Hypertension Review and Management Strategies for APRNs

2 contact hours

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Acknowledgments

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Purpose and Objectives

The purpose of this two contact hour course for APRNs is to provide an in-depth review of current pharmacological management guidelines for hypertension, so that the nurse can improve medication compliance in hypertensive patients.

After successful completion of this continuing education self-study course, the APRN will be able to:

1. Describe the epidemiology and prevalence of hypertension, heart failure and dyslipidemia with respect to prevalence and associated risks
2. Discuss risk factors for hypertension as well as the basic pathogenesis of hypertension
3. Review the national consensus guidelines on pharmacological management of patients with hypertension
4. Identify medications that can exacerbate or complicate the management of patients with hypertension
5. Discuss the most common clinical scenarios where certain medications may be preferred or contraindicated when used to treat hypertension

6. Review strategies that nurses can implement to improve medication adherence in patients with hypertension

Introduction

Hypertension is defined as blood pressure (BP) readings that exceed 140/90 mm Hg (American Heart Association, 2013).

Approximately, one third of all Americans have hypertension. This statistic amounts to about 77.9 million US adults, or approximately 29.1% of adults over 18 years old.

At present, the prevalence of hypertension is approximately equal in men and women, but some ethnic minority groups have higher rates in women, such as African Americans, who have a 42.6% prevalence rate in men, compared with a 47% occurrence rate in women.

Note! Hypertension remains one of most important, potentially modifiable, independent risk factors for cardiovascular disease (CVD).

Epidemiology of Hypertension

The relationship between hypertension and the risk of cardiovascular disease (CVD), such as stroke, myocardial infarction, and heart failure is continuous and consistent. (Saseen et al., 2011, Roger et al., 2012 & Chobanian et al., 2003)

Did You Know?

Aggressive BP lowering is associated with:

- 35-40% decrease in stroke
- 20-25% decrease in myocardial infarction
- 50% decrease in heart failure

Pre-Hypertension

Individuals who have a systolic BP (SBP) between 120–139 mmHg or a diastolic BP (DBP) between 80–89 mmHg are in the “pre-hypertensive stage” and require health-promoting lifestyle modifications to prevent CVD.

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Each increment of 20/10 mmHg doubles the risk of CVD across the entire BP range starting from 115/75 mmHg.

**Note!** Individuals who are normotensive at age 55 have a 90% lifetime risk for developing hypertension.

**Test Yourself**

The “prehypertensive” stage is when:

A. Systolic BP is between 120-139 mmHg  
B. Diastolic BP is between BP 80-89 mmHg  
C. Health-promoting lifestyle modifications are required to prevent CVD  
D. All of the above  

The correct answer is: D. All of the above.

**Etiology: Essential Hypertension**

Hypertension can be classified as either essential, where the exact cause is unknown, or secondary, where a cause can be identified.

Essential hypertension is associated with several risk factors including:

- Sedentary lifestyle  
- Obesity  
- Smoking  
- Nutritional factors (e.g. hypokalemia)  
- Excessive alcohol intake  
- Genetic factors  
- Metabolic syndrome (e.g. diabetes, dyslipidemia, obesity)  

(Saseen et al., 2011)

**Etiology: Secondary Hypertension**

Secondary hypertension results from identifiable medical conditions, such as:

- Obstructive sleep apnea  
- Hyperthyroidism  
- Cushing’s disease
• Renovascular disease
• Pheochromocytoma (tumor of the adrenal glands)

Secondary hypertension can also be drug-induced:
• NSAIDS drugs (e.g. ibuprofen)
• Corticosteroids (e.g. fludrocortisone, prednisone)
• Estrogens
• Amphetamines and related CNS stimulants
• Tacrolimus, cyclosporine

(Chobanian et al., 2003, Hulisz & Lagzdins, 2008)

Pathogenesis of Hypertension

The most commonly recognized mechanisms in hypertension include activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS).

Increased activation of the sympathetic nervous system causes stimulation of the heart and kidneys. Cardiac output and vascular resistance are increased as a result.

Arterial and aortic baroreceptors become reset to a higher pressure in the hypertensive patient.

(Oparil & Calhoun, 2003)

Pathogenesis of Hypertension

Angiotensin II may also contribute to exaggerated sympathetic stimulation.

Chemoreflex pathways may also become altered in those experiencing apnea, leading to an overall increase in sympathetic stimulation.

Ultimately, chronic sympathetic stimulation contributes to left ventricular hypertrophy and vascular remodeling.

This forms a major basis for treating hypertension, namely, targeting the RAAS and adrenergic system.

