The 2001 Canadian Hypertension Recommendations: What's New and What's Not So New but Is Still Important

Canadian Hypertension Recommendations Working Group

This summary of the 2001 Canadian hypertension recommendations, developed by the Canadian Hypertension Recommendations Working Group, is being submitted to a broad range of journals, including *CJHP*. The aim is to disseminate the recommendations to as many Canadian health care professionals as possible, to help ensure that patients receive consistent, up-to-date information and optimum care. Pharmacists are closely involved in hypertension therapy and have participated in the development of these recommendations. One pharmacist serves on the steering committee for the recommendations themselves (Seema Nagpal) and two have served on the steering committee for implementation (Seema Nagpal and Carol Repchinsky). The recommendations are updated yearly, and a new summary should be available early in 2003. The members of the Canadian Hypertension Recommendations Working Group and its subgroups are listed at the end of this article.

INTRODUCTION

Hypertension is one of the most common reasons for an adult patient to visit a physician and is estimated to be the third leading risk associated with death worldwide.[1] The most recent reliable data on hypertension prevalence and control in Canada are 10 to 15 years old.[2] At that time 22% of adult Canadians had high blood pressure and only 16% of those with hypertension were treated and controlled. Preliminary data (N.R.C. Campbell, unpublished data) suggest a significant increase in prescriptions of major classes of antihypertensive agents coinciding with the introduction of the annual recommendations and implementation process; however, whether this trend reflects an improvement in treatment and control of hypertension is uncertain. Unfortunately, our national health surveillance is inadequate to determine whether hypertension prevalence, awareness, treatment, or control has changed. Given the data that are available, it behooves all health care professionals to prioritize hypertension as a public health issue and to aggressively identify, treat, and control hypertensive patients according to the best available evidence and recommendations.

This is the third year that the Canadian Hypertension Recommendations Working Group has comprehensively updated its hypertension recommendations.[3-5] The recommendations are linked to an expanding implementation effort.[6] The current report is a brief summary of the 2001 recommendations, highlighting those that are new, revised, or simply important to improve blood pressure control in Canada. New recommendations of specific interest include an updated section on management of hypertension in people with diabetes, especially new recommendations for initial therapy, and a new recommendation to lower blood pressure following the acute phase of stroke or transient ischemic attack. The arbitrary classification of elderly people as those age 60 or older has been removed. Evidence for an age effect is required, as opposed to the previous requirement for evidence in specific age categories. This has resulted in a more aggressive threshold for initiating therapy in those over age 60. The recommendation to switch first-line therapies when there is inadequate response has been changed to a recommendation to combine first-line therapies, in recognition of the need for multiple drugs to control hypertension as well as the sequential method

of adding medications used in major therapeutic trials. There are also new comprehensive sections on management of patients with pheochromocytoma and hyperaldosteronism.

The purpose of this summary is to provide a rapid update to the 2000 hypertension recommendations.[4,5] A full publication of the comprehensive recommendations will be published separately. The latter publication is intended to be a scientific reference and not a clinical practice guideline. A slide kit and clinical practice algorithms supporting the full 2001 recommendations will be available to download at the Web site of the Canadian Hypertension Society (www.chs.md).

The methods for producing the recommendations have been published previously,[7] but there have been some revisions. In 2001 a separate meeting of those involved in the production of recommendations was held to discuss new, changed, or controversial recommendations and evidence. A voting process adopted in 2000 to exclude recommendations with which 30% or more of those involved on the subgroups, central review committee, and steering committee disagreed was continued, but individuals with a direct conflict of interest on specific recommendations were excluded from voting on those recommendations. Those with conflict of interest participated in the discussions following disclosure. The recommendations were based on the results of literature searches (to at least March 2001), personal knowledge of published literature, contact with authors, and major clinical trials published prior to November 2001.

