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With increased longevity, the quality of life and general health of the elderly have become important topics of discussion and research. It is projected that there will be 213 million hypertensives in India by the year 2025. It is estimated that 25-30% of adults in urban areas and 15-18% rural adults suffer from hypertension. The current estimate of hypertensives in India are more than 84 million.

The probability of having hypertension increase with age. At age ≥ 70, approximately 70% of men and women have hypertension, compared with less than 20% among those aged ≤ 44. The residual lifetime risk of hypertension among person ≥ 60 years who had not developed hypertension is approximately 90%. In the 2007-2008 NHANES data, only 50% of all patients with hypertension were controlled to <140/90 mm Hg. The proportion of patients with controlled hypertension was lower among those ≥ 60 years than in younger (<40) individuals. The characterisation and definition of what constitutes hypertension in the elderly has changed over the years. Data obtained during the Framingham Heart Study, which followed patients for 30 years, agreed that systolic blood pressure (SBP) shows a continuous increase between the ages of 30 and 84 years or over. Diastolic blood pressure (DBP), however, has a varying pattern with ageing, increasing until the fifth decade and slowly decreasing from the age of 60 to at least 84 years of age.

A great number of studies have shown that aging and hypertension are associated with impairment of endothelium-dependent vascular relaxation in coronary, forearm and renal arteries, and endothelial dysfunction, which is involved in the development of atherosclerosis, was found to increase the risk of cardiovascular and cerebrovascular diseases.

Aging may alter the structure and function of vascular components, such as the endothelium, intimas and smooth muscle cells, resulting in an increase in the risk of development of cardiovascular and cerebrovascular diseases, which are related to hypertension. Several possible mechanisms by which advanced aging and hypertension impair endothelial function have been postulated. An imbalance of reduced production of nitric oxide (NO) or increased production of reactive oxygen species (ROS), mainly superoxide, may promote endothelial dysfunction.
function is restored by appropriate interventions, including pharmacological therapy, such as renin-angiotensin system inhibitors and statins, supplementation therapy and lifestyle modifications.\textsuperscript{10}

Isolated systolic hypertension (ISH) is consequently most prevalent in those aged 50 or over. The third National Health and Nutrition Examination Survey (NHANES III) in the US showed that almost 80% of those individuals aged 50 or over with high BP, at least on a single occasion, have systolic hypertension.\textsuperscript{11} Hypertension in older subjects may be defined as SBP $\geq$ 140 mm Hg or SBP $\geq$ 160 mmHg and/or a DBP $\geq$ 90 mm Hg. Systolic hypertension is either observed de novo or as a development after a long period of systolic-diastolic hypertension with or without treatment. The great majority of older patients with hypertension have ISH, with diastolic hypertension occurring in a minority (10% among those aged 70). ISH is primarily due to decreased compliance of the large arteries and increased pulse wave velocity. Age-related changes in the histology of the large vessels (especially the aorta) with a decrease in elastic fibers and replacement with collagen result in increased aortic wall stiffness and decreased compliance. High pulse wave velocity, which results in the reflected pulse waves arriving at the central aorta during systole rather than after the dicrotic notch (as occurs in younger individuals). These physiologic and pathologic effects of aging are modulated to significant extent by behavioural and environmental influences including physical activity, die the autonomic nervous system undergoes significant change with aging. Drowseregulation and decreased responsiveness of beta-receptors and increased ambient catecholamine concentrations. The increased norepinephrine concentrations common in older individulas may be due to homeostatic mechanisms counterbalancing decreased responsiveness of the adrenergic receptors.

The differences in Systolic and Diastolic Blood pressure with increasing age, systolic blood pressure (SBP) increases in all populations studied. Diastolic blood pressure (DBP) increases until approximately the fifth or sixth decade and declines thereafter, the increase of blood pressure (BP) with age is more pronounced in women. Stroke and CHD are the major causes of death in people over 65 years of age. The most common treatable risk factor is hypertension. The danger of cardiovascular complications associated with a widening Pulse Pressure was also shown in a meta-analysis that included results from several major trials including SHEP, EWPHE, Syst-Eur and Syst-China.\textsuperscript{12}

In some individuals BP decreases with ageing. This is mostly as a consequence of illness such as Alzheimer’s and other forms of dementia, cancer or impaired ventricular function which may occur after myocardial infarction. A similar inverse association between BP and mortality was also found in the Helsinki Ageing study, a population-based study of over 500 people aged 75 or over. the study suggested that antihypertensive treatment in those aged 80 years or over could be problematic due to falling BP and increased mortality.\textsuperscript{13}

Elderly hypertensives usually have low renin, low aldosterone, salt-sensitive hypertension because of decreased natriuretic activity of the nephrosclerotic kidney and increased sodium reabsorption.

Between the ages of 30 and 85, approximately one quarter of the cortex is lost due to glomerulosclerosis and interstitial fibrosis with impairment of renal hemodynamics. Renal changes from nephrosclerosis and changes of the juxtaglomerular apparatus result in low renin and aldosterone levels. This may be related to expansion of total body water and suppression of renin activity.\textsuperscript{14} The decreased renal function in hypertension may impair excretion of medications or their metabolites, especially in the elderly with polypharmacy and associated comorbidities (e.g. Coronary Heart Disease (CHD), diabetes, dyslipidemia, and osteoarthritis). Renal dysfunction predicts cardiovascular (CV) outcomes and
mortality in older hypertensive.\textsuperscript{15} There is a wealth of evidence that antihypertensive pharmacologic therapy decreases mortality and morbidity. Even in the very old, antihypertensive therapy decreases mortality. In the HYVET clinical trial of patients with hypertension (mean age 83.6 years), indapamide/perindopril therapy resulted in decreased mortality and was well tolerated. Intervention exercise programs were also implemented in elderly hypertensive patients such as that conducted by Motoyama and co-workers. The first drug of choice for elderly patients still seems to be a thiazide or in some cases a calcium channel blocker.\textsuperscript{16}

The nutritional status of the elderly also affects the rate of drug metabolism and in the frail elderly drug metabolism is reduced. ACE inhibitors, often used as second line agents, can cause persistent dry cough in as many as 10–20\% of patients due to inhibition of bradykinin breakdown. This leads to discontinuation and poor compliance. Long-term therapy with diuretics and the decrease in body water and reduction of fluid intake in the elderly could lead to an increased risk of hypokalaemia and hyponatraemia, especially in females, when compared with younger patients.

Co-morbidities need to be taken in consideration in the use of medication both in terms of advantages such as the use of β-blockers in angina or contra-indications such as β-blockers in peripheral vascular disease.\textsuperscript{17}

The TONE trial (Trial of Nonpharmacological Intervention in the Elderly) showed a reduction in cardiovascular complications and requirement for drugs after a reduction in salt intake.\textsuperscript{18} Salt reduction may also have other health related benefits independent of the BP effect, such as a reduction in target organ damage.\textsuperscript{19} Salt reduction is possibly effective in the elderly because of decreased arterial compliance and hence a decrease in arterial blood volume which leads to a larger drop in BP.\textsuperscript{20}

In conclusion, the life expectancy of the population in India has changed over the decades from 54 years to 70 years. The criteria used to define hypertension have changed with time, but although the cut-off points are not agreed by all physicians, it is certain that the elderly have predominantly isolated systolic hypertension and that its treatment can reduce the risk of cardiovascular events. The treated elderly have increased orthostatic and postprandial hypotension and increased BP variability. These problems and the increased burden of side effects and comorbidities with ageing, need to be taken into consideration when treating elderly and particularly very elderly hypertensive patients, in whom the balance of risk and benefit from anti-hypertensive treatment remains to be determined.

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Hypertensive Stroke: Guidelines to Treat Blood Pressure

Bhupendra Chaudhary¹, Rakesh Kumar Aran²

THE BURDEN OF HYPERTENSION

Hypertension remains one of the most important preventable contributors to disease and death. Most patients with hypertension have other risk factors including lipid abnormalities, glucose intolerance and diabetes, family history of early cardiovascular events, obesity and tobacco use with or without alcohol excess. According to a review on “The Global Burden of Hypertension”, the estimated prevalence of hypertension (in people aged 20 years and over) in India in the year 2000 was 20.6% among males and 20.9% among females and is projected to increase to 22.9% and 23.6% respectively by year 2025. Between 1 and 5 percent of children and 15% of young adults suffer from hypertension while more than 60% of adults above the age of 65 years have hypertension. If the child’s blood pressure (BP) is more than the 90th percentile, the incidence of hypertension in adulthood rises 2-4 fold. Therefore, it is postulated that childhood diseases such as reflux nephropathy (RN) are the reason of hypertension in adulthood. About one-third of adults in developed and developing world have hypertension and it is estimated to cause over seven million deaths each year, which is about 13% of the total number of deaths worldwide.

Based on the World Health Organization (WHO) reports, hypertension is the cause of 62% of cerebrovascular accidents (CVA) and 49% of ischemic heart diseases. For every 5 mmHg increase in diastolic BP, there is a 35% and 20% increase in the risk of CVA and coronary artery disease, respectively. In addition, hypertension is the cause of up to 50% of end stage renal diseases (ESRD) requiring dialysis and transplantation in adults.

Hypertension (HTN) is the second most common cause of death after diabetes in adults worldwide. Untreated hypertension leads to life-threatening complications that include CAD, MI, stroke, and kidney disease. So it is called “the silent killer” because symptoms generally appear only after the disease has caused damage to vital organs such as the brain, eyes, kidneys and the heart.

STROKE AND HYPERTENSION

Hypertension is the most important modifiable risk factor for stroke. It is estimated that 25% or more of strokes may be attributable to hypertension. This is well established that lowering

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BP reduces the risk of stroke. Epidemiological studies have shown that for each 10 mm Hg lower systolic blood pressure (SBP), there is a decrease in risk of stroke of approximately one third in persons aged 60 to 79 years. This association is continuous down to levels of at least 115/75 mm Hg and is consistent across sexes, regions, stroke subtypes, and even for fatal and nonfatal events. Lowering diastolic blood pressure (DBP) was once the main target to achieve stroke and other cardiovascular event reduction, but SBP has now become the target. Although hypertension in the immediate post-stroke period is frequently observed, BP tends to spontaneously fall within the first hours and days following the acute event, with the pattern of blood pressure change varying with stroke subtype. Precipitous falls in BP have, however, been associated with poor outcome and should be avoided. A ‘U-shaped’ association between admission BP and stroke outcome has been identified, with very high and very low BP at the onset of stroke largely being associated with poor post-stroke outcome. The role of longer-term BP control to improve outcomes in patients with stroke is undisputed, BP management immediately after a stroke still remains controversial.

HYPERTENSIVE HEMORRHAGE: THE GUIDELINES TO TREAT BLOOD PRESSURE

While treating the patient of acute intracerebral hemorrhage the question of controlling the blood pressure in domain of when, how and how much always remains in mind of internist. Despite of vast experience in treating such situation many times one find himself in a difficult way to deal such an emergency situation. The argument against lowering BP in acute ICH is based on the possible existence of a perihematomal ischemic zone. Recent studies, however, indicate that low blood flow around the hematoma may be a consequence of reduced cerebral metabolism in this area rather than a primary reduction of blood flow. In addition, chronic hypertensives (due to a shift in the autoregulatory curve) and patients with increased intracranial pressure (ICP; due to lowered cerebral perfusion pressure) may develop cerebral ischemia if BP is acutely lowered but majority of the patients with intracerebral hemorrhage (ICH) often have elevated BP. Approximately one third of all patients with ICH presenting within 3 hours of symptom onset have a significant expansion of the hematoma over the next 20 hours. Initial hematoma volume and hematoma expansion are powerful predictors of mortality after ICH. Some studies have suggested an association between high BP and hematoma expansion and BP is often lowered under the assumption that high BP promotes hematoma expansion.

TREATING BLOOD PRESSURE: THE QUESTION OF WHEN, HOW AND HOW MUCH?