(Oparil & Calhoun, 2003)

Hypertension and Diabetes

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There is a strong connection between hypertension and diabetes. Many people who have diabetes also have hypertension or will eventually develop hypertension.

The connection between diabetes and hypertension is insulin resistance. When your patient’s body does not allow insulin to enter cells, not only does their blood glucose rise, but they also begin to retain sodium.

The major risk to patients that have both diabetes and hypertension is the development of atherosclerosis and its subsequent cardiovascular consequences.

**Blood Pressure Control to Minimize CV Risk**

Patients with high BP are clearly at increased risk for:

1. Stroke (cerebrovascular accident, or CVA)
2. Heart failure
3. Myocardial infarction
4. Chronic kidney disease

Aggressive and appropriate BP control is essential at decreasing the risk for these diseases (Chobanian et al., 2003).

**Test Yourself**

Patients with high BP are clearly at increased risk for:

A. Stroke
B. Heart failure
C. Chronic kidney disease
D. All of the above

The correct answer is: D. All of the above.

**Blood Pressure Control and Cost**

Did you know that only about 50% of persons with hypertension have their BP under good control, defined as a level below 140/90 mmHg?

Hypertension costs the US about $76 billion in health care services, medications and work absenteeism, and an estimated 57,000 deaths in US per year are due to hypertension.

Projections indicate that by 2030, prevalence of hypertension will increase 7.2% from 2013 estimates.
Risk Factors

While uncontrolled, hypertension leads to the development of CVD, the following risk factors are also associated with CVD and must be addressed in patients with hypertension:

- Cigarette smoking
- Obesity* (Body Mass index or BMI ≥30 kg/m²)
- Physical inactivity
- Dyslipidemia
- Diabetes mellitus
- Renal insufficiency
- Age (older than 55 for men, 65 for women)
- Family history of premature CVD, where premature is defined as men under age 55 or women under age 65 years of age

Lifestyle Modification

Lifestyle modification is the cornerstone of initial management of hypertension and should include measures to reduce intake of sodium (salt), saturated fats, sugars, red meat, alcohol, caffeine, and nicotine.

It is recommended that 2.3 grams of sodium daily be the upper limit for those with hypertension and that potassium intake be increased in most patients to 4.7 grams daily.

This should be achieved through increased intake of potassium-rich fruits and vegetables.

Males should consume no more than one or two alcoholic drinks per day, where one drink is considered 12oz of beer, 5oz of wine, or 1.5oz of 80-proof liquor.

Test Yourself

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What is the recommended maximum daily sodium allowance for hypertensive patients?

A. 2.3 grams  
B. 3.2 grams  
C. 4.3 grams  
The correct answer is: A. 2.3 grams.

**Hypertension Treatment Overview**

The eighth report from the Joint National Committee (JNC-8) on hypertension management was released in early 2014. There are nine recommendations which will be summarized in this course. These guidelines should be applied in the initial approach to managing patients with hypertension, but subsequent monitoring and titration of medications must be individualized.

**Did You Know?**

*Over 75% of patients with hypertension require two or more medications to achieve optimal BP goals and only about 48% of patients who are aware they have hypertension are well-controlled.*

**Hypertension Treatment Overview**

The 2014 JNC-8 guidelines recommend that:

- Co-morbidities, such as heart failure, diabetes, high cholesterol and the need for laboratory tests will increase the frequency of visits.
- Since hypertension is asymptomatic, the consequences of poorly controlled BP should be explained to patient.
- Benefits of good BP control should also be explained to improve long-term medication adherence.
- The amount of BP reduction is the major determinant of reduction in cardiovascular risk, rather than the initial antihypertensive drug prescribed, unless very compelling indications exist with concurrent diseases.
- A thiazide diuretic has been considered the first-line hypertensive in the absence of compelling indications that would favor a different agent.
- Once BP goals are met, follow-up visits are done at three to six month intervals.

(Appel et al., 2007, Bui et al., 2010, Sarafidis & Bakris., 2008, Turnbull et al., 2008)

**Note! Lifestyle modification should be continued after decisions are made to initiate medications.**

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Evaluating Resistant Hypertension

When evaluating resistant hypertension, the clinician should assure that BP is properly measured, and rule out excess sodium intake as a cause of elevated BP.

Health care professionals should also consider medication issues as a cause of resistant hypertension:

- Inadequate drug doses and poor adherence
- Drug actions and interactions, illicit drugs (cocaine), sympathomimetics, oral contraceptives, stimulants
- OTCs (pseudoephedrine) and herbal supplements (e.g. Ginseng)

Secondary causes of hypertension should also be considered.