DIAGNOSIS

Although there are no substantive changes to this section, diagnosis is critical to the management of hypertension. The recommendations highlight the importance of assessing the blood pressure of all adults using proper measurement technique at all appropriate visits. Hypertension can be diagnosed immediately if there is a hypertensive urgency or crisis or over the course of 3 visits in the presence of target organ damage in patients who are clinically stable. However, diagnosis requires up to 5 visits if there is no target organ damage and the initial blood pressure is less than 180/105 mm Hg. Although the recommendation for 5 visits represents a substantial workload, those whose blood pressure falls to less than 140/90 mm Hg with observation have a normal prognosis and can avoid labeling and interventions that may be harmful.[8] Self-measurement and 24-h ambulatory measurement continue to be recommended for consideration in assessing office-induced blood pressure elevation, and the former is recommended to improve patient compliance. Only devices meeting international standards should be used.[9] Daytime blood pressures of less than 135/85 mm Hg with ambulatory and self-measurement are associated with a normal prognosis.

Table 1. Characteristics of Candidates for Angioplasty or Revascularization Who Should Be Screened for Renovascular Hypertension by Means of Post-Captopril Renography

Uncontrolled hypertension despite therapy with 3 or more drugs
Deteriorating renal function
Recurrent episodes of flash pulmonary edema

Table 2. Characteristics of Patients Who Should Be Considered for Screening for Pheochromocytoma with a 24-h Urine for Metanephrines and Creatinine*

Paroxysmal and/or severe sustained hypertension refractory to usual antihypertensive therapy
Hypertension and symptoms suggestive of catacholamine excess (2 or more of headaches, palpitations, sweating, etc.)
Hypertension triggered by ß-blockers, monoamine oxidase inhibitors, micturation, or changes in abdominal pressure
Incidentally discovered adrenal adenoma
Multiple endocrine neoplasia 2A or 2B, von Recklinghausen's neurofibromatosis, or von Hippel-Lindau disease

*Assessment of urinary vanilmandelic acid is inadequate in these situations.

LABORATORY INVESTIGATION

Routine laboratory assessment should be performed at diagnosis and includes blood for electrolytes, creatinine, fasting glucose, complete blood count, and lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides), urinalysis, and electrocardiography. Criteria for screening patients for renovascular hypertension with post-captopril renography (Table 1) and for pheochromocytoma with a 24-h urine for metanephrines and creatinine (Table 2) are provided. Screening patients for pheochromocytoma by assessment of urinary vanilmandelic acid is inadequate. More recent studies have confirmed that hyperaldosteronism is relatively common. Screening for hyperaldosteronism should include assessment of a plasma aldosterone and plasma renin activity measured in morning samples taken from patients in a sitting position after resting for at least 15 min. (Antihypertensive drugs, with the exception of

Table 3. Characteristics of Hypertensive Patients for Whom Screening for Hyperaldosteronism Should Be Considered*

Spontaneous hypokalemia
Profound diuretic-induced hypokalemia (<3.0 mmol/L)
Hypertension refractory to treatment with 3 or more drugs
Incidental adrenal adenomas

*Screening for hyperaldosteronism should include assessment of a plasma aldosterone and plasma renin activity, measured in morning samples taken from patients in a sitting position after resting at least 15 min. Antihypertensive drugs, with the exception of aldosterone antagonists, may be continued before testing.

Table 4. Methods of Cardiovascular Risk Assessment on the Basis of Framingham Data

Technology	Source
Desktop computer	www.hyp.ac.uk/bhs/managemt.html
Palm-type devices	www.statcoder.com/cardiac.htm
Risk charts	www.hyp.ac.uk/bhs/managemt.html *J Hypertens* 1999;17:151-83 (reference 10)
Calculators incorporating the formula	*JAMA* 2001:285:2486-97 (reference 11) *Circulation* 1999;100:1481-92 (reference 12) *J Hum Hypertens* 1999;13:569-92 (reference 13) *BMJ* 2000;320:709-10 (reference 14)

aldosterone antagonists, may be continued prior to testing.) The criteria for selecting patients to be screened for hyperaldosteronism are shown in Table 3. Comprehensive recommendations for the diagnosis and management of pheochromocytoma and hyperaldosteronism will be published with the detailed 2001 hypertension recommendations.

