

# Review: Cardioselective $\beta$ -blockers did not reduce respiratory function in chronic obstructive pulmonary disease

Salpeter S, Ormiston T, Salpeter E, Poole P, Cates C. Cardioselective beta-blockers for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2002(2):CD003566 (latest version 18 Oct 2001).

## QUESTIONS

What are the effects of cardioselective  $\beta_1$ -blockers on the respiratory function of patients with chronic obstructive pulmonary disease (COPD)? How does treatment with  $\beta_1$ -blockers affect response to  $\beta_2$ -agonists?

## DATA SOURCES

Clinical trials published in any language from 1966 to May 2001 were identified by searching MEDLINE, EMBASE/Excerpta Medica, and CINAHL and by scanning clinical symposia abstracts and references of identified studies and reviews.

## STUDY SELECTION

Studies were selected if they were randomized, controlled, blinded trials that assessed the effects of intravenous or oral cardioselective  $\beta$ -blockers on airway function (FEV<sub>1</sub> at rest as liters or percentage of normal predicted value at baseline and follow-up) or symptoms in patients with COPD (baseline FEV<sub>1</sub> < 80% of normal predicted value or as defined by the American Thoracic Society guidelines).

## DATA EXTRACTION

2 investigators independently extracted data on study design, patient characteristics, interventions, comparison groups, and outcomes (change in FEV<sub>1</sub>; FEV<sub>1</sub> response to  $\beta_2$ -agonists given after study drug or placebo; and self-reported symptoms such as wheezing,

dyspnea, or exacerbation). Only published data were included in the analysis.

## MAIN RESULTS

19 crossover trials met the inclusion criteria ( $n = 267$ )\*; of these,  $\{17\}$ \* trials ( $n = 226$ )\* included a placebo-control group). Only the results of these placebo-controlled trials are reported here.  $\beta$ -blockers assessed were atenolol, metoprolol, bisoprolol, practolol, celiprolol, and acebutolol.

Meta-analysis of 2 trials ( $n = 50$ ) showed that single-dose  $\beta$ -blockers did not differ from placebo for change in FEV<sub>1</sub> (Table). Meta-analysis of  $\{9\}$ \* trials ( $n = 114$ )\* found no differences for respiratory symptoms (risk difference [RD] 0, 95% CI -0.03 to 0.03). Meta-analysis of 2 trials ( $n = 50$ ) showed that single-dose  $\beta$ -blockers had no effect on change in FEV<sub>1</sub> in patients receiving an inhaled  $\beta_2$ -agonist (weighted mean difference [WMD] -1.21, CI -10.97 to 8.56).

Meta-analysis of 4 trials ( $n = 140$ ) showed that longer-term  $\beta$ -blocker therapy (duration

of therapy ranged from 1 to 12 wk) did not differ from placebo for change in FEV<sub>1</sub> (Table). Meta-analysis of  $\{7\}$ \* trials ( $n = 98$ )\* showed no differences for respiratory symptoms (RD 0, CI -0.04 to 0.04). 1 trial ( $n = 30$ ) found that longer-term  $\beta$ -blocker therapy had no effect on change in FEV<sub>1</sub> in patients receiving an inhaled  $\beta_2$ -agonist (WMD -2.0, CI -13.78 to 9.78).

## CONCLUSION

In trials that enrolled a total of < 300 patients, cardioselective  $\beta$ -blockers did not reduce respiratory function in patients with chronic obstructive pulmonary disease and did not reduce FEV<sub>1</sub> response to  $\beta_2$ -agonists.

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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.

\*Information provided by author.

## Percentage of change in FEV<sub>1</sub> for cardioselective $\beta$ -blockers vs placebo in chronic obstructive pulmonary disease†

Type of therapy	Number of trials	Follow-up	WMD (95% CI)
Single dose	2 ( $n = 50$ )	{1 to 6 h}*	-2.05 (-6.05 to 1.96)
Longer duration	4 ( $n = 140$ )	1 to 8 wk	-2.55 (-5.94 to 0.84)

†WMD = weighted mean difference. Other abbreviations defined in Glossary. All analyses used a fixed-effects model.

## COMMENTARY

The review by Salpeter and colleagues reinforces an important clinical message:  $\beta$ -blockers are not contraindicated in COPD (1). The issue is not trivial. About 20% of patients discharged after hospitalization for acute myocardial infarction have a diagnosis of COPD or asthma (2), whereas patients with COPD often have ischemic heart disease, and many have hypertension (3). In such conditions,  $\beta$ -blockers have been proven to save lives, with most patients with COPD having a mortality reduction equivalent to those without COPD on  $\beta$ -blockers after acute myocardial infarction (2).

At the same time, the review shows the scarcity of randomized-trial data regarding  $\beta$ -blockers in COPD. Salpeter and colleagues identified only a few trials of short duration and small numbers of patients; many lacked blinding or placebo controls. Consequently, this meta-analysis adds only a small increment to our existing clinical knowledge. Reassuringly, its results are concordant with those of a large epidemiologic study that found no increase in hospital admissions for COPD exacerbations with  $\beta$ -blocker therapy (2).

These data suggest that clinicians can consider a cardioselective  $\beta$ -blocker for patients with stable COPD, as they would for patients without chronic lung disease. However, neither this study nor any others to date have shown the long-term safety of  $\beta$ -blockers in COPD. Careful monitoring after drug administration remains prudent. Unexplained respiratory deterioration shortly after starting a  $\beta$ -blocker warrants discontinuation, and any unexplained exacerbations thereafter should prompt reevaluation of therapy.

Matthew B. Stanbrook, MD  
University of Toronto  
Toronto, Ontario, Canada

## References

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