Understanding Systolic Hypertension in the Elderly

R Gupta, RR Kasliwal

Abstract
Among the various causes of blood pressure in the elderly population, isolated systolic hypertension (ISH) is the commonest. Its prevalence increases with age. Age related rigidity of aorta is the primary cause of ISH. Systolic rise in blood pressure is at least as important as the diastolic blood pressure. Several non-pharmacological and pharmacological therapies are well-established for reduction of blood pressure in this age group. Among different groups of anti-hypertensive drugs, the preference depends primarily on co-morbidities and overall cardiovascular risk. Lifestyle modification should also be an integral part of therapy for each patient. Various studies suggest that control of blood pressure definitely decreases the incidence of mortality as well as coronary artery disease, stroke and other morbidities.

INTRODUCTION
Isolated systolic hypertension (ISH) is the commonest cause of raised blood pressure in the older population. As the age progresses, more and more persons will be hypertensives, a disease, which is definitely the most prevalent, remediable risk factor for cardiovascular diseases.

Definition
Although no threshold of values are established that clearly identify potential risk for cardiovascular diseases, but the long-term risk rises progressively over the entire range of blood pressure.

ISH is defined as systolic BP 140mmHg or more and diastolic BP less than 90mmHg, when patient is not taking antihypertensive drugs and not acutely ill.

Classification
Classification of ISH for adults (≥18 yrs of age) is given in Table 1.

Prevalence
Hypertension is found in one-fourth of all adults. As discussed earlier, the incidence increases with progressing age, as approximately, 55% of the whole population will be hypertensive by age 60 and, 65% over age 70. In the elderly population (age ≥ 60 years) with hypertension, 65% are suffering from ISH.

Causes of ISH
As we all know, blood pressure is a product of cardiac output and total peripheral resistance, so increase in any of the two (or both) will cause ISH as shown in Table 2.

Increased cardiac output is seen in hyperkinetic states of circulation like thyrotoxicosis, Paget’s disease of bone, beri-beri, AV fistula, PDA and aortic regurgitation.

Rigidity of aorta is primarily because of loss of elasticity of the aorta with progression of age. It increases the total peripheral resistance (TPR). It is the main bulk of ISH, especially, in the elderly population and we will primarily direct our discussion to it.

Etiopathogenesis of ISH
There are several factors, contributing more or less to the development of ISH like:

* Increased rigidity/decreased elasticity of the large capacitance arteries

<table>
<thead>
<tr>
<th>Table 2 : Causes of ISH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Increased cardiac output</td>
</tr>
<tr>
<td>- Hyperkinetic circulation</td>
</tr>
<tr>
<td>- AR</td>
</tr>
<tr>
<td>- Paget’s disease of bone, beri-beri, thyrotoxicosis</td>
</tr>
<tr>
<td>- AV fistula, PDA</td>
</tr>
<tr>
<td>2. Increased peripheral resistance</td>
</tr>
<tr>
<td>- Rigid aorta</td>
</tr>
</tbody>
</table>
* Increased total peripheral resistance
* With the advancement of age, obesity, stress, decreased physical activities, altered dietary patterns specifically increased sodium and decreased potassium intake are contributory
* Decreased blood volume combined with run-off because smaller reservoir provided by rigid large arteries lowers diastolic blood pressure and widens pulse pressure.
* Aging impairs baroreceptor function and renal functions.

**SIGNIFICANCE OF ISH IN ELDERLY**

Previously, many physicians used to consider that age + 100= ‘acceptable’ systolic pressure. For example, at the age of 70 years, 170 mmHg of SBP used to be considered ‘acceptable’. Now, it is clearly seen in different studies that hypertension is as great a risk factor for elderly males as it for younger males. It is rather more risky in elderly females in comparison to younger females. The significance of ISH becomes more important in Indian perspective as hypertension is more risky in non-whites.

