Do beta-blockers reduce short-term mortality following acute myocardial infarction: a systematic review and meta-analysis


CRD summary
The authors concluded that beta-blockers given with 72 hours of an acute myocardial infarction did not reduce short-term mortality but may be of benefit in low-risk patients (Killip class 1). This was generally a well-conducted and clearly-reported review and the authors’ conclusion is likely to be reliable.

Authors’ objectives
To determine if beta-blockers given within 72 hours of an acute myocardial infarction reduce mortality at six weeks compared to placebo.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews, HealthStar, ACP Journal Club, DARE and Conference Papers Index were searched up to 2007. Search terms were reported. Only English language studies were eligible. In addition, reference lists of reviews and included studies were screened, and manufacturers of beta-blockers were contacted for unpublished studies. Two experts were also consulted in order to identify any missing studies.

Study selection
Parallel-group randomised controlled trials (RCTs) that compared the effects on six-week mortality of beta-blockers (given intravenously, orally or both) within 72 hours of acute myocardial infarction symptom onset, compared to placebo or no additional treatment, were eligible for inclusion. Trials could be set in emergency departments, coronary care units or other in-patient settings.

Most of the included trials evaluated either propranolol or metoprolol. Treatment was generally initiated within 24 hours or less of acute myocardial infarction (range four to 72 hours). Most patients (77%) were men. All trials excluded patients with hypotension, cardiogenic shock and severe bradycardia; all but one trial excluded patients with congestive heart failure.

Two reviewers independently selected studies and resolved disagreements by consensus.

Assessment of study quality
Two blinded reviewers independently assessed validity using the Jadad criteria (randomisation, blinding and reporting of withdrawals) and allocation concealment. Disagreements were resolved with the aid of a third reviewer if required. Trials were classified as high-quality if: they scored 2 out of 5 points on the Jadad scale and had adequate allocation concealment; or they had unclear allocation concealment and a Jadad score of at least 3 points.

Data extraction
Two blinded reviewers independently extracted data onto a database. Mortality outcomes were expressed as odds ratios (OR) with 95% confidence intervals (CI).

Methods of synthesis
Pooled odds ratios and 95% confidence intervals were calculated using a random-effects model. Heterogeneity was assessed using the χ² and the I² statistics. Sensitivity analysis was undertaken by limiting analysis to high-quality trials, trials enrolling patients within 24 hours of acute myocardial infarction and trials with adequate allocation concealment. The analysis was repeated after excluding one trial that included Killip class III patients with congestive heart failure. Publication bias was assessed using a funnel plot.

Results of the review
Eighteen RCTs were included in the review (n=74,643 patients). Sample size ranged from 94 to 45,852 patients. Thirteen RCTs were classified as high-quality.

There was no statistically significant difference in mortality at six weeks between beta-blockers and control (OR 0.95, 95% CI 0.90 to 1.01). No statistically significant heterogeneity was found (p=0.57, I²=0%).

Results were similar for high-quality studies and studies with adequate allocation concealment.

After excluding the trial that included Killip class III patients with congestive heart failure, beta-blockers were associated with a statistically significant reduction in six-week mortality compared to control (OR 0.93, 95% CI 0.88 to 0.99). No statistically significant heterogeneity was found (p=0.67, I²=0%).

The funnel plot showed no clear evidence of publication bias.

**Authors' conclusions**

Beta-blockers given with 72 hours of an acute myocardial infarction did not reduce short-term mortality but may be of benefit in low-risk patients (Killip class 1).

**CRD commentary**

The review question and inclusion criteria were clearly stated. Several relevant sources were searched. Attempts were made to minimise publication but not language bias. Appropriate methods were used to minimise reviewer error and bias during the review process. Only RCTs were included and validity was assessed, but only an aggregated score was reported. Limited information was provided about the patients. Appropriate methods were used for the meta-analyses, heterogeneity was assessed and various subgroup analyses conducted. The cautious conclusions regarding low-risk patients appear appropriate, since findings were based on a sub-group analysis. This was generally a well-conducted and clearly-reported review and the authors’ conclusion is likely to be reliable.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that there is a need for further research to determine the optimal time to start treatment with beta-blockers after acute myocardial infarction and to determine the optimal route of administration.

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