

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 FEV₁ 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 FEV₁, FEV₁ 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 FEV₁ compared with placebo or baseline controls and did not increase respiratory symptoms (Table). Longer-duration of cardioselective β -blockers also did not change FEV₁ (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 FEV₁ (Table). Subgroup analyses showed that single-dose or longer-duration cardioselective β -blockers did not affect change in FEV₁ in patients with severe COPD (baseline FEV₁ < 1.4 L or < 50% of

normal predicted value) or in patients with COPD with a reversible component as shown by $\geq 15\%$ improvement in FEV₁ after β_2 -agonists.

CONCLUSION

In patients with chronic obstructive pulmonary disease, cardioselective β -blockers do not change FEV₁ or increase respiratory symptoms.

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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 FEV₁ < 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.

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