As far as the issue that which fragment of blood pressure is more important is still not fully answered. Contrary to the popular beliefs in past, systolic rise in blood pressure is equally (or may be more) risky than diastolic rise. National high blood pressure education program than DBP working group reported SBP is a stronger predictor of all cardiovascular events (stroke, heart failure, cardiovascular diseases, coronary artery disease, and end-stage renal disease) and all cause mortality in elderly population. The investigators of SHEP trial found that higher SBP was associated with more incidence of postural hypotension. Silagy and McNeiletal have shown that 1 mm rise in systolic blood pressure increases long term mortality by 1%. Verdecchia et al found that wide pulse pressure is the most important predictor of cardiovascular risk.

Blood pressure has to be controlled as if left untreated, half of the all hypertensives die of CAD or CHF, about one-third of stroke and one-sixth of renal failure.

The vascular complications of hypertension may be because of hypertension per se or may be because of increased atherosclerosis process. The complications like heart failure, haemorrhagic stroke and nephrosclerosis are primarily because of raised blood pressure per se, and coronary artery disease, peripheral vascular disease, sudden cardiac death, arrhythmias and non-haemorrhagic strokes are primarily caused through increased atherosclerosis mechanism.

**Why to Treat?**

As there is no specific symptom of raised blood pressure but even during almost asymptomatic course of uncomplicated hypertension, the patient may be unaware of the consequent progressive damage to the cardiovascular system for even ten to twenty years.

For all practical purposes, hypertension needs to be treated to prevent these cardiovascular complications as well as the target organ damage.

**Goal of Therapy**

According to the JNC-VI and WHO-ISH guidelines, for most hypertensives, including elderly the values should be kept below 140/90 mmHg. Those at higher risk, including diabetics and suffering from nephropathy, the target is even lower i.e. <130/90 mmHg.

But the issue is at which level (values) the treatment should be initiated and how aggressively it needs to be treated? It can not be generalised as we discussed earlier, we need to identify hypertensives, those at risk for cardiovascular complications (by history) and to establish TOD (Target Organ Damage) or CCD (Clinical Cardiovascular Disease) by clinical examination and few simple investigations (Table 3, 4 and 5).

**Management of ISH**

It can be divided into pharmacological and non-pharmacological treatment.

**NON-PHARMACOLOGICAL TREATMENT**

The value and effectiveness of lifestyle modification cannot be underestimated. Although, it is so talked about issue, but poorly practiced.

The reasons are:
* Lack of faith among physicians
* Poor adherence of patients, especially those

<table>
<thead>
<tr>
<th>Table 3 : Hypertensives at risk of cardiovascular complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smokers</strong></td>
</tr>
<tr>
<td><strong>Dyslipidemics</strong></td>
</tr>
<tr>
<td><strong>Diabetics</strong></td>
</tr>
<tr>
<td><strong>Age &gt; 60 years</strong></td>
</tr>
<tr>
<td><strong>Males and post-menopausal females</strong></td>
</tr>
<tr>
<td><strong>Positive family history of cardiovascular disease</strong></td>
</tr>
<tr>
<td>- Women &lt; 65 years</td>
</tr>
<tr>
<td>- Men &lt; 55 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4 : TOD/CCD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart disease</strong></td>
</tr>
<tr>
<td>- Angina/prior MI/ prior coronary revascularization</td>
</tr>
<tr>
<td>- LVH</td>
</tr>
<tr>
<td>- Heart failure</td>
</tr>
<tr>
<td><strong>Stroke/TIA</strong></td>
</tr>
<tr>
<td><strong>Nephropathy</strong></td>
</tr>
<tr>
<td><strong>Retinopathy</strong></td>
</tr>
<tr>
<td><strong>Peripheral artery disease</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 5 : Risk Stratification &amp; Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPB (mmHg)</strong></td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>High normal (130-139)</td>
</tr>
<tr>
<td>Stage 1 (140-159)</td>
</tr>
<tr>
<td>Stage 2 &amp; 3 (≥160)</td>
</tr>
</tbody>
</table>

Risk group A - no risk factors, no TOD/CCD. Risk group B - at least one risk factors (not including diabetics), no TOD/CCD. Risk group C - TOD/CCD and/ or diabetics, with or without other risk factors. * upto 12 months. ** upto 6 months. LSM - Lifestyle modification
asymptomatic
* Too many and too drastic changes are very difficult to be accepted
* And, the most unfortunate and disappointing fact that a large number of patients on even religious LSM, ultimately have to take pills.