In absence of definitive supportive evidence, majority of experts believe that a SBP of >180 mm Hg or a mean arterial pressure (MAP) of >130 mm Hg would warrant immediate lowering. In the presence of conditions such as acute heart failure, hypertensive encephalopathy, active cardiac ischemia, and so on, lower BP targets may be appropriate. It has been suggested that rapidly lowering MAP by approximately 15% does not lower cerebral blood flow, whereas reductions of >20% can do so. Therefore, if BP-lowering is considered, current guidelines suggest cautious lowering of BP by no more that 20% in the first 24 hours. Therefore immediately after an ICH, it is perhaps more appropriate to tailor the target BP to each patient rather than using a generalized approach. The possibility of increased ICP and a history of chronic untreated hypertension should be considered while choosing the target. Presently, the American Heart Association/American Stroke Association (AHA/ASA) guidelines suggest maintaining a cerebral perfusion pressure of 60 to 80 mm Hg in patients with possible increased ICP and a
BP of 160/90 or a MAP of 110 mm Hg in other patients.

Short and rapidly acting intravenous anti hypertensive agents are preferred. Drugs like labetalol, hydralazine, esmolol, nicardipine, enalapril, nitroglycerin, and nitroprusside have been recommended. While treating the stroke patient sodium nitroprusside and nitroglycerin should be used with caution because these agents can potentially increase ICP. It is the target of BP lowering which is more important than the agent used.

**HYPERTENSIVE ISCHEMIC STROKE: THE GUIDELINES TO TREAT BLOOD PRESSURE**

Spontaneous elevation of blood pressure in the first 24-48 h after stroke onset with a significant spontaneous decline after a few days is established phenomenon. Several mechanisms may be responsible for the increased blood pressure including stress, pain, urinary retention, Cushing effect due to increased intra cranial pressure and the activation of the sympathetic, renin-angiotensin and ACTH-cortisol pathways. Several arguments speak for lowering this elevated BP due to risks of hemorrhagic transformation, cerebral edema, recurrence of stroke and hypertensive encephalopathy. On the other hand, it may be important to maintain the hypertensive state due to the damaged autoregulation in the Ischemic brain and the risk of cerebral hypoperfusion exacerbated by the lowered systemic blood pressure as cerebral perfusion becomes dependent upon systemic arterial BP following stroke due to impairment of cerebral autoregulation, and therefore changes in systemic BP can directly influence cerebral perfusion. Hypertension may sustain cerebral perfusion to the ischemic penumbra, with BP having been shown to fall spontaneously in response to successful recanalization of cerebral vessels following thrombolytic treatment, perhaps suggesting the restoration of cerebral autoregulation.

**TREATING BLOOD PRESSURE: THE QUESTION OF WHEN, HOW AND HOW MUCH?**

In thrombolysis eligible patients the AHA/ASA guidelines recommends that before intravenous thrombolytic treatment, BP should be lowered if >185 mm Hg systolic or >110 mm Hg diastolic. During thrombolytic treatment, SBP should be kept <180 mm Hg and DBP <110 mm Hg and it should also be maintained for first 24 hrs. Intravenous labetalol, nitropaste, nicardipine infusion, and, if BP remains elevated, sodium nitroprusside are the recommended agents. Intravenous labetolol is the preferred agent with t-PA use as it maintain cerebral and coronary blood flow. It should be given in dosage of 10-20 mg over 2 min and may even be repeated once. If BP is not reduced and maintained <180/110 mmHg do not administer t-PA so it is a golden rule that “Treat BP prior to t-PA” because clinical experiences have shown that uncontrolled BP with thrombolysis may worsen cerebral oedema and increases risk of intracerebral hemorrhage. Despite the absence of supporting evidence, these recommendations are often applied to patients receiving other forms of reperfusion therapy (e.g., intra-arterial thrombolysis, clot retrieval, and so on). Patients with other indications for BP-lowering such as acute heart failure, aortic dissection, and so on should have the BP lowered. One should be cautious about abruptly lowering BP in other patients due to the risk of worsening cerebral ischemia. In other subset of patients i.e. in non-thrombolysis patient guidelines suggest withholding antihypertensive agents in these patients unless the DBP is >120 mm Hg or the SBP is >220 mm Hg and limiting the drop in BP during the first 24 hours by approximately 15%.

Thus strategies focussing on achieving target BP with aim to maintain an adequate cerebral perfusion pressure and thus restoration of cerebral autoregulation to prevent the ongoing normal injury may result is favourable neurological outcome.
REFERENCES


By the year 2050, our patient population will mainly consist of older adults and the very old adults (those in the 8th, 9th, 10th decade of life). It has been projected that in 2050, the population of our country will rise by 60% and that of adults more than 60 years of age will rise by 360% (i.e. 20% of the entire population). There is a direct positive relation between advancing age and rise in blood pressure (BP). It is very important to recognize hypertension in this age group and institute appropriate intervention to improve their quality of life (QoL).

Both systolic and diastolic BP rise with age. Systolic BP (SBP) rises progressively until the seventh or eighth decade of life; while diastolic BP (DBP) increases until the age of 50 or 60, after which it stabilizes or may decline slightly depending on the arterial compliance. Therefore, most often in older adults there is systolic hypertension (Isolated Systolic Hypertension - ISH) and Pulse Pressure (PP) has assumed significance.

Statistics show that more than 50% of persons above 60 years have hypertension. It is also important to note that after the fifth decade, the prevalence of hypertension is higher in women (40-50%) than in men (30-40%).

Framingham Study data has depicted that systolic hypertension is a major risk factor for stroke, various cardiac ailments (left ventricular hypertrophy, congestive cardiac failure, coronary artery, peripheral arterial disease, end-stage kidney disease, vision impairment, cognitive impairment, and dementia). Paradoxically, there is an increased risk of cardiovascular mortality with a low DBP (<65 mm Hg) which could be attributed to the “J-curve” phenomenon. Both HYVET and SHEP trials found that lowering BP with medications reduced the risk of cardiovascular disease in older adults. These studies are important, because for a long time doctors thought that high BP was a “normal” part of aging, and hence did not think it worthwhile to treat it. SHEP trial and HYVET convinced most doctors to take hypertension in older adults seriously.

Certain features of hypertension in older adults, are different from the younger population of <60 years of age. This paper will highlight these differences, and the ensuing clinical and practical implications.

**PATHOPHYSIOLOGY**

Cardiac output and vascular resistance are two determinants of arterial pressure. The rise in BP with age is a consequence of stiffening of blood vessels and reduced arterial compliance predominantly of the aorta and large arteries, resulting in increased systemic
vascular resistance. It is the Central Systolic Aortic Pressure (CAP) that increases and not brachial artery pressure (BAP).

Pulse pressure has been shown to be the best predictor of structural alterations in the arteries

Other aspects in pathophysiology that are of practical and therapeutic significance in the older age group are:

1. Baroreceptor sensitivity:
   a. Decreased baroreceptor sensitivity results in an impairment of postural reflexes, making elderly hypertensive individuals more sensitive to orthostatic hypotension.

b. Fluctuations in BP levels because of age-related alterations in baroreceptor reflex mechanisms. This is demonstrated by continuous ambulatory BP monitoring (ABPM). Specific attention should be paid to the timings and dosage of medications.

c. Autonomic Nervous System Imbalance:
   a. Sodium retention due to increased intake and decreased excretion contributes to development of hypertension. That is why diuretics are good antihypertensives in the elderly.

b. A fall in plasma renin with increasing age has been demonstrated. The renin response to salt intake is more reduced with age in hypertensive than in normotensive elderly subjects. It is advisable to restrict salt in the diet of the elderly.

Physiologic changes with age and their consequences on therapy are elaborated in Table 1.
<table>
<thead>
<tr>
<th>Decrease in the function of various organ systems</th>
<th>Challenges to Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CVS</td>
<td>• Deal with vascular resistance without affecting function of the heart</td>
</tr>
<tr>
<td>• Cardiac output reduced,</td>
<td>• Ensure adequate blood volume</td>
</tr>
<tr>
<td>• Increased Vascular resistance, Central Arterial Pressure (CAP)</td>
<td>• Therapy:</td>
</tr>
<tr>
<td>• The heart becomes more dependent on blood volume (preload).</td>
<td>• Ca channel blockers are ideal,</td>
</tr>
<tr>
<td>• Autonomic nervous system responsiveness reduced</td>
<td>• diuretics recommended with caution</td>
</tr>
<tr>
<td>• Liver</td>
<td>• Postural Hypotension</td>
</tr>
<tr>
<td>• hepatic blood flow reduced</td>
<td>• Therapy</td>
</tr>
<tr>
<td>• decreased metabolism and prolonged excretion of medications</td>
<td>• β &amp; α-blockers not recommended as initial therapy. They are adjunct / 2nd line agents in specific situations</td>
</tr>
<tr>
<td>• most medications are metabolized by the liver</td>
<td>• CCBs – may have a longer half-life</td>
</tr>
<tr>
<td>• Renal function declines</td>
<td>• Dose reduction may be required</td>
</tr>
<tr>
<td>• Toxic accumulation of drugs and metabolites</td>
<td>• Adverse effects like edema which is coupled with incompetent veins of lower extremities</td>
</tr>
<tr>
<td>• Diabetes, hypertension and vascular disease play a significant role in worsening renal function.</td>
<td>• Accumulation of drugs</td>
</tr>
<tr>
<td>• Strict monitoring when these conditions co-exist</td>
<td>• Profound effects &amp; ADRs</td>
</tr>
<tr>
<td>• Beware of drug interactions &amp; ADRs</td>
<td>• To be cautious with diuretics</td>
</tr>
</tbody>
</table>

or functional impairment, causing significant disability in this population.

**INITIATING TREATMENT**

The BP level and general condition of the patient is important rather than the age of the patient for consideration of therapy.

Before initiating medical therapy, the following variables should be reviewed:

1. Screening for frailty of the patient
   a. To help identify patients at higher risk for adverse clinical outcomes.
   b. The degree of frailty will also help to guide treatment targets. A higher BP goal in frail individuals may be more appropriate in order to avoid postural hypotension and other adverse effects that may induce iatrogenic falls, fatigue, or significant disability

2. Their mental status, cognition and ability to follow instructions
3. Current medications
   • NSAIDs and nasal decongestants should be discontinued
4. Screening of organ function: Tests to estimate liver, kidney and heart function should be performed. Certain anti-hypertensives like ACE Inhibitors and ARBs can cause renal function impairment.
5. Support from caregivers – Very important for compliance from the patient.
6. In order to achieve the maximal benefit of any prescribed regimen, it is important to understand extraneous factors such
as psychosocial barriers, comorbidities, compliance history and the direct cost to patient.

7. It is important to encourage lifestyle modifications. This can make a large difference in medical therapy required by older patients, and spare them from potential adverse effects of multiple drug regimens. Taste sensation reduces with age and the elderly often paradoxically increase salt intake. Stress should be laid on reduced salt intake.

SELECTION OF ANTIHYPERTENSIVE AGENTS IN THIS AGE GROUP

Evidence

Literature has recommended the use calcium channel blockers and diuretics in older adults. In some studies, ACE-I have also found favor (HYVET). JNC-7 had recommended a diuretic as first line of therapy. Instead, JNC-8 has recommended any class of antihypertensives - diuretic, CCB, ACE-I, or ARB, depending on the clinical situation. ESC/ESH guidelines recommend either a calcium channel blocker or diuretic for treatment of older patients with ISH. The ALLHAT data concluded that low-dose diuretic is ideal, but a combination of calcium channel blocker and ACE-I has a good BP lowering effect in this age group.

Practical Implications

CAP is a more important determinant of outcome in elderly than conventional brachial artery pressure (BAP). CCBs & diuretics cause greatest reduction in CAP & are best indicated in elderly hypertensives. β-blockers reduce BAP but not CAP and hence do not find favor in the elderly. β-blockers should not be used unless there is another primary indication for which they are mandatory.

Some important facts about these antihypertensives have been illustrated in (Table 2).

Principles Behind Therapeutic Decisions:
The main aim is to prevent and ward off adverse drug reactions.

- Age-related basic physiologic changes are to be taken into consideration before starting medications.
- It is important to treat these patients conservatively. Treating an elderly hypertensive similar to a younger patient with equivalent BP can be detrimental to the older patient.
- BP should be lowered gradually. Start with a low dose.
- More than one drug should not be added at a time even if the baseline BP is > 20 mm Hg above goal BP. There is a high risk of developing hypotension.

