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Hypertension Management:

Making Sense of Guidelines and Therapy Options for the Elderly

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1.5 Contact Hour (.15 CEU's)

This is a knowledge based activity.

See the end of the article for CE details.

Target Audience: Pharmacists

Faculty Disclosure: Faculty have no
conflicts of interest to disclose

Goal:

The goal of this activity is to increase the awareness of the pharmacist on the complications surrounding hypertension management in the elderly individual, clarify the differences in current guideline recommendations, and aid in making the most appropriate drug therapy decisions regarding the management of hypertension.

Objectives

1. Identify the differences and similarities in clinical practice guideline recommendations for management of hypertension in the elderly patient.
2. List changes in the physiology of elderly individuals that create more complicated management scenarios
3. Discuss potential adverse drug effects that may be experienced by an elderly individual when prescribed anti-hypertensive medications
4. Select an appropriate drug therapy regimen and treatment goals for an elderly patient with uncontrolled hypertension

Introduction:

Hypertension affects 70.8% of individuals over the age of 65, making this population the most likely to experience complications of uncontrolled hypertension such as organ damage and cardiovascular disease.¹ However, data to support the target blood

pressure goal of <140/80 mm Hg in the elderly population as suggested in previous guidelines has not been robust. Further complicating matters, most trials evaluating hypertensive goals and pharmacological management in recent years only included individuals <80 years of age. When pooling results of studies including individuals between 80 and 90 years of age, treated patients showed a reduction in both stroke and cardiovascular morbidity, but also a significant increase in all-cause mortality compared to controls. As a result, many practitioners are without clear direction when treating elderly patients.^{2,3} Built upon the results of these trials that included the elderly population, the 2014 Evidence Based Guideline for the Management of High Blood Pressure in Adults (JNC8), along with the Clinical Practice Guidelines for the Management of Hypertension in the Community also released in 2014 by the American Society of Hypertension and International Society of Hypertension (ASH/ISH) have resulted in a new approach to managing hypertension in the aging population.

Pathophysiology

Hypertension is seen with increased frequency in the elderly population due to age-associated changes in vasculature complicated by lifestyle changes, comorbidities, and use of certain medications (Table 1). In the aging individual, large vessels become less distensible, endothelial dysfunction occurs, forward flow is reduced, and coronary stenosis is enhanced. Glomerulosclerosis and interstitial fibrosis then results in

progressive renal dysfunction and causes increased intracellular sodium, reduced sodium-calcium exchange, and volume expansion which further contributes to the patient's hypertension due to increased sodium sensitivity.² These pathological changes in the elderly paired with a more sedentary lifestyle and medication use cause an elevation in systolic blood pressure (SBP) to become more likely. Untreated hypertension in the elderly is the first step in a cascade of events that may result in additional comorbidities. Poor blood pressure control in this population can result in cerebrovascular disease; coronary artery disease (CAD); disorders of the left ventricular structure and function; rhythm disorders; aortic and peripheral arterial disease; chronic kidney disease (CKD), ophthalmic disorders; and decreased quality of life.²

Patients of African descent pose different challenges in the management of hypertension. This population is more sensitive to the blood pressure raising effects of sodium than other groups, potentially explaining why these individuals tend to experience hypertension earlier in life and have more severe hypertension than other ethnicities. African Americans are particularly vulnerable to strokes and are 3 to 5 times more likely than Caucasians to have renal complications or end-stage kidney disease as a result of uncontrolled hypertension.^{4,5}

Evaluating Blood Pressure Goals and Management

Prior to the release of the JNC 8 and ASH/ISH guideline statements, the

American College of Cardiology Foundation and American Heart Association's (ACCF/AHA) 2011 Expert Consensus Document on Hypertension in the Elderly was available to aid in setting blood pressure goals in the elderly population. According to the ACCF/AHA 2011 document, the blood pressure goal for all individuals with uncomplicated hypertension was <140/90 mm Hg. The expert panel noted that this recommendation was based on opinions of the writing panel, rather than randomized controlled trials, and stated for individuals 80 years of age and older a SBP of 140 to 145 mm Hg would be acceptable.²

More recently, JNC 8 and ASH/ISH guidelines have indicated new blood pressure targets for the elderly population. As outlined in Table 2, JNC8 utilizes the blood pressure goal of <150/90 mmHg for those patients 60 years of age and older; while ASH/ISH imposes this same target for patients 80 years of age and older.^{4,5}

When initiating antihypertensive medications in the elderly, the ACCF/AHA 2011 Expert Panel recommends starting at the lowest possible dose and gradually increasing, depending on response, to the maximum tolerated dose. A second medication is then added if the patient has not reached their blood pressure goal.^{2,4,5} On the other hand, the strategies proposed by JNC8 and ASH/ISH indicate some patients may need multiple pharmacologic agents at time of diagnosis to achieve their goals when >20/10 mmHg above the desired blood pressure.^{4,5}

Why a Difference?