The different aspects of LSM are-

a) **Weight reduction**: Increment in body weight increases the incidence of hypertension and the vise-versa is also true. Staessen et al have shown that decrease in 1.0kg body weight decreases blood pressure by 1.6/1.3 mmHg. It improves insulin sensitivity, sleep apnea and the sensitivity to sodium decreases.

b) **Dietary sodium restriction**: Moderate degree of sodium restriction is 100mmol sodium, or 2.4 gm/day. Indian patients with ISH are more responsive to sodium restriction, because of their lower renin responsiveness. Response is not generalised but even in the non-responders, patient may still benefit by improved beta-receptor responsiveness, less diuretic-induced potassium wastage and by decreasing left ventricular hypertrophy. In practical terms, no added salts may suffice. In typical Indian food, avoidance of APC (Achar, Papad, Chatni) may serve the purpose grossly. Coming back to natural foods, instead of Western style processed foods is also helpful as processing takes out ‘good’ potassium and adds ‘bad’ sodium.

c) **Potassium supplementation**: More than 30 randomised controlled trials have shown the beneficial role of potassium supplementation. It decreases blood pressure by an average of 3.1/2.0mmHg. As potassium supplementation is very costly and hazardous for routine use in normal serum levels, its routine use is not recommended. Protection of potassium depletion and to increase dietary potassium intake appear sufficient. Moreover, decreased sodium intake itself increases potassium content.

d) **Moderation of alcohol**: Alcohol abuse is the commonest cause of reversible hypertension. One to two portions containing 0.5 to 1.0 oz of ethanol per day are associated with fewer coronary events and strokes in comparison to teetotaters.

e) **Other dietary changes**: Role of diet has been proven in DASH (Dietary Approaches to Stop Hypertension), TONE (Trial of Nonpharmacological Interventions in the Elderly), and many more trials. In nutshell, diet should be rich in fruits, vegetables and high fiber content.

f) **Avoidance of tobacco**: Smoking is prevalent in urban as well as rural population and a significant contributory factor for cardiovascular risk, along with other detrimental effects on other body systems.

g) **Physical exercise**: After regular exercise programmes, resting blood pressure decreases as it increases vascular compliance. For practical purpose, brisk walk appears sufficient.

**DOES THERAPY IMPROVE PROGNOSIS?**

This fact has been established on the basis of many meta-analyses. A popular meta-analysis conducted by Jan A Staessen of Belgium included eight RCT namely HOPE, SECURE, STOP-Hypertension, STOP - II, TRACE, UKPDS, HOT and Syst-China trial. This meta-analysis included more than 15,000 patients and mean follow up of 3.8 years. The results were decrease in mortality as well as morbidity from cardiovascular events (Table 6).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Odd Ratio Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes mortality</td>
<td>13%</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>18%</td>
</tr>
<tr>
<td>All cardiovascular events</td>
<td>26%</td>
</tr>
<tr>
<td>All stroke events</td>
<td>30%</td>
</tr>
<tr>
<td>All coronary events</td>
<td>23%</td>
</tr>
</tbody>
</table>

Treatment of high blood pressure also decreases incidence of dementia is proved by Syst-Eur trial, in which more than 2000 patients were treated with nitrendipine ± enalapril ± hydrochlorothiazide versus placebo for two years and the incidence of dementia decreased by 50% in the treatment arm.

An important and large trial SHEP trial, in which about five thousand elderly patients were followed for 4.5 years and treated with chlorthalidone (12.5 mg/d) ± atenolol (25 mg/d) or reserpine (0.05 mg/d) versus placebo. Significantly fewer incidences of ischaemic stroke, haemorrhagic stroke, TIA, MI, CABG, angioplasties and left ventricular failure in the treatment group (Fig. 1).