Adverse drug reactions among elderly patients are a major healthcare issue and a problem for all healthcare practitioners treating elderly patients. Adverse reactions are electrolyte imbalance and hypovolemia because of diuretics, edema of the lower extremities caused by dihydropyridine calcium channel blockers and orthostatic hypotension due to inappropriate fall in BP. The consequences are falls, injuries, alteration in level of consciousness, confusion. Elderly persons can react inappropriately to medications compared to the younger age group.

### Table 2: Antihypertensive Agents

<table>
<thead>
<tr>
<th></th>
<th>Diuretics</th>
<th>CCBs</th>
<th>ACE-I / ARBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP lowering</td>
<td>Good</td>
<td>Good</td>
<td>Less</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Combination therapy)</td>
</tr>
<tr>
<td>Overall mortality reduction</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CVS</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CNS</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Kidney</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>LVH regression</td>
<td>8</td>
<td>11</td>
<td>10 / 13</td>
</tr>
<tr>
<td>Diast Dysfunc improvement (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>+</td>
<td>neutral</td>
<td>↓</td>
</tr>
<tr>
<td>Other Effects</td>
<td>Edema</td>
<td>Cough - ACEI</td>
<td></td>
</tr>
</tbody>
</table>
Table 3: Factors that make it difficult to generalize the effect a drug will have on an older individual

**Pharmacokinetics and pharmacodynamics of drugs**
- particularly in the central nervous and cardiovascular systems
  - benzodiazepine effects potentiated (50%)
  - Sedation, disturbances of balance

**The volume of distribution changes depending on**
- renal and hepatic function
- total body water and fat content (Hydrophilic / Lypophilic drugs)
- Albumin (ACE-I, ARBs)

**Comorbidities**
- Higher number of concomitant medications required

aggravating the pharmacologic effect and turning it into an adverse event.

Developing an effective pharmacotherapeutic plan for an elderly patient requires a clear understanding of the principles of pharmacokinetics and pharmacodynamics, which may be altered in the geriatric population because of alterations in the basic physiology. This understanding is lacking because of paucity of drug trials in older adults.

Table 4 enumerates the factors that make it difficult to generalize the effect a drug will have on an older individual.

Table 4: Age-associated trends in clinical hypertension

| 1. Sodium sensitivity increases with age, as does the hypotensive response to diuretics |
| 2. The renin response to salt intake is more reduced with age in hypertensive than in normotensive elderly subjects |
| 3. Isolated systolic hypertension becomes more frequent than systolic-diastolic hypertension |
| 4. Arterial stiffness increases |
| 5. There is a greater incidence of endothelial dysfunction |
| 6. The frequency of ‘white coat effect’ increases |
| 7. Baroreceptor Reflex sensitivity reduced |

**GOAL BP TO BE ACHIEVED**

**The Evidence**

Different guidelines have recommended different goal BP to be achieved. JNC 7 used <140/90. This recommendation was based on weak evidence and expert opinion. The new JNC 8 Guidelines 2016 have recommended that hypertensive patients > 60 years of age be treated to a goal BP of 150/90. Compared to the JNC-7 report, JNC-8 is more evidence-based. AHA/ACC/ASH Guidelines 2016 endorsed the goal of JNC 7 to a BP of < 140/90. SPRINT has sprung a surprise. Intensive SBP treatment to a level of < 120 mm Hg was more effective in reducing CV events and all-cause mortality than in the standard treatment group; with comparable adverse outcome rates. The ACP/AAFP Guidelines also recommend initiating treatment in all ≥60 years of age with a SBP >150 mmHg and target it to <150 mmHg. Those with associated co-morbidities like CNS, cardiovascular disease, diabetes mellitus should have a goal BP of <140 mmHg.

**Practical Implications**

Targets are for Guidelines. The practicing physician should address the patient in front of him and treat as per his needs. Start treatment with a SBP of > 160 mm Hg and reduce it to as much as can be without interfering with quality of life (QoL) and without...
the risk of causing adverse events due to too low BP.

The optimal target BP among very elderly patients has yet to be defined. In my opinion and experience of managing very old hypertensives and those with Frailty Syndrome, treatment targets need to be individualized. In the absence of certainty, each particular case must be carefully assessed, and the possible benefits of antihypertensive treatment weighed against the risks, which tend to increase with age. Reducing BP by approximately 20 mm Hg is a safe alternative that will not produce adverse effects of therapy and ensure good quality of life.

**COGNITIVE DYSFUNCTION & DEMENTIA AS A RESULT OF HYPERTENSION**

High BP itself, as well as medications used for its treatment can result in cognitive impairment and dementia. Most studies have demonstrated a positive correlation between BP levels and the development of cognitive abnormalities and dementia years later.

High mid-life BP has been shown to be a strong and independent predictor of later cognitive impairment. Paradoxically, a low BP in the very elderly (DBP) can also result in cognitive impairment; possibly a J-shaped curve effect. Hypertension appears to be the strongest risk factor for all forms of vascular dementia.

The HYVET-COG Study which examined quality of life and cognitive function showed that antihypertensive treatment in elderly patients does not statistically reduce incidence of dementia. This negative finding might have been due to the short follow-up, owing to the early termination of the trial

**Mechanisms**

- The relationship between cognition and BP is complex, and factors such as age, education, effective follow-up, hyperinsulinemia, hypercholesterolemia diabetes mellitus, may potentiate the negative effects of high BP on cognitive functions.

- Long term hypertension leads to vascular remodeling with narrowing of the lumen and wall thickening. This might affect cerebral blood flow and disturb cerebral metabolism and structure.

- High BP levels have a negative effect on intellectual performance could also be linked to alterations in the cerebral white matter. Some studies have suggested that hypertension, particularly high SBP, was the main risk factor for white-matter lesions, while some have reported either no or an inverse association with BP.

**HYPERTENSION IN VERY OLD ADULTS**

The benefit of antihypertensive treatment is well established in patients aged 60 or 65 years to about 80 years of age.

**The Evidence**

Evidence in literature is more discordant in patients 80 or 84 years and older.

Studies like EWPHE and STOP-Hypertension Trial have not demonstrated significant benefit of antihypertensive therapy. In contrast, the SHEP trial and the Syst-Eur trial have concluded that the effect of treatment was found to be beneficial compared with placebo on the relative risk of stroke, but all-cause mortality did not decrease. An important finding in the Syst-Eur trial is that active treatment significantly reduced by half the incidence of dementia. One more study that included 1810 subjects aged 75 years and older had a significantly reduced incidence of dementia with BP control. On the contrary, no reduction in dementia is shown in the SHEP study. A meta-analysis of data from 1670 patients aged 80 years and older suggested that treatment reduced the incidence of strokes, cardiovascular events and heart failure, but no reduction in mortality. The HYVET has studied hypertension in the very elderly. It summarizes that lowering the BP of hypertensive patients over the age of 80 is associated with reductions in total mortality and rate of cardiovascular events. The
beneficial effects outweighed the risks from treatment and should be considered for the general ambulant very elderly population. However, further evidence is needed in the frail elderly. The “SPRINT-Senior” Trial – a subgroup of SPRINT Trial – included subjects > 75 years. Treating hypertension to a goal of SBP <120 in this population resulted in better cardiovascular health outcomes, compared to treating to a goal of SBP <140. This trial illustrated that in frail elderly also, intensive treatment with SBP reduction to < 120 mm Hg provided a similar risk reduction (for cardiovascular events and for mortality) as in non-frail participants, and the adverse events recorded were not statistically different between the two treatment groups.

Practical Implications
It is clear that antihypertensive treatment in very old patients preserves the quality of life and reduces morbidity by preventing strokes and heart failure and should be instituted. Large-scale specific trials are needed for definite conclusions on the benefit of treatment in very old patients.

PHARMACOECONOMICS: IT’S RELEVANCE IN THIS AGE GROUP
The cost of health-care is on a continuous upsurge. The financial resources in this age group generally dwindle because of obvious reasons.

The cost-effectiveness and the cost:benefit ratio is most beneficial in those aged 60-75 years. Management of hypertension in this group reduces the morbidity and mortality for cardiovascular risk factors. They decline in those > 75 years because of the increasing cost of non-CVD and other morbidity. In younger adults with low absolute risk of CVD, cost-effectiveness and cost:benefit ratio becomes meaningless.

SUMMARY
The population of adults over 60 years of age is growing. Hypertension is one of the common age-related disorders. It entails a high morbidity and mortality, attributed to its consequences. Treatment clearly benefits this age group, and also the very old adults (> 80 years).

BP should be checked in both arms, and in the erect and lying down positions. Pseudo-hypertension, masked hypertension, and situational hypertension are common. Situational hypertension should be confirmed by ambulatory BP measurements. Renal Artery Stenosis is one of the important causes of secondary hypertension in this age group.

Initially non-pharmacologic interventions should be tried, and if they are not successful at lowering BP to target, a long-acting dihydropyridine calcium channel blocker or a diuretic should be administered.

Adverse effects are common, especially in frail elderly. They are due to age-related physiologic changes and inappropriate/excessive response to pharmacologic agents.

Evidence points that the individual patient should be treated with the aim of lowering the BP without affecting his QoL and without exposing him to ADRs. BP should be lowered to 140/90 and lower if the situation demands. Be wary of the “lower is better” approach because of the J-curve effect and a possible increase in adverse events at very low DBPs.

To conclude, the objective of this discussion is not merely a review of evidence-based medicine and academics; but primarily to promote healthy aging and help older adults to live a long, productive life and enjoy a good Quality of Life. Management of older adults is a social challenge and the need of the hour.

REFERENCES


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National Annual Conference of Hypertension Society of India

**Programme**

Advances in Hypertension-Obesity-Lipid-Diabetes

Date: 18th-20th August 2017 • Venue: Hyatt Regency, Kolkata

**PROGRAMME OVERVIEW**

- Hypertension, Obesity, Lipid, Diabetes
- Postgraduate Prog
- Paper Presentation
- HTN - New Concepts
- Research in Hypertension
- Clinical Dilemma
- Common issues in Practice
- Problems in HTN
- Advances in Lipid, Diabetes & Obesity
- Recent Update
- Newer Therapy

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Many pathophysiologic factors are concerned in the genesis of essential hypertension: redoubled sympathetic nervous system activity, maybe associated with heightened exposure or response to psychosocial stress; overrun of sodium-retaining hormones and vasoconstrictors; long-run high metallic element intake; inadequate dietary intake of metallic element and calcium; redoubled or inappropriate peptidase secretion with resultant redoubled production of Hypertensin and aldosterone.

Deficiencies of vasodilators, like prostacyclin, nitric oxide (NO), and therefore the symptom peptides; alterations in expression of the kallikrein—plant hormone system that affect tube-shaped structure tone and nephritic salt handling; abnormalities of resistance vessels, as well as selective lesions within the nephritic microvasculature; polygenic disease mellitus; hormone resistance; obesity; increased activity of tube-shaped structure growth factors; alterations in adrenergic receptors that influence pulse rate, inotropic properties of the center, and tube-shaped structure tone; and altered cellular particle transport

Understanding these complex mechanisms has important implications for the targeting of antihypertensive therapy to achieve benefits beyond lowering blood pressure.

The pathogenesis of essential hypertension is multifactorial and highly complex. It tends to cluster in families and represents a collection of genetically based diseases or syndromes with several resultant inherited biochemical abnormalities. The resulting phenotypes can be modulated by various environmental factors, thereby altering the severity of blood pressure elevation and the timing of hypertension onset. A small number of patients (between 2% and 5%) have an underlying renal or adrenal disease as the cause for their raised blood pressure.

Multiple factors modulate blood pressure (BP) for adequate tissue perfusion; these include the following:

- Humoral mediators
- Vascular reactivity
- Circulating blood volume
- Vascular caliber
- Blood viscosity
- Cardiac output
• Blood vessel elasticity
• Neural stimulation

After a long, invariable, asymptomatic period, persistent hypertension develops into complicated hypertension, in which target organ damage to the aorta and small arteries, heart, kidneys, retina, and central nervous system is evident.

