

# 2006 Canadian Hypertension Education Program Recommendations

## What Are the New Messages?

Hypertension remains a significant health problem that is predicted to become a greater global burden in the next 20 years. The estimated total number of adults with hypertension in 2000 was 972 million. The number of adults with hypertension in 2025 is predicted to increase by about 60% to a total of 1.56 billion.<sup>1</sup> Hence, hypertension is an important public health challenge. Prevention, detection, treatment and control of this condition should receive high priority. The Canadian Hypertension Education Program (CHEP) has a mandate to improve hypertension management, to develop tools to aid health care professionals and to evaluate the impact of these activities. CHEP continues to provide the most current evidence-based recommendations to Canadian health care workers.

On behalf of the Evidence-based Recommendations Task Force of the Canadian Hypertension Education Program

This marks the seventh consecutive year that CHEP has updated recommendations for the diagnosis, management and treatment of hypertension. This year, CHEP's recommendations focus on adherence to antihypertensive therapy. In addition, based on new and additional evidence, a few changes relating to pharmacologic treatment were introduced. Furthermore, CHEP identified that treated hypertensive patients with masked hypertension (BP controlled in the office but not at home) should monitor home/self BP.

### *The new message identified in the 2006 recommendations*

This new message must also be incorporated into what remains as the older but still important, considerations for the diagnosis, management and treatment of the patient with hypertension, namely:

- Assess BP in all adults, at all appropriate visits
- The diagnosis of hypertension can and should be expedited
- Assess and manage global cardiovascular risk
- Treat to target

- Use combination of antihypertensive medications and lifestyle changes to achieve recommended targets

### *Key elements of the 2006 recommendation process*

The 2006 Canadian Hypertension Recommendations process incorporated all trials and epidemiologic studies published in the past 12 months, which were considered to be relevant for the diagnosis, management and treatment of individuals with hypertension. The impact of these studies was considered in the context of the cumulative evidence of the past 50 years of major clinical trials in hypertension and of prior iterations of the evidence-based Canadian Hypertension Recommendations developed over the past 25 years.

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For the 2006 CHEP Recommendations, the incorporated clinical studies included:

- the ASCOT-BPLA Study,<sup>2,3</sup>
- ALLHAT,<sup>4</sup>
- VALIANT Trial<sup>5</sup> and
- SHEAF Study,<sup>6</sup> as well as a number of smaller studies, systemic reviews and the Cochrane Database.

## *The new key messages in the 2006 Recommendations*

### *Improve patient adherence to antihypertensive therapy*

Adherence with an antihypertensive prescription can be improved by a multi-pronged approach, which includes:

#### *1. Assisting your patient to adhere*

- Teach patients to take their pills on a regular schedule, associated with a routine or daily activity (*e.g.*, brushing teeth).
- Simplify medication regimens using long-acting once-daily dosing.
- Utilize fixed-dose combination pills.
- Utilize unit-of-use packaging (*e.g.*, blister packaging).

#### *2. Assisting your patient to get more involved in his/her treatment*

- Educate patients and their families about their disease and treatment regimens verbally and in writing.
- Encourage greater patient responsibility/autonomy in regular monitoring of their BP.

#### *3. Improving your management in the office and beyond*

- Assess adherence to non-pharmacologic and pharmacologic therapy at every visit.
- Encourage adherence to therapy by health-care, practitioner-based telephone contact, particularly in the first three months of therapy.
- Coordinate with work-site health-care providers, if available, to improve hypertension management and monitoring.

These recommendations were based on an initial survey of related studies from PsycInfo (including 210 original papers and reviews) and Medline (including 769 original papers and reviews) over the past 3 years.

Low adherence of patients to prescribed, self-administered antihypertensive drugs is a major problem that contributes, in part, to poor control of hypertension. In general, patients who are prescribed self-administered medications typically take less than half the prescribed dose. Efforts to assist patients to follow medication protocols may improve the efficiency of care and enhance the benefits. In Canada, suboptimal control of hypertension is attributed, in part, to patients who stop taking their antihypertensive drugs after one year. Accordingly, adherence needs to be stressed and this is a major focus of the 2006 CHEP recommendations.

With the cut-off point between normal and high BP being pushed increasingly downward, particularly for patients with multiple cardiovascular risk factors, most hypertensive patients need more than one antihypertensive agent to reach target BP. Furthermore, guidelines indicate that low doses of multiple drugs may be even more efficacious than higher doses of fewer drugs.

