

Q: Can patients with COPD or asthma take a beta-blocker?**ELSY VIVIANA NAVAS, MD**

Department of Cardiovascular Medicine, Cleveland Clinic

DAVID O. TAYLOR, MD

Department of Cardiovascular Medicine, Critical Care Center, and Transplantation Center, Cleveland Clinic

A: Yes. Treatment with beta-adrenergic receptor blockers decreases the mortality rate in patients with coronary artery disease or heart failure, as well as during the perioperative period in selected patients (eg, those with a history of myocardial infarction, a positive stress test, or current chest pain due to myocardial ischemia). The current evidence supports giving beta-blockers to patients with coronary artery disease and chronic obstructive pulmonary disease (COPD) or asthma, which lowers the 1-year mortality rate to a degree similar to that in patients without COPD or asthma, and without worsening respiratory function.¹ However, many clinicians still hesitate to start patients with COPD or asthma on a beta-blocker due to the fear of bronchoconstriction.²

■ THE RISKS

In patients with reversible airway disease, beta-blockers may increase airway reactivity and bronchospasm, as well as decrease the response to inhaled or oral beta-receptor agonists.³ Even topical ophthalmic nonselective beta-blockers for glaucoma can cause a worsening of pulmonary function.⁴ However, these data are from small trials in the 1970s and 1980s.

On the other hand, not giving beta-blockers can pose a risk of death. In a retrospective study of more than 200,000 patients with myocardial infarction, Gottlieb et al⁵ found that beta-blockers were associated with a 40% re-

duction in mortality rates in patients with conditions often considered a contraindication to beta-blocker therapy, such as congestive heart failure, pulmonary disease, and older age.⁵

■ CARDIOSELECTIVE BETA-BLOCKERS

Cardioselective beta-blockers with an affinity for the beta-1 receptor theoretically result in fewer adverse effects on the lungs. They competitively block the response to beta-adrenergic stimulation and selectively block beta-1 receptors with little or no effect on beta-2 receptors, except perhaps at high doses. However, this possible high-dose effect requires further study.

The effect of cardioselective beta-blockers on respiratory function was evaluated in two meta-analyses,^{6,7} one in patients with mild to moderate reactive airway disease, the other in patients with mild to severe COPD. Patients with reactive airway disease who received a single dose of a beta-blocker had a 7.46% reduction in forced expiratory volume in the first second of expiration (FEV₁), an effect that was completely reversed by treatment with a beta-agonist inhaler. The FEV₁ increased by a statistically significantly greater amount in response to beta-agonists in patients who received beta-blockers (a single dose or continuous therapy) than in those who did not receive beta-blockers. Patients who received continuous cardioselective beta-blockers experienced no significant drop in FEV₁, and no new symptoms developed. These results led the authors to conclude that cardioselective beta-blockers do not cause a significant reduction in pulmonary function in patients with mild to moderate reactive airway disease and COPD and are therefore safe to use. A single dose of a cardioselective beta-blocker may produce a small decrease in FEV₁, especial-

Beta-blockers may increase airway reactivity and bronchospasm, but not giving one can pose a risk of death

doi:10.3949/ccjm.77a.09133

ly in patients with reactive airway disease, but as therapy is continued over days to weeks, there is no significant change in symptoms or FEV₁ and no increase in the need for beta-agonist inhalers.

A major limitation of the two meta-analyses was that the patients were younger than most patients who require beta-blockers: the average age was 40 in patients with reactive airway disease, and 54 in patients with COPD. Also important to consider is that only patients with mild to moderate reactive airway disease were included. Patients with severe asthma, especially those with active bronchospasm, may react differently to even cardioselective beta-blockers.

■ NONSELECTIVE BETA-BLOCKERS

Recent studies suggest that nonselective beta-blockers can affect respiratory function in patients with COPD, but they have failed to show any harm. For example, propranolol (Inderal) was shown to worsen pulmonary function and to decrease the sensitivity of the airway to the effects of long-acting beta-2-agonists, but the 15 patients included in this study had no increase in respiratory symptoms.⁸

It has also been suggested that combined nonselective beta- and alpha-receptor blockade—eg, with labetalol (Trandate) or carvedilol (Coreg)—might be better tolerated than nonselective beta-blockers in patients with COPD.⁹ However, from limited data, Kotlyar et al¹⁰ suggested that carvedilol may be less well tolerated in patients with asthma than with COPD. All current evidence on combined nonselective beta- and alpha-blockade is observational, and it is not yet clear whether this class of beta-blockers is better tolerated due to alpha-blockade or merely because nonselective beta-blockers themselves are well tolerated.