ASSESSMENT OF RISK

It is recommended to quantitatively assess a patient's cardiovascular risk and adopt a multifactorial approach for treating hypertension. A variety of methods can be used (Table 4).[10-14]

LIFESTYLE MODIFICATION

Individualized lifestyle modification is recommended for all patients with hypertension and those at risk for hypertension. A diet consistent with Canada's "Guide to Healthy Eating" (i.e., high in fresh fruit and vegetables and low-fat dairy products and low in saturated fat) and limitation of salt additives and foods with excessive added salt will lower blood pressure. Other lifestyle changes that are effective at reducing blood pressure include weight loss (4.5 kg minimum) in those who are overweight, regular physical activity (optimum 45 to 60 min of moderate activity, such as brisk walking, 4 or 5 times a week), and low-risk alcohol consumption (0 to 2 drinks per day; fewer than 14 drinks per week in men, fewer than 9 drinks per week in women). Cognitive behaviour modification for stress management is effective in some individuals. Because smoking is a major cardiovascular risk factor, has greater than additive risk in hypertensive persons, and reduces or abolishes the beneficial outcomes associated with antihypertensive therapy, smoking cessation should be strongly encouraged for all hypertensive patients.

Table 5. Drugs To Be Combined for Additive Hypotensive Effect in Dual Therapy*

Column 1	Column 2
Low-dose thiazide diuretic	ß-Blocker
Long-acting dihydropyridine calcium-channel blocker	Angiotensin-converting enzyme inhibitor†

*Combination therapy consists of a drug from column 1 combined with a drug from column 2. Dual combinations of agents within column 1 and within column 2 have less than additive hypotensive effect but may be indicated in specific settings (e.g., column 2 drugs are used after myocardial infarction)
†Angiotensin receptor blockers are an alternative initial choice in patients with diabetes and nephropathy.

PHARMACOTHERAPY

Drug treatment is recommended if the diastolic blood pressure is greater than 90 mm Hg and there is cardiovascular disease or other target organ damage or cardiovascular risk factors. Most hypertensive patients have additional risk factors or target organ damage; however, if such are not present, the lower cardiovascular risk has resulted in a recommendation to treat diastolic blood pressure of 100 mm Hg or above or systolic blood pressure of 160 mm Hg or above. Initial drugs for diastolic and combined systolic and diastolic hypertension include diuretics, long-acting dihydropyridine calcium-channel blockers, and angiotensin-converting enzyme inhibitors. α-Blockers are recommended as first-line therapy in those under but not age 60 or over. α-Blockers are not recommended as first-line therapy, and short-acting calcium-channel blockers should not be used as antihypertensive agents. For isolated systolic hypertension, initial therapy should be with a low-dose thiazide-like diuretic or a long-acting dihydropyridine calcium-channel blocker.

In people with diabetes mellitus, angiotensin-converting enzyme inhibitors are recommended as first-line therapy in all situations. Low-dose thiazide-like diuretics and long-acting dihydropyridine calcium-

Table 6. Considerations in the Individualization of Antihypertensive Therapy*

Risk Factor or Disease	Initial Therapy	Second-Step Therapy	Notes and Cautions
Uncomplicated hypertension	Low-dose thiazide-like diuretics, ß-blockers, ACE inhibitors, long-acting dihydropyridine calcium-channel blockers	Combinations of first-line drugs (see Table 5)	α-Blockers not recommended as initial therapy. ß-Blockers not recommended as initial therapy in those over age 60. Hypokalemia should be avoided by using potassium-sparing agents in those prescribed diuretics.
Isolated systolic hypertension	Low-dose thiazide-like diuretics, long-acting dihydropyridine calcium-channel blocker		Hypokalemia should be avoided by using potassium-sparing agents in those prescribed diuretics.
Diabetes mellitus with nephropathy	ACE inhibitors; alternatively angiotensin II receptor blockers	One or more of low-dose thiazide-like diuretics, cardioselective ß-blockers, long-acting calcium-channel blockers	If serum creatinine > 150 µmol/L, a loop diuretic should be used as a replacement for low-dose thiazide diuretic if volume control is required.
Diabetes mellitus without nephropathy	ACE inhibitors	One or more of angiotensin II receptor blockers, low-dose thiazide-like diuretics, cardioselective ß-blockers, long-acting calcium-channel blockers	
Diabetes mellitus without nephropathy and with systolic hypertension	ACE inhibitors; alternatively, low-dose thiazide diuretics, long-acting calcium-channel blockers		
Angina	ß-Blockers (consider ACE inhibitors as add-on therapy)	Long-acting calcium-channel blockers	
Prior myocardial infarction	ß-Blockers with or without ACE inhibitors	Combinations of additional agents	
Systolic dysfunction	ACE inhibitors (thiazide or loop diuretics, ß-blockers, spironolactone as additive therapy)	Angiotensin II receptor blockers, hydralazine/isosorbide dinitrate, amlodipine	Avoid non-dihydropyridine calcium-channel blockers (diltiazem, verapamil).
Past cerebrovascular accident or transient ischemic attack	Strongly consider blood pressure reduction after the acute phase		Blood pressure reduction reduces recurrent cerebrovascular events.
Renal disease	ACE inhibitors (diuretics as additive therapy)	Combinations of additional agents	Give ACE inhibitors if patient has bilateral renal artery stenosis.
Left ventricular hypertrophy	Does not affect initial treatment recommendations	recommendations	Avoid hydralazine and minoxidil.
Peripheral arterial disease	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	Avoid ß-blockers in patients with severe disease.
Dyslipidemia	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	

