

# Review: Single-dose and longer-duration cardioselective $\beta$ -blockers do not increase respiratory symptoms in reversible airway disease

Salpeter S, Ormiston T, Salpeter E. Cardioselective beta-blocker use in patients with reversible airway disease. *Cochrane Database Syst Rev.* 2001;(3):CD002992 (latest version 26 May 2001).

## QUESTION

In patients with reversible airway disease, what is the effect of cardioselective  $\beta$ -blockers on respiratory function?

## DATA SOURCES

Randomized, blinded, placebo-controlled trials were identified by searching EM-BASE/Excerpta Medica, MEDLINE, and CINAHL databases (1966 to 2001) by using the Cochrane Airways Group registry and scanning abstracts at clinical symposia and bibliographies of identified studies.

## STUDY SELECTION

Studies in any language were selected if they reported the effects of single-dose or longer-duration cardioselective  $\beta_1$ -blockers (atenolol, metoprolol, bisoprolol, procatolol, celiprolol, acebutolol, and xamoterol) and patients had clearly documented reversible airway disease (mean increase of  $\geq 15\%$  in FEV<sub>1</sub> in response to  $\beta_2$ -agonist, decrease in FEV<sub>1</sub> during methacholine challenge, or asthma as defined by the American Thoracic Society).

## DATA EXTRACTION

2 reviewers independently extracted data on study methods, patient characteristics, details of the interventions, and outcomes. Main

outcomes were change in FEV<sub>1</sub> and symptoms and, for studies of longer duration, weekly use of inhaled short-acting  $\beta_2$ -agonists.

## MAIN RESULTS

29 studies (381 patients) met the selection criteria: 19 trials of single-dose cardioselective  $\beta_1$ -blockers and 10 of longer-duration  $\beta_1$ -blockers. Single doses of  $\beta_1$ -blockers reduced FEV<sub>1</sub> 8% more than placebo, but respiratory symptoms did not increase in any of the studies (Table). In longer-duration treatment, FEV<sub>1</sub> did not change, and treatment and placebo groups did not differ for reported symptoms or inhaler use (Table).

## CONCLUSION

In patients with reversible airway disease, single-dose and longer-duration cardioselective  $\beta_1$ -blockers do not increase respiratory symptoms, and in longer-duration studies, they do not reduce FEV<sub>1</sub> more than does placebo.

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### Single-dose or longer-duration $\beta_1$ -blockers (SD-BB or LD-BB) vs placebo (PI) in patients with reversible airway disease\*

Outcomes	Comparison	Weighted mean difference (95% CI)		
FEV <sub>1</sub>	SD-BB vs PI	-7.98 (-9.77 to -6.19)		
	LD-BB vs PI	-0.42 (-3.75 to 2.91)		
Inhaler use	LD-BB vs PI	-0.106 (-6.75 to 6.54)		
	Comparison	Weighted event rates	RRI (CI)	NNH
Symptoms	SD-BB vs PI	0.8% vs 0.3%	55% (-62 to 537)	Not significant
	LD-BB vs PI	1.3% vs 0.4%	92% (-57 to 763)	Not significant

\*FEV<sub>1</sub> = forced expiratory volume at 1 second. Other abbreviations defined in Glossary; RRI, NNH, and CI calculated from data in article. A fixed effects model was used for all meta-analyses.

## COMMENTARY

Long-term administration of  $\beta$ -adrenergic blockers for primary or secondary prevention of myocardial infarction has been shown to improve survival. Physicians are reluctant to administer  $\beta$ -blockers to many patients, including those with asthma, chronic pulmonary disease, and the elderly (1). Less than one third of such patients receive  $\beta$ -blockers after myocardial infarction, despite a 40% reduction in mortality in this patient population (1).

This well-done meta-analysis by Salpeter and colleagues tries to assess the effect of cardioselective  $\beta$ -blockers on respiratory function in patients with reversible airway disease. The most important result of this study was the finding that multiple doses of cardioselective  $\beta$ -blockers lead to no increase in symptoms, inhaler use, or decrement in FEV<sub>1</sub> when compared with placebo. Additionally, regular use of cardioselective  $\beta$ -blockers without intrinsic sympathomimetic activity resulted in a 13% increase over that of placebo in  $\beta_2$ -agonist response. This finding suggests that these drugs are sufficiently cardioselective to preserve clinical bronchial responsiveness to  $\beta_2$ -agonists (2).

The authors point out several limitations of this meta-analysis. Selection criteria included only mild-to-moderate airway obstruction

with significant reversibility. This eliminates most patients with chronic obstructive pulmonary disease who are at greater risk for ischemic heart disease. Furthermore, these studies were of short duration and could not assess the effect on frequency or severity of asthma exacerbations. Nevertheless, Salpeter and colleagues' findings suggest that patients with mild-to-moderate obstructive lung disease may tolerate cardioselective  $\beta$ -blockers, and these drugs should not be withheld in patients who could clinically benefit from them.

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## References

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