

## Q: Does salmeterol increase mortality in patients with COPD?

**ROBERT B. GERBER, MD**

Department of Pulmonary and Critical Care Medicine,  
Cleveland Clinic

**MANI KAVURU, MD\***

Department of Pulmonary and Critical Care Medicine,  
Cleveland Clinic

**A:** No. The long-acting beta<sub>2</sub> agonist salmeterol (Serevent) is approved by the US Food and Drug Administration for use in asthma, exercise-induced bronchospasm, and chronic obstructive pulmonary disease (COPD). It can be used as a single-agent treatment for symptoms of mild to moderate COPD.

On the other hand, salmeterol probably does not produce objective improvements in lung function, decrease the mortality rate, or alter the course of the disease. If symptoms do not improve, there is no reason to continue its use. Moreover, it should be part of a comprehensive treatment program that includes education, smoking cessation, oxygen supplementation, drug therapy, and rehabilitation.

Only one study<sup>1</sup> indicated a possible trend toward increased mortality with salmeterol. This European study compared salmeterol with salbutamol (a short-acting beta<sub>2</sub> agonist) in patients with asthma. There was a trend towards increased mortality in the salmeterol group, but the difference between the groups was not statistically significant.

Contraindications to salmeterol include hypersensitivity to salmeterol or adrenergic amines, the need for acute bronchodilatation, or use of a monoamine oxidase (MAO) inhibitor within the previous 2 weeks.

### ■ SMOKING CESSATION, HOME OXYGEN

Two measures *do* affect the course of COPD and should be part of its initial outpatient

management: smoking cessation and assessment of need for home oxygen therapy.<sup>2</sup>

Pharmacotherapy, though important and frequently used for symptom relief, has not been shown to alter the natural history of COPD or improve survival.

### ■ THERAPY FOR ACUTE EXACERBATIONS

Drug therapy for acute exacerbations of COPD usually consists of:

- Systemic steroids
- Inhaled ipratropium (Atrovent) and albuterol (Proventil, Ventolin)
- An antibiotic (possibly) if an infection is suspected as the cause of the exacerbation. Currently, no studies show any benefit of antibiotic use for COPD exacerbations if infection is not apparent.

### ■ LONG-TERM THERAPY

For long-term maintenance therapy, the emphasis is on treating bronchoconstriction and increased cholinergic tone with inhaled agents. Studies have shown the anticholinergic agent ipratropium, given on a regular schedule, to be more beneficial than either short-acting beta agonists delivered by metered-dose inhalers or placebo.<sup>3</sup> Because ipratropium has a slower onset of action, it should be used on a regular schedule rather than on an as-needed basis.


Should symptoms persist despite maximum anticholinergic therapy (up to 6 puffs four times a day), consideration should be given to adding sustained-release theophylline or a long-acting inhaled beta<sub>2</sub> agonist such as salmeterol or both.

### ■ SALMETEROL BOOSTS QUALITY OF LIFE

In a study comparing salmeterol with placebo, salmeterol was associated with significant

Salmeterol  
should only  
be part of a  
total  
program

\*The author is on the speakers' bureau of and has received grant support from the Glaxo Corporation.




improvements in quality of life as assessed by the St. George's Respiratory Questionnaire, which evaluates symptoms (such as cough and sputum), impact on physical activity, and the psychosocial impact of the disease.<sup>4</sup>

## ■ BETA AGONISTS DO NOT AFFECT LUNG FUNCTION

Even though salmeterol significantly improved lung function in one study,<sup>5</sup> beta<sub>2</sub> agonists are generally thought not to improve lung function (as objectively measured by spirometry) or exercise tolerance (as measured by the standardized 6-minute walk). Given this information, one should not use spirometry with a bronchodilator challenge to decide whether or not to try a beta<sub>2</sub> agonist.

Beta<sub>2</sub> agonists also do not appear to change the frequency of exacerbations, nor do they make a difference in the degree of resting or exercise-induced hypoxemia.<sup>6</sup>

If symptoms remain poorly controlled despite treatment with ipratropium, theophylline, and salmeterol, it is appropriate to consider a short trial of an oral corticosteroid to evaluate reversibility of airflow obstruction due to underlying airway inflammation. 

## ■ REFERENCES

1. Castle W, Fuller R, Hall J, et al. Serevent nationwide surveillance study: comparison of salmeterol with salbutamol in asthmatic patients who require regular bronchodilator treatment. *BMJ* 1993; 306:1034–1037.
2. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1995; 152:S77–S120.
3. Ferguson GT, Cherniack RM. Management of chronic obstructive pulmonary disease. *N Engl J Med* 1993; 328:1017–1022.
4. Jones PW, Bosh TK. Quality of life changes in COPD patients treated with salmeterol. *Am J Respir Crit Care Med* 1997; 155:1283–1289.
5. Mahler DA, Donohue JF, Barbee RA, et al. Efficacy of salmeterol xinafoate in the treatment of COPD. *Chest* 1999; 115:957–965.
6. Patakas D, Andreadis D, Mavrofridas E, et al. Comparison of the effects of salmeterol and ipratropium bromide on exercise performance and breathlessness in patients with stable chronic obstructive pulmonary disease. *Resp Med* 1998; 92:1116–1121.

---

ADDRESS: Mani Kavuru, MD, Department of Pulmonary and Critical Care Medicine, A90, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail [kavurum@ccf.org](mailto:kavurum@ccf.org).