ACE = angiotensin-converting enzyme.
*When using 2 drugs specifically to lower blood pressure, use Table 5 to maximize the hypotensive effect. Short-acting calcium-channel blockers are not recommended in the treatment of hypertension.

channel blockers are recommended as alternative first-line agents in isolated systolic hypertension. Angiotensin II receptor blockers are recommended as alternative first-line agents to angiotensin-converting enzyme inhibitors in the presence of diabetic renal disease (e.g., microalbuminuria greater than 30 mg/24 h).

CONTROLLING HIGH BLOOD PRESSURE

As per the previous year's recommendations, one of the most important aspects of the current recommendations is the need to control blood pressure in treated patients. It is recommended to reduce blood pressure to less than 140/90 mm Hg in most patients including the elderly and to less than 130/80 mm Hg in patients with diabetes mellitus or renal dysfunction. Lowering blood pressure to less than 125/75 mm Hg is recommended for patients with renal dysfunction and greater than 1 g/day proteinuria. A modification to the recommendations suggests the use of combinations of medication if the initial choice is ineffective and to switch to an

alternative first-line agent only if there is intolerance or adverse effects. The average blood pressure lowering of a single drug is about 10/5 mm Hg. In the large outcome trials, stepwise additions of antihypertensive medications were prescribed to achieve blood pressure targets, and the use of multiple agents was necessary in a large proportion of patients. Table 5 indicates combinations of first-line agents that have additive hypotensive effect when used in combination for the treatment of uncomplicated hypertension. Other first-line dual-agent therapies have less than additive hypotensive effects and are recommended only for specific indications (e.g., ß-blockers and angiotensin-converting enzyme inhibitors after myocardial infarction). In the treatment of uncomplicated hypertension with triple or quadruple therapy, all potential antihypertensive combinations of first-line agents are effective. Individual physicians need to assess their personal skill and experience in determining the need for specialty consultation for resistant hypertension. In patients who have little response to appropriate single or combination medications, non-adherence, secondary hypertension, interfering drugs or lifestyle, and/or office-induced increases in blood pressure (the "white coat effect") should be considered.

In specific patient subgroups there are further treatment recommendations (see Table 6). A notable change is the recommendation to strongly consider antihypertensive therapy in anyone who has had a nondisabling stroke or transient ischemic attack after the acute phase. A recent trial (PROGRESS) demonstrated a reduction in recurrent cerebrovascular events when blood pressure was lowered in both hypertensive and normotensive persons.[15]

Patient compliance is still a major challenge and should be addressed by health care professionals at each medical visit.

SUMMARY OF VOTING

There were 105 recommendations produced and 38 eligible voters (subgroup, central review committee, and steering committee membership). For 22 recommendations there was no disagreement, 74 recommendations had 1 vote in disagreement, 7 recommendations had 2 votes in disagreement, and 2 recommendations had 3 votes in disagreement. The recommendation that had the greatest disagreement was voted against by 8% of the eligible voters. It is important to note that individuals involved in the recommendations process or in a subgroup may have personally opposed specific recommendations. Therefore, acknowledgement of an individual's contribution to the hypertension recommendations process does not indicate personal support for any specific recommendation.

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