotics are presumed to differ, further research is appropriate to determine if adding bronchodilators to antibiotics is more effective than either treatment alone.

In summary, this double-blinded, randomized trial of treatment of acute bronchitis with albuterol in comparison with erythromycin demonstrated that albuterol was more effective at clearing patients' cough in 7 days. Albuterol appeared to be equally effective in both smokers and nonsmokers and in patients with purulent sputum.

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