The progression of essential hypertension begins with prehypertension in persons aged 10-30 years (by increased cardiac output) and then advances to early hypertension in persons aged 20-40 years (in which increased peripheral resistance is prominent), then to established hypertension in persons aged 30-50 years, and finally to complicated hypertension in persons aged 40-60 years.

FACTORS INFLUENCING BP REGULATION

Regulation of normal blood pressure (BP) is a complex process. Arterial BP is a product of cardiac output and peripheral vascular resistance.

Cardiac output and peripheral resistance

Maintenance of a normal blood pressure is dependent on the balance between the cardiac output and peripheral vascular resistance. Most patients with essential hypertension have a normal cardiac output but a raised peripheral resistance. Peripheral resistance is determined not by large arteries or the capillaries but by small arterioles, the walls of which contain smooth muscle cells. Contraction of smooth muscle cells is thought to be related to a rise in intracellular calcium concentration, which may explain the vasodilatory effect of drugs that block the calcium channels. Prolonged smooth muscle constriction is thought to induce structural changes with thickening of the arteriolar vessel walls possibly mediated by angiotensin, leading to an irreversible rise in peripheral resistance. It has been postulated that in very early hypertension the peripheral resistance is not raised and the elevation of the blood pressure is caused by a raised cardiac output, which is related to sympathetic overactivity. The subsequent rise in peripheral arteriolar resistance might therefore develop in a compensatory manner to prevent the raised pressure being transmitted to the capillary bed where it would substantially affect cell homeostasis.

The factors affecting cardiac output include sodium intake, renal function, and mineralocorticoids; the inotropic effects occur via extracellular fluid volume augmentation and an increase in heart rate and contractility.

Peripheral vascular resistance is dependent upon the sympathetic nervous system, humoral factors, and local autoregulation. The sympathetic nervous system produces its effects via the vasoconstrictor alpha effect or the vasodilator beta effect. Recent studies with bilateral radiofrequency renal nerve ablation have shown a significant reduction of blood pressure in drug-resistant patients. Similar reductions in blood pressure have shown bilateral carotid artery stimulation in the same populations. These studies confirm the important role of the sympathetic nervous system in the pathogenesis of hypertension. The humoral actions on peripheral resistance are also influenced by other mediators, such as vasoconstrictors (eg, angiotensin, catecholamines) or vasodilators (eg, prostaglandins, kinins).

Blood viscosity, vascular wall shear conditions (rate and stress), and blood flow velocity (mean and pulsatile components) have potential relevance with regard to the regulation of BP in humans by vascular and endothelial function. Circulating blood volume is regulated by renal salt and water handling, a phenomenon that plays a particularly important role in salt-sensitive hypertension.

Reninangiotensin system

The reninangiotensin system may be the most important of the endocrine systems that affect the control of blood pressure. Renin is
secreted from the juxtaglomerular apparatus of the kidney in response to glomerular underperfusion or a reduced salt intake. It is also released in response to stimulation from the sympathetic nervous system. Renin is responsible for converting renin substrate (angiotensinogen) to angiotensin I, a physiologically inactive substance which is rapidly converted to angiotensin II in the lungs by angiotensin converting enzyme (ACE). Angiotensin II is a potent vasoconstrictor and thus causes a rise in blood pressure. In addition it stimulates the release of aldosterone from the zona glomerulosa of the adrenal gland, which results in a further rise in blood pressure related to sodium and water retention.

The circulating reninangiotensin system is not thought to be directly responsible for the rise in blood pressure in essential hypertension. In particular, many hypertensive patients have low levels of renin and angiotensin II (especially elderly and black people), and drugs that block the reninangiotensin system are not particularly effective.

There is, however, increasing evidence that there are important noncirculating “local” reninangiotensin epicrine or paracrine systems, which also control blood pressure. Local renin systems have been reported in the kidney, the heart, and the arterial tree. They may have important roles in regulating regional blood flow (Figure 1).

**Autonomic nervous system**

Sympathetic nervous system stimulation can cause both arteriolar constriction and arteriolar dilatation. Thus the autonomic nervous system has an important role in maintaining a normal blood pressure. It is also important in the mediation of short term changes in blood pressure in response to stress and physical exercise. There is, however, little evidence to suggest that epinephrine (adrenaline) and norepinephrine (noradrenaline) have any clear role in the aetiology of hypertension. Nevertheless, their effects are important, not least because drugs that block the sympathetic nervous system do lower blood pressure and have a well established therapeutic role. It is probable that hypertension is related to an
interaction between the autonomic nervous system and the renin-angiotensin system, together with other factors, including sodium, circulating volume, and some of the more recently described hormones (Figure 2).

**Autoregulation of BP**

Autoregulation of BP occurs by way of intravascular volume contraction and expansion regulated by the kidney, as well as via transfer of transcapillary fluid. Through the mechanism of pressure natriuresis, salt and water balance is achieved at heightened systemic pressure, as proposed by Guyton. Interactions between cardiac output and peripheral resistance are autoregulated to maintain a set BP in an individual. For example, constriction of the arterioles elevates arterial pressure by increasing total peripheral resistance, whereas venular constriction leads to redistribution of the peripheral intravascular volume to the central circulation, thereby increasing preload and cardiac output.

**Vasoreactivity and the role of the vascular endothelium**

The vascular endothelium is considered to be a vital organ, in which synthesis of various vasodilating and constricting mediators occurs. The interaction of autocrine and paracrine factors takes place in the vascular endothelium, leading to growth and remodeling of the vessel wall and to the hemodynamic regulation of BP.

Dysfunction of the endothelium has been implicated in human essential hypertension. Modulation of endothelial function is an attractive therapeutic option in attempting to minimise some of the important complications of hypertension. Clinically effective antihypertensive therapy appears to restore impaired production of nitric oxide, but does not seem to restore the impaired endothelium dependent vascular relaxation or vascular response to endothelial agonists.

This indicates that such endothelial dysfunction is primary and becomes irreversible once the hypertensive process has become established. The vasoreactivity of the vascular bed, an important phenomenon mediating changes of hypertension, is influenced by the activity of vasoactive factors, reactivity of the smooth muscle cells, and structural changes in the vessel wall and vessel caliber, expressed by a lumen-to-wall ratio.

Numerous hormonal, humoral vasoactive, and growth and regulating peptides are produced in the vascular endothelium. These mediators include angiotensin II, bradykinin, endothelin, nitric oxide, and several other growth factors. Endothelin is a potent vasoconstrictor and growth factor that likely plays a major role in the pathogenesis of hypertension. Angiotensin II is a potent vasoconstrictor synthesized from angiotensin I with the help of an angiotensin-converting enzyme (ACE).

Another vasoactive substance manufactured in the endothelium is nitric oxide. Nitric oxide is an extremely potent vasodilator that influences local autoregulation and other
vital organ functions. Additionally, several growth factors are manufactured in the vascular endothelium; each of these plays an important role in atherogenesis and target organ damage. These factors include platelet-derived growth factor, fibroblast growth factor, insulin growth factor, and many others.

Many other vasoactive systems and mechanisms affecting sodium transport and vascular tone are involved in the maintenance of a normal blood pressure. It is not clear, however, what part these play in the development of essential hypertension. Bradykinin is a potent vasodilator that is inactivated by angiotensin converting enzyme. Consequently, the ACE inhibitors may exert some of their effect by blocking bradykinin inactivation.

Endothelin is a recently discovered, powerful, vascular, endothelial vasoconstrictor, which may produce a salt sensitive rise in blood pressure. It also activates local renin-angiotensin systems. Endothelial derived relaxant factor, now known to be nitric oxide, is produced by arterial and venous endothelium and diffuses through the vessel wall into the smooth muscle causing vasodilation. Atrial natriuretic peptide is a hormone secreted from the atria of the heart in response to increased blood volume. Its effect is to increase sodium and water excretion from the kidney as a sort of natural diuretic. A defect in this system may cause fluid retention and hypertension. Sodium transport across vascular smooth muscle cell walls is also thought to influence blood pressure via its interrelation with calcium transport. Ouabain may be a naturally occurring steroidlike substance which is thought to interfere with cell sodium and calcium transport, giving rise to vasoconstriction (Figure 3).

**Hypercoagulability**

Patients with hypertension demonstrate abnormalities of vessel wall (endothelial dysfunction or damage), the blood constituents (abnormal levels of haemostatic factors, platelet activation, and fibrinolysis), and blood flow (rheology, viscosity, and flow reserve), suggesting that hypertension confers a prothrombotic or hypercoagulable state. These components appear to be related to target organ damage and long term prognosis, and some may be altered by antihypertensive treatment.

**Insulin sensitivity**

Epidemiologically there is a clustering of several risk factors, including obesity, hypertension, glucose intolerance, diabetes mellitus, and hyperlipidaemia. This has led to the suggestion that these represent a single syndrome (metabolic syndrome X or Reaven’s syndrome), with a final common pathway to cause raised blood pressure and vascular damage. Indeed some hypertensive patients who are not obese display resistance to insulin. There are many objections to this hypothesis, but it may explain why the hazards of cardiovascular risk are synergistic or multiplicative rather than just additive.

**Genetic factors**

Although separate genes and genetic factors have been linked to the development of essential hypertension, multiple genes are most likely contribute to the development of the disorder in a particular individual. It is therefore extremely difficult to determine accurately the relative contributions of each of these genes. Nevertheless, hypertension is about twice as common in subjects who have one or two hypertensive parents, and many epidemiological studies suggest that genetic factors account for approximately 30% of the variation in blood pressure in various populations. This figure can be derived from comparisons of parents with their monozygotic and dizygotic twin children, as well as their other children, and with adopted children. Some familial concordance is, however, due to shared lifestyle (chiefly dietary) factors.

Some specific genetic mutations can rarely cause hypertension. Experimental models of genetic hypertension have shown that the inherited tendency to hypertension resides primarily in the kidney. For example, animal
and human studies show that a transplanted kidney from a hypertensive donor raises the blood pressure and increases the need for antihypertensive drugs in recipients coming from “normotensive” families. Conversely a kidney from a normotensive donor does not raise the blood pressure in the recipient.

Increased plasma levels of angiotensinogen, the protein substrate acted on by renin to generate angiotensin I, have also been reported in hypertensive subjects and in children of hypertensive parents. Hypertension is rarely found in rural or “tribal” areas of Africa, but it is very common in African cities and in black populations in Britain and the United States. Whereas the rural/urban differences in Africa are clearly due to lifestyle and dietary factors, the finding that hypertension is commoner in black people compared with white people may have some genetic basis. There is some evidence from salt loading studies in medical students that black Americans are more susceptible to a given salt load than white Americans, and may be more sensitive to the beneficial effects of salt restriction. (Figure 4)

**Intrauterine influences**

There is increasing evidence that fetal influences, particularly birth weight, may be a determinant of blood pressure in adult life. For example, babies who are small at birth are more likely to have higher blood pressure during adolescence and to be hypertensive as adults. Babies who are small for their age are also more likely to have metabolic abnormalities that have been associated with the later development of hypertension and cardiovascular disease, such as insulin resistance, diabetes mellitus, hyperlipidaemia, and abdominal obesity (the “Barker hypothesis”). Insulin resistance almost certainly contributes to the increased prevalence of coronary disease seen in adults of low birth weight.

It is possible, however, that genetic factors influence the Barker hypothesis. Mothers with above average blood pressure in pregnancy give birth to smaller babies who subsequently develop above average blood pressure themselves and eventually hypertension. It is entirely likely that the similarity of blood pressures in mother and child are genetic and, in a modern “healthy” society, unrelated to intrauterine undernutrition. (Figure 5)

**Hypertension and metabolic syndrome**

The metabolic syndrome is an assemblage of metabolic risk factors that directly promote the development of atherosclerotic cardiovascular disease. Dyslipidemia, hypertension, and hyperglycemia are the most widely recognized metabolic risk factors. The combination of these risk factors leads to a prothrombotic, proinflammatory state in humans and identifies individuals who are at elevated risk for atherosclerotic cardiovascular disease.