An echo subgroup of the SHEP trial has shown that treatment with chlorthalidone ± atenolol causes LV mass reduction, which is an independent risk factor.

Treatment of ISH also prevents development of heart failure among elderly, whether have no previous history of heart failure (NIH trial - low dose diuretics decreased heart failure incidence by 50%) or have experienced heart failure earlier (SHEP trial - low dose diuretics ± atenolol or reserpine decreases incidence of heart failure by 80%).

Even after the multiple documentations of multiple benefits of treating hypertension, out of all Western hypertensives, only 27% have proper control. The situation is worse in older population, with only 18% having proper control. Although the Indian data is not much, but probably worse results are expected. In one study, it was 9%.
By and large, presence of more cardiovascular risks means more benefit of pressure reduction.

A very recent trial, ECG-LVH, a subset of previously published LIFE study, suggested that losartan may be better than atenolol in patients with ISH and left ventricular hypertrophy on electrocardiogram (ECG-LVH), despite similar reduction in blood pressure with both drugs.

**Pharmacotherapy for ISH**

No single drug is considered unanimously the best drug for ISH. Most authorities consider diuretics are the best choice, but the data are conflicting in present scenario (Table 7).

**Table 7: Drugs for ISH**

| A | ACE inhibitors & ARBs |
| B | Beta blockers |
| C | Calcium channel blockers |
| D | Diuretics |
| E | Eplerenone* |

* Selective Aldosterone blocker

The choice of the anti-hypertensive drug depends on several factors like the presence or absence of target organ damage, vascular risk profile and the cost of therapy and the possibility of drug interactions.

It has been clearly shown that all the drugs mentioned in the table (except eplerenone) are of equal efficacy at equipotent doses. On an average, they decrease SBP by 10mmHg and 5mmHg on standard doses. According to the WHO-ISH guidelines, in case of uncomplicated hypertension, any of the aforementioned drugs can be used as first line. ACEI, ARBs, beta blockers and diuretics have been shown to reduce cardiovascular morbidity and mortality. According to the Syst-eur trial and Syst-china trial, calcium channel blockers provide more reduction in stroke, but reduction in coronary events are less, especially in older population without proteinuria. On an average, all antihypertensives have similar long-term safety and efficacy. Although, elderly hypertensives are more at risk of pharmacotherapy (Table 8), still 140/90 value has to be achieved.

**Table 8: Factors contributing to increased risk of pharmacological treatment of HT in the elderly**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Preferred drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild to moderate HT</td>
<td>Low - dose thiazide</td>
</tr>
<tr>
<td>Normal RFT (S Cr &lt; 2.0)</td>
<td>Indapamide</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Abnormal RFT (S Cr &gt; 2 or Cr clearance &lt; 25ml/min)</td>
<td>Furosemide</td>
</tr>
<tr>
<td></td>
<td>Toremide</td>
</tr>
<tr>
<td></td>
<td>Metolazone</td>
</tr>
</tbody>
</table>

Side effects - ↓K+, ↓Mg, ↑Uric acid, ↑Lipids, ↑Ca++, hyperglycemia, insulin resistance, impotence & renal cell carcinoma.

By and large, presence of more cardiovascular risks means more benefit of pressure reduction.

The greater reduction in blood pressure and risk reduction in fatal as well as in non-fatal stroke with diuretic based therapy (Perindopril + indapamide) than perindopril alone has been seen, according to the PROGRESS trial.7

The mechanism of action of diuretics and their relative choice and side effects are shown in Table 9 and 10 respectively.

On average, diuretics decrease blood pressure by 10mmHg. Its effect persists indefinitely and they actually increase the effect of all anti-hypertensive drugs used concomittantly, except ACE inhibitors and calcium channel blockers.

