Special Focus Issue on Hypertension Guidelines

A Canadian Perspective on the Eighth Joint National Committee (JNC 8) Hypertension Guidelines

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The Eighth Joint National Committee (JNC 8) guidelines process presents a striking contrast to the Canadian Hypertension Education Program (CHEP). Whereas 10 years have passed since the last update of JNC 7, the CHEP guidelines have been revised annually since 1999. During the first few years, CHEP made numerous revisions to its forerunner, the 1993 guidelines of the Canadian Hypertension Society. Thereafter, the annual reviews focused on the few important developments in the previous 12 months, leading to specific changes in the existing recommendations. As with JNC 7, the CHEP guidelines have been comprehensive, covering both the diagnosis and treatment of hypertension. In contrast, JNC 8[1] addresses thresholds for initiating drug therapy but says nothing about the actual measurement of blood pressure (BP) for making a diagnosis of hypertension.

Both CHEP 2013[2] and JNC 8 take an evidence-based approach to evaluating the literature supporting individual recommendations. CHEP follows a long tradition of evidence-based guidelines in Canada starting with an evidence-based approach developed in 1975.[3] Since then, all Canadian hypertension guidelines have been based on a rigorous assessment of the evidence. The JNC 8 paper stated that "the panel limited its evidence review to RCTs"(randomized controlled trials); nonetheless, many of the JNC 8 recommendations were made based upon grades C and E evidence, the latter being expert opinion. In adhering to an evidence-based approach, CHEP also formulates recommendations on lower grades of evidence when data from RCTs are not available.

WHAT JNC DID NOT INCLUDE

Many experts believe that the foremost issue in hypertension today is how to measure BP. The value of office BP measurement has been questioned in recent hypertension guidelines.[4–6] Most noteworthy are the conclusions of the British National Institute for Health and Clinical Excellence (NICE) document, which stated that a diagnosis of hypertension should be based primarily on readings obtained using 24-hour ambulatory BP monitoring (ABPM). Following a detailed assessment of the available evidence, the NICE panel concluded that measurement of BP in the office was inherently inaccurate, subject to a white-coat response, and significantly less useful in determining future cardiovascular risk in relation to an individual's BP status in comparison with 24-hour ABPM or home BP.

CHEP first recommended 24-hour ABPM for the diagnosis of hypertension in its 1999 guidelines.[7] The role of ABPM became more prominent in the CHEP 2005 update,[8,9] which stated that the preferred method for making a diagnosis of hypertension should be 24-hour ABPM. In CHEP 2013, home BP readings are included as a method for the diagnosis of hypertension. JNC 8 says nothing about the limitations of conventional office BP measurement. This omission is somewhat paradoxical since the United States was the first country to provide funding for 24-hour ABPM from a government agency, in this case under Medicare in 2001.

THRESHOLDS AND TARGETS FOR DRUG THERAPY

The thresholds for initiating drug therapy based on office BP are quite similar for both JNC 8 and CHEP 2013 (Table). However, CHEP also provides thresholds for treatment based on 24-hour ABPM and home BP readings. When it comes to the targets for treatment, the two guidelines diverge. In its first recommendation, JNC 8 proposes a unique target for systolic BP (SBP) of 150 mm Hg instead of 140 mm Hg, which has been in use throughout the modern era of antihypertensive therapy. This single innovation dominated initial commentaries on JNC 8. From a Canadian perspective, the benefits of national guidelines in contributing to a reduction in cardiovascular mortality have been almost without precedent. From 1992 to 2004, there has been a progressive decrease in mortality from stroke (−35%), heart failure (−27%), and myocardial infarction (−45%), with the steepest decline occurring since 1999 when the annual CHEP recommendation process was initiated.[10] The assumption that a lower SBP target 140 mm Hg may lead to harm is also offset by the epidemiologic evidence in the context of relatively low mean BP levels reported in recent Canadian population surveys in the community.[11,12]

Even in studies involving older hypertensive patients cited in the JNC 8 report, ABPM substudies reveal a marked, white coat effect with the mean baseline ambulatory SBP at entry being 22 mm Hg to 36 mm Hg lower than the carefully recorded clinic