Hypertensive patients who are obese have a sympathetic overdrive, higher cardiac output, and a rise in peripheral vascular resistance due to reduced endothelium-dependent vasodilation. Plasma aldosterone and endothelin are increased, the increase in cardiac output

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![Fig. 4: Renin and electrolytes in black and white people](image)

![Fig. 5: Possible mechanisms to explain why low birthweight babies are more likely to develop in later life](image)
manifests secondary to increased preload, and the end-diastolic volume and pressure are elevated, leading to left ventricular dilatation. Left ventricular wall thickening occurs secondary to increased afterload, heightening the risk of congestive heart failure. The concomitant diabetes that is often present in patients who are obese produces a devastating effect on the kidneys and leads to a much higher incidence of renal failure. Obstructive sleep apnea confers additional risk of resistant hypertension.

**Etiology of Essential Hypertension**

A possible etiology of essential hypertension has been proposed in which multiple factors, including genetic predisposition, excess dietary salt intake, and adrenergic tone, may interact to produce hypertension.

Patients who develop hypertension are known to develop a systemic hypertensive response secondary to vasoconstrictive stimuli. Alterations in structural and physical properties of resistance arteries, as well as changes in endothelial function, are probably responsible for this abnormal behavior of vasculature. Furthermore, vascular remodeling occurs over the years as hypertension evolves, thereby maintaining increased vascular resistance irrespective of the initial hemodynamic pattern.

Changes in vascular wall thickness affect the amplification of peripheral vascular resistance in hypertensive patients and result in the reflection of waves back to the aorta, increasing systolic BP.

One form of essential hypertension, termed high-output hypertension, results from decreased peripheral vascular resistance and concomitant cardiac stimulation by adrenergic hyperactivity and altered calcium homeostasis. A second mechanism manifests with normal or reduced cardiac output and elevated systemic vascular resistance (SVR) due to increased vasoreactivity. Another (and overlapping) mechanism is increased salt and water reabsorption (salt sensitivity) by the kidney, which increases circulating blood volume.

**Hypertensive Emergencies and Target Organ Damage**

The pathophysiology of hypertensive emergencies is not well understood. Failure of normal autoregulation and an abrupt rise in systemic vascular resistance (SVR) are typically initial steps in the disease process. Increases in SVR are thought to occur from the release of humoral vasoconstrictors from the wall of a stressed vessel. The increased pressure within the vessel then starts a cycle of endothelial damage, local intravascular activation of the clotting cascade, fibrinoid necrosis of small blood vessels, and the release of more vasoconstrictors. If the process is not stopped, a cycle of further vascular injury, tissue ischemia, and autoregulatory dysfunction ensues.

Single-organ involvement is found in approximately 83% of patients presenting with hypertensive emergencies. Two-organ involvement is found in 14% of patients, and multiorgan involvement (>3 organ systems) is found in approximately 3% of patients presenting with a hypertensive emergency.

**Hypertension and cardiovascular disease**

During hypertensive emergencies, the left ventricle is unable to compensate for an acute rise in SVR. This leads to left ventricular failure and pulmonary edema or myocardial ischemia.

Chronic hypertension causes increased arterial stiffness, increased systolic blood pressure (BP), and widened pulse pressures. These factors decrease coronary perfusion pressures, increase myocardial oxygen consumption, and lead to left ventricular hypertrophy (LVH). In LVH, the myocardium undergoes structural changes in response to increased afterload. Cardiac myocytes respond by hypertrophy, allowing the heart to pump more strongly against the elevated pressure. However, the contractile function
of the left ventricle remains normal until later stages. Eventually, LVH lessens the chamber lumen, limiting diastolic filling and stroke volume. The left ventricular diastolic function is markedly compromised in long-standing hypertension.

The mechanisms of diastolic dysfunction apparently include an aberration in the passive relaxation of the left ventricle during diastole. Over time, fibrosis may occur, further contributing to the poor compliance of the ventricle. As the left ventricle does not relax during early diastole, left ventricular end-diastolic pressure increases, further increasing left atrial pressure in late diastole. The exact determinants of left ventricular diastolic dysfunction have not been well studied; possibly, the abnormality is governed by abnormal calcium kinetics.

Cardiac involvement in hypertension manifests as LVH, left atrial enlargement, aortic root dilatation, atrial and ventricular arrhythmias, systolic and diastolic heart failure, and ischemic heart disease. LVH is associated with an increased risk of premature death and morbidity. A higher frequency of cardiac atrial and ventricular dysrhythmias and sudden cardiac death may exist. Possibly, increased coronary arteriolar resistance leads to reduced blood flow to the hypertrophied myocardium, resulting in angina despite clean coronary arteries. Hypertension, along with reduced oxygen supply and other risk factors, accelerates the process of atherogenesis, thereby further reducing oxygen delivery to the myocardium.

Hypertension and cerebrovascular disease

Cerebral autoregulation is the inherent ability of the cerebral vasculature to maintain a constant cerebral blood flow (CBF) across a wide range of perfusion pressures. Rapid rises in BP can cause hyperperfusion and increased CBF, which can lead to increased intracranial pressure and cerebral edema.7 Patients with chronic hypertension can tolerate higher mean arterial pressures before they suffer disruption of their autoregulatory system. However, such patients also have increased cerebrovascular resistance and are more prone to cerebral ischemia when flow decreases, especially if BP is decreased into normotensive ranges.

Hypertension and renal disease

Hypertension is commonly observed in patients with kidney disease, with chronic hypertension causing pathologic changes to the small arteries of the kidney. As hypertensive damage occurs, the renal arteries develop endothelial dysfunction and impaired vasodilation, which alter renal autoregulation. When the renal autoregulatory system is disrupted, the intraglomerular pressure starts to vary directly with the systemic arterial pressure, thus offering no protection to the kidney during BP fluctuations. During a hypertensive crisis, this can lead to acute renal ischemia.

Volume expansion is the main cause of hypertension in patients with glomerular disease (nephrotic and nephritic syndrome). Hypertension in patients with vascular disease is the result of the activation of the renin-angiotensin system, which is often secondary to ischemia. The combination of volume expansion and the activation of the renin-angiotensin system is believed to be the main factor behind hypertension in patients with chronic renal failure.

Renovascular hypertension

The term renovascular hypertension (RVHT) denotes the causal relationship between anatomically evident arterial occlusive disease and elevated BP. RVHT is the clinical consequence of renin-angiotensin-aldosterone activation. As demonstrated by Goldblatt, renal artery occlusion creates ischemia, which triggers the release of renin and a secondary elevation in BP. Hyperreninemia promotes conversion of angiotensin I to angiotensin II, causing severe vasoconstriction and aldosterone release. The ensuing cascade of events varies,
depending on the presence of a functioning contralateral kidney. In the setting of 2 kidneys, aldosterone-mediated sodium and water retention is handled properly by the nonstenotic kidney, precluding volume from contributing to the angiotensin II–mediated hypertension. By contrast, a solitary, ischemic kidney has little or no capacity for sodium and water excretion; hence, volume plays an additive role in the hypertension.

**Hypertension and end-stage renal disease**

Despite widespread treatment of hypertension in the United States, the incidence of end-stage renal disease continues to rise. The explanation for this rise may be concomitant diabetes mellitus, the progressive nature of hypertensive renal disease despite therapy, or a failure to reduce BP to a protective level. A reduction in renal blood flow in conjunction with elevated afferent glomerular arteriolar resistance increases glomerular hydrostatic pressure secondary to efferent glomerular arteriolar constriction. The result is glomerular hyperfiltration, followed by development of glomerulosclerosis and further impairment of renal function.

**Hypertension and ocular changes**

The pathophysiologic effects of hypertensive ocular changes can be divided into acute changes from malignant hypertension and chronic changes from long-term, systemic hypertension.

Optic changes that can result from malignant hypertension include the development of the following acute retinal lesions:

- Focal intraretinal periarteriolar transudates
- Inner retinal ischemic spots (cotton-wool spots)
- Microaneurysms
- Shunt vessels
- Collaterals

Chronic hypertensive retinal changes include the following:

- Arteriolosclerosis - Localized or generalized narrowing of vessels
- Copper wiring and silver wiring of arterioles as a result of arteriolosclerosis
- Arteriovenous (AV) nicking as a result of arteriolosclerosis
- Retinal hemorrhages
- Nerve fiber layer losses
- Increased vascular tortuosity
- Remodeling changes due to capillary nonperfusion, such as shunt vessels and microaneurysms

**CONCLUSION**

Essential hypertension is primarily due to an increase in systemic vascular resistance and not only increase in cardiac output. Hypertension is associated with impaired kidney sodium excretion, reset baroreflexes, and reset local autoregulation responses. Alterations in the renin-angiotensin-aldosterone system and sympathetic nervous system are likely to play a role in the generation and maintenance of hypertension, due to their direct effects on kidney vascular tone and sodium excretion.

**REFERENCES**

Hypertension is one of the leading cause of death globally. At least one of every five adult Indian is suffering from hypertension. It is responsible for 57% of all stroke deaths and 24% of all cardiac deaths in India.

Often it becomes difficult to diagnose hypertension on the basis of variable blood pressure (BP) readings observed in a clinic or hospital settings because of various associated factors. Also the diurnal variation is difficult to measure. Two important and easy techniques have been developed to overcome these issues. One of them is Ambulatory Blood Pressure Monitoring (ABPM) and another is home blood pressure monitoring.

ABPM involves measuring blood pressure (BP) at regular intervals (usually every 20–30 minutes) over a 24 hour period while patients undergo normal daily activities, including sleep. The use of ABPM is increasing day by day in routine clinical practice.

### INDICATIONS OF ABPM

Various indications of ABPM includes:

1. Suspected white-coat hypertension (including in pregnancy)
2. Suspected masked hypertension (untreated subject with normal clinic BP and elevated ABP)
3. Suspected nocturnal hypertension or no night time reduction in BP (dipping)
4. Hypertension despite appropriate treatment
5. Patients with a high risk of future cardiovascular events (even if clinic BP is normal)
6. Suspected episodic hypertension.

It may also be useful in certain other situations which include:

- Titrating antihypertensive therapy
- Borderline hypertension
- Hypertension detected early in pregnancy
- Suspected or confirmed sleep apnea
- Syncope or other symptoms suggesting orthostatic Hypotension, where this cannot be demonstrated in the clinic.

### Procedure

The portable monitor is worn on a belt connected to a standard cuff on the upper arm. The BP readings are taken for a period of 24 to 48 hours, usually every 15 to 20 minutes during daytime and every 30 to 60 minutes at night. Ambulatory BP monitors use cuff oscillometry. The cuff is inflated until the pressure occludes flow within the brachial
artery. As the pressure is released, blood begins to flow causing fluctuations (oscillations) in the arterial wall that are detected by the monitor. These oscillations increase in intensity then diminish and cease when blood is flowing normally. The monitor defines the maximal oscillations as mean arterial BP and then uses an algorithm to calculate systolic and diastolic BP.

Although the day and night timings can be set, but by default the day and night cut-off are 9 AM to 9 PM for daytime and 1 AM to 6 AM for night time. The intermediate periods are usually variable and are termed as Rising period which is from 6 AM to 9 AM and Retiring period from 9 PM to 1 AM. For a satisfactory result, at least 70% of all recordings should be appropriate.

When complete, the device is connected to a computer that prepares a report of the 24 hour, day time, night time, and sleep and awake (if recorded) average systolic and diastolic BP and heart rate.

**ANALYSIS OF ABPM READINGS**

**Defining hypertension**

As per the ESC guidelines 2013, the cut off the normal readings of ABPM and cut offs for hypertension are shown in table 1. On the basis of these reading hypertension can be defined in patients who have discrepancy in office and home blood pressure readings.

**Dipping**

Another important parameter to be obtained from ABPM recording is about dipping of blood pressure during night time. The night-to-day BP ratio represents the ratio between average night-time and daytime BP. BP normally decreases during the night which is defined as ‘dipping’. Although the degree of night-time dipping has a normal distribution in a population setting, it is generally agreed that the finding of a nocturnal BP fall of >10% of daytime values (night–day BP ratio ,0.9) will be accepted as an arbitrary cut-off to define subjects as ‘dippers’. Various patterns are shown in Table 2.

Possible reasons for absence of dipping are sleep, disturbance, obstructive sleep apnoea, obesity, high salt intake in salt sensitive subjects, orthostatic hypotension, autonomic dysfunction, chronic kidney disease (CKD), diabetic neuropathy and old age.

