Blood pressure lowering treatment for preventing stroke recurrence: a systematic review and meta-analysis
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CRD summary
The authors concluded that blood pressure lowering agents reduced the risk of subsequent stroke and cardiovascular events, but not myocardial infarction or all-cause mortality in patients who had experienced a transient ischaemic attack or stroke. In light of significant statistical heterogeneity and the unclear quality of the included trials, the authors' conclusions should be treated with caution.

Authors’ objectives
To investigate the association between blood pressure reduction, anti-hypertensive agents use and stroke recurrence.

Searching
MEDLINE and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched in April 2009. In addition, ClinicalTrials.gov was searched to identify complete, ongoing and enrolling registered trials. Search terms were reported. Bibliographies of the retrieved articles were also searched.

Study selection
Randomised placebo-controlled trials that evaluated the use of anti-hypertensive medications to lower blood pressure were eligible for inclusion. Clinical outcome measures were stroke recurrence, cardiovascular events, myocardial infarction or all-cause mortality. Eligible trials were also required to have one arm containing solely patients with a previous stroke or transient ischaemic attack. Trials of anti-hypertensive treatment during acute stroke or trials where blood pressure reduction was part of an integrated approach to stroke reduction were excluded.

Included trials assessed the following medications: atenolol, candesartan, deserpidine plus methyclothiazide, indapamide, nicardipine, perindopril, perindopril plus indapamide, ramipril and telmisartan. In one trial, the control group received no treatment; in the remaining trials, the treatment was compared with placebo. Included patients had prior transient ischaemic attack, ischaemic stroke, hemorrhagic stroke or reversible ischaemic neurologic defect.

The authors did not state how the studies were selected for the review.

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

Data extraction
The number of participants with a clinical outcome was extracted for each group and used to calculate odds ratios (ORs) with 95% confidence intervals (CI).

Two reviewers independently extracted the data, with differences resolved by consensus.

Methods of synthesis
Pooled odds ratios with 95% confidence intervals were calculated using the Mantel-Haenszel method. Statistical heterogeneity was assessed using the $\chi^2$ test and quantified using the $I^2$ test. Where significant heterogeneity was present, the authors identified differences between the trials. Funnel plots were used to assess publication bias.

Results of the review
Ten RCTs were included for review (n=37,737 patients); one was an open trial (n=264 patients). The length of follow-up ranged from one to five years. Where stated, the mean decrease in systolic blood pressure ranged from -0.4 to 25mmHg and the mean decrease in diastolic blood pressure ranged from 1.5 to 12.3mmHg.
Stroke recurrence: Lowering blood pressure using anti-hypertensive medication significantly reduced the risk of stroke recurrence compared with placebo or no treatment (OR 0.71 95% CI 0.59 to 0.86; ten RCTs; n=37,737 patients). There was evidence of significant statistical heterogeneity (I²=78%). The authors reported that the trials differed according to age of participants, race, time of follow-up, medication used and baseline levels of hypertension. Excluding one trial (that contributed to significant funnel plot asymmetry) did not significantly alter the findings. Cardiovascular event: Blood pressure reduction significantly reduced the risk of cardiovascular event compared with placebo (OR 0.69 95% CI 0.57 to 0.85; nine RCTs, n=37,473 patients). There was evidence of significant statistical heterogeneity (I²=87%). Blood pressure reduction did not significantly reduce the risk of myocardial infarction or all-cause mortality. Statistical heterogeneity for these outcomes was low (myocardial infarction I²=24%; all-cause mortality I²=29%).

Forest plots were only available online as additional files (see URL for Additional Data).

Authors' conclusions
Blood pressure lowering agents reduced the risk of subsequent stroke and cardiovascular events, but not myocardial infarction or all-cause mortality in patients who had experienced a transient ischaemic attack or stroke.

CRD commentary
The review addressed a clear question with well-defined inclusion criteria. Three relevant databases were searched, but it was unclear whether language restrictions were applied, so the possibility of language bias could not be ruled out. Limited attempts were made to identify unpublished data. Whilst the authors stated that they assessed publication bias, they did not report the findings in the results, so there may be a possibility of publication bias. Appropriate steps were taken during the data extraction process to minimise reviewer error and bias, but it was unclear whether similar steps were taken in the study selection process, which may have introduced reviewer error and bias.

It appeared that a validity assessment was not carried out and insufficient trial characteristics were provided in the paper to independently ascertain trial quality. Given the high levels of statistical heterogeneity found for some outcomes, it was unclear whether the most appropriate method of synthesis was used. Differences between trial characteristics were reported, but statistical heterogeneity was not explored using statistical methods.

In light of significant statistical heterogeneity and the unclear quality of the included trials, the authors' conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that treatment following stroke should include at least one blood pressure lowering agent.

Research: The authors did not state any implications for research.

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Other publications of related interest

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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.