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TABLE. Comparison of JNC 8 Recommendations to CHEP 2014 Recommendations

Recommendation 1 JNC 8: Age 60+. Rx threshold is ≥150/90 mm Hg and target is <150/90 mm Hg.
CHEP: For hypertension of all ages, Rx threshold is ≥160/100 mm Hg and target is <140/90 mm Hg unless age 80+, then target for systolic BP is <150 mm Hg. Rx is indicated for BP 140/90–159/99 mm Hg in patients with cardiovascular risk factors or target organ damage. Otherwise, use nonpharmacologic therapy for BP 140–159/90–99 mm Hg in association with low cardiovascular risk and no target organ damage.
Recommendation 2 JNC 8: Age <60. Rx threshold is diastolic BP ≥90 mm Hg and target is <90 mm Hg.
CHEP: Same as recommendation 1.
Recommendation 3 JNC 8: Age <60. Rx threshold is systolic BP ≥140 mm Hg and target is <140 mm Hg.
CHEP: Same as recommendation 1.
Recommendation 4 JNC 8: For chronic kidney disease, Rx threshold is ≥140/90 mm Hg and target is <140/90 mm Hg.
CHEP: Same.
Recommendation 5 JNC 8: For diabetes, Rx threshold is ≥140/90 mm Hg and target is <140/90 mm Hg.
CHEP: For diabetes, Rx threshold is ≥130/80 mm Hg and target is <130/80 mm Hg.
Recommendation 6 JNC 8: In the general nonblack population with diabetes, initial Rx should be with a thiazide-type diuretic, CCB, ACE inhibitor, or ARB.
CHEP: Same, but also recommends a β-blocker for patients <60 years.
Recommendation 7 JNC 8: In the general black population with diabetes, initial Rx should be with a thiazide-type diuretic or CCB.
CHEP: In black patients without diabetes same as recommendation 6, but also includes an ARB and β-blocker if <60 years.
Recommendation 8 JNC 8: In all patients with chronic kidney disease, include an ACE inhibitor or ARB as part of Rx.
CHEP: Same but applies only to patients with chronic kidney disease with proteinuria.
Recommendation 9 JNC 8: Treat to attain and maintain target BP.
CHEP: Same as JNC 8.

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; CHEP, Canadian Hypertension Education Program; DBP, diastolic blood pressure; JNC 8, Eighth Joint National Committee; Rx, pharmacologic treatment; SBP, systolic blood pressure.

BP.[13] Thus, reducing BP to relatively low levels within the normal range in placebo-controlled studies did not seem to adversely affect clinical outcomes. There was no evidence that patients in these trials were harmed because their (24-hour) BP values were much below the actual target BP in the protocols. The Perindopril Protection Against Recurrent Stroke Study (PROGRESS)[14] also compared antihypertensive therapy with placebo in elderly patients who had experienced a recent stroke. There was a consistent decrease in clinical events in patients in relation to baseline BP, with the lowest event rate in the quartile with the lowest baseline SBP (<120 mm Hg) who went on to have a median office BP of 112/72 mm Hg on therapy. Thus, having lower BP on treatment would appear to be beneficial in the general hypertension population and not harmful, as postulated in JNC 8.

It is quite likely that some hypertensive patients may be receiving more antihypertensive medication than required to protect against future cardiovascular events as a consequence of inappropriate treatment of white-coat hypertension. However, there is an alternative to raising the threshold for initiating drug therapy for all patients simply because office BP is inaccurate and incorrectly diagnoses hypertension in about 25% of patients with mild increases in BP. The simple answer is found in the NICE recommendations,[4] wherein the solution is not to raise the threshold for defining hypertension but to perform a better assessment of an individual's BP in order to avoid unnecessary drug therapy. The CHEP 2013 guidelines are consistent with the approach recommended by NICE except CHEP continues to maintain a role for office BP measurement in the diagnosis of hypertension.