There is considerable data which suggest measurement of night time blood pressure yields additional prognostic data in terms of all-cause mortality and cardiovascular events. It is estimated that around 7% of patients with hypertension have isolated nocturnal hypertension. MAPEC study (Prognostic value of ABPM in prediction of CV events and effects of chronotherapy in relation to risk) was a 5 years follow up study on 3344 patients. It showed a 17% reduction in CVD risk or each 5 mm Hg decrease in mean asleep BP. Also, the mean Nocturnal BP is most significant

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**Table 1: Showing cut offs for defining hypertension**

<table>
<thead>
<tr>
<th>Category</th>
<th>Normal mm Hg</th>
<th>Hypertension mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 Hours Average</td>
<td>&lt; 115/75</td>
<td>≥ 130/80</td>
</tr>
<tr>
<td>Day Time / Awake</td>
<td>&lt; 120/80 mm Hg</td>
<td>≥135/85</td>
</tr>
<tr>
<td>Asleep / Night time</td>
<td>&lt; 105/65</td>
<td>≥120/70</td>
</tr>
</tbody>
</table>

**Table 2: Various patterns of dipping**

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Description</th>
<th>Night to Day BP ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipping</td>
<td>Nocturnal BP fall of &gt;10% of daytime values</td>
<td>0.8 to 0.9</td>
</tr>
<tr>
<td>Non-dipping</td>
<td>Absence of nocturnal fall in BP</td>
<td>0.9 to 1.0</td>
</tr>
<tr>
<td>Reverse Dipping or rising</td>
<td>Increase in BP levels during sleep to levels higher than in daytime</td>
<td>&gt;1.0</td>
</tr>
<tr>
<td>Extreme Dipping</td>
<td>A marked fall in BP during the night.</td>
<td>&lt; 0.8</td>
</tr>
</tbody>
</table>
predictor of event free survival. Based on these findings the American Diabetes Association has suggested that one of the antihypertensive drugs should be administered at night.

Classification based on ABPM (Figure 1).

**WHITE COAT HYPERTENSION**

White coat hypertension is a common phenomenon and is essential to evaluate true hypertension. It refers to an abnormal stress response of visiting a clinic leading to higher blood pressure reading in clinic setting as compared to that measured in home environment. White-coat hypertension is defined as “a clinic blood pressure of 140/90 mm Hg or higher on at least three occasions, with at least two sets of measurements of less than 140/90 mm Hg in non-clinic settings, plus the absence of target-organ damage”.5

Several studies have shown that, in patients diagnosed as being hypertensive on a first visit to a new clinician, there is a mean 15 and 7 mmHg fall in the systolic and diastolic blood pressure, respectively, by the third visit, with some patients not reaching a stable value until the sixth visit.7 In cross-sectional studies, the prevalence of white coat hypertension ranges from 10 to more than 20 percent, and it appears to be higher in children and the elderly.8

A white coat effect is also described which is defined as a rise in BP occurring in medical environment regardless of the daytime ABPM level or antihypertensive medications. It is clinically important when Office BP is ≥ 20 mm Hg systolic of ≥ 10 mm Hg diastolic higher than awake ABPM reading. It is an important cause of pseudo – resistant HTN.

Patients with white coat hypertension are also at high risk for developing sustained hypertension in future. In a study of 81 patients with office hypertension (mean blood pressure 154/97 mmHg) and normal 12-hour ambulatory blood pressure (mean blood pressure 125/77 mmHg), 60 had a mean ambulatory blood pressure above 140/90 mmHg after five to six years of follow-up (74 percent).9

**MASKED HYPERTENSION**

It is defined as a normal clinic blood pressure and a high ambulatory blood pressure. This condition is the reverse of white-coat hypertension. The clinic blood pressure of patients with masked hypertension may underestimate the risk of cardiovascular events.

As many as 10 to 40 percent of patients who are normotensive by conventional clinic measurement are hypertensive by ABPM10. Masked hypertension has been associated with an increased long-term risk of sustained hypertension and cardiovascular morbidity11. Because of the risk associated with masked hypertension, ABPM should be considered in patients referred for possible hypertension (for a variety of reasons, such as LVH) despite repeatedly normal blood pressure when measured in the clinic.

**INFLUENCE ON THERAPY OF HYPERTENSION**

Based on the ABPM monitoring various adjustments can be done in the antihypertensive regimes of a patient. The drugs, doses and timings of the medications can be adjusted on basis of the peaks found in the ABPM readings. This is especially useful in patients with resistant and labile hypertension.

**CONCLUSION**

Although the use of ABPM monitoring may
not help in all the cases of hypertension but its use in selected cases is of utmost importance in altering the long term outcomes. The night time blood pressure is a very important parameter which is obtained by ABPM. It is a strong predictor of long term cardiovascular outcomes. ABPM can also be used in adjusting the antihypertensive medications in difficult to treat cases.

REFERENCES

Case Report

Amlodipine Induced Gum Hypertrophy - Rare Case Studies

Naga Raghunandan Thota¹, Yeshavanth G², Sandeep Yamasani¹, Shruthi R³, Promod Jali³

ABSTRACT

Background: Gingival enlargement is a result of variety of inflammatory, systemic disorders, neoplasia and adverse effects of drugs. It is commonly encountered as a side effect of three classes of drugs, namely, anticonvulsants, calcium channel blockers and immunosuppressant cyclosporine. The present case study refers to two middle aged hypertensive females on long term treatment of Amlodipine with no other co-morbidities. They developed soft tissue enlargement of gums which on biopsy revealed as gingival hyperplasia with fibrosis and super-added inflammatory changes. Treating physicians should have a clear knowledge regarding the etiology of gingival enlargement and should be vigilant regarding the treatable causes as like those of drugs by simple discontinuation of the offender.

INTRODUCTION

Gingival enlargement is a well-known consequence of administration of some anticonvulsants, the immunosuppressant drug cyclosporine A, and calcium channel blockers, and it may create speech, mastication, tooth eruption, and esthetic problems. Calcium channel blockers are used in the management of various cardiovascular disorders such as angina and hypertension. The prevalence with amlodipine, 33.3%, is much lower.²

MATERIALS AND METHODS

It is study of two middle aged females, hypertensive since 5 years and on regular treatment of Amlodipine 5mg twice daily. Based on the clinical evaluation of the soft-

Fig. 1: Gingival hyperplasia at the time of presentation

1Postgraduate, ²Assistant Professor, Department of General Medicine, SSIMS&RC, Davangere, Karnataka; ³Assistant Professor, Department of Oral Pathology, College of Dental Sciences, Davangere, Karnataka;
tissue response to scaling and the persistence of fibrotic component on the lingual aspect of mandibular incisors, gingivectomy was performed. The patients were placed on periodic recall of 3 months for the evaluation of the gingival hyperplasia.

Intraoral examination revealed generalized pink gingiva with rolled gingival margins, lobulated papillae, and fibrous overgrowth throughout the maxilla and mandible, particularly on the labial and buccal side (Figure 1). Histologically, the lesions were diagnosed as fibro-epithelial hyperplasia, and were indicative of amlodipine-induced gingival hyperplasia based on clinical and histological evidence (Figure 2).

**DISCUSSION**

Calcium channel blockers are one of the chief etiologic agents for drug-induced gingival enlargement. Amlodipine is a third-generation dihydropyridine calcium antagonist. However, amlodipine has a unique physio-chemical profile, which is characterized by nearly complete resorption, late peak plasma concentrations, high bioavailability, and slow hepatic degradation. Owing to its slow elimination and long duration of its action, has a better patient compliance in reducing hypertension. Clinically, drug-induced gingival overgrowth normally heralds at the interdental papillae and is more frequently found in the anterior segment of the labial surfaces. Gradually, gingival lobulations are formed that may later become fibrotic due to associated superadded inflammation.

There occurs characteristic accumulation of extracellular matrix in the form of collagen. Histologically, hyperplasia of connective tissue and overlying epithelium in the form of acanthosis. Rete pegs extend deep in to the connective tissue which signify collagen bundles with intervening blood vessels and fibroblasts. Over time there occurs inflammatory infiltration in the form of plasma cells.

The pathogenesis of gingival overgrowth is unclear as of now. It has been proposed that the resistance or suspectibility to gum hypertrophy induced by drugs is due to the presence varying degree of fibroblast progenitors which exibit functional heterogeneity in genetically predisposed patients.

Another theory of fibrogenesis is due to reduction in the influx of calcium ions across the cell membrane which in turn reduces the secretory functions of the fibroblasts and extracellular matrix degrading collagenases. Thus, increased fibroblastic proliferation and collagen synthesis occurs.

Inflammatory and non-inflammatory mechanisms have also been suggested. The non-inflammatory mechanisms include defective folic acid uptake resulting in collagenase functional disturbance, keratinocyte growth factor upregulation, aldosterone block resulting feed back increase in adreno cortico trophic harmone excess. Inflammatory mechanism are more or less directly toxic and depend on upregulation of Transforming growth factor beta and have addictive effects with poor oral hygiene.

The treating physician should identify the culprit drug and immediately with hold the same or substituting with an alternative antihypertensive depending on the disease profile of the patient with advocation of serial oral hygiene and plaque removal techniques. Usually there occurs considerable regression over a three month period. Unresolved or rather aesthetically unacceptable gingival over growth portions of the oral cavity have to be excised. Gingivectomy and follow up in association with a periodontist is always advisable for refractory cases.
CONCLUSION
The reported cases are examples of a combined type of gingival enlargement—basically a drug-induced one, complicated by inflammatory changes due to plaque accumulation. The case studies, thus, would help treating physicians immensely to encounter such gingival hyperplasia in the absence of systemic disorders and treat them efficiently.

REFERENCES
Secondary Hypertension Complicating Pregnancy - A Case Report

G Usha¹, K Abhishek², Manjula Rao³, Abhishek Mufkalwar⁴, G Karuna⁴

ABSTRACT

Secondary hypertension is a type of hypertension with an underlying potential correctable cause. An underlying cause for hypertension must be entertained if the onset of hypertension is early in life; associated with symptoms and signs of the pathology which is causing the hypertension; the hypertension is resistant to treatment with medications and follows a severe or accelerated course. Amongst all the secondary aetiologies of hypertension, Reno Vascular Hypertension (RVH) is the most common. When RVH complicates pregnancy, it is associated with serious maternal and foetal consequences. Here we present a young woman who was diagnosed with RVH during her pregnancy, underwent a therapeutic procedure and went on to have a successful subsequent pregnancy.

CASE REPORT

A 20yr old female at 9+4 weeks of gestation with a history of chronic hypertension and previous intrauterine foetal death at 20 weeks of gestation was referred to us in view of persistently high blood pressure recordings. She was asymptomatic at the time of admission and was on combination antihypertensive therapy, nifedipine retard plus labetalol, since 8 months i.e., from the time of her previous pregnancy loss.

Her BP on admission was 180/120mmHg, and there was no significant pressure difference recorded between both upper and upper& lower limbs; Ankle Brachial Pressure Index (ABPI) was found to be 0.9., pulse rate 116/min, regular, all her peripheral pulses were felt. No renal bruit was heard on auscultation. Fundus examination showed changes of grade 2 hypertensive retinopathy. Cardiovascular and Respiratory system examination was normal.

She was initiated on treatment with Inj. Labetalol in incremental doses and switched over to NTG infusion because of lack of response to IV Labetalol, after which her pressures were optimized. She was investigated for any secondary cause of hypertension. Her Complete Blood Count, Serum Creatinine, Blood Urea, Serum Electrolytes, Complete Urine Examination, Lipid profile and Liver Function Tests were normal. Transthoracic echocardiogram revealed a...
mild concentric left ventricular hypertrophy with grade 1 diastolic dysfunction, no systolic and regional wall motion abnormalities were present.

On evaluating causes for her secondary hypertension, Renal Artery Doppler was done which showed a parvus tardus flow pattern at bilateral intrarenal arteries (L>R), features suggestive of **Bilateral Renal Artery Stenosis at origin secondary to fibromuscular dysplasia.** Small for size left kidney in comparison with right, and normal corticomedullary differentiation was found.

