CRD summary
This review assessed the effect of atenolol on cardiovascular morbidity and mortality in patients with hypertension. The authors concluded that atenolol may not be a suitable treatment option for patients with hypertension, and queried its use as a reference drug in trials. Limitations in the reporting of the review process and the lack of a validity assessment weaken this conclusion.

Authors’ objectives
To assess the effect of atenolol on cardiovascular morbidity or mortality in patients with primary hypertension.

Searching
The Cochrane Library, MEDLINE and relevant textbooks were searched to identify studies; the database search terms were given. Researchers in the field of hypertension were also contacted.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. The follow-up in the included studies ranged from 2.6 to 9 years.

Specific interventions included in the review
Studies that compared atenolol alone as first-line therapy with placebo or an antihypertensive drug were eligible for inclusion. The dosage of atenolol ranged from 50 to 100 mg. The comparator antihypertensive treatments were hydrochlorothiazide (25 or 50 mg), bendroflumethiazide (5 mg), captopril (50 to 100 mg), losartan (50 to 100 mg) and lacidipine (4 to 6 mg). Studies that evaluated atenolol as add-on therapy or atenolol plus other drugs in the same treatment group were excluded, as were multidrug strategies.

Participants included in the review
Studies of participants with primary hypertension were eligible for inclusion. The mean age of the included participants ranged from 52.2 to 70.4 years.

Outcomes assessed in the review
Studies that evaluated cardiovascular mortality, myocardial infarction and stroke using predefined criteria were eligible for inclusion. The included studies also assessed all-cause mortality.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data on the occurrence of all-cause mortality, cardiovascular mortality, myocardial infarction and stroke were extracted from the individual studies and used to calculate a relative risk (RR). Data on the mean blood-pressure (BP) change were also extracted.
Methods of synthesis
How were the studies combined?
The results from the included studies were combined using a fixed-effect meta-analysis. A pooled RR with 95% confidence intervals (CIs) was calculated separately for each outcome of interest. Data on the mean BP change were tabulated.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test. Forest plots allowed a visual assessment of differences between the studies. A sensitivity analysis was also conducted to examine the impact of one large trial on the conclusions.

Results of the review
Eight RCTs (n=23,394) were included in the review.

Atenolol compared with placebo or no treatment (4 RCTs, n=6,825).
No significant difference was found on all-cause mortality (RR 1.01, 95% CI: 0.89, 1.15), cardiovascular mortality (RR 0.99, 95% CI: 0.83, 1.18), or myocardial infarction (RR 0.99, 95% CI: 0.83, 1.19). The risk of stroke was lower in patients given atenolol than those given placebo, although this was not statistically significant (RR 0.85, 95% CI: 0.72, 1.01). No evidence of statistical heterogeneity was found for any outcome.

The mean BP (systolic/diastolic) changes were -4.0/-3.0, -5.8/-2.9, -13.5/-7 and -18/-11.0 mmHg.

Atenolol compared with other antihypertensive treatments (5 RCTs, n=17,671). Atenolol was associated with a significant increase in the risk of all-cause mortality (RR 1.13, 95% CI: 1.02, 1.25) and stroke (RR 1.30, 95% CI: 1.12, 1.5). No evidence of statistical heterogeneity was found (P=0.49 and P=0.63, respectively).

The risk of cardiovascular mortality was also slightly higher in those given atenolol (RR 1.16, 95% CI: 1.00, 1.34), but there was no significant difference in the risk of myocardial infarction (RR 1.04, 95% CI: 0.89, 1.2). There was evidence of statistical heterogeneity for both these outcomes (P=0.08 and P=0.03, respectively).

The mean BP (systolic/diastolic) changes were 0/-1, -1.0/0.5, -1.0/-1.0, 1.1/0.2 and -0.2/-0.1 mmHg.

The sensitivity analysis revealed that the conclusions did not differ when the large RCT was not included in the meta-analysis.

Authors' conclusions
Atenolol may not be a suitable treatment option for patients with hypertension. The authors also stated that the use of atenolol as a reference drug in studies evaluating treatments for hypertension may not be appropriate.

CRD commentary
The review addressed a clear research question and the inclusion criteria appeared appropriate. The search used to identify the included studies was limited to two databases, although some attempt was made to identify unpublished studies. No details were given of the languages of publication that were eligible for review, thus the potential for language bias could not be assessed. The methods used to select studies for inclusion and extract data from the included studies were not reported; therefore, the potential for reviewer bias and error could not be assessed either. Furthermore, the authors did not state whether methods were used to assess the quality of the included studies; this makes it difficult to assess the validity of the studies on which the results of the review were based.

Some details of each of the included studies were provided. The methods used to combine the results were appropriate for some outcomes. However, the presence of heterogeneity for some of the outcomes suggests that statistical pooling may not have been appropriate. Limitations in the reporting of the review process and the apparent lack of a validity assessment weaken the evidence presented.
Implications of the review for practice and research

Practice: The authors stated that atenolol may not be suitable for first-line treatment in patients with hypertension.

Research: The authors stated that the use of atenolol as a reference drug in outcome trials of patients with hypertension may not be appropriate.

Bibliographic details

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Other publications of related interest
These additional published commentaries may also be of interest. Cruickshank JK. Review: atenolol may be ineffective for reducing cardiovascular morbidity or all cause mortality in hypertension. Evid Based Med 2005;10:74. Cruickshank JK. Review: atenolol may be ineffective for reducing cardiovascular morbidity or all cause mortality in hypertension. ACP J Club 2005;142:59.

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Subject indexing assigned by NLM

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.