



REVIEW ON RATIONAL AND EFFECTIVE MANAGEMENT OF HYPERTENSION IN ELDERLY

Mohammed Safi Ur-Rahman¹, Syed Muneb Ahmed², Govinda Nayak³, Juzer Sabuwala⁴ and S. P. Srinivas Nayak^{5*}

^{1,2}(PharmD), Sultan-ul-Uloom College of Pharmacy, Hyderabad, Telangana.

³(PharmD), Krishna Teja Pharmacy College, Tirupati, Andrapradesh.

⁴(PharmD), Sultan-ul-Uloom College of Pharmacy, Hyderabad, Telangana.

⁵Assistant Professor, Department of Pharmacy Practice, Sultan-ul-Uloom College of Pharmacy, Hyderabad, Telangana.

Corresponding Author: S. P. Srinivas Nayak

Assistant Professor, Department of Pharmacy Practice Sultan-ul-Uloom College of Pharmacy, Hyderabad, Telangana.

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ABSTRACT

Hypertension is an important risk factor for cardiovascular morbidity and mortality, particularly in the elderly. It is defined as persistently elevated arterial blood pressure (BP). Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease (CHD) deaths in India. Both SBP and DBP increase with age. In elderly persons there are specific underlying mechanisms of HTN, including mechanical hemodynamic changes, arterial stiffness, neurohormonal and autonomic dysregulation, and the aging kidney. The goals and strategies for treating hypertension in the elderly population are different from, and more challenging than, in younger patients. Lifestyle modification is effective in this population, but it is difficult to maintain. There is often a debate about which antihypertensive drug class should be used first in elderly patients with hypertension. Combination of low dose diuretic (chlorthalidone) and a beta blocker (Atenolol) appears to be suitable first line therapy in vast majority of elderly hypertensive patients, even CCB's (Amlodipine) can be substituted for Atenolol. Complex and multiple drug regimes should be avoided in elderly patients as they may be confusing.

KEYWORDS: Elderly, Hypertension, Management.

INTRODUCTION

Hypertension (HTN) has been identified by WHO,^[1] as one of the most significant risk factors for morbidity and mortality worldwide and is responsible for the deaths of approximately 9 million people annually.^[1] The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNCVI) and the World Health Organization/International Society of Hypertension guidelines subcommittees have agreed that both SBP and DBP should be used for the classification of hypertension. Systolodiastolic hypertension is diagnosed when SBP is ≥ 140 mm Hg and DBP is ≥ 90 mm Hg. Isolated systolic hypertension (ISH) refers to an SBP of ≥ 140 with a DBP of < 90 mm Hg.^[2,3] Treating hypertension results in significant reductions in risk of subsequent cardiovascular disease.^[4,5] Hypertension is a major public health issue, particularly in developing countries as a whole. It's now well established that over 80% of the burden of the disease is in low-income and middle income regions.^[6] Aging is an inevitable part of life and brings along two

inconvenient events: physiologic decline and disease state.^[7] In 2000 the estimated total number of people with hypertension was 972 million, with 333 million in economically developed countries.^[8] Hypertension is an important risk factor for cardiovascular morbidity and mortality, particularly in the elderly. It is a significant and often asymptomatic chronic disease, which requires optimal control and persistent adherence to prescribed medication to reduce the risks of cardiovascular, cerebrovascular and renal disease.^[9] This disorder can be further classified as hypertensive urgency or hypertensive emergency when there is evidence of acutely progressive end-organ damage.^[10] The JNC-7 has defined criteria for normal BP, prehypertension and stage 1 and 2 of hypertension.^[11] classified below (Table 1).

Table 1: Classification of blood pressure for adults according to JNC-7.

Classification	SBP (mmHg)	DBP (mmHg)
Normal	≤ 120	And ≤ 80
Pre-hypertension	120-139	Or 80-89
Stage 1 hypertension	140-159	Or 90-99
Stage 2 hypertension	≥ 160	Or ≥ 100

Epidemiology

As our population ages, the importance of cardiovascular disease (CVD) as the leading cause of death in adults becomes increasingly clear.^[12] One major reason for this trend is the patterns of BP changes and increasing hypertension prevalence with age (about 1 billion people worldwide).^[13] Hypertension prevalence is less in women than in men until 45 years of age, is similar in both sexes from 45 to 64 and is much higher in women than men over 65 years of age.^[12] Study carried out by Indian Council of Medical Research (ICMR) among Indian population during 1994 observed that the prevalence of hypertension was 29% and 25% among urban and 13% and 10% among rural men and women, respectively.^[14] Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease (CHD) deaths in India.^[15] Study carried out among elderly tribal in Orissa observed high prevalence of hypertension (32% and 42% among men and women),^[16] while another study among Lepchas of the Sikkim Himalayas also observed high prevalence of HTN.^[17] According to World Health Organization (WHO), HTN is one of the most important causes of premature death globally.^[18]

