

Hypertension

Canadian Diabetes Association
Clinical Practice Guidelines Expert Committee

BLOOD PRESSURE TARGETS

The recommended blood pressure (BP) targets are $\leq 130/80$ mm Hg. Systolic BP >130 mm Hg and diastolic BP >80 mm Hg are the thresholds recommended to initiate treatment and apply regardless of whether nephropathy is present. Vascular protection and control of hypertension are more important than measures aimed solely at protecting renal function (see Table 1 in “Vascular Protection” chapter and “Nephropathy” chapter).

Results of the Hypertension Optimal Treatment (HOT) and UKPDS 38 trials provide strong evidence for the diastolic BP target of 80 mm Hg (1,2). Both trials demonstrated clinically important reductions in microvascular and macrovascular complications (1,2), CV death (1) and diabetes-related death (2) in patients with diabetes who were randomized to treatments yielding diastolic BP as low as 81 mm Hg.

The evidence for a systolic BP target of 130 mm Hg is less strong and includes 2 prospective cohort studies (3,4) and the normotensive Appropriate Blood Pressure Control in Diabetes (ABCD) trial (5). In the cohort studies, direct relationships were observed between higher systolic BP levels and death, coronary artery disease, nephropathy and proliferative retinopathy (3,4). Although this relationship extended to systolic BP as low as 110 mm Hg, the Canadian Diabetes Association Clinical Practice Guidelines Expert Committee did not judge the evidence to be sufficient to recommend a systolic BP target lower than 130 mm Hg. Results of the normotensive ABCD trial also support the systolic BP target of 130 mm Hg (5), but, again, not to a level that justified a Grade A recommendation. Stronger evidence for the optimal systolic BP target awaits completion of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial in which thousands of people with diabetes are being randomized to systolic BP targets of <120 mm Hg or <140 mm Hg.

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TREATMENT OF HYPERTENSION

If BP cannot be controlled with lifestyle intervention in people with diabetes without nephropathy, any 1 of the following drugs is recommended as the initial choice of therapy, in the following order: ACE inhibitor, ARB, cardioselective beta blocker or thiazide-like diuretic. This recommendation reflects the results of studies that have compared, as a prespecified primary goal, clinically important vascular outcomes in people with diabetes who were randomized to either a drug from the studied class or to placebo (6,7), or to an active comparator control group (8-10). Because the efficacy of long-acting calcium channel blockers (CCBs) has not been proven in similarly designed trials, but was demonstrated in post-hoc analyses of randomized trials (11), CCBs remain an attractive option for patients unable to use drugs from any of the 4 aforementioned classes.

In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), >12 000 people with diabetes were randomized to treatment with a CCB, ACE inhibitor, thiazide-like diuretic or alpha-adrenergic blocker (9,10), and CV outcomes were compared over 5 years. Early termination of the alpha-adrenergic blocker arm occurred because of excess heart failure relative to the diuretic arm (10). This is the reason to avoid alpha-adrenergic blockers, at least as first-line therapy, for the treatment of hypertension.

More recently, the primary ALLHAT results were reported (9). No differences were observed in people with diabetes among the 3 remaining drug classes with respect to the primary outcome (fatal coronary heart disease or nonfatal myocardial infarction [MI]), but a lower rate of prespecified secondary vascular outcomes, including heart failure, occurred among those randomized to the thiazide-like diuretic. Although glycemic control was also worse in this group relative to the ACE inhibitor and CCB groups (9), the lack of differences in the primary outcome, the lower incidence of selected secondary outcomes in the diuretic group, and the lower cost of diuretics suggest that diuretics should be used before the other ALLHAT drug classes for patients with diabetes, hypertension and no nephropathy (9). However, a complete description of the ALLHAT results in the subgroup with diabetes—including whether there were any differences among the 3 drug classes in their effects on microvascular outcomes, such as nephropathy, or on macrovascular outcomes in those with nephropathy at baseline—was not available at the

time of development of the Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Therefore, a thiazide-like diuretic was not recommended as first-line therapy before the other drug choices.

Multiple drugs will often be required to approach, if not meet, the recommended BP targets. For example, in the UKPDS, 29% of subjects randomized to tight BP control required at least 3 antihypertensive drugs by the trial's end (2). The issue of which drug to use first may therefore be less important than the need to use more than 1 drug to control BP in most people with diabetes. The prospect of prescribing several antihypertensive drugs to patients with diabetes can be discouraging, particularly when the same people are likely to need several other drugs to reach the stringent lipid and glycemic targets that are now advocated. For each patient, treatment decisions will have to weigh the potential benefits of lowered BP against the potential adverse effects of polypharmacy. This judgement can be guided by the fact that a direct

relationship exists between the size of the incremental BP reduction and subsequent reduction in hypertension-related complications (3,4). While any reduction in BP is associated with a lower risk of complications, small reductions in BP are associated with small reductions in risk. Thus, it may be reasonable to be less aggressive (e.g. not adding a third or fourth antihypertensive drug) in patients whose BP is already close to 130/80 mm Hg and for whom the clinician is especially concerned about possible side effects from additional drug therapy. Larger BP reductions are associated with larger reductions in risk—justifying a more aggressive approach in the patient with diabetes whose BP levels are particularly high.

RECOMMENDATIONS

1. Lifestyle interventions to reduce BP, including achieving and maintaining a healthy weight, and limiting sodium and alcohol intake, should be considered [Grade D, Consensus].
2. BP should be measured at every diabetes visit. Patients with systolic BP >130 mm Hg or diastolic BP >80 mm Hg should have their BP remeasured on a separate visit [Grade D, Consensus].
3. Persons with diabetes should be treated to target a systolic BP <130 mm Hg [Grade C, Level 3 (3-5)] and a diastolic BP ≤80 mm Hg [Grade A, Level 1A (1)]. Systolic BP >130 mm Hg and diastolic BP >80 mm Hg are the thresholds recommended to initiate treatment [Grade D, Consensus].
4. For people with diabetes, no diabetic nephropathy, and BP levels >130 mm Hg and/or >80 mm Hg despite lifestyle modification, any 1 of the following drugs is recommended as the initial choice of therapy, in the following order [Grade D, Consensus for the order]:
 - ACE inhibitor [Grade A, Level 1A (6)];
 - ARB [Grade A, Level 1A for co-existent left ventricular hypertrophy (LVH) (7); Grade B, Level 2 if LVH is not present (7)];
 - cardioselective beta blocker [Grade B, Level 2 (8)];
 - thiazide-like diuretic [Grade A, Level 1A (9)]; or
 - long-acting CCB [Grade B, Level 2 (11)].
5. If BP targets cannot be reached despite the use of 1 of the above drug choices as monotherapy, use of 1 or more of these or other antihypertensive drugs in combination should be considered [Grade D, Consensus].
6. Alpha-adrenergic blockers are not recommended as first-line agents for the treatment of hypertension in persons with diabetes [Grade A, Level 1A (10)].

OTHER RELEVANT GUIDELINES

Definition, Classification and Diagnosis of Diabetes and

Other Dysglycemic Categories

Screening and Prevention

Targets for Glycemic Control

Physical Activity and Diabetes

Nutrition Therapy

Management of Obesity in Diabetes

Vascular Protection

Dyslipidemia in Adults with Diabetes

RELATED WEBSITES

Canadian Hypertension Society. Available at: <http://www.hypertension.ca>. Accessed June 12, 2006.

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