The reason for differences between the various guidelines lies in the evidence upon which each document was built. As mentioned previously, the blood pressure goal set by the ACCF/AHA 2011 document was set by opinions of the expert panel.² ASH/ISH was similar in that the blood pressure goals were also set based on opinions of the expert writing panel, while JNC8 was different in that blood pressure goals were formulated based on reviews of randomized controlled trials.^{4,5} As dictated in the statement of purpose for the ASH/ISH guidelines, the authors were focused on practical applicability in the clinical setting. This panel further relied upon the evidence for a defined goal blood pressure of <140/90 mm Hg from trials such as ACCOMPLISH, ALLHAT, and VALUE that included individuals over the age of 60 and the SBP goal of <150 mm Hg from the HYVET trial for individuals >80 years of age.⁵⁻¹⁰ On the other hand, JNC8 chose to utilize evidence-based criteria using trials that evaluated individuals over the age of 60 such as SHEP, Syst-EUR, and others.¹¹⁻¹⁴ Table 3 outlines the studies that supported each guideline's recommendations.

Drug Therapy

The majority of elderly individuals presenting with uncontrolled hypertension will have an additional comorbidity indicating the need for a specific antihypertensive medication or drug class. Table 4 compares recommended initial drug therapy options amongst the guidelines previously discussed. It is important to note initial drug therapy is based on race, not age;

however, when selecting appropriate therapy for elderly individuals the adverse effects of each medication (Table 5) must be considered as this population is more prone to dehydration, hypotension, and bradycardia due to changes in physiology.²

While the JNC8 and ASH/ISH guidelines are more flexible in initial drug therapy choice, the ACCF/AHA 2011 expert consensus panel recommends a thiazide diuretic as the initial drug of choice.²

Thiazide diuretics have been associated with reduced cardiovascular, cerebrovascular, and renal adverse outcomes in trials, but may exacerbate age-related physiological changes such as contracted intravascular volumes, orthostatic hypotension due to sodium and water depletion, exacerbation of gout, and an increased risk of arrhythmias due to electrolyte depletion.^{2,6,12,13}

Dihydropyridine (DHP) calcium channel blockers have been supported by positive evidence in controlled trials for the elderly population.^{8,9} Since an elderly individual's hypertension is characterized by arterial stiffness, decreased vascular compliance, and diastolic dysfunction, the drug's ability to promote vasodilator activity make these drugs appealing. It is important to note that similar effects are not seen with non-DHP calcium channel blockers such as verapamil and diltiazem and, when selected for therapy, these agents require close monitoring for bradycardia in this population.

Other agents that may be appropriate to initiate in an elderly patient based on comorbidities require additional monitoring to ensure safety in this sensitive population.

Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) must be accompanied by diligent monitoring of renal function and serum potassium levels but are often times used for their renal protective properties in patients with kidney disease or diabetes mellitus. Beta blockers lack evidence for use as a primary antihypertensive agent in the elderly population, except in patients with an existing comorbidity noted in Table 5. When these agents are selected, practitioners should be aware these drugs mask the signs of hypoglycemia in diabetic patients and non-selective agents may exacerbate pulmonary diseases. Loop diuretics can be used as adjuvant therapy in the elderly with hypertension complicated by heart failure or chronic kidney disease; however, caution and close monitoring should be utilized due to these agents' large adverse effect profile including increased glucose, electrolyte disturbances, and dehydration. Finally, mineralocorticoid antagonists and epithelial sodium transport channel antagonists may be useful in combination with other agents for patients with refractory hypertension or an additional indication such as heart failure; however, close monitoring of serum potassium is important.

Some antihypertensive agents, on the other hand, should be avoided in the elderly population and are listed on the Beers criteria and STOPP/START criteria.^{15,16} Both tools outline potentially inappropriate medications for older patients based on the medication's potential side effects and/or the changing physiology of the elderly individual's body. For example, alpha

blockers and non-specific vasodilators, such as hydralazine and minoxidil, are recommended as last line agents due to the ability of these medications to increase fall risk secondary to the orthostatic hypotension these agents cause. Additionally, alpha blockers should be avoided due to the proven excessive cardiovascular events seen in the ALLHAT trial.⁷ Alpha-agonists, such as clonidine, also meet Beers criteria for their ability to produce central nervous system adverse effects.

