

The 2001 Canadian hypertension recommendations: take-home messages

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Case

Mrs. J, a 72-year-old woman whom you are treating for continuing hip pain related to arthritis (diclofenac 75 mg/d), has been relatively healthy, but her blood pressure has been increasing recently. Over the last 3 visits it has been 184/92 mm Hg on average. Mrs. J is physically active and uninterested in dietary advice. She is a nonsmoker who does not drink alcohol. Her body mass index is 26 kg/m², and physical examination reveals a pulsatile mass in the upper abdomen. The rest of the examination is unremarkable. Electrolyte and creatinine levels, complete blood count, and urinalysis and electrocardiography results are all within normal ranges. The fasting glucose level is 5.6 mmol/L, total cholesterol 5.4 mmol/L, high-density lipoprotein cholesterol 1.1 mmol/L and triglycerides 1.3 mmol/L. Ultrasonography of the abdomen shows a tortuous aorta with no aneurysm. What drugs are recommended as starting therapy? Once this therapy has been started, what will you add as a second drug? As a third drug? Does the most recent evidence concerning treatment of hypertension, reflected in the 2001 revisions of the Canadian recommendations for the management of hypertension, mandate any changes from previous practice in the approach to therapy?

This article summarizes the “take-home messages” from the 2001 Canadian recommendations for the management of hypertension^{1,2} and describes how they might affect the care of a patient such as Mrs. J. The Canadian hypertension recommendations are based on a systematic review of the relevant literature, assessed according to an evidence-based grading scheme.³ Since 1999 there have been annual updates to Canada’s hypertension recommendations.⁴⁻⁷ The 2001 version includes an updated section on the management of hypertension in people with diabetes and new recommendations for therapy after the acute phase of stroke or transient ischemic attack. The new recommendations also specify a lower threshold for initiating therapy in those over 60 years of age. The previous recommendation to switch first-line therapies when response is inadequate has been dropped in favour of a recommendation to combine first-line therapies in this situation. There are also new and comprehensive sections on management of patients with hyperaldosteronism and pheochromocytoma. The full recommendations and their scientific rationale are published elsewhere.^{1,2}

Diagnosis of hypertension

Was Mrs. J’s blood pressure measured accurately?

Accurate measurement of blood pressure is the first step in diagnosing hypertension and should be carried out at all appropriate visits (Box 1).

One of the most important aspects of blood pressure measurement is having the patient rest in a quiet, comfortable room for 5 minutes immediately before readings are taken. The patient should rest in the room and in the position (usually seated) in which the first readings will be taken. Talking increases blood pressure by, on average, 7 mm Hg,⁸ so speech should be discouraged. It is also important to assess blood pressure in various positions (seated or prone, standing) and in different limbs (both arms and one or both legs). These simple steps can help to determine if there is an obstruction of blood flow to one arm that could obscure a diagnosis of hypertension; they can also provide clues to secondary causes of hypertension or atherosclerosis. A drop in blood pressure of more than 20/10 mm Hg when the patient is standing (relative to the seated or prone position) indicates the need for caution during antihypertensive therapy.

Hypertension can be diagnosed immediately if there is a hypertensive urgency or crisis or in 3 visits if the patient is clinically stable but has target-organ damage (Table 1). 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. The recommendation to take up to 5 visits for a diagnosis represents a substantial workload for the physician, but patients whose blood pressure falls to less than 140/90 mm Hg with observation are not at greater risk of cardiovascular disease because of their blood pressure.⁹⁻¹¹

Box 1: Recommended technique for measurement of blood pressure

If possible, measure blood pressure with a mercury manometer. A recently calibrated aneroid or a validated and recently calibrated electronic device can be used. Aneroid devices and mercury columns must be clearly visible at eye level.

Choose a cuff with an appropriate bladder width: (bladder width \times 2.5) \pm 4 cm = circumference of patient's arm.

