Hypertension in the Elderly

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It is worthwhile to review the issue of hypertension in the elderly not only because it will become an ever-increasing problem with our aging population, but also because of the robust database currently at our disposal concerning improved risk assessment and efficacious therapy.

The Epidemiology

Generally, the elderly are considered those above 65 years of age. Dealing with hypertension in this age group, we quickly realize that this disease is a major epidemic with far-reaching consequences for both the health status of this segment of the population as well as our health care system.

The Canadian Heart Health Survey ascertained that among people in the age group 65–74 years, 56% of males and 58% of females were hypertensive.1 This survey defined hypertension as systolic blood pressure (SBP) > 140mmHg or diastolic blood pressure (DBP) > 90mmHg, or current treatment with a prescription antihypertension medication or non-pharmacological treatment of blood pressure (weight control or sodium/salt restriction). The problem of hypertension in the elderly will continue to increase steadily in importance. During the next 20 years, there will be a 6% increase in the number of Canadian elderly, with a corresponding increase in the number of hypertensive patients requiring medical care (Table 1).

The treatment of hypertension in this population must incorporate many aspects that will influence their clinical management. Elderly hypertensives have reduced distension and elasticity in the large capacitance arteries, which results in increased pulse wave velocity and early return of pulse wave reflection in systole. Thus, the blood pressure has a tendency to fluctuate, creating an increased stress on the vascular system. These patients usually have lower intravascular volume, lower renal blood flow, lower plasma renin activity and higher peripheral vascular resistance. Because the elderly have reduced baroreceptor responsiveness compared to younger individuals, they are also more likely to have asymptomatic postural changes. Postural hypotension was found in 10.4% of respondents in the Systolic Hypertension in the Elderly Program (SHEP) at one minute after rising from a seated position.2 It is therefore likely that a higher proportion would manifest postural hypotension after rising from supine position. The potential for orthostatic hypotension should be kept in mind when initiating antihypertensive treatment and choosing dosages in elderly patients.

Is Hypertension in Elderly Associated with Increased Cardiovascular Risk?

Not so long ago, there were widely held views that older patients required higher blood pressure to perfuse narrowed and stiffened arteries. In fact, textbooks published in the mid-’70s to early ’80s defined hypertension in those older than 65 as a blood pressure of 210/110mmHg or more3, and stated that “blood pressure level of 180/100 is less abnormal and menacing at the age of 70 than at 45”.4

Today we have a wealth of information documenting that total mortality, from both coronary disease and stroke, is much higher among elderly hypertensives than in comparable middle-aged populations. In particular, the risk of cerebrovascular events associated with elevated systolic blood pressure is now well documented.

The Framingham Study5, the Multiple Risk Factors Intervention Trial6 and a recent meta-analysis by Staessen et al.7 showed the importance of isolated systolic hypertension (ISH) and concluded that elevated systolic pressure in the elderly is more significant than elevated DBP. Pulse pressure (PP), defined as the systolic-diastolic BP difference, also widens with age8 since DBP tends to remain constant or decline after the fifth or sixth decade.9 Both ISH and wide pulse pressure in the elderly are markers of age-related vascular damage. Each of these markers is an independent cardiovascular (CV) risk factor that reflects similar diagnostic and prognostic information.10,11 Framingham Study data support the use of PP in risk prediction, indicating that for any given level of SBP > 130mmHg, those with higher PP had a significant increase in coronary heart disease (CHD) risk.10

While the above analysis slightly favoured PP over SBP as a predictor of CHD, a recent study found that after adjustment for all potential confounders, SBP was a better predictor of CV events than DBP or pulse pressure.12 There is, however, one caveat to this finding: The evidence for a strong

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**Table 1**

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>2000</td>
<td>12.84</td>
</tr>
<tr>
<td>2010</td>
<td>14.61</td>
</tr>
<tr>
<td>2020</td>
<td>18.59</td>
</tr>
<tr>
<td>2030</td>
<td>22.39</td>
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Taken from Internet site: www.hccsj.nf.ca/seniors/demogr.htm
positive association between increased SBP and greater CV risk is not available for the very old (i.e., people over age of 80). Starr et al. observed that among 603 men and women aged 70–88, the survival after four years was better in those with initial casual SBP below 150mmHg than in those with higher BP levels.

