Hypertension in the elderly: implications and generalizability of randomized trials


Authors' objectives
To estimate the benefits of drug therapy, in terms of morbidity and mortality, for hypertensive elderly patients; to compare these benefits with effects in younger patients; and to provide a framework for generalising results derived from trials to actual patients.

Searching
MEDLINE was searched from 1966 to 1993, and references obtained from the identified reviews and trials were examined. Experts were consulted for additional material. Only English language articles were considered. For comparisons between elderly and younger patients, the data were derived from a meta-analysis published in 1990 (see Other Publications of Related Interest no.1).

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) lasting more than 1 year.

Specific interventions included in the review
Antihypertensive drug therapy (mainly diuretics, but also beta-blockers and centrally-acting hypotensives) in trials lasting more than 1 year.

Participants included in the review
Hypertensive elderly persons aged over 60 years. The patients in the trial were healthier than the general population of elderly hypertensives. The hypertensive adults in the trials included in the meta-analysis published in 1990 (see Other Publications of Related Interest no.1) were younger patients.

Outcomes assessed in the review
The following were assessed: cardiovascular morbidity and mortality; cerebrovascular morbidity and mortality (nonfatal and fatal strokes); coronary heart disease (CHD) morbidity (non-fatal myocardial infarction) and mortality (fatal myocardial infarction and sudden or rapid cardiac death); total mortality.

How were decisions on the relevance of primary studies made?
The papers were independently assessed by two reviewers.

Assessment of study quality
The criteria used to assess the validity of the studies were: blinding; a drop-out rate of less than 25%; and more than 25% of patients on assigned active or placebo therapy at completion. Four independent reviewers performed the validity assessment.

Data extraction
The data were extracted by four reviewers, and included on an intention to treat basis.

Methods of synthesis
How were the studies combined?
Data were combined using the method of Yusuf et al. (see Other Publications of Related Interest no.2). The outcomes were expressed as the number-needed-to-treat to prevent one adverse outcome, and were standardised for a 5-year period. Analyses were also performed using the random-effects model of DerSimonian and Laird (see Other
How were differences between studies investigated?

Chi-squared tests for heterogeneity showed all outcome data, with the exception of combined cardiovascular mortality and morbidity events from the beta-blocker arm of the Medical Research Council Trial in Older Adults (MRCOA; see Other Publications of Related Interest no.4), were compatible with the assumption of a uniform risk ratio (P>0.05). The data were re-analysed excluding small trials (N less than 200) and those that were not placebo-controlled or blinded. The results showed the same directions, magnitudes of effects (within 12%) and significance levels, as the primary analyses. Regression of entry diastolic blood-pressure onto the ‘observed minus expected’ value was performed to assess the effects of diastolic pressure on the observed treatment benefits.

Results of the review

Thirteen trials with 16,564 patients were included. Data on younger patients were derived from a meta-analysis of 12 RCTs including 33,000 adults.

Eighteen patients (95% confidence interval, CI: 14, 25) needed to be treated for 5 years to prevent 1 fatal or nonfatal cardiovascular event, 43 (95% CI: 31, 69) to prevent 1 cerebrovascular event, and 61 (95% CI: 39, 141) to prevent one CHD event.

When the studies of patients with isolated systolic hypertension were combined, the results showed that 15 patients (95% CI: 11, 22) needed to be treated for 5 years to prevent one cardiovascular event. The inclusion of small or low-quality trials did not substantially affect this. Higher levels of diastolic blood-pressure at entry were associated with greater benefits (P<0.05). When the beta-blocker arm of the MRCOA was combined with the only other trial that initially assigned patients to a beta-blocker or control group, no significant effects on cardiovascular outcomes were found. The numbers withdrawing because of adverse effects of therapy varied significantly between the studies, with particularly high levels of withdrawal from the beta-blocker arm of the MRCOA.

Comparisons made between elderly and younger patients suggested that 2 to 4 times as many younger persons need to be treated to prevent an equivalent number of cardiovascular events.

Authors’ conclusions

Antihypertensive treatment for healthy elderly people is highly efficacious; the evidence is strong, consistent and convincing. The 5-year morbidity and mortality benefits are greater for older than younger adults, although it is possible that long-term cumulative benefits in younger people may exceed those in the elderly. Extrapolating benefits from trials to individual patients is difficult, but should take into account multiple issues including the patient’s risk factors, pre-existing cardiovascular disease and co-morbid illness.

CRD commentary

The review was rigorous and systematic, and its presentation was reasonably clear and straightforward. There was little consideration of differential effects of different drugs, and it is unclear whether the results can be generalised to treatment with beta-blockers. The inclusion of cardiovascular outcomes and mortality only suggests that other potential, treatment-associated changes in morbidity may be missed. The problem of adverse effects was reported to vary significantly from trial to trial, but few details were given. The evidence of cardiovascular benefit needs to be considered alongside potential adverse effects on the quality of life.

Implications of the review for practice and research

Antihypertensive therapy using diuretics and/or centrally acting hypotensives prevents cardiovascular accidents and reduces cardiovascular mortality, particularly in elderly people without other disease, but at unknown cost (both financial and in terms of the quality of life). Treatment of hypertension in elderly people should be considered, but taking other co-morbidities into account.
Bibliographic details

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Other publications of related interest

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Subject indexing assigned by NLM

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