Place the cuff so that the lower edge is 3 cm above the elbow crease and the bladder is centred over the brachial artery. Before the reading is taken, the patient should rest comfortably for 5 minutes in the seated position with the back supported. The arm should be bare and should be supported, with the antecubital fossa at heart level. The patient should not talk, and his or her legs should not be crossed. In addition to resting blood pressure measurements, blood pressure should also be assessed after 2 minutes of standing and whenever the patient reports symptoms suggestive of postural hypotension.

Increase the bladder pressure rapidly to 30 mm Hg above the level at which the radial pulse is extinguished (to exclude the possibility of auscultatory gap).

Place the head of the stethoscope gently but firmly over the brachial artery.

Open the control valve so that the rate of drop in pressure in the vicinity of the systolic and diastolic levels is 2 mm Hg per beat.

Read the systolic pressure (the first appearance of a clear tapping sound [the phase I Korotkoff sound]) and the diastolic pressure (the point at which the sounds disappear [the phase V Korotkoff sound]).

Record the blood pressure to the nearest 2 mm Hg on a manometer (or to the nearest 1 mm Hg on an electronic device); also record the arm used and whether the patient was supine, sitting or standing. Record the heart rate.

The seated blood pressure is used to determine and monitor treatment decisions. The standing blood pressure is used to examine for postural hypotension (if postural hypotension is present, the treatment may be different).

If Korotkoff sounds persist as the pressure approaches 0 mm Hg, then the point of muffling of the sound (the phase IV Korotkoff sound) is used to indicate diastolic pressure.

In a patient with arrhythmia, additional readings may be required to estimate the average systolic and diastolic pressure. Ignore isolated extra beats. Note the rhythm and pulse rate.

Leaving the cuff partially inflated for too long will allow the venous system to fill, which makes the sounds difficult to hear. To avoid venous congestion, it is recommended that at least 1 minute elapse between consecutive readings.

Blood pressure should be measured at least once in both arms. If one arm has a consistently higher pressure, that arm should be used for subsequent measurements.

What other laboratory tests should be ordered?

All hypertensive patients should undergo routine laboratory assessment (Table 2). Determination of serum electrolyte levels is particularly important, since hypokalemia is a marker of primary or secondary hyperaldosteronism. Elevated serum creatinine level and abnormal urinalysis results (e.g., casts, hematuria or proteinuria) are important as potential indicators of renal causes of hypertension or hypertensive target-organ damage and as cardiovascular risk factors. Electrocardiography is recommended both to assess for target-organ damage (e.g., old myocardial infarction) and to indicate the prognosis (e.g., left ventricular hypertrophy indicates a poor prognosis). A complete blood count is recommended to screen for systemic disease.

Patients with features of secondary hypertension should undergo further testing. The 2001 update includes new recommendations for screening patients for renovascular hypertension (Table 3), hyperaldosteronism (Table 4) and pheochromocytoma (Table 5). It is estimated that renovascular hypertension occurs in approximately 1% of hypertensive patients, hyperaldosteronism in 1% to 15% and pheochromocytoma in approximately 0.1%. (Comprehensive recommendations for the diagnosis and management of hyperaldosteronism and pheochromocytoma are included with the detailed hypertension recommendations.¹) False-positive results are common in unselected patients, so these tests should not be ordered routinely.

A fasting glucose and lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides) is essential to determine the patient's cardiovascular prognosis. Because cardiovascular risk can vary more than 10-fold at a given pressure level, it is important to assess the patient's global cardiovascular risk and adopt a multifactorial approach for treating hypertension. A variety of methods, including charts, formulas, and programs for desktop computers or personal digital assistants, can be used.¹²⁻¹⁶ For example, the use of a risk chart can improve a patient's reduction in sys-

Table 1: Examples of target-organ damage due to hypertension

Cerebrovascular disease (stroke, transient ischemic attack or dementia)
Hypertensive retinopathy
Coronary artery disease
Left ventricular hypertrophy
Left ventricular systolic dysfunction
Aortic and other arterial aneurysms
Renal impairment
Proteinuria
Peripheral arterial disease
Overt atherosclerotic disease