The thiazides help in preservation of bone mineral density, which is an additional benefit in elderly population.17

**b) Calcium channel blockers**

It has become the most popular class of anti-hypertensive therapy. They have vasodilatory as well as negative inotropic effect. Dihydropyridines have greatest peripheral vasodilatory action. This group of drugs is effective in hypertensives of all ages and races, and in hypertensive diabetics, a combination very commonly seen in clinical practice. A unique character of CCBs is that its antihypertensive efficacy is not blunted by non-steroidal anti-inflammatory agents. More or less, all NSAIDs produce retention of salt and water(including newer COX - 2 inhibitors), but COX -2 inhibitors preserve renal haemodynamics in comparison with conventional NSAIDs. As arthritis is prevalent in older population, NSAIDs are largely consumed in this group. Statistically significant increment of 3-6 mmHg...
pressure is observed with NSAIDs in several studies and further increase in cardiovascular risk. So this issue should be considered while selecting antihypertensive agent. Although, not commonly used, drugs like IV nicardipine and SL nifedipine are available for hypertensive emergencies. Among the commonly seen side effects of CCBs, leg edema is worth mentioning and is probably due to local hydrostatic effect and very poorly responds to diuretics.

The efficacy of CCBs in the treatment in ISH has been established in SyS-Eur trial and SyS-Eur 2 trial. SyS-China trial has shown the lesser incidence of stroke in CCB treatment group. The usefulness of CCB was compared with ACE inhibitors in hypertensive nephrosclerosis in AASK trial.9 Lercanidipine, a newer long-acting dihydropyridine is promising to have lesser incidence of leg edema and has associated antiatherogenic properties. Its antihypertensive efficacy and tolerability have been established in recent ELYPSE trial.10 Mechanism of action of CCBs is shown in Table 11.

c) Angiotensin converting enzyme inhibitors (ACEI)

In the pathogenesis of hypertension, the role of increased activity of Renin-Angiotensin System (RAS) is well known.11 This has an adverse affect on the endothelial function and has major role in high cardiovascular events. Hypertensives with high-renin levels (plasma renin activity ≥ 0.65 ng/mL/hr) are more prone to cardiovascular events and show maximum benefit with ACEI therapy. Other beneficial roles of ACEI are: prevention of remodeling, regression of left ventricular hypertrophy, prevention of target organ damage like CHF, renal failure, improvement in endothelial function and prevention of atherosclerosis.

The efficacy of ACEI in hypertension has been established in CAPP trial (Captopril) and HOPE trial (Ramipril). Here, a word of caution is its first dose effect i.e. unpredictable precipitous fall in blood pressure with first dose of ACEI. So, the ACEI should be started in low dose and to be increased gradually, instead of starting with higher doses.

ACEI are usually considered second-line drug therapy ISH. ACEI are considered standard therapy in hypertension with renal disorders, diabetes, diabetic nephropathy and LV dysfunction.

In HOPE trial,12 Ramipril decreased cardiovascular deaths by 25%, stroke by 31% and myocardial infarction by 20%. The use of ACEI in all high-risk patients for both primary and secondary prevention is a growing consensus. Mechanism of action of ACEI shown in Table 12.

d) Angiotensin II receptor blockers (ARBs)

This group of drugs was initially introduced as an alternative to ACEI, for those who are intolerant to them. As ARBs completely block RAS activity, so blockade of angiotensin II and bradykinin occurs, which prevents dry cough, a very common side effect of ACEI. The antihypertensive efficacy is similar of ACEI, with lesser side effects. The superiority of losartan over atenolol was found in recently published LIFE trial.13 Losartan was found to have more reduction in cardiovascular event as well as in stroke, more LVH regression and lesser incidence of new onset diabetes. Losartan was even more beneficial in diabetic hypertensives.

As far as survival is concerned, ARBs were not found superior to ACEI in the recent heart failure (ELITE II) trial.14 At present, the status of ARBs is as an alternative to ACEI, especially in intolerant to ACEI and in patients with DM type 2 with proteinuria.

