Therapeutics

Review: cardioselective β₁ blockers given for 3 days to 4 weeks do not reduce respiratory function in reactive airway disease


QUESTIONS: In patients with reactive airway disease, what is the effect of cardioselective β₁ blockers on respiratory function? In these patients, how does treatment with β₁ blockers affect response to β₂ agonists?

Data sources
Studies were identified by searching Medline, EMBASE/Excerpta Medica, and CINAHL (all between 1966 and May 2001), and by scanning bibliographies of relevant studies and reviews.

Study selection
Studies in any language were selected if they were randomised, blinded, placebo controlled trials that assessed the effects of intravenous or oral cardioselective β₁ blockers, given as a single dose or as continued treatment lasting ≥ 3 days, on airway function (FEV₁ or symptoms) in patients with reactive airway disease (defined as asthma or chronic obstructive pulmonary disease with a reversible obstructive component).

Data extraction
Data were extracted on study quality, study design, patient characteristics, interventions, comparison arms, and outcomes (change in FEV₁; FEV₁ response to β₂ agonist given after study drug or placebo; symptoms reported, such as wheezing, dyspnoea, or exacerbation of asthma; and, for trials of continued treatment, weekly use of inhaled short acting β₂ agonists).

Main results
19 crossover studies on single dose treatment (n=240, mean age 40 y, 70% men) were included; β₁ blockers assessed were atenolol, metoprolol, bisoprolol, practolol, celiprolol, acebutolol, and xamoterol. Compared with placebo, single doses of cardioselective β₁ blockers reduced FEV₁, and increased FEV₁ after a β₂ agonist was given (table), with no increase in respiratory symptoms. Continued treatment with cardioselective β₁ blockers dose not reduce respiratory function and increases FEV₁ response to β₂ agonists.

Cardioselective β₁ blockers v placebo in reactive airway disease*

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>Outcomes (β₁ blocker v placebo)</th>
<th>Follow up</th>
<th>WMD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single dose of β₁ blocker</td>
<td>Change in FEV₁</td>
<td>1–6 hours</td>
<td>−7.46% (−9.32 to −5.59)</td>
</tr>
<tr>
<td></td>
<td>FEV₁ response to β₂ agonist</td>
<td>1–6 hours</td>
<td>4.63% (2.47 to 6.78)</td>
</tr>
<tr>
<td>Continued treatment with β₁ blocker</td>
<td>Change in FEV₁</td>
<td>3 days to 4 weeks</td>
<td>−0.42% (−3.74 to 2.91)†</td>
</tr>
<tr>
<td></td>
<td>FEV₁ response to β₂ agonist</td>
<td>3 days to 4 weeks</td>
<td>8.74% (1.96 to 15.52)</td>
</tr>
</tbody>
</table>

†Not statistically significant.

COMMENTARY
β₁ blockers have become the standard of care for a wide variety of cardiovascular disorders. Despite their widespread use, many physicians worry about potential adverse reactions in patients with reactive airway disease. Cardioselective β₁ blockers are > 20 times more selective for the β₁ than β₂ receptors and should carry less risk of bronchoconstriction in reactive airway disease.

The meta analysis by Salpeter et al lends further support to the position that cardioselective β₁ blockers do not cause clinically significant interactions in patients with mild to moderate reactive airway disease. Although a small asymptomatic reduction in FEV₁ occurred after a single dose of cardioselective β₁ blocker compared with placebo, this initial effect did not persist with continued treatment. In addition, FEV₁ increased in response to β₂ agonist administration, with short and long term use of cardioselective β₁ blockers.

Several challenges are notable with this meta analysis, some of which may have been unavoidable given the nature of the study. The included patients had only mild to moderate airway obstruction and no recent asthma exacerbations. Because only previously published studies were included, a selection bias may have existed.

This meta analysis lends additional weight to the argument that use of cardioselective β₁ blockers in reactive airway disease is without clinically significant interactions. Although many of the studies in the continuing treatment group had a relatively short duration, the results would suggest that cardioselective β₁ blockers may be safe for long term use. Agents such as metoprolol and atenolol should be the first agents considered. In contrast to non-cardioselective agents, the effects of cardioselective agents are believed to be easier to reverse. Safety in acute exacerbations remains to be established; if used, a short acting agent such as esmolol should be considered.

Given their mortality benefit in numerous conditions, it is our recommendation that the use of cardioselective β₁ blockers not be restricted in patients with mild to moderate reactive airway disease.

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