DIFFERENCES BETWEEN JNC 8 AND CHEP IN THE MANAGEMENT OF SUBGROUPS

In recommendation 5 from JNC 8, the target office BP of <140/90 mm Hg for patients with hypertension and diabetes is also different from the target of <130/80 mm Hg in CHEP (Table). In recent years, various guidelines have made different interpretations of the evidence for greater benefit when treating diabetic patients with hypertension to lower BP targets. Regarding the primary outcome in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial,[15] there was no added benefit to treating hypertensive patients with diabetes to a target BP <120/80 mm Hg compared with <140/90 mm Hg. CHEP did not increase the existing target BP of <130/80 mm Hg because of these results. One reason is that the ACCORD trial compared <140/90 mm Hg with <120/80 mm Hg. The actual SBP levels achieved on treatment in ACCORD were 133.3 mm Hg vs 119.5 mm Hg. Moreover, the findings in the Hypertension Optimum Treatment (HOT) study,[16] provided further support for the target BP of <130/80 mm Hg.

In HOT, patients with a mean baseline diastolic BP of ≥105 mm Hg were randomly allocated to treatment with 1 of 3 target diastolic BP values: <90 mm Hg, <85 mm Hg, or <80 mm Hg. The overall findings in this trial were negative, primarily because the achieved differences in BP on drug therapy were not sufficiently different to answer the question being posed. However, 1501 of 18,790 patients enrolled in the HOT trial had both hypertension and diabetes. In this numerically large subgroup, there were significantly fewer cardiovascular events when diastolic BP was reduced to a target of <80 mm Hg compared with <90 mm Hg.

JNC 8 excluded these findings because they considered that the size of the subgroup was too small and that the analysis was post hoc and not prespecified. However, the article describing the design of the HOT trial at the time of its initiation[17] did state that the data analysis would include outcomes in relation to target diastolic BP *in patients with diabetes mellitus*, thus making this analysis prespecified. As outlined in detail in a recent publication,[18] CHEP has maintained a target BP of <130/80 mm Hg for treating hypertensive patients with diabetes while recognizing the need for further research in this area.

There are some minor differences in the choice of antihypertensive medications for different types of patients (Table). In recommendation 6, JNC 8 does not include β-blockers as initial therapy for hypertensive patients who are younger than 60 years, whereas CHEP 2013 includes this option. It is true that the benefits of treating younger patients with β-blockers are somewhat uncertain. As a consequence, some guidelines such as NICE[4] concur with the JNC 8 approach, whereas others, such as ESH/ISH 2013,[5] agree with the CHEP recommendations. The evidence for the CHEP position on β-blockers has recently been evaluated in a formal meta-analysis.[19]

Another difference in the approach to the initiation of drug therapy can be seen in the treatment of black patients with both hypertension and diabetes. Whereas JNC 8 recommends only initiating therapy with thiazide-type diuretics or calcium channel blockers (CCBs) in this population, CHEP 2013 also includes angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) as first-line therapy. CHEP bases its position on the additional benefit provided by ACE inhibitors and ARBs beyond lowering BP, including protection against both renal and cardiovascular disease.

One difference between JNC 8 and CHEP 2013 appearing in Table 6 of the JNC publication is incorrect. The CHEP 2013 guidelines did include long-acting CCB drugs as initial treatment for hypertension in the general population younger than 80 years. This information appears to have been inadvertently omitted.

CONCLUSIONS FROM A CHEP PERSPECTIVE

One might ask what impact will JNC 8 have on the diagnosis and treatment of hypertension in clinical practice? Most of the recommendations are either similar to the consensus of existing guidelines, including CHEP, or else contain relatively minor modifications, which are unlikely to have much impact on patient care. The one exception is the higher threshold for the target BP with antihypertensive therapy. Much of this article has focused on the currently available methods for measuring BP given the mounting evidence that 24-hour ABPM and home BP are significantly better than office BP in determining future cardiovascular risk in relation to BP status. Debating different thresholds for the initiation of drug therapy and target BP on the basis of office BP readings may already be irrelevant as 21st-century techniques for the measurement of BP replace the mercury manometer and other manual sphygmomanometers currently in use. The debate on target BP is already shifting to how low treatment should reduce ambulatory BP and home BP with special interest in nocturnal BP readings. As the management of hypertension continues to evolve, there would seem to be little advantage in recommending higher targets for office BP, especially if the effort required to implement the new guidelines into clinical practice is taken into consideration.

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