The increase in complexity of self-administration, with the use of multiple drugs and the consequent likelihood for reduction in adherence remains an ongoing problem. A possible way to simplify dosages involves the use of fixed-dose combination pills (*i.e.*, pills that include two or more drugs in fixed proportions in the same formulation). Rational antihypertensive drug combinations are based on their ability to produce additive BP lowering and to reduce the incidence of dose-dependent side effects.<sup>7</sup>

Other interventions that aim to simplify dosages involve utilizing unit-of-use packaging (*e.g.*, blister packaging of several medications in fixed combination to be taken together). For example, a recent retrospective analysis of medication adherence by Taylor and Shoheiber<sup>7</sup> compared 2,754 patients who were prescribed a single capsule, fixed-dose combination of amlodipine besylate/ benazepril HCl, with 2,978 patients who were prescribed an angiotensin-converting enzyme (ACE) inhibitor and a dihydropyridine calcium channel blocker as separate drugs. Results indicated improved adherence and fewer medical resource requirements for the fixed-dose combination pill group. Therefore, to improve adherence, the 2006 CHEP Recommendations suggest simplifying medication regimes.<sup>8</sup>

While once-daily dosing and utilizing electronic medication aids are currently recommended as ways of simplifying the medication regime and improving adherence, the increase in complexity of self-administration with the use of multiple drugs and the consequent possibility for reduction in adherence remains a problem requiring further attention.

A systematic review of randomized trials evaluating the effects of fixed-dose combination pills

and unit-of-use packaging<sup>9</sup> concluded that in 12 of 15 trials identified, there were trends to improve clinical and/or adherence outcomes. While the trials reviewed were heterogeneous in their settings, the medical conditions being treated and the outcome measures used, three of the four trials that involved unit-of-use packaging for the treatment of hypertension reported clinically significant reductions in BP. Although interpretation of these findings is limited by the methodologic quality of the studies

(most were small or had inadequate follow-up time), those with greater methodologic rigor were typically associated with larger improvements in measures of adherence and clinical outcomes, including BP reduction.

### *Looking at patient follow-up*

The proposed revision to the recommendations in regards to encouraging a role of telephone follow-ups is primarily based on generalization from management of dyslipidemia and specifically based on the systematic review by Schedlbauer *et al.*<sup>10</sup> In that review, reinforcement and reminders via telephone and postal backups were the interventions of interest in three studies selected among 2,380 articles. Weekly phone calls were reported as improving adherence to lovastatin and colestipol in the intervention group judged by prescription refill rate (rate was improved by 24%; 63% in the intervention group vs. 39% in the control group, *p*-value less than 0.05; *n* = 30).<sup>11</sup> It is notable that telephone and postal reminders in the remaining two RCT did not result in any significant improvement (79.7% in the intervention group vs. 77.4% in the control group, *p*-value reported as non significant;

n = 4,548<sup>12</sup>; and 88% in the intervention group vs. 82% in the control group, p = 0.32, n = 120).<sup>13</sup>

However, the study by Faulkner *et al.*<sup>11</sup> was viewed as being of higher quality than the other two (notwithstanding the smaller sample size) and is the primary basis of the proposed revision in the 2006 CHEP Recommendations. In addition, studies that predominantly enrolled adherent patients will not be able to improve the adherence of these patients regardless of the intervention.

*New and additional evidence in the pharmacological treatment of patients with hypertension*

Beta blocker therapy is strongly recommended in hypertensive patients of all ages who have specific indications such as post MI, angina and congestive heart failure. However, new evidence further supports the use of beta blockers as a first-line therapy in uncomplicated hypertension only in patients younger than 60 years old. These findings were based on recent meta-analysis.<sup>14,15</sup> The recommendation is not new, but is further supported by the new evidence. Trials demonstrate the inferiority of beta blockers in reducing cardiovascular events in uncomplicated hypertension in older patients compared to diuretics, angiotensin receptor blockers and calcium channel blockers (CCB).

Additional antihypertensive drugs should be used if target BP levels are not achieved with standard dose mono-therapy (Grade B). Add-on drugs should be chosen from first-line choices. Useful choices include a thiazide diuretic or CCB

with either an ACE inhibitor, ARB or beta blocker (Grade D and/ or Grade C for the combination of dihydropyridine CCB and ACE inhibitor). Caution should be exercised in combining a non-dihydropyridine CCB and a beta blocker (Grade D).