(Saseen et al., 2011 & Chobanian et al., 2003)

Drug Therapy Management Pearl

Did you know that:

- In general, a low dose of the initial drug should be used, slowly titrating upward.
- Optimal formulation should provide 24-hour efficacy with once-daily dose with at least 50% of peak effect remaining at end of 24 hours.
- Combination therapies may provide additional efficacy with fewer adverse effects.
Benefits of Lifestyle Modification for Hypertension

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<tr>
<td>Dietary sodium reduction</td>
<td>2-8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>4-9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>2-4 mmHg</td>
</tr>
</tbody>
</table>

(Saseen et al., 2011 & Chobanian et al., 2003)

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)

The ALLHAT study is the largest, randomized, double-blind, multi-center clinical hypertension trial ever conducted.

A major aim of the study was to determine whether occurrence of fatal coronary heart disease (CHD) or nonfatal myocardial infarction (MI) is lower for high-risk hypertensive patients treated with newer agents.

The newer agents are:

- Calcium channel blockers (CCB): Amlodipine
- Angiotensin Converting Enzyme Inhibitor (ACEI): Lisinopril
- Alpha-blocker: Doxazosin, as compared with a diuretic

The study enrolled 42,418 high-risk hypertensive patients ≥ 55 years of age.

(ALLHAT, 2002)

Overall Conclusions from ALLHAT: ACE-Inhibitors versus Diuretics

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Findings of the ALLHAT trial showed that Lisinopril (representing ACEI) was about equivalent to chlorthalidone (representing thiazide-type diuretics) in preventing major coronary events or increasing overall survival, but Chlorthalidone is superior to lisinopril in preventing aggregate cardiovascular events, principally stroke, heart failure, angina, and urgent coronary vessel surgery.

Results were generally consistent for most outcomes by age, gender, race and diabetic status.

(Chobanian et al., 2003 & ALLHAT, 2002)

**JNC-8 Recommendations**

There are nine JNC-8 Recommendations:

**Recommendation 1**
In the general population aged ≥60 years, initiate pharmacologic treatment to lower (BP) at systolic blood pressure (SBP) ≥150mmHg or diastolic blood pressure (DBP) ≥90mmHg and treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.

**Recommendation 2**
In the general population <60 years, initiate pharmacologic treatment to lower BP at DBP ≥90mmHg and treat to a goal DBP <90mmHg.

**Recommendation 3**
In the general population <60 years, initiate pharmacologic treatment to lower BP at SBP ≥140mmHg and treat to a goal SBP <140mmHg.

**Recommendation 4**
In the population aged ≥18 years with chronic kidney disease (CKD), initiate pharmacologic treatment to lower BP at SBP ≥140mmHg or DB ≥90mmHg and treat to goal SBP <140mmHg and goal DBP <90mmHg.

**Recommendation 5**
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In the population aged ≥18 years with diabetes, initiate pharmacologic treatment to lower BP at SBP ≥140mmHg or DBP ≥90mmHg and treat to a goal SBP <140mmHg and goal DBP <90mmHg.

**Recommendation 6**

In the general non-black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor (ACEI), or angiotensin receptor blocker (ARB).

**Recommendation 7**

In the general black population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic or CCB.

**Recommendation 8**

In the population aged ≥18 years with CKD, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status.

**Recommendation 9**

The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug (e.g. thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with two drugs, add and titrate a third drug. Do not use an ACEI and ARB together in the same patient. If goal BP cannot be reached using only the drugs recommended previously, or because of a contraindication, or the need to use more than three drugs to reach goal BP, antihypertensive drugs from other classes can be used. Referral to a hypertension specialist may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed.

**Test Yourself**

Which of the following recommendations is INCORRECT?

A. Never use an ACEI and ARB together in the same patient.
B. Titrate as many antihypertensive drugs as necessary to maintain BP within goal range.
C. Only add a second antihypertensive drug if the first antihypertensive fails to maintain BP in the desired range after 9 months of therapy.

The correct answer is: C.

**Hypertension in Minority Patients**

Socioeconomic factors and lifestyle are important barriers to BP control.

African Americans have a reduced BP response to monotherapy with beta blockers (BB), ACEI, or angiotensin receptor blockers (ARB), as compared to diuretics or calcium channel blocker (CCB).

These differences can usually be eliminated by adding adequate doses of a diuretic, or increasing the antihypertensive dose.