Her blood pressure could not be controlled with Labetalol, Nifedipine and Clonidine. So, in view of maternal risk her pregnancy was terminated and she underwent a renal angiogram which revealed right renal artery-90% ostial stenosis, and left renal artery- total ostial occlusion. After informed consent Percutaneous Transluminal Renal Angioplasty (PTRA) and Stenting to right renal artery was done; procedure was uneventful. She was discharged on Nifedipine, Clonidine and Dual Antiplatelet Therapy. She was counselled to avoid her next pregnancy for at least one year, so that all her parameters could be monitored and maintained at normal levels.

She conceived spontaneously 9 months post procedure. She was managed with Labetalol, Nifedipine and low dose Aspirin. She continued till term and delivered a healthy live girl baby. She is on regular follow up since then and now her blood pressure is under control with Nifedipine. 6 months after delivery she underwent MR angiography to look for other arteries involvement and it revealed bilateral renal artery stenosis, status post stenting right renal artery, complete occlusion of left renal artery, **possible narrowing at the origin of left common carotid artery,** with normal aortic arch and rest of aorta being normal.

**DISCUSSION**

Prevalence of hypertension in general population ranges between 2-15% in urban India and 2-8% in rural India. The prevalence has been steadily increasing over the years.¹ Though essential hypertension is the commonest type, about 5-10% of the patients² have secondary forms of hypertension. It is important for the clinician to look for an underlying cause especially when there are clinical clues which point to it because this is a potentially reversible form of hypertension. Though Reno Vascular Hypertension (RVH), along with hypertension secondary to renal parenchymal disease (2-3%) remains the commonest form of secondary hypertension, many aspects of it such as the prevalence, natural history, diagnosis and treatment remain unclear.
The prevalence of RVH is around 1-2%.3 The pathophysiology of RVH is well understood. This was identified by Goldblatt et al., in animal models4 by clamping both main renal artery of dogs, which resulted in renal ischemia because of hypoperfusion. This resulted in increased renin level, resulting in activation of Renin Angiotensin Aldosterone System(RAAS) which is responsible largely for the hemodynamic response that ensues (Figure 1). Though there are multiple types of intrinsic and extrinsic lesions associated with RVH, the two major forms of Renal Artery Stenosis(RAS) are Atherosclerosis and Fibro Muscular Dysplasia(FMD).

FMD is defined as an idiopathic, segmental, nonatherosclerotic, noninflammatory disease of renal artery and other medium sized arteries (especially the carotid artery) that can lead to stenosis, occlusion, dissection and aneurysm. FMD afflicts the younger age group and women, and should be considered in the evaluation of women with secondary hypertension in the childbearing age group. FMD must be suspected in a patient under the following circumstances:

Consider the diagnosis of FMD in the following circumstances5

<table>
<thead>
<tr>
<th>Onset of hypertension before age 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistant hypertension</td>
</tr>
<tr>
<td>Epigastric bruit and high blood pressure</td>
</tr>
<tr>
<td>Cervical bruit before age 60</td>
</tr>
<tr>
<td>Pulsative tinnitus</td>
</tr>
<tr>
<td>Severe or recurrent headaches</td>
</tr>
<tr>
<td>TIA or stroke before age 60</td>
</tr>
<tr>
<td>Dissection of a renal, carotid or vertebral artery</td>
</tr>
<tr>
<td>Aortic aneurysm before age 60</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
</tr>
<tr>
<td>Renal infarction</td>
</tr>
</tbody>
</table>

Three main types of renal FMD has been identified depending on the most affected part of the arterial wall- intimal FMD(5%), medial FMD(>85%) and perimedial FMD(10%). Angiographically FMD is classified as multifocal (string of beads appearance), unifocal(solitary stenosis <1cm in length), and tubular(stenosis of at least 1cm in length). FMD usually involves middle main and distal main renal artery. But unifocal FMD can be at ostium, the trunk or the bifurcation of the renal artery. As this feature lacks specificity, the diagnosis can be established in young (usually <40 yrs) patients with no atherosclerosis or other less frequent diseases. It is important to screen patients with renal artery involvement in FMD, for cervicocephalic lesions as this may guide the future management of these patients, and also other medium sized arteries. Familial FMD has been described in the literature.

The diagnosis of RVH requires a high index of suspicion for which a clinical prediction rule may be helpful.6 It is reasonable to go for non-invasive duplex ultrasonogram as initial investigation when the index of suspicion is high. This has to be confirmed by either CT angiography or MR angiography. Both display good sensitivity and specificity. Renal scintigraphy is not in the diagnostic algorithm. Renal Digital Subtraction Angiography(DSA) is recommended after CT or MR angiography in patients whom revascularisation is justified.7

The treatment modalities are medical, revascularisation by percutaneous transluminal angioplasty (PTA) or surgical method. Introduction of ACE inhibitors and ARB’s have resulted in marked improvement in patients with RAS. Revascularisation is recommended when there is failure of medical treatment, renal insufficiency or deterioration of renal function after administration of ACE inhibitors and ARB’s. Renal PTA is the procedure of choice in patients with FMD associated with RAS; it can be curative in FMD. Stenting following PTA is not routinely recommended but can be performed if required. After revascularisation it is mandatory to monitor the patient especially in the first 6months of procedure for restenosis, renal failure, dose adjustments of antihypertensives and thereafter at regular intervals.

Since FMD commonly affects women of child bearing age the diagnosis should be
considered in women with secondary hypertension.

The case reported here was a young woman with severe uncontrolled hypertension on 3 drugs with features suggestive of RAS on ultrasonogram presenting for the first time in pregnancy (Figure 2). With these findings the possibility of FMD was high in her and the renal angiogram confirmed the diagnosis (Figure 3).

Though hypertension is a common medical disorder in pregnancy, RVH complicating pregnancy is uncommon. The data is limited, a small number of case reports suggest it can lead to significant maternal and foetal complications. Managing these patients in pregnancy could be challenging if there is superimposed preeclampsia which is a common association. The other issue that complicates the management of these patients is the potential teratogenic effects of radiation exposure for diagnostic purposes. The mainstay drugs used for treatment (ACEI/ARB’s) are contraindicated in pregnancy. Young women with hypertension should be evaluated for FMD, if detected before pregnancy and the diagnosis should be considered in those patients who present with severe hypertension early in pregnancy.

A case series reports 6 pregnancies in 4 patients with FMD. 2 patients had hypertension prior to pregnancy; 1 had a vaginal delivery and the other patient opted for termination at 10 weeks of gestation. 2 patients developed hypertension during pregnancy, one patient underwent bilateral renal angioplasty after termination of pregnancy; another patient presented at 20 weeks of gestation with preeclampsia, placental abruption and intrauterine foetal death. She underwent an angioplasty and delivered a healthy baby in the following year.

There are case reports where successful revascularisation in second trimester was done with subsequent favourable maternal and foetal outcome. Appropriate shielding must be implemented and dose of radiation must be limited to less than 5 rads.

**CONCLUSION**

To conclude causes of secondary hypertension should be looked for, in young patients. Women of childbearing age group presenting with secondary hypertension prior to pregnancy or severe hypertension early in pregnancy should be evaluated for FMD as this is a potentially reversible cause of hypertension.
Fig. 3: MR Angiogram showing stent in situ for right renal artery and total occlusion of left renal artery
ACKNOWLEDGEMENT
We thank Dr. V. Dayasagar Rao, Consultant Cardiologist at KIMS, Hyderabad for performing the therapeutic intervention and helping us manage the patient.

REFERENCES

2nd International Conference on Hypertension & Health Care
11-13 September 2017, Amsterdam, Netherlands

2nd International Conference on Hypertension & Healthcare during the beautiful month of Sep 11-13, 2017 at Amsterdam, Netherlands, the place which sees the largest influx of tourists in Amsterdam. Working under the theme “New insights in diagnosis and management for hypertension” we bring together the brightest and most productive minds to discuss the intricate concepts of Hypertension diagnosis and management.

The conference aims to provide an opportunity to share knowledge, expertise along with unparalleled networking opportunities between a large number of medical professionals like Directors, Heads, Deans, Professors, Scientists, Researchers, Cardiologists and Writers of the Hypertension or Cardiology and related departments, Founders and Employees of the related companies, Associations, Organizations, Laboratory members and Young researchers working in the field of hypertension treatment and management. This conference mainly focuses on spreading the awareness about challenges in this field and how to prevent and manage hypertension.

For more information log on to: http://echocardiography.conferenceseries.com/
A Rare Cause of Hypertension in Youngs-Mid-Aortic Dysplastic Syndrome

Harshita Sharma, Rajesh Manocha, Chandan Kumar, Sailesh Bansiwala, Harshit Khosla
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Mid aortic syndrome, coarctation of abdominal aorta is a rare disease with only 200 reported cases. It is characterized by constriction of distal thoracic and/or abdominal aorta and its branches, therefore it is also known as abdominal aortic coarctation. MAS is characterized radiologically by severe narrowing of abdominal aorta and its branches and most of these patients usually die due to progressive severe hypertension before the age of 35-40, if left untreated.

Case Report: A 24 year old male was admitted with complain of pain abdomen, burning micturition and decreased urine output for 1.5 months. His blood pressure was 200/100 in left upper limb and 180/120 in right upper limb while it was not recordable in lower limb as well as peripheral pulses of lower limb were not palpable (tibial arteries). Ultrasonography showed bilateral MRD grade-I with shrunken left kidney. Further renal Doppler revealed, small sized left kidney with flow study showing turbulence at the site of origin of both the renal arteries, most likely due to a large atheroma filled in abdominal aorta distal to the origin of SMA. CT angiography of aorta and its branches was also done and patient was further evaluated.

Conclusion: We diagnosed a case of mid aortic coarctation with left renal artery occluded and right renal artery stenosis leading to secondary hypertension in a young adult presenting with pain abdomen and decrease urine output. The hypertensive male was referred for vascular surgery to higher centre.

A Study of Newly Diagnosed Hypertensive Patients with Special Reference to Carotid Intima Media Thickness

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Background: Hypertension is an iceberg phenomenon where atherosclerosis and vascular diseases are common. Studies have shown that increased intima media thickness is a surrogate marker for atherosclerosis. The purpose of this study was to test whether carotid intima-media thickness (CIMT) is already increased in newly diagnosed hypertensive patients, independent of other known determinants of vessel wall thickness.

Methods: 50 cases (≥18 years) of newly diagnosed hypertensive patients were recruited along with age, sex and BMI matched controls. Patients with body mass index (BMI) >30 kg/m², diabetes mellitus and secondary causes of hypertension were ruled out. All patients underwent carotid ultrasonography for assessment of CIMT.

Results: In the study group 29(58%) were males and 21(42%) were females and in the control group 28(56%) were males and 22(44%) were females. The mean age was 43±10.98 years in study group and 41±10.99 years in control group. The mean SBP was 160.08±17.82 mmHg in cases and 116.86±10.80 mmHg in controls, the mean DBP was 96.6±7.52 mmHg in cases and 70.38±7.61 mmHg in controls. The mean CIMT was found to be 0.74±0.175 mm in cases and 0.53±0.08 mm in control group. There was a significant correlation between CIMT and SBP (r=0.432, p=0.001) CIMT and age (r=0.472, p<0.001), but not with DBP (r=0.025, p=0.86), BMI (r=0.301, p=0.124), LDL-cholesterol (r=0.186, p=0.196) and HDL-cholesterol (r=-0.25, p=0.080).

Conclusion: Increased blood pressure correlates significantly with increase in CIMT even in newly diagnosed hypertensive patients as compared to normotensive counterparts independent of other known factors which causes increase in intimal thickness. Thus, CIMT can be used as early marker for detection of subclinical atherosclerosis even in newly diagnosed asymptomatic hypertensive patients and thus early intervention can be done to prevent future cardiovascular events.

Assessment of Insulin Resistance in Non-Diabetic Patients with Essential Hypertension

Aasish Peddu, V. Rathna Mitreyee, Jaya Prakash
Kasturba Medical College and Hospital, Manipal University

Introduction: The Global Burden of Disease Study in 2010 described hypertension as the leading risk factor for global disease burden, accounting for 18% of all deaths and 7% of global disability adjusted life years.

