Treatment of hypertension reduces risk of complications in type 2 diabetes


QUESTION: In patients with type 2 diabetes mellitus, what are the optimal blood pressure (BP) goals and pharmaceutical agents to reduce risk of complications?

Data sources
The Cochrane Collaboration Diabetes Group report was used to identify studies published before 1997. Recent studies were identified by searching Medline in May 2000 and again in April 2002. Bibliographies of meta-analyses and review articles were scrutinised, and experts in the field were contacted for further studies.

Study selection
Studies were selected if they were randomised controlled trials (RCTs) that compared an antihypertensive drug with placebo, the effects of different target BP levels, or the effects of different classes of drugs, and measured relevant clinical end points in patients with type 2 diabetes mellitus.

Data extraction
Data were extracted on sample size, interventions, and outcomes. Main outcomes included all cause mortality; total cardiovascular events (TCEs) including cardiovascular mortality, myocardial infarction, and stroke; and microvascular end points (MEPs) including photocoagulation, nephropathy, neuropathy, and amputation.

Main results
16 RCTs met the selection criteria. Antihypertensive drugs were more effective than placebo for reducing the risk of TCEs (3 RCTs), all cause mortality (1 RCT), and MEPs (3 RCTs) (table). A target diastolic BP of 80 compared with 90 mm Hg reduced risk of TCEs (RRR 34%, CI 0.67 to 0.78 [1 RCT]); a target diastolic BP of 75 compared with 80–89 mm Hg reduced risk of all cause mortality (RRR 49%, CI 0.50 to 0.70) [1 RCT]; and a target systolic BP of 150/85 compared with 180/105 mm Hg reduced risk of TCEs (RRR 51%, CI 0.22 to 0.86) [1 RCT].

Outcomes NRCTs (n) Comparison RRR (95% CI) NNT (CI)
Total cardiovascular events 1 (583) Chlorothalidone plus atenolol or reserpine v placebo or usual care 34% (6 to 54) 13 (8 to 100)
1 (492) Nifedipine v placebo 62% (19 to 80) 13 (8 to 34)
1 (3577) Ramipril v placebo 25% (12 to 36) 20 (15 to 50)
1 (470) Enalapril v nisoldipine 57% (27 to 75) 12 (8 to 25)
1 (380) Fosinopril v amlodipine 51% (5 to 74) 15 (8 to 100)
1 (572) Captopril v thiazide diuretic or β blocker 41% (9 to 62) Not reported
1 (1195) Losartan v atenolol 24% (2 to 42) 20 (10 to 100)
1 (1195) Losartan v enalapril 24% (8 to 37) 34 (20 to 100)
1 (1195) Losartan v amlodipine 24% (4 to 69) Not reported
1 (1195) Losartan v enalapril 39% (16 to 55) 17 (10 to 50)
All cause mortality 1 (3577) Ramipril v placebo 26% (1 to 29) Not significant
1 (1513) Losartan v placebo 21% (5 to 34) Not significant
1 (590) Irbesartan v placebo 70% (39 to 86) 10 (7 to 25)
1 (1715) Irbesartan v amlodipine 23% (7 to 37) 12 (8 to 34)
Microvascular end points 1 (3577) Ramipril v placebo 26% (1 to 29) Not significant
1 (1513) Losartan v placebo 21% (5 to 34) Not significant
1 (590) Irbesartan v placebo 70% (39 to 86) 10 (7 to 25)
1 (1715) Irbesartan v amlodipine 23% (7 to 37) 12 (8 to 34)

*NRCTs = number of randomised controlled trials. Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in articles.

Conclusion
In patients with type 2 diabetes mellitus, aggressive treatment of hypertension reduces the risk of complications including stroke, myocardial infarction, and all cause mortality.

COMMENTARY
Vijan and Hayward reviewed large, multisite RCTs that provide strong evidence for aggressive control of hypertension in people with type 2 diabetes. The authors also examined different pharmaceutical approaches to BP control, concluding that thiazide diuretics, angiotension II receptor blockers (ARBs), and perindopril converting enzyme (ACE) inhibitors are first line treatment choices and that multiple agents may be necessary to reach target BP. However, many ACE inhibitors are relatively inexpensive generic medications that offer additional renoprotective benefits in diabetes, whereas thiazide diuretics at high doses may worsen glycaemia. As the authors indicate, none of the studies directly compared ACE inhibitors with ARBs.

A limitation of this review is the use of only a Cochrane Diabetes Group Report for studies published before 1997 and only Medline searches for more recent studies. The authors also restricted their review to major trials, excluding smaller RCTs and epidemiological studies, which may have influenced their findings. For example, Vijan and Hayward suggest that the data do not support current BP guidelines that specify a systolic BP goal of <135 mm Hg. However, in their review, Arauz-Pacheco et al found beneficial macrovascular and microvascular effects of systolic BP targets at ≤130 mm Hg, suggesting that patients with type 2 diabetes and a systolic BP of 130 mm Hg would benefit from pharmaceutical or other interventions designed to reduce their BP.

Finally, Vijan and Hayward suggest that control of hypertension should have a higher priority than control of blood glucose, based on findings from the UK Prospective Diabetes Study. This suggestion may be misleading because most patients with type 2 diabetes require glycaemic control interventions, whereas only a subgroup requires hypertension interventions. However, if present, both hypertension and hyperglycaemia need aggressive treatment.

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1 Arauz-Pacheco C, Parrott MA, Raskin P. Diabetes Care 2002;25:134–47.