

Review: Long-term β -blocker use reduces mortality after myocardial infarction

Freemantle N, Cleland J, Young P, Mason J, Harrison J. β Blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ*. 1999 Jun 26;318:1730-7.

QUESTION

In patients with myocardial infarction (MI), do β -blockers reduce all-cause mortality and recurrent MI without adverse effects?

DATA SOURCES

Studies were identified by searching databases from their inception to 1997 (MEDLINE, EMBASE/Excerpta Medica, Biosis, Sigle, HealthStar, IHTA, Conference Papers Index, Derwent Drug File, Dissertation Abstracts, International Pharmaceutical Abstracts, Pascal, and Science Citation Index). Bibliographies of relevant studies and reviews were also checked.

STUDY SELECTION

Randomized controlled trials were selected if treatment lasted ≥ 1 day, patients had had an MI, and β -blockers were compared with placebo or other therapies.

DATA EXTRACTION

Data were extracted on patient numbers and characteristics; type, route, and dose of

therapies; duration of treatment and follow-up; loss to follow-up; blinding; concealment of randomization; study inclusion and exclusion criteria; and outcomes (deaths, recurrent MI, and withdrawals).

MAIN RESULTS

82 trials met the inclusion criteria (54 234 patients). Short-term (treatment duration < 6 wk from onset of pain) studies ($n = 51$) had an overall mortality rate of 10.5%. In these studies, β -blockers did not reduce mortality (odds ratio [OR] for random-effects model 0.96, 95% CI 0.85 to 1.08); subgroup analyses did not differ in mortality for individual drugs.

Long-term (treatment duration 6 to 48 mo) studies ($n = 31$) had a mortality rate of 9.7%. Mortality was reduced for all β -blockers combined (OR 0.77, CI 0.69 to 0.85) and also for metoprolol (OR 0.80, CI 0.66 to 0.96, 7 studies), propranolol (OR 0.71, CI 0.59 to 0.77, 7 studies), and timolol (OR 0.59, CI 0.46 to 0.77, 2 studies). Drugs with cardioselectivity showed no reduction in mortality (OR 1.10,

CI 0.89 to 1.39). Drugs with intrinsic sympathomimetic activity showed a trend toward increased mortality (OR 1.19, CI 0.96 to 1.47). Data on reinfarction showed similar trends for a reduction with long-term β -blocker use. No additional benefit was shown if the initial treatment started with an intravenous dose (OR 0.87, CI 0.61 to 1.22). Subgroup analyses did not differ in reductions in mortality over time. Withdrawal rates ranged from 10% to 30% and were similar in the treatment and control groups.

CONCLUSION

Long-term treatment (6 to 48 mo) with β -blockers reduces mortality in patients who have had a myocardial infarction.

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COMMENTARY

β -adrenergic receptor blockade in the acute and the convalescent phases of MI is the standard of care (1) established in a remarkable series of clinical trials. Despite the evidence, β -blockers after MI continue to be underused (2). Freemantle and colleagues, who have collated data from many β -blocker trials, have shown that, although short-term β -blocker use does not decrease mortality, long-term β -blockade trials show consistent benefit. Early intravenous β -blocker therapy in acute MI is recommended by the joint American College of Cardiology and American Heart Association guidelines for the management of patients with acute MI (1). The present review calls into question the benefit of early intravenous use of β -blockers in acute MI. The widespread use of thrombolysis and primary percutaneous coronary angioplasty (where available) improves prognosis so markedly that any additional short-term benefit of β -blockers may be hard to prove. Clinicians faced with this question can wonder what role β -blockers have in treating acute MI. However, the clinical setting often includes an important subset of patients in whom thrombolysis either fails or results in suboptimal outcomes (3). Here, β -blockers are likely to improve mortality, attenuate ischemic pain, and prevent tachyarrhythmias.

Long-term use of β -blockers after MI remains unchallenged and is highlighted by the present review. After an MI, patients often

develop further clinical and subclinical myocardial damage, which can increase the chance of arrhythmias by altering the heart muscle with more scar tissue. Therefore, β -blockers should probably be used indefinitely. Should the β -blockers used be those with selective, non-selective, or intrinsic sympathomimetic activity? This meta-analysis raises interesting but unanswered questions about their relative clinical efficiency. It also seems prudent to use the actual agents that have shown benefit at established doses. The low withdrawal rates with β -blockers emphasize the tolerability of the therapy.

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References

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