■ REFERENCES

1. **Chen J, Radford MJ, Wang Y, Marciniak TA, Krumholz HM.** Effectiveness of beta-blocker therapy after acute myocardial infarction in elderly patients with chronic obstructive pulmonary disease or asthma. *J Am Coll Cardiol* 2001; 37:1950–1956.
2. The sixth report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med* 1997; 157:2413–2446.
3. **Benson MK, Berrill WT, Cruickshank JM, Sterling GS.** A comparison of four beta-adrenoceptor antagonists in patients with asthma. *Br J Clin Pharmacol* 1978; 5:415–419.
4. **Fraunfelder FT, Barker AF.** Respiratory effects of timolol. *N Engl J Med* 1984; 311:1441.
5. **Gottlieb SS, McCarter RJ, Vogel RA.** Effect of beta-blockade on mortality among high-risk and low-risk patients after myocardial infarction. *N Engl J Med* 1998; 339:489–497.
6. **Salpeter SR, Ormiston TM, Salpeter EE, Poole PJ, Cates CJ.** Cardioselective beta-blockers for chronic obstructive pulmonary disease: a

TABLE 1

Categories and examples of beta-blockers

<p>Nonselective beta-blockers</p> <ul style="list-style-type: none"> Nadolol (Corgard) Penbutolol (Levitol) Pindolol (Visken) Propranolol (Inderal) Sotalol (Betapace) Timolol (Blocadren) 	<p>Selective beta-blockers (beta-1-receptor blockers)</p> <ul style="list-style-type: none"> Acebutolol (Sectral) Atenolol (Tenormin) Betaxolol (Kerlone) Bisoprolol (Zebeta) Sotalol (Betapace) Esmolol (Brevibloc) Metoprolol (Toprol) Nebivolol (Bystolic)
<p>Combined nonselective alpha- and beta-blockers (cardioselective)</p> <ul style="list-style-type: none"> Carvedilol (Coreg) Labetalol (Trandate) 	

■ OUR RECOMMENDATIONS

Beta-blockers improve survival rates in patients with chronic systolic heart failure and after myocardial infarction, including in those patients with coexisting COPD and reactive airway disease. But not all beta-blockers are the same (TABLE 1). Cardioselective beta-blockers (ie, those that block predominantly beta-1 receptors) are our beta-blockers of choice based on stronger evidence from clinical studies. Nonselective agents that include alpha-adrenergic blockade can be considered, although less is known about their effect on respiratory function. However, the use of even beta-1-selective drugs merits caution and close follow-up in patients with severe asthma (for which clinical study data are limited).

- meta-analysis. *Respir Med* 2003; 97:1094–1101.
7. **Salpeter SR, Ormiston TM, Salpeter EE.** Cardioselective beta-blockers in patients with reactive airway disease: a meta-analysis. *Ann Intern Med* 2002; 137:715–725.
8. **van der Woude HJ, Zaagsma J, Postma DS, Winter TH, van Hulst M, Aalbers R.** Detrimental effects of beta-blockers in COPD: a concern for nonselective beta-blockers. *Chest* 2005; 127:818–824.
9. **Sirak TE, Jelic S, Le Jemtel TH.** Therapeutic update: non-selective beta- and alpha-adrenergic blockade in patients with coexistent chronic obstructive pulmonary disease and chronic heart failure. *J Am Coll Cardiol* 2004; 44:497–502.
10. **Kotlyar E, Keogh AM, Macdonald PS, Arnold RH, McCaffrey DJ, Glanville AR.** Tolerability of carvedilol in patients with heart failure and concomitant chronic obstructive pulmonary disease or asthma. *J Heart Lung Transplant* 2002; 21:1290–1295.

ADDRESS: David O. Taylor, MD, Department of Cardiovascular Medicine, J3, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail taylor2@ccf.org.