Hypertension in Geriatric Population

There are specific underlying mechanisms of HTN in older persons, including mechanical hemodynamic changes, arterial stiffness, neurohormonal and autonomic dysregulation, and the aging kidney.^[19] Both SBP and DBP increase with age.^[20] SBP rises progressively until the age of 70 or 80, whereas DBP increases until the age of 50 or 60 and then tends to level or even decline slightly.^[20,21] This combination of changes probably reflects stiffening of the blood vessels and reduced arterial compliance and leads to a large increase in pulse pressure with aging.^[20] Aging results in several structural and functional changes in the arterial vasculature. Over time, the arteries stiffen, with fracturing of the elastic lamellae and intimal hyperplasia is seen in the aorta. The stiffened arteries have decreased capacitance, and limited recoil, with subsequent difficulty to accommodate volume changes throughout the cardiac cycle. Both systolic BP (SBP) and diastolic BP (DBP) increase with age, however, after the age of 60 years, the central arterial stiffness predominates, and as a consequence, SBP continues to rise while the DBP declines thereafter.^[22] Fracture of elastic lamellae is seen in the aorta with aging and can account for both dilation and for stiffening (through transfer of stresses to the more rigid collagenous components of the arterial wall).^[23] Autopsy studies of perfusion-fixed human arteries have

shown that thickening is mostly confined to intimal hyperplasia.^[24] The result is a stiff artery that has decreased capacitance and limited recoil and is thus unable to accommodate the changes that occur during the cardiac cycle.^[25]

Furthermore, there are hemodynamic mechanical changes that alter wave reflection causing a reduction in the aortic elasticity, as well as loss of recoil during diastole. There is also increase in pulse pressure and pulse-wave velocity. The change in arterial structure causes an increase in the reflected pressure waves added to the forward pressure waves in the ascending aorta that further augments the central SBP. Over time, endothelial dysfunction occurs, inducing an elevation in endothelin and decreasing bioavailability of nitric oxide, which affects arterial dilation.^[26] Neurohormonal mechanisms such as the renin-angiotensin-aldosterone system decline with age. Plasma renin activity at age of 60 years is 40% to 60% of the levels found in younger individuals.^[27] This has been attributed to the effect of age-associated nephrosclerosis on the juxtaglomerular apparatus. Plasma aldosterone levels also decrease with age. Consequently, elderly patients with hypertension are more prone to drug-induced hyperkalemia.^[28] Baroreceptor sensitivity is modified with age. Alterations in baroreceptor reflex mechanisms may explain the variability of BP revealed by continuous monitoring.^[29] Decreased baroreceptor sensitivity results in an impairment of postural reflexes, making elderly hypertensive individuals more sensitive to orthostatic hypotension.^[30] Changes in the balance between β -adrenergic vasodilation and α -adrenergic vasoconstriction are in favor of vasoconstriction that increases peripheral vascular resistance and BP.^[31] The aging changes in the kidney are increased salt sensitivity due to a decline in the activity of the sodium/potassium and calcium adenosine triphosphate pumps, which prompts vasoconstriction and vascular resistance.^[32] HTN in the elderly is also associated with increased risk of ischemic and hemorrhagic strokes, vascular dementia, Alzheimer's disease, coronary artery disease and events, atrial fibrillation, chronic kidney disease and retinal diseases.^[33-36]

Management of Hypertension in Elderly

The goals and strategies for treating hypertension in the elderly population are different from, and more challenging than, in younger patients. Lifestyle modification is effective in this population, but it is difficult to maintain.^[37] There is often a debate about which antihypertensive drug class should be used first in

elderly patients with hypertension. Several classes of antihypertensive drugs are effective in preventing cardiovascular events. Treatment decisions should be guided by the presence of compelling indications such as diabetes mellitus, stroke or HF and by the tolerability of individual drugs or drug combinations. The initial antihypertensive drug should be started at the lowest dose and gradually increased depending on the BP response to the maximum tolerated dose. If the antihypertensive response to the initial drug is inadequate after reaching full dose, a second drug from another class should be added. If the antihypertensive response is inadequate after reaching the full dose of 2 classes of drugs, a third drug from another class should be added.^[38] Not all hypertensive old people need drug treatment; this is especially so in patients over 60 years of age. Treatment should be considered for those elderly patients whose BP exceeds 150/90 mm Hg. Rapid lowering of BP and postural hypotension can be dangerous. The low dose thiazides/CCB would appear to be relatively safe in these patients. ACEI/ARB are also well tolerated. Doses of diuretic larger than the equivalent of 25 mg of hydrochlorothiazide per day should be avoided and even mild hypokalemia treated.^[39] The American College of Cardiology (ACC) and the American Heart Association (AHA) recently released the first expert consensus statement to help clinicians effectively manage hypertension in the elderly population.^[40] The ACC/AHA document recommends BP measurement of <140/90 mm Hg for those aged 65 to

