Therapeutics

Review: cardioselective β_1 blockers given for 3 days to 4 weeks do not reduce respiratory function in reactive airway disease

Salpeter SR, Ormiston TM, Salpeter EE. *Cardioselective beta-blockers in patients with reactive airway disease: a meta-analysis*. *Ann Intern Med* 2002;137:715–25.

QUESTIONS: In patients with reactive airway disease, what is the effect of cardioselective β_1 blockers on respiratory function? In these patients, how does treatment with β_1 blockers affect response to β_2 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 β_1 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 groups, and outcomes (change in FEV₁; FEV₁ response to β_2 agonists 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 β_2 agonists).

Main results

19 crossover studies on single dose treatment (n=240, mean age 40 y, 79% men) were included; β_1 blockers assessed were atenolol, metoprolol, bisoprolol, practolol, celiprolol, acebutolol, and xamoterol. Compared with placebo, single doses of cardioselective β_1 blockers reduced FEV₁, and increased FEV₁ after a β_2 agonist was given (table), with no increase in respiratory symptoms.

10 crossover studies on continued treatment (n=141, mean age 51 y, 77% men) were included. Compared with placebo, continued treatment with cardioselective β_1 blockers did not differ from placebo for FEV₁ response (table), respiratory symptoms, or incidence of inhaler use. However, cardioselective β_1 blockers did increase FEV₁ more than placebo did after a β_2 agonist was given (table).

Conclusions

In patients with reactive airway disease, single doses of cardioselective β_1 blockers reduced FEV₁ but increased FEV₁ after β_2 agonist was given, with no increase in

respiratory symptoms. Continued treatment with cardioselective β_1 blockers dose not reduce respiratory function and increases FEV₁ response to β_2 agonists.

*Cardioselective β_1 blockers v placebo in reactive airway disease**

Type of treatment	Outcomes (β_1 blocker v placebo)	Follow up	WMD (95% CI)
Single dose of β_1 blocker	Change in FEV ₁	1–6 hours	–7.46% (–9.32 to –5.59)
	FEV ₁ response to β_2 agonist	1–6 hours	4.63% (2.47 to 6.78)
Continued treatment with β_1 blocker	Change in FEV ₁	3 days to 4 weeks	–0.42% (–3.74 to 2.91)†
	FEV ₁ response to β_2 agonist	3 days to 4 weeks	8.74% (1.96 to 15.52)

*WMD = weighted mean difference. CI defined in glossary.

†Not statistically significant.

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COMMENTARY

β_1 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 β_1 blockers are > 20 times more selective for the β_1 than β_2 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 β_1 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 β_1 blocker compared with placebo, this initial effect did not persist with continued treatment. In addition, FEV₁ increased in response to β_2 agonist administration, with short and long term use of cardioselective β_1 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 β_1 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 β_1 blockers may be safe for long term use. Agents such as metoprolol and atenolol should be the first agents considered.¹ 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 β_1 blockers not be restricted in patients with mild to moderate reactive airway disease.

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- 1 Tafreshi MJ, Weinacker AB. Beta-adrenergic-blocking agents in bronchospastic diseases: a therapeutic dilemma. *Pharmacotherapy* 1999;19:974–8.