This year, the grade of evidence supporting the combination of a dihydropyridine CCB and an ACE inhibitor was increased from a D to a C. This change is based in large part on the results of the Anglo Scandinavian Cardiac Outcomes

*Patients with uncontrolled hypertension and cardiac failure may benefit from combined ACE inhibitors and ARBs.*

Trial-Blood Pressure Lowering Arm (ASCOT-BPLA), which showed significantly lower rates of coronary and stroke events in individuals allocated an amlodipine-based combination drug regimen than in those allocated an atenolol-based combination drug regimen.<sup>2,3</sup> This trial was complicated by the use of beta blockers as initial therapy in a predominantly older study population. Therefore, the design of the trial would be expected to favour the amlodipine-based combination therapy.

Initial therapy in patients with hypertension who have had a recent ST-elevation MI or non ST-segment elevation MI should include both a beta adrenergic antagonist and an ACE inhibitor. An ARB can be used if the patient is intolerant to an ACE inhibitor.

These recommendations are based on findings from the VALsartan In Acute myocardial infarction (VALIANT) Trial,<sup>5</sup> which assessed effects of valsartan or captopril, or the combination of the two, in patients with post-MI with heart failure or systolic dysfunction or both. Total mortality and the combined secondary end point of cardiovascular death (CVD), MI or heart failure were not significantly different in the three groups after 24.7 months of follow up. Valsartan

was not inferior to captopril in terms of total mortality and cardiovascular death, MI and heart failure. Hence, valsartan can be considered an alternative treatment to ACE inhibitors in these patients.

Although ACE inhibitors combined with ARBs have a positive role in the management of cardiac failure, a higher rate of hospitalization for hypotension, hyperkalemia and worsening renal failure has been seen in clinical practice. Careful monitoring is required to ensure patient safety during this combination of therapies.

### *Potentially important in the diagnosis and management of hypertension*

#### *Home/self measurement of BP*

Certain issues appeared to dominate the literature in the area of home/self-measurement of BP in 2004-2005. In 2004, release of the SHEAF study demonstrated not only the prognostic strength of home BP measuring, but provided for the first time data documenting the mortality risk of masked hypertension.<sup>16</sup> Masked hypertension is defined as clinic BP < 140/90 mmHg (three measurements at two office visits) and home BP > 135/85 mmHg (three measurements in the morning and the evening over two days). More recent analyses of SHEAF data focused on the number of measurements necessary to determine masked hypertension.<sup>17</sup> The SHEAF data provide perhaps the clearest evidence that the risk profile of those with masked hypertension is similar to the risk profile of those with sustained hypertension.

*Studies have shown that the value of home BP is better than clinic BP. Home heart rate has also been shown to be a powerful independent predictor of cardiovascular risk.*

The prognostic significance of home BP measurement was demonstrated again in an 11 year follow-up study of elderly patients.<sup>18</sup> The study results suggest that the prognostic value of home BP is better than clinic BP and is similar to daytime ambulatory BP. Results further demonstrated the importance of the setting for BP measurement (home vs. clinic), strengthening the need to emphasize “home” rather than “self” in the terminology used to describe these measurements.

With respect to prognosis, more data from the Ohasama Study<sup>19</sup> show that in addition to the BP measured at home, the home heart rate is a powerful independent predictor of cardiovascular risk.

The concept of masked hypertension is not new. In general, the term describes the phenomena when clinic BP is normal, but out-of-office readings are in the hypertensive range. Masked hypertension has been variously called: reverse-white coat hypertension, isolated home or isolated ambulatory hypertension, depending on the type of method used to find it. Several of the issues and the history surrounding masked hypertension were discussed in the 2005 subcommittee report.

Important issues still to be resolved centre around how to define ‘Masked hypertension’ in a patient and what method (ambulatory BP or home BP) is most appropriate for making the diagnosis.