79 years. For patients aged ≥ 80 years, most experts, including the ACC/AHA statement, recommend a less-stringent systolic BP goal of 140 to 145 mm Hg, to minimize side effects.^[40] This ACC/AHA document further recommend starting the evaluation of the elderly patient with known or suspected hypertension with 3 measurements of BP, including in the standing position, to obtain an accurate BP value. If BP is elevated, the cause should be isolated later. Any organ damage should be assessed. Other CV disease (CVD) risk factors or comorbid conditions should be identified, along with any potential barriers to treatment adherence.^[40] According to this ACC/AHA statement, lifestyle modifications may be all that is necessary to treat milder forms of hypertension in elderly patients. In patients with resistant hypertension, drug therapy is recommended and should be started at the lowest dose possible, with gradual increases depending on response. Diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs) are effective in lowering BP and reducing CV outcomes in the elderly. Beta-blockers are inferior in benefits compared with these drug classes, but they may be used in selected cases in the elderly population.^[40] Complex, multiple-drug regimes are best avoided in the elderly as they may be confusing.^[39] The therapeutic strategies for hypertension in the elderly as well as the basic effects and the main cardiovascular benefits of the pharmacological agents are summarized in Table 2.^[41]

Table 2: Therapeutic strategies in Elderly.

Non-Pharmacological Strategy	Pharmacological Strategy- Main Pharmacological Agents
Weight reduction	1. Thiazide diuretic: inhibiting reabsorption of sodium (Na+) and chloride (Cl-) ions from the distal convoluted tubules in the kidneys $\rightarrow \rightarrow$ \downarrow BP, \downarrow stroke, \downarrow CV mortality
Dietary sodium reduction	2. Calcium antagonists: disrupts the movement of calcium through calcium channels in cardiac muscle and peripheral arteries $\rightarrow \rightarrow$ vasodilation (\downarrow SVR), \downarrow BP, \downarrow CV complications in elderly patients with ISH
Physical activity	3. ACEIs: block the conversion of angiotensin I to angiotensin II $\rightarrow \rightarrow$ \downarrow SVR, \downarrow BP, \downarrow mortality in patients with MI and left ventricular dysfunction, \downarrow progression of diabetic renal disease
Moderate alcohol consumption	4. ARBs: direct blockage of angiotensin II receptors $\rightarrow \rightarrow$ vasodilation (\downarrow SVR), \downarrow secretion of vasopressin, \downarrow aldosterone, \downarrow BP, \downarrow stroke. Generally, in patients who cannot tolerate ACEs
Dash diet	5. β blockers: \downarrow heart rate, \downarrow cardiac contractility, \downarrow cardiac output, inhibit renin release, \uparrow nitric oxide, \downarrow vasomotor tone $\rightarrow \rightarrow$ \downarrow BP
Smoking secession	6. Other agents: direct renin inhibitors, aldosterone receptor antagonists, centrally acting agents, direct vasodilators, α -adrenergic blocking agents
Combination therapy	
ACEIs or ARBs/Diuretic	
ACEIs or ARBs/Calcium antagonist (especially in patients with high CV risk)	
CV: Cardiovascular; BP: Blood pressure; ACEIs: Angiotensin converting enzyme inhibitors; ARBs: Angiotensin receptor blockers; SVR: Systemic vascular resistance.	

Review of Drug Therapy In Elderly

As there is areuncertainties among the doctors about the usage of and choice of the drug for the treatment of hypertension in the elderly hypertensive patients. It's a need of an hour to clear all puzzlement doctors are carrying for the drug of choice in elderly. Aneetpatel et al. Research article 2015 "Hypertension in the Eldely: An Epidemiologic Shift" concludes that based on the accurate diagnosis of blood pressure, if the systolic blood pressure is exceeding 150mmHg and diastolic blood pressure exceeding 90 mmHg in such situation the elderly patient should be given Hypertension treatment starting with non-pharmacological management plans(includes lifestyle modifications), if non-pharmacological plan have not been successful then the patient is initiated with monotherapy of Calcium Channel Antagonist's in elderly unless there is co-morbid diabetes mellitus, ischemic heart disease, or CKD in which ACEI's is preferred, Beta blocker's BB may worsen CVS outcome in Geriatric patients, regularly monitoring of BP and in follow up of patient medications, ask questions about low tissue perfusion , orthostasis and falls. Targeting for initial SBP below 150mmHg and a DBP below below 90mmHg in elderly patient, it was suggested that low dose Chlorthalidone in ALLHAT i.e. The Anti-HTN and Lipid-lowering Treatment, which prevents Heart attack. Combo therapy of CCB's+ACEI's was seen with overall mortality benefit on comparing with combo of BB+thiazide.

