High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal
Grossman E, Messerli F H, Goldbourt U

Authors' objectives
To assess the benefits of antihypertensive therapy in hypertensive patients with diabetes mellitus.

Searching
The authors searched MEDLINE (from inception to June 1999) using the terms 'diabetes mellitus', 'hypertension' or 'blood pressure' and 'therapy'. The authors also searched the references of identified articles for additional relevant studies. The search was limited to English language publications.

Study selection
Study designs of evaluations included in the review
Randomised placebo-controlled studies of more than 12 months duration.

Specific interventions included in the review
Antihypertensive therapy (diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists) versus placebo, or a combination of two active treatments versus placebo. Follow-up ranged from 2 to 8.4 years.

Participants included in the review
Participants were hypertensive patients with diabetes mellitus. The mean age of participants ranged from 55.0 to 70.5 years.

Outcomes assessed in the review
Morbidity and mortality. Outcomes were classified as follows: coronary heart disease (including fatal and nonfatal myocardial infarction and sudden cardiac death); cerebrovascular events (including fatal and nonfatal stroke, and transient ischemic attacks); cardiovascular mortality (including coronary heart disease and cerebrovascular mortality); and adverse events.

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

Assessment of study quality
The authors do not report the method used to assess validity, or how the validity assessment was performed.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Data were extracted for the categories of: patients' baseline characteristics, follow-up period, change in blood pressure, percentage of patients continuing to receive monotherapy, and the incidence of morbidity and mortality.

Methods of synthesis
How were the studies combined?
The authors determined that a meta-analysis was not possible due to differences between studies in inclusion criteria, initial blood pressure, age and time of follow-up.
The individual studies were presented in tables and a narrative summary of the trials was given in the discussion.

**How were differences between studies investigated?**
The authors do not state a formal test for assessing heterogeneity.

### Results of the review
Eight RCTs were included in the review with 5,244 participants.

The co-existence of diabetes mellitus doubled the risk of cardiovascular events, cardiovascular mortality, and total mortality in hypertensive patients (RR ranging from approximately 1.73 to 2.77 for cardiovascular events, 2.25 to 3.66 for cardiovascular mortality, and 1.73 to 2.18 for total mortality).

Intensive blood pressure control to levels lower than 130/85 mm Hg was beneficial in diabetic hypertensive patients.

All four drug classes (diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, and calcium antagonists) were effective in reducing cardiovascular events in diabetic hypertensive patients.

In elderly diabetic patients with isolated systolic hypertension, calcium antagonists reduced the rate of cardiac end points by 63%, stroke by 73%, and total mortality by 55%.

In more than 60% of diabetic hypertensive patients, combination therapy was required to achieve a blood pressure of 130/85 mm Hg.

Reported side effects included malaise and fatigue, edema, gastrointestinal tract disease, kidney failure, cough, erectile dysfunction, headache, depression, rash, allergic reaction, intermittent claudication, bronchospasm, cold and numb hand, hypokalemia and hyponatremia.

**Authors' conclusions**
The authors state that intensive control of blood pressure reduced cardiovascular morbidity and mortality in diabetic patients regardless of whether low-dose diuretics, beta-blockers, angiotensin-converting enzyme inhibitors or calcium antagonists were used as a first-line treatment. A combination of more than one drug is frequently required to control blood pressure and may be more beneficial than monotherapy.

**CRD commentary**
The authors have clearly stated the research question and inclusion and exclusion criteria. The literature search was limited by only searching one database and including only English-language publications. There is also no mention of searches for unpublished data. It is possible that additional relevant studies have been missed.

Heterogeneity was not assessed since the authors decided that the studies could not be statistically combined. The authors do not report how the articles were selected or who performed the validity assessment or the data extraction. Study details are reported and are listed along with review results in tables and discussed in the text.

The review states that the contact author has received grants from pharmaceutical companies and is on several companies' speaker lists. This could be a potential conflict of interest.

The authors' conclusions appear to follow from the results but these should be viewed with caution because of possible biases arising from the missing details in the performance of this review.

**Implications of the review for practice and research**
Practice: The authors state that a combination of more that one drug is frequently required to control blood pressure and may be more beneficial than monotherapy. Use of a combination of an ACE inhibitor and calcium antagonist is strongly recommended to maximally protect the kidney in diabetic hypertensive patients with nephropathy.
Research: The authors did not state any implications for research.

Bibliographic details
Grossman E, Messerli F H, Goldbourt U. High blood pressure and diabetes mellitus: are all antihypertensive drugs created equal. Archives of Internal Medicine 2000; 160(16): 2447-2452

PubMedID
10979055

Original Paper URL
http://archinte.ama-assn.org

Other publications of related interest
This additional published commentary may also be of interest. Montori VM. Review: intensive blood pressure control and drugs reduce morbidity and mortality in hypertension and diabetes mellitus. Evid Based Med 2001;6:44.

Indexing Status
Subject indexing assigned by NLM

MeSH
Angiotensin-Converting Enzyme Inhibitors /therapeutic use; Antihypertensive Agents /therapeutic use; Calcium Channel Blockers /therapeutic use; Diabetes Complications; Diabetic Angiopathies /drug therapy /mortality; Humans; Hypertension /complications /drug therapy /mortality; Prognosis; Randomized Controlled Trials as Topic; Risk Assessment; Treatment Outcome

AccessionNumber
12000008599

Date bibliographic record published
30/04/2001

Date abstract record published
30/04/2001

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.