Table 2: Recommended initial routine laboratory assessments

Test	Purpose
Electrolytes, creatinine level	To screen for renal target-organ damage and secondary causes of hypertension (e.g., hypokalemia or elevated serum creatinine)
Fasting blood glucose	To screen for diabetes and global cardiovascular risk
Complete blood count	To screen for systemic disease and polycythemia
Lipid profile (total, HDL and LDL cholesterol; triglycerides)	To screen for dyslipidemia and global cardiovascular risk
Urinalysis	To screen for renal target-organ damage and secondary hypertension
Electrocardiography	To screen for target-organ damage (left ventricular hypertrophy and ischemia) and heart blocks that may influence therapeutic choices

Note: HDL = high-density lipoprotein, LDL = low-density lipoprotein.

Table 3: Patient characteristics suggesting screening 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

*If patient is a candidate for angioplasty or revascularization.

Table 4: Patient characteristics suggesting screening for hyperaldosteronism*

Spontaneous hypokalemia
Profound diuretic-induced hypokalemia (potassium < 3.0 mmol/L)
Uncontrolled hypertension despite therapy with 3 or more drugs
Incidental adrenal adenomas

*Screening for hyperaldosteronism should include assessment of plasma aldosterone and plasma renin activity from morning samples. The patient should be in a sitting position for sampling and should rest for at least 15 minutes before samples are taken. Antihypertensive drugs (except aldosterone antagonists) may be continued before testing.

tolic blood pressure.¹⁷ According to the New Zealand risk chart shown in Fig. 1, Mrs. J's 5-year risk of a cardiovascular event is 15% to 20%.

Is office-based measurement of blood pressure enough?

Self-measurement and 24-hour ambulatory measurement of blood pressure continue to be recommended for assessing office-induced elevation of blood pressure; self-measurement is also recommended as a way to improve patient compliance with therapy. Only devices meeting international standards should be used for this purpose.^{18,19} Daytime blood pressures above 135/85 mm Hg obtained with self-measurement or ambulatory measurement are associated with elevated cardiovascular risk.

Table 5: Patient characteristics suggesting screening for pheochromocytoma by means of a 24-h urine sample for metanephrines and creatinine*

Paroxysmal or severe sustained hypertension refractory to usual antihypertensive therapy
Hypertension and symptoms suggestive of catecholamine excess (2 or more of headaches, palpitations, sweating and other typical symptoms)
Hypertension triggered by β -blockers, monoamine oxidase inhibitors, micturition or changes in abdominal pressure
Incidental adrenal adenomas
Multiple endocrine neoplasia 2A or 2B, von Recklinghausen's neurofibromatosis or von Hippel-Lindau disease

*Assessment of urinary vanillylmandelic acid is inadequate.

Management

What lifestyle modifications should Mrs. J undertake?