Is Treatment of Hypertension in Elderly Beneficial: What are the Target Values?

There have been several large trials showing the beneficial effect of therapy in elderly hypertensive patients. All of these trials documented a significant reduction (range ~17–40%) in the incidence of major cardiovascular events in the active treatment arm.

The only randomized clinical trial addressing the issue of treatment targets has been the Hypertension Optimal Treatment study. The trial addressed two issues: how far pressure should be lowered, and whether there is any benefit to adding low-dose (75mg) Aspirin to
the antihypertensive treatment. A total of 18,790 men and women aged 50–80 years were randomized to one of three diastolic pressure ranges (below 80, 80–85 or 86–90mmHg). The trial arms were further divided into either placebo or active Aspirin groups. Based on intention-to-treat analysis of the primary endpoint, no difference was seen between the three groups. However, when data from all three groups were pooled, the optimum effect of Aspirin on major cardiovascular events was seen in patients with DBP of 83mmHg and systolic pressures of 138.5mmHg. At one year, the percentage of patients in the elderly subgroup who were at target BP levels was higher in all three groups. Patients with heart disease and diabetes mellitus benefited most if their diastolic pressures were reduced to below 80mmHg.

Based on this evidence, the Canadian Hypertension Working Group recommends reducing BP to less than 140/90mmHg in most patients, including the elderly. The goal for patients with diabetes or renal dysfunction is less than 130/80mmHg.

Non-pharmacological Treatment of Hypertension in Elderly

Salt restriction and weight reduction are efficacious interventions in the elderly. It is desirable to reduce the average Canadian daily salt intake of 8–12g daily to less than 5g/day. However, we must keep in mind that more than 80% of salt intake is involuntary, as it is consumed from industrially processed foods. This can make it difficult for the patient to achieve the required reduction of dietary sodium intake. Clearly, without the cooperation of the government and food industry, the future reduction of the population’s salt intake will be hard to implement. Better labeling of food products and incentives for the industry to gradually reduce the salt content of processed foods will help.

It should also be kept in mind that most strategies for achieving permanent weight reduction are unsuccessful. Since effectiveness of non-pharmacological intervention is usually unsatisfactory, effective pharmacological treatment should not be postponed. Only if the patient succeeds in reducing excessive body weight and salt intake should drug therapy be modified or possibly withdrawn.

Pharmacological Treatment of Hypertension in Elderly

For uncomplicated hypertension without contraindications, low-dose thiazide diuretics (e.g., 12.5–25mg hydrochlorothiazide) or long-acting dihydropyridine calcium channel antagonists are recommended as first-line therapy. Since it is possible for even low-dose diuretics to lead to hypokalemia (potassium concentration < 3.5mEq/L), close monitoring is necessary and potassium-sparing diuretics or potassium supplements may be required for those at risk. In the SHEP study, patients who were treated with 12.5–25mg of chlorthalidone o.d. had a significant reduction in the incidence of strokes to 5.2% compared to 8.2% in the placebo group. There was also a one-quarter to one-third reduction in cardiovascular events in the active treatment group. Data from several trials have shown that long-acting dihydropyridine calcium channel blockers may be a substitute first-line therapy for patients with ISH who cannot take a diuretic or who show poor response to diuretic therapy.

Angiotensin-converting enzyme (ACE) inhibitors are considered an alternative therapy when diuretics or calcium channel blockers are ineffective, contraindicated or not tolerated, as well as for cases of recent myocardial infarction (MI). ACE inhibitors have been shown to be comparable to diuretics and calcium antagonists in reducing blood pressure, and to favourably affect cardiovascular outcomes in the elderly. Angiotensin II receptor antagonists (ARBs) are well tolerated and produce clinically significant reductions in blood pressure, with lower incidence of treatment-related cough. Although up until recently there was no evidence of their effects on incidence of CV outcomes in the elderly, the results of two important trials addressing this issue were released just this year.

