

# Review: Intensive blood-pressure control and drugs reduce morbidity and mortality in hypertension and diabetes mellitus

Grossman E, Messerli FH, Goldbourt U. High blood pressure and diabetes mellitus. Are all anti-hypertensive drugs created equal? *Arch Intern Med.* 2000 Sep 11;160:2447-52.

## QUESTION

In patients with hypertension and diabetes mellitus, what is the effectiveness of various antihypertensive treatments?

## DATA SOURCES

Studies were identified by searching MEDLINE (to June 1999) with the terms diabetes mellitus, hypertension, blood pressure, treatment, and therapy. Bibliographies of relevant studies were also checked.

## STUDY SELECTION

English-language studies were selected if they were randomized controlled trials > 12 months of duration that compared the effects of active drug treatments with placebo on morbidity and mortality in patients with hypertension and diabetes mellitus.

## DATA EXTRACTION

Data were extracted on patient characteristics, follow-up period, blood pressure, rate of

patients continuing to receive monotherapy, and cardiovascular morbidity and mortality.

## MAIN RESULTS

8 studies (5244 patients) met the selection criteria. 3 studies compared 2 active treatments, 1 study reported the effects of intensive blood-pressure lowering, and 3 studies compared active treatment with placebo. In 6 studies, mean ages ranged between 55 and 71 years; in 2 studies, patients were  $\geq 60$  years of age. Follow-up duration ranged between 2 and 8 years. Intensive blood-pressure control reduced cardiovascular morbidity and mortality. One study showed that the calcium antagonist nisoldipine increased the incidence of fatal or nonfatal myocardial infarction more than did the angiotensin-converting enzyme (ACE) inhibitor enalapril maleate (11% vs 2%, relative risk increase 4%, 95% CI 1 to 11, number needed to harm 12, CI 7 to 23). In the 3 studies that compared active treatment with placebo, a

diuretic (chlorthalidone) and a calcium antagonist (nitrendipine) reduced cardiac end points, stroke, and total mortality. Comparisons between antihypertensive drugs were not possible because study populations differed. Except for nisoldipine, adverse events did not differ among drugs.

## CONCLUSION

Intensive blood-pressure control reduces cardiovascular morbidity and mortality in patients with hypertension and diabetes mellitus regardless of which of 4 classes of antihypertensive drugs (low-dose diuretics,  $\beta$ -blockers, ACE inhibitors, and calcium antagonists) is used as first-line therapy.

*Sources of funding: Various pharmaceutical companies.*

*For correspondence: Dr. F.H. Messerli, Ochsner Clinic, 1514 Jefferson Highway, New Orleans, LA 70121, USA. FAX 504-842-4220.* ■

## COMMENTARY

Achieving tight blood-pressure control in patients with diabetes requires drug therapy, with most patients needing combination drug therapy (1). The choice of agent has been complicated by conflicting evidence of efficacy and safety. The review by Grossman and colleagues shows that currently used agents are more effective than is placebo for lowering cardiovascular risk in patients with diabetes and hypertension.

Does this mean that these agents are equivalent? Differences among agents are better assessed in head-to-head comparisons. The results of the review are consistent with a recently published meta-analysis (2) that reviewed the same 4 randomized trials comparing ACE inhibitors with calcium antagonists, diuretics, and  $\beta$ -blockers. In 3 trials, ACE inhibitors lowered the risk for cardiovascular events (relative risk reduction [RRR] 51%, CI 33 to 64) and all-cause mortality more than did other agents (RRR 62%, CI 13 to 62) with no effect on the risk for stroke. The fourth trial (the U.K. Prospective Diabetes Study) may not have had sufficient power to show differences between ACE inhibitors and  $\beta$ -blockers (3). These reports show that ACE inhibitors are similar to, if not better than, other antihypertensive drug classes for patients with diabetes.

Should ACE inhibitors be used as first-line treatment in patients with diabetes and hypertension? Treatment with ramipril in patients

with diabetes and hypertension lowers cardiovascular risk by 25% (CI 12 to 36) (4), a reduction beyond its antihypertensive effect. This evidence supports the consideration of ACE inhibitors in all patients with diabetes and hypertension. Whatever the choice of agent, patients with diabetes and their clinicians should choose tight blood-pressure control.

*Victor M. Montori, MD  
Mayo Clinic  
Rochester, Minnesota, USA*

## References

1. U.K. Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ.* 1998;317:703-13.
2. Pahor M, Psaty BM, Alderman MH, et al. Therapeutic benefits of ACE inhibitors and other antihypertensive drugs in patients with type 2 diabetes. *Diabetes Care.* 2000;23:888-92.
3. U.K. Prospective Diabetes Study Group. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. *BMJ.* 1998;317:713-20.
4. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. *Lancet.* 2000;355:253-9.