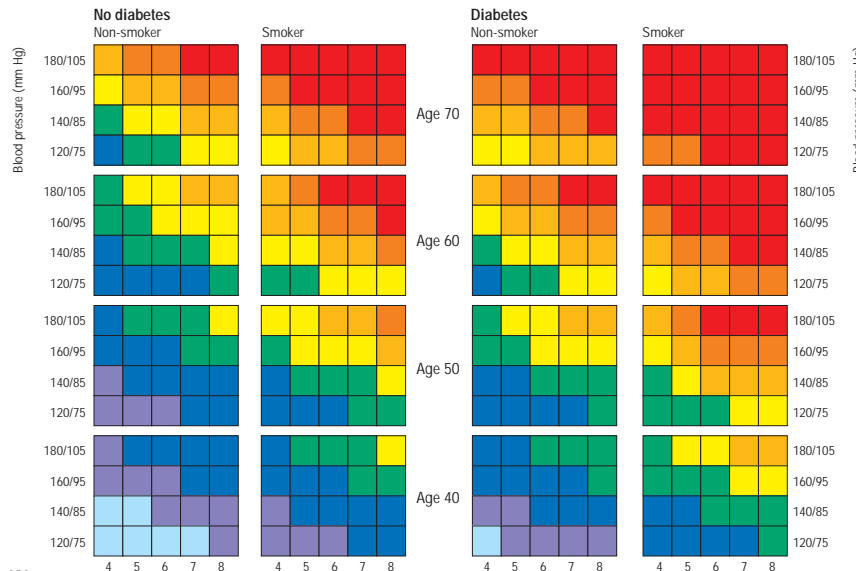
Individualized lifestyle modification is recommended for all patients who have or are at risk for hypertension. In selected patients, a single lifestyle intervention can prevent hypertension from developing or can reduce blood pressure to an extent similar to that accomplished by a single antihypertensive medication. The lifestyle modification might be the sole therapy or it might be used in conjunction with pharmacotherapy to significantly enhance the effectiveness of the medication.²⁰ All of the lifestyle modifications suggested in the hypertension recommendations improve general health, in addition to lowering blood pressure. A diet high in fresh fruit, vegetables and low-fat dairy products and low in saturated fat and salt is effective at reducing blood pressure. Commonly referred to as the DASH diet,²¹ this diet is also consistent with Canada's guide to healthy eating.²² Regular cardiorespiratory physical activity (e.g., brisk walking) is also a highly effective means of lowering blood pressure.²³ Low-

New Zealand cardiovascular risk prediction charts

Risk level		Benefit (1)	Benefit (2)
5 year cardiovascular risk (non-fatal and fatal)		Cardiovascular events prevented per 100 treated for 5 years*	Number needed to treat for 5 years to prevent 1 event*
Very high	>30%	>10	<10
	25-30%	9	11
	20-25%	7.5	13
High	15-20%	6	16
	10-15%	4	25
Moderate	5-10%	2.5	40
	2.5-5%	1.25	80
	<2.5%	<0.8	>20

* Based on a 20% reduction in total cholesterol or a reduction in blood pressure of 10-15 mm Hg systolic or 5-8 mm Hg diastolic, which reduces risk of cardiovascular disease by about one third over five years

