Review: β-blockers reduce mortality and morbidity in congestive heart failure

ACP Journal Club. 1999 Jan-Feb;130:7. ***(All 1999 articles were reviewed for relevancy, and abstracts were last revised in 2003.)***

Avezum A, Tsuyuki RT, Pogue J, Yusuf S. **Beta-blocker therapy for congestive heart failure: a systemic overview and critical appraisal of the published trials.** Can J Cardiol. 1998;14:1045-53.[PubMed ID: 9738164]

Question

In patients with congestive heart failure (CHF), what effect do β-blockers have on mortality and morbidity?

Data sources

Studies were identified by searching MEDLINE (1966 to March 1997) using the terms beta adrenergic blocking agents and heart failure.

Study selection

Randomized controlled trials comparing β-blockers with placebo in patients with CHF and reduced left ventricular ejection fraction (LVEF) were selected if treatment was > 1 month, follow-

up was 95%, and analysis was by intention to treat.

Data extraction

β-blocker type and class (New York Heart Association), randomization ratio, length of follow-up, cause of CHF, mortality, hospitalization for CHF, heart transplantation, LVEF, maximum exercise duration, and adverse effects.

Main results

123 articles were identified, and 18 trials (weighted mean follow-up 13 mo) of 2986 patients with various causes of CHF met the selection criteria. 7 trials (n = 562) of metoprolol, 4 (n = 209) of bucindolol, 2 (n = 1509) of carvedilol, 2 (n = 36) of nebivolol, 1 (n = 641) of bisoprolol, 1 (n = 17) of acebutolol, and 1 (n = 12) of labetalol were selected. Relative risks were calculated using a fixed-effects model. Patients who received a β-blocker compared with those who received placebo had reduced risk for mortality {P = 0.008}* (10 trials), hospitalization for CHF {P < 0.001}* (5 trials), and heart transplantation {P = 0.016}* (6 trials) (Table); improved LVEF (P < 0.001) (11 trials); higher rates of bradycardia, hypotension, and dizziness (P < 0.001) (13 trials); and a decreased rate of worsening of heart failure (P < 0.001) (13 trials). In 9 trials, no difference existed between β-blockers and placebo for maximum exercise duration.

Conclusion

In patients with congestive heart failure, β-blockers reduce mortality, hospitalization, and heart transplantation and improve left ventricular ejection fraction.

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**P* value calculated from data in article.

β-blocker vs placebo for patients with congestive heart failure†

Outcomes (variable mean follow-up times)	Weighted β-blocker	Weighted control	RRR (95% CI)	NNT (CI)
Mortality (13 mo)	8.2%	12.6%	25% (7 to 40)	32 (19 to 93)
Hospitalization (20 mo)	18.1%	28.8%	37% (24 to 48)	11 (8 to 18)
Heart transplantation (10 mo)	1.1%	2.7%	54% (13 to 75)	115 (53 to 580)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

Commentary

For many years, there has been an interest in the somewhat paradoxical treatment of CHF with β-blocking agents. Recent studies have led to the approval of carvedilol by the U.S. Food and Drug Administration for the treatment of CHF. This well-designed meta-analysis by Avezum and colleagues shows the strengths and weaknesses of current studies.

The evidence suggests that the use of β-blockers in patients with CHF reduces mortality and improves other outcomes. Because of the small sample size of the relevant trials, the data are not as powerful as those available to support the use of angiotensin-converting enzyme inhibitors in CHF, and it is possible that we are overestimating any benefit from the use of β-blockers in this

setting. The authors highlight the limitations of meta-analyses involving small trials and suggest the need for larger trials to conclusively answer these questions.

Evidence clearly supports the use of β-blockers in ischemic heart disease, even in such "high-risk" circumstances as poor LVEF after myocardial infarction (1); their anti-ischemic properties and their effects on preventing sudden death are beneficial. Patients with left ventricular dysfunction benefit from β-blockers through modulation of cardiac and peripheral adrenergic mechanisms.

Because of the diverse pharmacologic properties of β-blockers, they probably should not all be considered equal. Agents with intrinsic sympathomimetic activity should probably be avoided, but agents with α-blocking (vasodilating) properties may have specific advantages over nonvasodilating agents in CHF (2). Until the clinical value of carvedilol is shown, not enough evidence exists to support switching to carvedilol for patients with heart failure who are stable on metoprolol. Until the results of larger trials are published, patients with compensated CHF should be considered for β-blocker therapy for the potential benefits of improved cardiac function and morbidity and reduced mortality.

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References

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2. Gilbert EM, Abraham WT, Olsen S, et al. Comparative hemodynamic, left ventricular functional, and antiadrenergic effects of chronic treatment with metoprolol versus carvedilol in the failing heart. Circulation. 1996;94:2817-25.[PubMed ID: 8941107]

Commentary Addendum (2003)

β-blockers have turned out to be a key treatment for heart failure, and many more data have emerged since the 1998 paper (3).

Reference

3. Goldstein S. Benefits of beta-blocker therapy for heart failure: weighing the evidence. Arch Intern Med. 2002;162:641-8.[PubMed ID: 11911717]