Review: cardioselective \(\beta\)-blockers did not reduce respiratory function in patients with chronic obstructive pulmonary disease


QUESTIONS: What are the effects of cardioselective \(\beta\)-blockers on the respiratory function of patients with chronic obstructive pulmonary disease (COPD)? How does treatment with \(\beta\)-blockers affect response to \(\beta\)-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 randomised, controlled, blinded trials that assessed the effects of intravenous or oral cardioselective \(\beta\)-blockers on airway function (FEV\(_1\), at rest as litres or percentage of normal predicted value at baseline and follow up) or symptoms in patients with COPD (baseline FEV\(_1\) < 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\(_1\); FEV\(_1\) response to \(\beta\)-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, \(n = 226^*\) 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\(_1\). 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\(_1\), after an inhaled \(\beta\)-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 treatment ranged from 1 to 12 wks) did not differ from placebo for change in FEV\(_1\). 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\(_1\) in patients receiving an inhaled \(\beta\)-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\(_1\) response to \(\beta\)-agonists.

*Information provided by author.

Type of treatment

<table>
<thead>
<tr>
<th>Number of trials</th>
<th>Follow-up</th>
<th>WMD (95% CI)</th>
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<tbody>
<tr>
<td>Single dose</td>
<td>2 ((n = 50))</td>
<td>(1 to 6 h)*</td>
</tr>
<tr>
<td>Longer duration</td>
<td>4 ((n = 140))</td>
<td>1 to 8 wk</td>
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</tbody>
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WMD = weighted mean difference; other abbreviations defined in glossary. All analyses used a fixed-effects model.

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

At the same time, the review shows the scarcity of randomised trial data regarding \(\beta\)-blockers in COPD. Salpeter et al identified only a few trials of short duration and small numbers of patients; many lacked blinded 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 epidemiological study that found no increase in hospital admissions for COPD exacerbations with \(\beta\)-blocker therapy.

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 re-evaluation of treatment.

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