LIFE Study

The Losartan Intervention For Endpoint (LIFE) reduction in hypertension study was a double-blind, randomized, parallel-group trial of more than 9,000 patients with essential hypertension and electrocardiographic evidence of left ventricular hypertrophy, who were assigned to once-daily losartan-based (n=4,605) or atenolol-based (n=4,588) therapy. The trial was designed to last for at least four years and until 1,040 patients had a primary CV event (death, MI, stroke). Because the average age of the respondents was 66.9 years, LIFE can be considered a study of elderly hypertension. This trial addressed a relatively high-risk group; average blood pressure was 174/97mmHg and only those patients who had EKG signs of left ventricular hypertrophy were eligible.

Results showed that treatment with losartan reduced the incidence of stroke and new-onset diabetes by 25% compared to beta-blocker therapy with atenolol. There was a significant difference between study groups in the primary composite endpoint that was driven by the difference in rates of stroke; rates of MI and cardiovascular mortality were not significantly different between the two groups.

These results are particularly interesting because both losartan and atenolol provided similar blood pressure lowering effects, so losartan therapy’s benefits on stroke prevention must be due to effects beyond simply lowering blood pressure. Another important benefit has been the significantly reduced incidence of new-onset diabetes by 25% in the losartan-treated group.

SCOPE Study

The primary objective of The Study on Cognition and Prognosis in the Elderly (SCOPE) was to assess the effect of the angiotensin II type I receptor blocker candesartan cilexetil (8–16mg once daily) on major CV events in elderly patients (70–89 years) with mild hypertension.
(DBP 90–99 and/or SBP 160–179 mmHg). Compared to the LIFE trial, the multicentre, prospective, double-blind, parallel-group SCOPE addressed a lower risk population. The secondary objectives of SCOPE were to test the hypothesis that antihypertensive therapy can prevent cognitive decline (as measured by the Mini Mental State Examination) and dementia, and to assess the effect of therapy on total mortality, MI, stroke, renal function and hospitalization.

A total of 4,964 patients from 15 participating countries were recruited during the randomization phase of SCOPE, exceeding the target population of 4,000. The mean age of the patients at enrolment was 76 years, the ratio of male to female patients was approximately 1:2, and 52% of patients were already being treated with an antihypertensive agent at enrolment. Patients were randomized to candesartan 8mg or hydrochlorothiazide 12.5mg. When necessary, the drugs were titrated upward and other drugs could be added if target BP levels were not achieved.

In this head-to-head comparison, the candesartan therapy proved to be not only as effective in reducing CV events as therapy with thiazides, but also significantly better in preventing non-fatal cerebrovascular strokes (~28%). It is important to note that SCOPE was planned as a placebo-controlled trial and it was not powered to detect differences versus an actively treated group. For sufficient power to detect such differences over the three- to five-year duration of this study, the trial would have needed to enroll approximately 7,000 additional patients. However, if the trial has shown an 11% reduction of major CV events and a 28% reduction of nonfatal strokes against these odds, it documents good efficacy as well as the importance of considering ARBs as first-line therapy for elderly hypertensives. Another important observation in SCOPE was the beneficial effect of candesartan therapy on preventing decline of cognitive function in a subgroup of patients.

SCOPE complements the LIFE study in confirming the beneficial effect of ARBs in treating not only high-risk elderly hypertensives, but also those with mild hypertension and with relatively low global CV risk.

Conclusions

As of this year, any doubts about the justification of aggressive treatment of hypertension in the elderly were put to rest. A robust database provides scientific evidence that non-pharmacological and pharmacological strategies can prevent or postpone the occurrence of major CV events. For the treatment of elderly hypertensives, the specificities of drug selection, comorbidity and the tendency toward postural hypotension must be taken into consideration. A detailed overview of the wide variety of drugs suitable for treatment of hypertension in elderly is beyond the scope of this paper. (For additional information in this respect, consult the Canadian Hypertension Society Guidelines.) Therefore, the policy should be “start low, go slow”: gradually titrate the dosages until the target levels are achieved with minimal side effects. In light of recent evidence, ARBs should play a major role in the treatment of elderly hypertensives.

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