Conclusion

Uncontrolled hypertension is an ubiquitous disease state in the elderly population; however, given the age-related changes in physiology, management of these individuals can be complicated. Patients should be evaluated on an individual basis for tolerability of a lower blood pressure to determine how restrictive their blood pressure goal may be, utilizing JNC8 or ASH/ISH guidelines in combination with the ACCF/AHA 2011 expert consensus

guidelines. Practitioners must also take comorbidities, drug burden, and potential for adverse effects into consideration when choosing an antihypertensive therapy appropriate for their elderly patient.



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TABLE 1

Factors That Worsen Hypertension in the Elderly²

Lifestyle Changes	Comorbidities	Medications
<ul style="list-style-type: none"> ▪ Smoking and alcohol use ▪ Limited physical activity ▪ Altered or reduced appetite ▪ Excessive sodium intake 	<ul style="list-style-type: none"> ▪ Renal artery stenosis ▪ Obstructive sleep apnea ▪ Primary aldosteronism ▪ Thyroid disorders 	<ul style="list-style-type: none"> ▪ Nonsteroidal anti-inflammatory drugs (NSAIDs) ▪ Glucocorticoids ▪ Sex hormones ▪ Antirheumatic agents (e.g. cyclosporine, leflunomide)

TABLE 2

Blood Pressure Goals ^{2,4,5}

	Uncomplicated Hypertension	DM	CKD
ACCF/AHA 2011	All patients: <140/90 mm Hg >80 years of age: 140 to 145 mm Hg systolic can be acceptable	<130/80 mm Hg	<130/80 mm Hg
JNC8	< 60 years of age: <140/90 mm Hg > 60 years of age: <150/90 mm Hg	<140/90 mm Hg	<140/90 mm Hg
ASH/ISH	<80 years of age: <140/90 mm Hg >80 years of age: <150/90 mm Hg	<140/90 mm Hg	<140/90 mm Hg

CKD: chronic kidney disease, DM: diabetes mellitus

TABLE 3

Hypertension Trials

Trial	Study Participants	Pharmacologic Intervention	Important Considerations and Results
ACCOMPLISH⁸	N= 11,506 Mean Age: 68	(Benazepril + amlodipine) vs. (benazepril + HCTZ)	<ul style="list-style-type: none"> ▪ Goal BP: <140/90 mm Hg, <130/80 mmHg in participants with history of DM ▪ ACEI/ CCB combination is superior to ACEI/ HCTZ in reduction in morbidity and mortality ▪ 40% of participants were 70 years of age or older ▪ No difference in morbidity and mortality in those >80 years of age
ALLHAT⁷	N=33,357 Mean Age: 67	Amlodipine, lisinopril or doxazosin vs. chlorthalidone	<ul style="list-style-type: none"> ▪ Goal BP: <140/90 mmHg ▪ 25% increase in CV events in doxazosin arm including a 204% increase in HF and 19% increase in stroke

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			<ul style="list-style-type: none"> 57% of participants were 65 years of age or older
HYVET⁶	N=3,845 Mean Age: 84	Indapamide +/- perindopril	<ul style="list-style-type: none"> Goal BP: <150/80 mmHg All patients were 80 years of age or older Reduction of stroke, HF, and CV events in the indapamide arm Significant reduction in all-cause death
INVEST¹⁰	N=22,576 Mean Age: 66	Verapamil vs. atenolol	<ul style="list-style-type: none"> Goal BP: <140/90 mmHg, <130/85 mmHg in participants with history of DM 33% of participants were 70 years of age or older No difference in outcomes in those >80 years of age
SHEP¹³	N=4,736 Mean Age: 72	Chlorthalidone	<ul style="list-style-type: none"> Goal SBP: <150 mmHg Reduced incidence of stroke in all patients in treatment arm

Syst-EUR¹⁴	N=4,695 Mean Age: 70	Nitrendipine	<ul style="list-style-type: none"> ▪ Goal SBP: <150 mmHg ▪ Treatment to goal BP improves CV and cerebrovascular outcomes and lowers mortality
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ACE: angiotensin converting enzyme; BP: blood pressure; CCB: calcium channel blocker; CV: cardiovascular; HCTZ: hydrochlorothiazide; HF: heart failure; SBP: systolic blood pressure