Men



Women

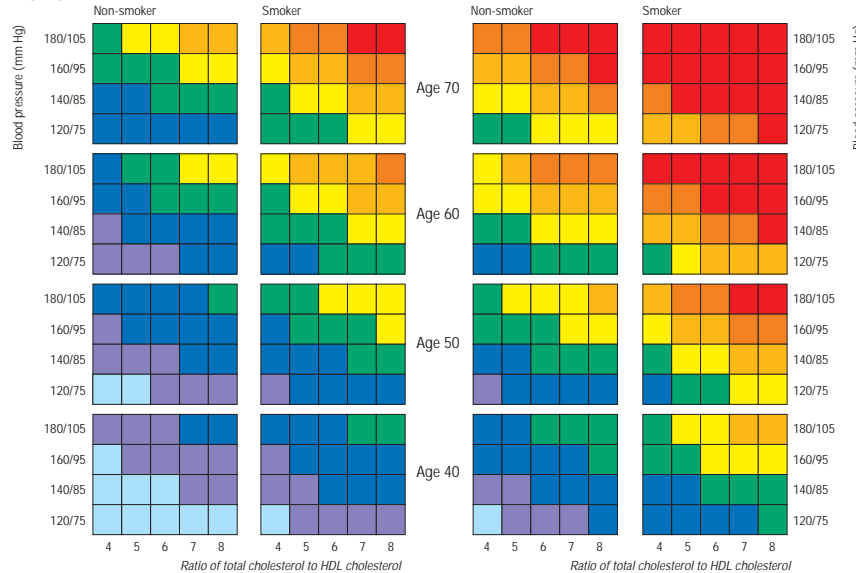


Fig. 1: The New Zealand risk charts represent a quick and easy method of categorizing a patient's 5-year cardiac risk on the basis of blood pressure, age, smoking status, presence of diabetes and ratio of total to high-density lipoprotein (HDL) cholesterol.¹² For people with the same blood pressure, there is substantially greater risk when other risk factors are present. To use the chart for the patient described in this article, select the bottom left column of risk panels (for women who are not diabetic and who are not smokers). Using the age category of 70 years and the highest of her systolic and diastolic pressure, select the blood pressure category of 180/105 mm Hg. Her ratio of total to HDL cholesterol is 4.9 or close to 5, which puts her in a yellow risk category. Yellow corresponds to a risk of 15% to 20% of a cardiovascular event within 5 years. Antihypertensive treatment would be expected to prevent 1 event for every 16 people treated. The Framingham 10-year risk assessment methods may also be used.¹³⁻¹⁶ Reproduced with permission from *BMJ*.

Table 6: Individualization of antihypertensive therapy

Risk factor or disease	Initial therapy	Second-step therapy	Notes and cautions*
Uncomplicated hypertension	Low-dose thiazide-like diuretics, β -blockers, ACE inhibitors or long-acting dihydropyridine calcium-channel blockers	Combinations of first-line drugs (see Table 7)	α -Blockers are not recommended as initial therapy. β -Blockers are not recommended as initial therapy in those over 60 years of age. Avoid hypokalemia by using potassium-sparing agents in patients receiving diuretics
Isolated systolic hypertension	Low-dose thiazide-like diuretics or long-acting dihydropyridine calcium-channel blockers		Avoid hypokalemia by using potassium-sparing agents in patients receiving diuretics
Diabetes mellitus with nephropathy	ACE inhibitors; alternatively, angiotensin II receptor blockers	One or more of low-dose thiazide-like diuretics, cardioselective β -blockers,† long-acting calcium-channel blockers	If serum creatinine > 150 μ mol/L, a loop diuretic should be used as a replacement for a low-dose thiazide diuretic if volume control is required; use caution with potassium-sparing diuretics
Diabetes mellitus without nephropathy	ACE inhibitors	One or more of angiotensin II receptor blockers, low-dose thiazide-like diuretics, cardioselective β -blockers,† long-acting calcium-channel blockers	
Diabetes mellitus without nephropathy and with isolated systolic hypertension	ACE inhibitors; alternatively, low-dose thiazide diuretics, long-acting dihydropyridine calcium-channel blockers		
Angina	β -Blockers (consider ACE inhibitors as add-on therapy)	Long-acting calcium-channel blockers	
Prior myocardial infarction	β -blockers or ACE inhibitors (or both)	Combinations of additional agents	
Systolic dysfunction	ACE inhibitors (thiazide or loop diuretics, β -blockers, or spironolactone as add-on therapy)	Angiotensin II receptor blockers, hydralazine/isosorbide dinitrate, amlodipine	Avoid non-dihydropyridine calcium-channel blockers (e.g., diltiazem, verapamil)
Prior cerebrovascular accident or TIA	Strongly consider blood pressure reduction after the acute phase		Blood pressure reduction reduces recurrence of cerebrovascular events
Renal disease	ACE inhibitors (diuretics as add-on therapy)	Combinations of additional agents	Give ACE inhibitors if there is bilateral renal artery stenosis
Left ventricular hypertrophy	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	Avoid hydralazine and minoxidil
Peripheral arterial disease	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	Avoid β -blockers in patients with severe disease
Dyslipidemia	Does not affect initial treatment recommendations	Does not affect initial treatment recommendations	

Note: ACE = angiotensin-converting enzyme, TIA = transient ischemic attack.

*When using 2 drugs specifically to lower blood pressure, use Table 7 to maximize the hypotensive effect. Short-acting calcium-channel blockers (i.e., regular-release formulations of nifedipine, diltiazem and verapamil) are not recommended for the treatment of hypertension.

†Commonly prescribed cardioselective β -blockers include atenolol, metoprolol and acebutolol.

risk alcohol consumption, defined as abstinence or moderate alcohol consumption (less than 2 standard drinks per day) is effective for heavy alcohol consumers. For those who are overweight, the single most effective intervention is weight loss. For comprehensive reduction of cardiovascular risk, a smoke-free environment is critical.

