Review: Cardioselective β-blockers do not produce adverse respiratory effects in COPD

Salpeter S, Omiston T, Salpeter E. **Cardioselective beta-blockers for chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2005;4:CD003566.

Clinical impact ratings: GIM/FP/GP ★★★★★★☆ Cardiology ★★★★★★☆ Pulmonology ★★★★★☆☆

QUESTION

In patients with chronic obstructive pulmonary disease (COPD), do cardioselective β-blockers cause adverse respiratory effects?

METHODS

Data sources: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE/Excerpta Medica, CINAHL, respiratory journals, meeting abstracts, and relevant references (up to May 2005).

Study selection and assessment: Randomized, blinded, controlled trials (RCTs) in any language that evaluated cardioselective β-blockers as a single dose or for an extended period in patients with COPD and reported change in FEV_1 or respiratory symptoms. Administration of β_2-agonists, either intravenously or by inhalation, after cardioselective β-blockers or placebo, was also studied. Study quality was assessed for randomization and blinding.

Outcomes: Change in FEV_1, FEV_1 response to β_2-agonists, and respiratory symptoms (wheezing, dyspnea, or COPD exacerbation).

MAIN RESULTS

20 RCTs (all crossover trials) met the selection criteria. 11 trials (n = 131, mean age 53.8 y, 80% men) evaluated a single dose of cardioselective β-blockers, and 9 trials (n = 147) reported longer duration (mean 3.7 wk). Meta-analyses showed that a single dose of cardioselective β-blockers was not associated with a change in FEV_1 compared with placebo or baseline controls and did not increase respiratory symptoms (Table). Longer-duration of cardioselective β-blockers also did not change FEV_1 (Table) or increase respiratory symptoms. Administration of β_2-agonists after a single dose or longer-duration cardioselective β-blockers or placebo did not change FEV_1 (Table). Subgroup analyses showed that single-dose or longer-duration cardioselective β-blockers did not affect change in FEV_1 in patients with severe COPD (baseline FEV_1 < 1.4 L or < 50% of normal predicted value) or in patients with COPD with a reversible component as shown by ≥ 15% improvement in FEV_1 after β_2-agonists.

CONCLUSION

In patients with chronic obstructive pulmonary disease, cardioselective β-blockers do not change FEV_1 or increase respiratory symptoms.

Source of funding: Garfield Weston Foundation UK.

For correspondence: Dr. S. Salpeter, Stanford University and Santa Clara Valley Medical Center, San Jose, CA, USA. E-mail shelley.salpeter@hhs.co.santa-clara.ca.us.

Cardioselective β-blockers vs placebo for chronic obstructive pulmonary disease*

Treatments	Number of trials (*n*)	Outcomes	WMD (95% CI) or RD (CI)
Single-dose β-blockers	4 (108) 9 (301)	FEV_1 Respiratory symptoms	WMD –2.08% (–5.25 to 1.09) RD 0.00% (–0.04 to 0.04)
Inhaled β_2-agonists after single-dose β-blockers	2 (50)	FEV_1	WMD –1.21% (–10.97 to 8.56)
Longer-duration (2 d to 12 wk) β-blockers	5 (170) 8 (224)	FEV_1 Respiratory symptoms	WMD –2.39% (–5.69 to 0.91) RD 0.00% (–0.05 to 0.05)
Inhaled β_2-agonists after longer-duration (2 d to 12 wk) β-blockers	2 (60)	FEV_1	WMD 1.12% (–4.97 to 7.20)

*WMD = weighted mean difference; RD = risk difference. CI defined in Glossary. A fixed-effects model was used. All results are not significant.

COMMENTARY

The well-conducted meta-analysis by Salpeter and colleagues vividly illustrates 1 of the assumptions of the new paradigm of evidence-based medicine: The rationales for treatments, which follow from basic pathophysiologic principles, may in fact be wrong and lead to inaccurate predictions about their effects (1). For many clinicians, the suggestion that (even cardioselective) β-blockers may be safely used in COPD is counterintuitive. In this regard, the conclusion of the meta-analysis is very important because COPD is highly prevalent and shares common risk factors with cardiovascular disease. Both conditions often coexist.

The results are only partially reassuring, however. Many patients have severe COPD (i.e., those with an FEV_1 < 30% predicted [2], which contrasts with the threshold of 50% used in the meta-analysis). More important, COPD is characterized by periods of clinical instability (acute exacerbations) that are often triggered by bronchial infection. Patients with COPD typically have about 3 exacerbations per year (3). Patients with such episodes were excluded from most studies included in the meta-analysis. During these periods, as lung function usually deteriorates, patients may have the most serious side effects of β-blockers. Further, only cardioselective β-blockers were assessed and the mean duration of the "long-term" studies included in the meta-analysis (3.7 wk) is too short to confirm absolute innocuousness of even cardioselective β-blockers in COPD. Clinical wisdom would dictate that patients at risk for frequent exacerbations (i.e., those we see every day in our walk-in clinics or hospitals) who are prescribed cardioselective β-blockers should be closely monitored.

Yves Lacasse, MD, MSc, FRCPC
Hôpital Laval, Université Laval
Sainte-Foy, Québec, Canada

References

1. Evidence-based medicine. A new approach to teaching the practice of medicine. Evidence-Based Medicine Working Group. JAMA. 1992;268:2420-5.
2. **Pauwels RA, Buist AS, Calverley PM, et al.** Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med. 2001;163:1256-76.
3. **Donaldson GC, Wedzicha JA.** COPD exacerbations. 1: Epidemiology. Thorax. 2006;61:164-8.