TABLE 4

Initial Treatment Options for Uncomplicated Hypertension ^{2, 4, 5}

	Non-African American Individuals		African American Individuals
ACCF/AHA 2011	Thiazide-type diuretic		Thiazide-type diuretic
JNC8	ACE inhibitor ARB CCB Thiazide-type diuretic		CCB Thiazide-type diuretic
ASH/ISH	<60 years of age	>60 years of age	CCB Thiazide-type diuretic
	ACE inhibitor ARB	CCB Thiazide-type diuretic	

ACE: angiotensin converting enzyme, ARB: angiotensin II receptor blocker, CCB: calcium channel blocker

TABLE 5

Drug Therapy Options for the Elderly ^{2,5}

Drug Class	Important Considerations	Monitoring
Thiazide diuretics	<ul style="list-style-type: none"> ▪ Promotes orthostatic hypotension, depletion of electrolytes, hyperuricemia, glucose intolerance and dyslipidemia 	<ul style="list-style-type: none"> ▪ Sodium, potassium, magnesium ▪ Volume status ▪ Blood glucose ▪ Fasting lipid panel ▪ Uric acid level ▪ CrCl: not effective in patients with CrCl <30 ml/min
Calcium channel blockers	<ul style="list-style-type: none"> ▪ Associated with postural hypotension with an increased risk of dizziness and falls ▪ Verapamil and diltiazem may precipitate heart block in those with underlying defects 	<ul style="list-style-type: none"> ▪ Bradycardia (most common with DHP CCB) ▪ Ankle edema ▪ Headache

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	<ul style="list-style-type: none">▪ Avoid verapamil, diltiazem, and nifedipine in those with preserved ejection fraction heart failure	<ul style="list-style-type: none">▪ Constipation (most common with verapamil)
ACE inhibitors	<ul style="list-style-type: none">▪ May cause chronic dry cough, angioedema, hyperkalemia, and renal failure▪ More effective in reducing BP in white patients than African Americans	<ul style="list-style-type: none">▪ Angioedema (more common in African American patients)▪ Potassium▪ Renal function; may increase SCr up to 30%▪ May need to start at lower initial dose for CrCl<30 ml/min
ARBs	<ul style="list-style-type: none">▪ May cause chronic dry cough, angioedema, hyperkalemia, and renal failure▪ More effective in reducing BP in white patients than African Americans	<ul style="list-style-type: none">▪ Angioedema (less common than ACE inhibitors)▪ Potassium▪ Renal function; may increase SCr up to 30%

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Direct renin inhibitors	<ul style="list-style-type: none"> ▪ May cause hypotension, hyperkalemia, and renal failure 	<ul style="list-style-type: none"> ▪ Potassium ▪ Renal function
Beta blockers Alpha-beta blockers	<ul style="list-style-type: none"> ▪ Useful in elderly patients who have CAD, HF, certain arrhythmias, migraine headaches, or tremor ▪ May mask signs of hypoglycemia in patients with DM 	<ul style="list-style-type: none"> ▪ Bradycardia ▪ Depression ▪ Sexual dysfunction ▪ Fasting lipid panel
Loop diuretics	<ul style="list-style-type: none"> ▪ Useful in patients with volume overload (ie. HF and CKD) ▪ May cause electrolyte disturbances and glucose intolerance 	<ul style="list-style-type: none"> ▪ Potassium, magnesium ▪ Volume status ▪ Fasting lipid panel ▪ Blood glucose ▪ Uric acid level
Mineralocorticoid antagonists	<ul style="list-style-type: none"> ▪ Does not cause metabolic disturbances ▪ May cause hyperkalemia; avoid in combination with ACE inhibitors and ARBs 	<ul style="list-style-type: none"> ▪ Gynecomastia and sexual dysfunction in men treated with spironolactone ▪ Potassium ▪ Dose adjusted with CrCl <50 ml/min, not

		recommended <30 ml/min
Epithelial sodium transport channel antagonists (amiloride and triamterene)	<ul style="list-style-type: none"> ▪ Does not cause metabolic disturbances ▪ Minimal effect on BP; used mostly for potassium sparing effect in combination with diuretics 	<ul style="list-style-type: none"> ▪ Potassium ▪ Use not recommended with CrCl <50 ml/min

ACE: angiotensin converting enzyme, ARB: angiotensin II receptor blocker, BP: blood pressure, CAD: coronary artery disease, CCB: calcium channel blockers; CKD: chronic kidney disease , CrCl: creatinine clearance, DHP: dihydropyridine, DM: diabetes mellitus, HF: heart failure, SCr: serum creatinine