Review: β-blockers benefit patients with chronic heart failure

ACP Journal Club. 1999 Mar-April;130:29. ***(All 1999 articles were reviewed for relevancy, and abstracts were last revised in 2003.)***
Evidence-Based Medicine. 1999 Mar-April;4:49.
Lechat P, Packer M, Chalon S, et al. **Clinical effects of beta-adrenergic blockade in chronic heart failure: a meta-analysis of double-blind, placebo-controlled, randomized trials.** Circulation. 1998;98:1184-91.[PubMed ID: 9743509]

Question

Are β-blockers effective for improving outcomes in patients with chronic heart failure (CHF)?

Data sources

Studies were identified by searching MEDLINE and meeting abstracts; by scanning bibliographies of relevant studies; and by contacting colleagues, investigators, and pharmaceutical sponsors.

Study selection

Studies were selected if they were randomized, double-blind, placebo-controlled studies of β-blockers in patients with CHF. Studies were excluded if patients had had a recent myocardial infarction, xamoterol was used, or the β-blocker was given only once.

Data extraction

Data were extracted on specific β-blockers and other drugs used, the cause of CHF, New York Heart Association (NYHA) class, treatment duration, and main outcomes: all-cause mortality, hospitalization for CHF, the combined end point of all-cause mortality and hospitalization for CHF, functional status, and left ventricular ejection fraction (LVEF).

Main results

18 trials met the inclusion criteria. Treatment duration ranged from 1.5 to 44 months (mean 7 mo). Most patients had NYHA class II or III symptoms during treatment with diuretics, angiotensin-converting enzyme inhibitors, and digoxin. Results were pooled by using a fixed-effects model for all outcomes except functional status, which used a random effects model. Compared with placebo, β-blockers reduced death (18 studies, $P = 0.003$), hospital admissions for CHF (18 studies, $P < 0.001$), death and hospitalization for CHF (9 studies, $P < 0.001$), and the number of patients with a deterioration in NYHA class (16 studies, $P = 0.03$) and increased the number of patients with an improvement in NYHA class (16 studies, $P = 0.04$) (Table) and mean LVEF (mean increase 29%, $P < 0.001$). Trials using nonselective β-blockers showed a greater reduction in mortality than did those using selective β-blockers. For all other outcomes, treatment effects were similar for selective and nonselective β-blockers.

Conclusion

In patients with CHF, β-blockers reduce death and hospitalization for CHF and improve functional status and left ventricular ejection fraction.

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β-blockers vs placebo for heart failure at a mean follow-up of 7 months*

Outcomes	Weighted event rates		RRR (95% CI)	NNT (CI)
	β-blockers	Placebo		
All-cause mortality	9%	12%	27% (10 to 41)	40 (24 to 149)
Hospitalization for CHF	13%	17%	35% (22 to 46)	24 (16 to 51)
Combined end point†	19%	25%	30% (18 to 39)	16 (11 to 28)
Functional deterioration	11%	15%	24% (1 to 41)	25 (13 to 220)
			RBI (CI)	
Functional improvement	26%	21%	22% (0 to 47)	20 (11 to 189)

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

†All-cause mortality plus hospitalization for heart failure.

Commentary

The merits of β-blockers in CHF have been vigorously debated for years. A class of drugs once thought forbidden in patients with CHF is now widely considered to be beneficial. The increasing number of positive trials has led to increased use of β-blockers, particularly carvedilol.

In this valuable review, Lechat and colleagues showed that ejection fraction, morbidity, and mortality outcomes were improved by β-blockers. They also pointed out that meta-analysis, as a

research tool, cannot always clarify the usefulness of certain agents in specific subsets of heterogeneous patient populations. 1 trial of bisoprolol (1) and 1 unpublished trial of metropolol (2) support the general conclusion that β-blockers benefit patients with NYHA class II and III CHF.

In addition to being a nonselective β-blocker, carvedilol has the pharmacologic properties of a β-blocker as well as putative antioxidant effects. Nonselective β-blockers (primarily carvedilol) were associated with a larger survival benefit in this review. The authors pointed out that ongoing studies are testing the hypothesis that nonselective β-blockers show a larger benefit than selective agents.

The question remains whether all patients with CHF can benefit from β-blockers. The answer will probably be “no.” The trials to date reflect an unavoidable selection bias and include patients with primarily NYHA class II and III symptoms. The present recommendations for slow titration of carvedilol therapy under direct supervision should be considered a necessary hemodynamic precaution. However, we have more data on outcomes with carvedilol now than we had on digitalis (until the Digitalis Investigation Group trial [3]) during centuries of use. Patients who tolerate carvedilol titration have better outcomes than similar patients who are treated with placebo.

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References

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3. The effect of digoxin on mortality and morbidity in patients with heart failure. The Digitalis Investigation Group. N Engl J Med. 1997;336:525-33.[PubMed ID: 9036306]