KaKeat Lim et' al cross sectional study 2015 "Antihypertensive drugs or elderly patients: a cross sectional study" cross sectional study involving 122 public health care clinics and 652 private health care clinics-from their study concluded that calcium channel blockers were the most common antihypertensive drug as a monotherapy was prescribed in the public health care clinics, where as Beta blockers were the most commonly prescribed as a monotherapy in private health care clinics, patients with comorbid conditions were prescribed with combination therapy, in public healthcare clinics for combo-therapy, comparing, the Angiotensine Receptor Antagonists rate of prescribing is higher than that of Angiotensine Converting Enzyme Inhibitors as ARB's have less or negligible incidence of persistent cough thus, leads to patient medication adherence, the combo-therapy of BB+Diuretics +Amilozide was linked with higher risk of diabetes mellitus, BB once was first line anti-HTN, but it has less BP lowering effect and less effective in stroke prevention.

Quang t. Nguyen et' al Review article 2012 "Managing Hypertension in the Elderly: A Common Chronic Disease with Increasing Age" their review study concluded that treatment target for hypertension in all aged group populations should be, the systolic blood pressure is less than or equal to 140 mmHg and diastolic blood pressure less than or equal to 90 mmHg. The initiation of treatment in elderly, priority was given to

non-pharmacological strategy(includes life style changes), encouraging lifestyle modification is the first line treatment, medications started was as appropriate, CCBs, ACEI's, ARB's and Diuretics, should be started with low dose and titrated as tolerated, these were considered as 1st line pharmacological anti-HTN agents in elderly. If any Contraindications is seen with Diuretics, ACEI's, ARB's; then CCB's is the best effective drug. Regular vigil monitoring on ADR's of drugs is needed to avoid treatment related Adverse Events. Clinical trials that included patients aged >65 years have shown that patients who receive treatment for their elevated BP have fewer strokes, fewer heart attacks, and less congestive HF compared with those with untreated hypertension. In very elderly patients (aged >80) the risks and benefits of tight control need to be frequently re-evaluated.

Santoshkar et' al in a comprehensive pharmacology and therapeutics Textbook stated that not all hypertensive elderly patients need drug treatment, treatment should only be considered for those elderly whose BP exceeds 150/90 mmHg. The low dose of CCB's or Thiazides would appear to be relatively safe, ACEI's and ARB's are well tolerated. Doses of diuretics should be maintained in the range of less than or equal to 25mg per day, and even mild hypokalemia should be treated. As per ALLHAT Trial in elderly, chlorthalidone 12.5-25mg in combination with CCB's or ACEI's was found to be effective in preventing the CVS events. Chlorthalidone was found to be twice potent and longer duration of action than Hydrochlorothiazide. Combination of low dose diuretic (chlorthalidone) and a beta blocker (Atenolol) appears to be suitable first line therapy in vast majority of elderly hypertensive patients, even CCB's (Amlodipine) can be substituted for Atenolol. Complex and multiple drug regimes should be avoided in elderly patients as they may be confusing. The aim of therapy in the elderly should be to lower BP as much below 180/100mmHg as the patient can tolerate comfortably, preferably to 150/90mmHg or less. No attempt should be made to make the BP 'normal' (>140mm Hg). In case an elderly attains BP<140/90 mmHg and tolerated drug/s well with no adverse effects on health and quality of life, no adjustment should be made in doses or drugs.

CONCLUSION

In conclusion of our review, it is clear that patients who receive treatment for their elevated BP have fewer strokes, fewer heart attacks, and less congestive HF compared with those with untreated hypertension. In very elderly patients (aged >80) the risks and benefits of tight control need to be frequently re-evaluated. However it is challenging fact to choose a single drug in elderly, Combo therapy of CCB's+ACEI's was seen with overall mortality benefit on comparing with combo of BB+thiazide. BB once was first line anti-HTN, but it has less BP lowering effect and less effective in stroke prevention. According to ALLHAT Trial in elderly, chlorthalidone 12.5-25mg in combination with CCB's or

ACEI's was found to be effective in preventing the CVS events. Combination of low dose diuretic (chlorthalidone) and a beta blocker (Atenolol) appears to be suitable first line therapy in vast majority of elderly hypertensive patients, even CCB's (Amlodipine) can be substituted for Atenolol. Complex and multiple drug regimes should be avoided in elderly patients as they may be confusing.

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