Table 7: Combinations of drugs for additive hypotensive effect in dual therapy*

Column 1	Column 2
Low-dose thiazide diuretic	β-blocker
Long-acting dihydropyridine calcium-channel blocker	ACE inhibitor†

*Combine any drug from column 1 with any drug in column 2. Avoid combinations of 2 drugs from the same column unless there is a specific indication (e.g., ACE inhibitor and β-blocker for patients who have had myocardial infarction). For triple or quadruple therapy in uncomplicated hypertension, all potential antihypertensive combinations of first-line drug classes are effective.

†Angiotensin receptor blockers are an alternative initial choice in patients with diabetes mellitus and nephropathy.

Table 8: Three most commonly prescribed drugs in each class of antihypertensive medication recommended as first-line therapy for uncomplicated hypertension*

Drug class and generic name	Dose, mg	
	Starting†	Moderate
Thiazide-like diuretics		
Hydrochlorothiazide	12.5	25
Chlorthalidone	2.5‡	25
Indapamide	1.25	2.5
Combinations of hydrochlorothiazide and potassium-sparing diuretic§		
Amiloride (50/5)	½ tablet	½ tablet
Triamterene (50/50)	½ tablet	1 tablet
Spirolactone (25/25)	½ tablet	1 tablet
β-Blockers		
Metoprolol	50¶	100–200¶
Atenolol	25	50
Acebutolol	100	400
ACE inhibitors		
Enalapril	5	20
Lisinopril	5	20
Ramipril	2.5	10
Dihydropyridine calcium-channel blockers		
Nifedipine XL	20	60
Amlodipine	2.5	10
Felodipine SR	2.5	10

*Frequency of drug prescriptions was obtained from IMS Canada data, which are based on prescriptions in 2001.

†Lower doses can be appropriate for older patients and for some other patient populations who might be expected to be more sensitive to the effects of the drugs.

‡Lower doses are preferred but not available in Canada.

§For medications in this drug class, the dose of each of the 2 drugs in a standard tablet (in milligrams) is given in column 1, and starting and moderate doses are given in terms of standard tablets.

¶Genetic variation in metabolism requires individualization of dose.

What pharmacotherapy would you recommend?

Drug treatment is recommended if the diastolic blood pressure is greater than 90 mm Hg and the patient has cardiovascular disease, 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 recommendation is to treat diastolic blood pressure of 100 mm Hg or more and systolic blood pressure of 160 mm Hg or more. Drugs suitable as initial treatment for hypertension are listed in Table 6 (and guidelines for combining drugs are given in Table 7; see also below). Table 8 summarizes the most common examples of the major drug classes and gives starting and moderate doses. β-blockers are not recommended as first-line therapy in those 60 years of age or older, and α-blockers are not recommended as first-line therapy. In these settings, these drugs are not as effective as diuretics in preventing cardiovascular complications. Short-acting calcium-channel blockers may increase cardiovascular complications and should not be used as anti-hypertensive agents. Low-dose thiazide diuretics are effective first-line drugs. Diuretics may not prevent cardiovascular complications if hypokalemia occurs.²⁴ Prevention of hypokalemia by using low doses and combinations of thiazide and potassium-sparing diuretics is important.

What blood pressure target would you set for Mrs. J?

Regardless of the approach used, perhaps the most important message from the recommendations is that we as physicians must do a better job in helping our patients to achieve the recommended blood pressure targets. Treatment targets for hypertension should be less than 140/90 mm Hg in general, less than 130/80 mm Hg in those with diabetes or renal disease, and less than 125/75 mm Hg in those with renal disease and proteinuria (greater than 1 g/24 hours).