Pregnancy, hyperkalemia and bilateral renal artery stenosis are compelling contraindication, as of ACEI.

e) Beta blockers

β blockers reduce mortality and morbidity in patients with concomitant coronary artery disease (secondary prevention). These are also suggested to have primary prevention of coronary artery disease but probably here, low-dose diuretics are better.

The mechanisms of action of beta blockers are shown in Table 13.
f) Eplerenone

This is latest addition in antihypertensive therapy. This drug is first Selective Aldosterone Blocker (SAB) and is currently under regulatory review for approval by FDA for treatment of hypertension. This drug is said to be effective in all types of hypertension. The role of eplerenone in ISH needs further work up.

MESSAGES FROM JNC VII REPORT

The Seventh report of the joint national committee (J NC VII) on prevention, detection, evaluation, and treatment of high blood pressure’ guidelines provide new insight on the issue. Although not universally accepted (especially, the concept of ‘pre hypertensives’), the key message are worth noting -

1. In persons older that 50 years, systolic blood pressure (BP) of more than 140 mmHg is a much more important cardiovascular disease (CVD) risk factor that diastolic BP.
2. The risk of CVD, beginning at 115/75 mmHg, doubles with each increment of 20/10 mmHg; individuals who are normotensive at 55 years of age have a 90% lifetime risk for developing hypertension.
3. Individuals with a systolic BP of 120 to 139 mmHg or a diastolic BP of 80 to 89 mmHg should be considered as prehypertensive and require health-promoting lifestyle modifications to prevent CVD.
4. Thiazide-type diuretics should be used in drug treatment for most patients with uncomplicated hypertension, either alone or combined with drugs from other classes. Certain high-risk conditions are compelling indications for the initial use of other antihypertensive drug classes (angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, beta-blockers, calcium channel blockers).
5. Most patients with hypertension will require two or more antihypertensive medications to achieve goal BP (<140/90 mmHg) or <130/80 mmHg for patients with diabetes or chronic kidney disease.
6. If BP is more than 20/10 mmHg above goal BP, consideration should be given to initiating therapy with two agents, one of which usually should be a thiazide-type diuretic.

CONCLUSIONS

Isolated systolic hypertension (ISH) is the commonest cause of high blood pressure in the elderly. The incidence increases with age advancement. It is more risky in non-White population. Even small reductions in BP have a substantial impact on patient outcome. In general < 140/90 mmHg is target for uncomplicated hypertension, < 130/85 mmHg for those with diabetes or renal disease with proteinuria. Earlier, alpha blockers were preferred in elderly hypertensives with BPH (benign prostatic hypertrophy). The investigators of ALLHAT study have reported that doxazosin is associated with more salt and water retention and higher cardiovascular event rate in comparison to thiazides. Whether pharmacological treatment is needed or not, non pharmacological measures have to be religiously implemented on every hypertensive.

Although, all major antihypertensive drugs cause similar reduction in BP in standard doses, low-dose diuretics are considered first choice for ISH. Selection of antihypertensive drug depends on the associated comorbid conditions as well as on the overall cardiovascular risks.

REFERENCES


---

**Announcement**

The Elected Executive Members of The Association of Physicians of India, Gurgaon Chapter, Haryana

Chairman : M Prabhakar
Vice Chairman : RS Rawat
Secretary : A Biswas
Joint Secretary : J Chakraborty
Treasurer : PD Pahwa
Editor Newsletter : R Gupta
Immediate Past Chairman : AK Taneja

---

**Announcement**

Regional CME on Recent Advances in Medicine on 7th and 8th August, 2004 at Hotel JP Residency, Manor, Mussorie (Uttaranchal).

Organised by : Association of Physicians of India, Saharanpur Branch.

For details contact : Dr. Rajneesh Dahuja, Chairman, Leela Heart and Medicare Centre, Bajoria Road, Saharanpur - 247001. Tel. : 9837029409; E_mail : dahuja_r@sancharnet.in

Dr. Naresh Nausaran, Convener, Nausaran Medical Centre, Bajoria Road, Saharanpur - 247001. Tel. : 9837049824