## *Old but still important messages in the 2006 Recommendations*

### *1. Measure BP in all adults at all appropriate visits.*

In the last survey of BP (1985-1992), 43% of adults with high BP were not aware that their BP was elevated. This places a large proportion of the Canadian population at preventable risk for cardiovascular disease due to uncontrolled hypertension. Recent data from the Framingham Study has indicated that over 90% of normotensive participants aged 55 to 65 years developed hypertension over the 20 to 30 years of follow up. Forty-six per cent of Canadians aged 55 to 65 years already have hypertension. It is, therefore, expected that the vast majority of Canadians will develop hypertension. Measuring the BP of all adults every time they visit is an important mechanism to detect hypertension and an opportunity to discuss preventive strategies using lifestyle modifications.

### *2. The diagnosis of hypertension can and should be expedited.*

A diagnosis of hypertension can be made at an initial hypertension-related visit for patients with BP >140/90 mmHg and with one of the following: target organ damage, chronic kidney disease or diabetes mellitus. If BP > 180/110 mmHg, hypertension is diagnosed.

A diagnosis of hypertension can be made at a second visit. For patients with BP between 160-179 mmHg and 100-109 mmHg (and not already diagnosed based on the criteria above), a diagnosis can be made at a third visit.

Diagnosis can be expedited by home/self measurement of BP. Office-based diagnosis of hypertension has remained the gold standard for the diagnosis of hypertension. However, it is now firmly established that out-of-office modalities for BP

measurement are as, or more, effective in assessing the prognostic importance of BP elevations. To be effective, these technologies, including automatic ambulatory BP monitoring and home/self blood BP monitoring must be used by properly educated practitioners and this assumes the use of validated, properly calibrated equipment. However, when available (and properly used) these modalities are effective and can expedite the diagnosis of hypertension, especially for those patients with Level I hypertension (and without diabetes, chronic kidney disease or target organ damage) that would otherwise require up to six visits and six months prior to a diagnosis being made.

### *3. Assess and manage global cardiovascular risk.*

Over 90% of hypertensive patients have additional cardiovascular risks that require assessment and management. Acetylsalicylic acid should be considered in controlled hypertensive patients. Statins are recommended in hypertensive patients with established cardiovascular disease or the presence of more than three other cardiovascular risks.

### *4. Lifestyle modifications are the cornerstone of antihypertensive therapy.*

Lifestyle modifications are safe, inexpensive and can prevent hypertension and lower BP in hypertensive patients. When combined with drug therapy, they may result in better BP control and improved quality of life. Many of the individual factors, if successfully adopted, may lead to BP changes in the magnitude of that associated with single-drug therapy. Although each factor typically has a modest effect, the combined effects may be substantial. From a public health perspective, even a small reduction in BP should

have a significant, beneficial effect on the occurrence of hypertension and its complications.

### Lifestyle changes recommended by CHEP to reduce BP include:

- Maintaining a diet low in salt and saturated fats and high in fresh fruit and vegetables and low in fat dairy products (DASH diet).
- 30 to 60 minutes of continuous or accumulated moderate intensity dynamic exercise (such as walking, jogging, cycling or swimming) four to seven days of the week.
- Weight reduction in those who are overweight.
- Reduction in alcohol consumption in those who drink more than two drinks per day.
- A smoke free environment and cessation to reduce cardiovascular risk.


### 5. Treat to target.

Population surveys demonstrate that small proportions of patients have BP treated to target resulting in suboptimal cardiovascular risk reduction. In particular in high risk patients greater benefits occur with achieving recommended targets. The systolic BP target is the more difficult to achieve in most patients. Achieving systolic BP targets, however, is important, as systolic BP is at least as important if not more so than diastolic BP in determining cardiovascular prognosis.

The current recommended target to reduce blood pressure is:

- < 140 mm Hg systolic and < 90 mmHg diastolic in general.
- < 130/80 mmHg in patients with diabetes or chronic kidney disease.

### 6. Use combinations of medications and lifestyle modifications to achieve BP targets.

Most patients require two or more drugs to achieve recommended BP targets. In general, the average reduction in BP with a single BP lowering medication is 10/5 mmHg. Combining medications is, therefore, to be expected in the therapy of hypertension. Lifestyle modifications can reduce the number and doses of medications that are required for BP control and should be recommended for all hypertensive patients. 

## Take-home message

As in previous years, it needs to be reiterated that the CHEP hypertension management recommendations are based solely on efficacy data. Considerations relating to individual patient/ physician preferences and cost-effectiveness of different drug classes have not been a component of this process and need to be considered by the physician and patient when individualizing therapy.

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