Combinations of medications should be used if the initial choice of drug is only partially effective in lowering blood pressure to the target level. Switching to an alternative first-line agent should be considered only if there is intolerance. Table 7 indicates recommended combinations of first-line agents. For patients with uncomplicated hy-

Target blood pressure for hypertensive patients

Patient group	Target blood pressure (mm Hg)
Most patients	< 140/90
Patients with diabetes or renal disease	< 130/80
Patients with renal disease and proteinuria (> 1 g/24 h)	< 125/75

pertension who are receiving triple or quadruple therapy, all potential combinations of first-line antihypertensive agents are effective. Several factors may explain lack of response to appropriate single or combination medications: nonadherence, secondary hypertension, interfering drugs or lifestyle (e.g., weight gain, excess sodium or alcohol consumption), or office-induced increases in blood pressure (the “white coat effect”).

Case revisited

Mrs. J’s blood pressure is probably being adversely affected by the nonsteroidal anti-inflammatory drug (diclofenac) that she is receiving for her arthritis.²⁵ Acetaminophen should be tried to determine if it will provide adequate pain relief. Antihypertensive pharmacotherapy is indicated to reduce the risk of cardiovascular disease. The first-line choice for systolic and diastolic hypertension is a low-dose thiazide diuretic, an angiotensin-converting enzyme (ACE) inhibitor or a long-acting dihydropyridine calcium-channel blocker. β -Blockers are less effective in those over 60 years of age, such as Mrs. J, and should not be used as first-line therapy in this age group.

The patient is first given a low-dose thiazide diuretic, but her serum potassium level is 3.2 mmol/L on follow-up, so treatment is switched to a potassium-sparing diuretic combination drug. You anticipate that additional agents will probably be required to achieve a target blood pressure of less than 140/90 mm Hg; use Table 7 to select an ACE inhibitor as the second agent. You may have to discontinue the potassium-sparing diuretic to avoid hyperkalemia. If a third agent is required, either a β -blocker or a dihydropyridine calcium-channel blocker would be reasonable (Table 7).

Comments

Hypertension is a growing concern in our society. The increase in the prevalence of this condition is in part related to changes in levels of physical activity and diet and increases in obesity and the average age of the Canadian population. Major pharmacological advances that should have made blood pressure control easier have instead resulted in an overreliance on single-drug therapy. This has in turn been associated with deterioration in blood pressure control and increases in treatment costs.²⁶ Systematic approaches to managing hypertension are needed. Physicians should become familiar with combination antihypertensive therapy to optimize patient outcomes and prevent disease. Future efforts to improve blood pressure management need to incorporate greater participation by patients and multidisciplinary health care teams.

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Subgroups for the 2001 recommendations: Office Measurement of Blood Pressure: Carl Abbott (Chair), Karen Mann; Follow-up of Blood Pressure: Peter Bolli; Self-Measurement of Blood Pressure: Don McKay (Chair), Brenda Ens; Ambulatory Blood Pressure Monitoring: Martin Myers (Chair), Simon Rabkin; Routine Laboratory Testing: Tom Wilson; Echocardiography: George Honos; Global Risk Assessment: Stephen Grover; Endocrine Hypertension: Ernesto Schiffrin; Lifestyle Modification: Ellen Burgess (Chair), Robert Petrella, Rhian Touyz; Pharmacotherapy of Uncomplicated Hypertension: Richard Lewanczuk (Chair), James Wright, Bruce Culleton; Elderly subsection: J. George Fodor (Chair), Pavel Hamet, Robert Herman; Pharmacotherapy for Hypertension in Patients with Cardiovascular Disease: Frans Leenen (Chair), Simon Rabkin, James Stone; Diabetes and Hypertension: Jeffrey Mahon (Chair), Charlotte Jones, Pierre Larochelle, Richard Ogilvie, Sheldon Tobe; Renal and Renovascular Hypertension: Marcel Lebel (Chair), Ellen Burgess, Sheldon Tobe; Concordance Strategies for Patients: Ross D. Feldman (Chair), Jane Irvine.

Librarian: Angela Eady.

Implementation Committee: Denis Drouin (Chair), Seema Nagpal (Chair), Norman R.C. Campbell, Arun Chockalingam, Ross D. Feldman, Alain Milot, Carol Repchinsky, Terrance Ruddy, Guy Tremblay, Elinor Wilson.

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