Hyperinsulinemia as a consequence of insulin resistance and reduced clearance could induce hypertension. Insulin resistance was demonstrated in non-diabetic hypertensive patients. This relationship persists even in the absence of glucose intolerance suggesting a more fundamental relationship between hypertension and insulin resistance.
Effect of Morning and Bedtime Dosing with Cilnidipine on Blood Pressure in Essential Hypertension

Yogesh Kumar Dubey, M.P.Singh, P.K.Agrawal, Faiyaz Alam, Karan Bhargav, Abhishek Kumar
Katihar Medical College Katihar

Introduction: Cilnidipine has a blocking action against N-type calcium channels as well as L-type calcium channels. We studied the effect of morning and bedtime dosing on circadian variation of blood pressure.

Blood Pressure in 39 essential hypertension patient B.P measure 6 hourly and patient was advised to measure B.P at home with automated B.P monitor device.

Material: 39 patient with essential hypertension diagnosed and under treatment in KMCH were selected and started dose of 5mg once daily. The dose was gradually increase until B.P at outpatient clinic reached optimal values <140mmhg SBP <90mmhg DBP) or until maximum dose of 20 mg reached for each patient the dose at this time was monitor for 12 week.

Observation: The average final dose of cilnidipine 11.2 +/- 1.5 mg /day. Night time dosing of cilnidipine reduce the average systolic diastolic B.P during both day and night time and consequently over 24 hours. Night time reduce the average systolic and diastolic B.P over 24 hours and in the day time and night time reduction in average night time systolic B.P with morning dose was not significant the minimum systolic and diastolic B.P during night time were significantly by bed time dosing, but not by morning dosing.

Conclusion: Cilnidipine was effective as a once daily antihypertensive agent.

The average final dosing of cilnidipine in this study (11.2 mg /day) is considered efficient to reduce Blood Pressure.

Management of Hypertension: Insights into Real-World Clinical Practice for Differential Usage of CCBs

Arup Dasbiswas, Tushar Tamboli, Shahu Ingole, Swati Naik, Rishi Jain
Emcure Pharmaceuticals Ltd, Pune, Maharashtra

Introduction: Calcium channel blockers (CCB) like amlodipine, S(-)amlodipine and cilnidipine, etc. have established place in the treatment of hypertension (HTN). As perceived by most of the physicians, they have comparative anti-hypertensive efficacy. However, available evidences suggest varied differences in incidence of pedal oedema. Therefore, this survey was planned to understand real-world clinical practice pattern of Indian physicians for usage of various CCBs and whether differential incidence of oedema is encountered in their clinical practice.

Materials: Survey questionnaire consisting of 10 questions about preferred antihypertensive choice for different subsets of patients with HTN and efficacy and safety of S(-)amlodipine was prepared and validated in small group of physicians. Overall, 494 general physicians and cardiologists practicing in India were approached for seeking their opinion on usage of various CCBs.

Observations: Most of the physicians (53.8%, 41.1%, 55.3%, and 30.8% respectively) preferred CCB as their initial drug of choice for patients with HTN, HTN with CKD, elderly and young patients. Amlodipine was preferred as the CCB of choice by most of the physicians (75.7%). Pedal oedema with Amlodipine was observed in >15% patients only by 14.2% physicians, while most of the physicians (55.3%) observed it in only <10% patients. Most of the physicians rated S(-)amlodipine to have better efficacy (79.4%) and safety profile (88.3%) with decreased incidence of pedal oedema than racemic Amlodipine.
Conclusion: Although available evidences suggest comparative efficacy of S(-)amlodipine and racemic amlodipine with varied differences in incidence of pedal oedema, our survey suggests greater efficacy and safety of S(-)amlodipine over racemic amlodipine as opined by most of the physicians of India. However, this needs to be further evaluated in randomised clinical trials.

Pheochromocytoma as a Rare Cause of Hypertension

Dharma Teja Dhulipalla, B. Bhaskara Rao, D. Harika, Gaparanji, Sahithi
NRI Medical College, Guntur, Andhra Pradesh

Introduction: Hypertension remains one of the most important preventable contributors to disease and death. Abundant evidence from randomized controlled trials (RCTs) has shown benefit of antihypertensive drug treatment in reducing important health outcomes in persons with hypertension. In fact, hypertension is the most prevalent chronic disease in India. The number of people with hypertension is projected to increase from 118 million in 2000 to 214 million in 2025, with nearly equal numbers of men and women. Pheochromocytoma is estimated to occur in 2-8 of 10 lakhs persons per year and 0.1 percent of hypertensive patients harbor a pheochromocytoma.

Case Report: A 62 year female came to outpatient department with complaints of headache, profuse sweating and palpitations since 1 year. Headache is sudden in onset relieved spontaneously. She gives history palpitations since 3 years which is sudden in onset it is associated with profuse sweating. H/o one episode of fall 1 month back.

Past History: She was diagnosed as having hypertension 1 year back and she was losartan 50 mg daily. There was no relief of symptoms with the drugs. Personal history was normal.no similar complaints in siblings and family members. On general examination blood pressure recorded was 198/110 mm hg and pulse rate was 92 bpm regular, ophthalmoscopic examination revealed grade 2 hypertensive retinopathy in both eyes.systemic examination was normal and patient was evaluated for hypertension. ECG was normal. Electrocardiography revealed grade 1 diastolic dysfunction with preserved lv systolic function. USG abdomen showed an right adrenal mass of size 7*4 cm.contract enhanced computed tomography was done and it revealed right adrenal pheochromocytoma of size 8.4*7.2 cms 24 hours urinary metanephrins were positive. Patient was treated with prazosin, calcium channel blocker and angiotensin receptor blocker. She was posted for surgery.

Prevalence of Metabolic Syndrome in patients with Essential Hypertension

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Katihar Medical College, Katihar, Bihar

Introduction: The metabolic syndrome consist of a constellation of metabolic abnormalities that thought to occur due to insulin resistance and abnormal obesity which confer increase risk of cardiovascular disease and diabetes mellitus. The major features of metabolic syndrome includes central obesity, hypertriglyceridermia, low levels of high density lipoprotein cholesterol, hyperglycemia and hypertension.

Material: The study was a non-interventional, observational study. 172 patients of essential hypertension attending hypertension clinic or indoor department of KMCH, katihar were selected and their investigations were carried out in a fasting state. The metabolic syndrome in these patients was defined by Adult Treatment Panel (III) Criteria.

Inclusion criteria:
- Age between 25-70 yrs
- Blood pressure >140/90 mmhg

Exclusion criteria:
- age >70 yrs
- age <25 yrs
- Renal failure, hypothyroidism, hyperthyroidism, hypercalcemia, eclampsia

Observations: Prevalence of metabolic syndrome was 55.23% in patients with essential hypertension and more common in females in age group between 40-50 yrs (39.60%). Low high density lipoprotein was most common abnormality detected in patients with metabolic syndrome followed by abnormal fasting blood sugar(FBS), abnormal waist circumference and triglyceride level. The FBS and triglyceride were abnormal in 60.3% and 50.7% female patients. The commonest abnormality in male was low HDL in 87.5% followed by abnormal TG level in 65.62% patients.

Conclusions: Study demonstrated that all patients of essential hypertension should be screened for metabolic syndrome. As the prevalence is more common in younger age group, screening should start at an early age.

Study of Clinical Profile of Dippers Vs Non Dippers Using 24 Hours ABPM

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Introduction: The reduction in nocturnal blood pressure compared with average daytime blood pressure is
referred to as the dipping phenomenon. The variation of dipping in nocturnal BP carries prognostic implications in hypertensive patients. The absence of this decline (non-dippers) may place patients at an increasing risk of cardiovascular disease, particularly elderly patients. Association with increased risk of renal and vascular target-organ injury has also been reported. ABPM is now an established tool to study the circadian rhythm of blood pressure.

**Material:** 100 indoor hypertensive patients in our hospital (2013-2015) formed the subject of the study. Target organ damage was observed by ECG, Fundus examination, Serum creatinine, BUN and Blood urea.

**Observations:** Out of total 100 hypertensives, 15% were detected extreme dippers (>20% dipping), 41% were dippers (10-20% dipping) and 44% were non dippers (<10% dipping) as per systolic class. Mean S.Creatinine and BUN levels were observed to be more in non dippers than dippers in both systolic and diastolic class, but the difference did not assume significance (p> 0.05). A negative correlation was observed between presence of retinopathy and systolic or diastolic class (p> 0.05), but it did not appear to be significant. Association was observed between presence of retinopathy and systolic or diastolic class (p> 0.05), but it did not appear to be significant. Association was observed between presence of abnormal ECG (LAD, LVH, ST-T changes) and systolic or diastolic class respectively (p< 0.05). Retinopathy was present in 25% systolic non-dippers compared to 14.3% dippers and in 20.5% diastolic non-dippers as compared to 17.9% dippers. Association was observed between presence of abnormal ECG (LAD, LVH, ST-T changes) and systolic or diastolic class (p> 0.05), but it did not appear to be significant.

**Conclusion:** The proportion of the non-dippers in this study was significantly high (approx. 40%) and the association of abnormal ECG among the non-dippers was not found to be significant. A negative correlation was also found between nocturnal BP fall and the patient age. It is concluded that ambulatory BP measurement is clinically important to get a better understanding of blood pressure variability over 24-hour periods compared to simple clinical measurements and that nondippers may fare poorly.

**To Study the Clinical Profile & Electrocardiography Criteria in Patients with Left Ventricular Hypertrophy and Correlate them with Echocardiography Findings**

**Suraj Kodak, Vikram B. Vikhe**
Dr D Y Patil Medical College and Hospital, Pimpri, Pune

**Introduction:** Left ventricular hypertrophy is an important complication of long standing hypertension and is proven to be associated with target organ damage. Left ventricular hypertrophy (LVH) refers to an increase in the size of myocardial fibres in the main cardiac pumping chamber. Such hypertrophy is usually the response to a chronic volume or pressure load. Hence presence of left ventricular hypertrophy in essential hypertension indicates a grave prognosis and should be diagnosed using the most accurate method.

**Material and Methods:** The study has been conducted at Tertiary care Hospital over a period of one and half years. The study group consisted of 50 patients with the inclusion and exclusion criteria who were evaluated with history, clinical examination and specific investigations like Electrocardiography and 2D Echocardiography.

**Result:** The sensitivity was 64% for ECG-Sokolov Lyon, 36% for ECG-Romhilt Estes Scoring and 91% for 2D echo. The specificity was 75% for ECG-Sokolov Lyon, 89% for ECG-Romhilt Estes Scoring and 86% for 2D echo. The accuracy was found to be 70% for ECG-Sokolov Lyon, 66% for ECG-Romhilt Estes Scoring, 2D Echo was found to have maximum accuracy i.e. 88%.

**Conclusion:** M-mode and two dimensional echocardiography are found to be more sensitive and accurate than Electrocardiography for detecting left ventricular hypertrophy in hypertensive patients.

**Thiazide Induced Benign Gynaecomastia**

Yamsani Sandeep, Yeshavanth G
SSIMS and RC, Devangere, Karnataka

**Introduction:** Gynaecomastia is a consequence of administration of thiazides. Thiazides is a class of diuretics derived from benzothiazide. Thiazides are used in the management of hypertension and heart failure. The prevalence of gynaecomastia with thiazides is 5 to 10% which is one of very rare presentation in patients.

**Material:** A study of 75 year old male patient, hypertensive and diabetic since 5 years on regular medication of olmesartan and hydrochlorothiazide, glimeperide and metformin respectively. Based on clinical examination, bilateral breast enlargement present, firm in consistency, tenderness present.

**Observation:** High resolution sonography of both breasts showed benign enlargement of both breasts in the form of fibrous tissue in subareolar region suggestive of gynaecomastia. Cytopathology report came as benign breast lesion with epiteliosis of right breast.

**Conclusion:** Reported case is an example of benign gynaecomastia, basically a drug induced one, i.e., thiazide group of drugs and other common causes of gynaecomastia are ruled out in the patient. Treating physician should have a clear understanding of drugs that cause this phenomenon and know how to manage these cases. Only management of this kind of patients is witching over to other group of antihypertensives.

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