(Saseen et al., 2011 & Chobanian et al., 2003)

**Hypertension and Heart Failure**

Hypertensive patients with heart failure are usually managed with combination therapy, consisting of:

- **Diuretic**
  - Loop diuretic for HF exacerbations
  - Thiazides for BP control if good renal function
- **Beta blocker (cardioselective agents)**
- **ACE inhibitor**
- **Angiotensin receptor blocker**
- **Aldosterone antagonist**

(Saseen et al., 2011 & Chobanian et al., 2003)

**Hypertension and MI**

Hypertensive patients with myocardial infarction are usually managed with combination therapy, consisting of:

- **Beta blocker (cardioselective)**
- **ACEI (preferred over ARB)**

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• Aldosterone antagonist (e.g. spironolactone, eplerenone)
(Saseen et al., 2011 & Chobanian et al., 2003)

Left Ventricular Hypertrophy (LVH)
LVH is an independent risk factor that increases the risk of CVD. Regression of LVH occurs with aggressive BP management using:
Weight loss and exercise
Sodium restriction
Aggressive treatment with all classes of antihypertensive drugs, except the direct vasodilators hydralazine and minoxidil
(Saseen et al., 2011 & Chobanian et al., 2003)

Peripheral Arterial Disease (PAD)
Peripheral arterial disease (PAD) is equivalent in risk to ischemic heart disease.
Any class of drugs can be used in most PAD patients, and daily aspirin use is recommended.
(Saseen et al., 2011 & Chobanian et al., 2003)

Other risk factors should be managed aggressively, such as dyslipidemia.

Hypertension in the Elderly
More than two-thirds of people over 65 have hypertension.
Treatment, including those who with isolated systolic hypertension (ISH), should follow same principles outlined for general care of hypertension.
Lower initial drug doses may be indicated to avoid symptoms; standard doses and multiple drugs will be needed to reach BP targets.
(Saseen et al., 2011 & Chobanian et al., 2003)

Did You Know?
ISH is very common in the elderly due to stiff, noncompliant arteriole walls, and many patients with ISH need more than one drug to regulate BP.
Postural Hypotension

Postural hypotension occurs when there is a decrease in standing systolic blood pressure of more than 10 mmHg, and is associated with dizziness/fainting.

It is more frequent in older hypertensive patients with diabetes, and elderly hypertensive patients who are taking diuretics, venodilators and some psychotropic drugs.

BP in these individuals should be monitored in the upright position.

Avoid volume depletion and excessively rapid dose titration of drugs.

(Saseen et al., 2011 & Chobanian et al., 2003)

Hypertension in Women

Estrogen-containing oral contraceptives may increase BP; thus BP should be checked regularly. If hypertension develops in women on birth control pills, another form of contraception (non-estrogen containing) should be considered.

Hypertension in Pregnancy

ACE inhibitors are contraindicated in pregnancy: ACEI can cause injury and death to the developing fetus when used in the second and third trimesters, and should thus be discontinued as soon as possible once pregnancy is detected.

ACE inhibitors have been associated with congenital malformations and have a Black-Box warning for use during pregnancy.

Females of child-bearing potential should be counseled on appropriate birth-control measures before initiation of ACEI.

Other drugs that act on the RAAS system, such as angiotensin receptor blockers (ARBs) and direct renin inhibitors (DRIs) are likewise contraindicated in pregnancy.

Note! Pregnant women with hypertension should be followed carefully.

Did You Know?

*Methyldopa, BBs, and vasodilators are preferred for women of child-bearing potential since they are not teratogenic; and ACEI, ARBs and DRIs contraindicated in pregnancy.*

(Saseen et al., 2011 & Chobanian et al., 2003)

Additional Considerations in Antihypertensive Drug Choices

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There are potential unfavorable side-effects that must be considered with the use of antihypertensive drugs:

- Thiazide diuretics should be used cautiously in gout or a history of significant hyponatremia.
- BBs should be generally avoided in patients with asthma, reactive airways disease, or second- or third-degree heart block.
- ACEIs, ARBs and DRIs are contraindicated in pregnant women or those likely to become pregnant.
- ACEIs should not be used in individuals with a history of angioedema.
- Aldosterone antagonists and potassium-sparing diuretics can cause hyperkalemia.

(Saseen et al., 2011 & Chobanian et al., 2003)

**Drug Therapy: ACEI**

**Method of Action:**
ACEIs inhibit Angiotensin Converting Enzyme to prevent the conversion of angiotensin I to angiotensin II. This decreases the production of angiotensin II results in vasodilatation (enlarging the opening of both arteries and veins), and decreased aldosterone secretion. This in turn leads to less sodium and water reabsorption and less potassium excretion.

The net effect is a reduced BP.

(Microdex, 2013 & Lexi-Comp, 2013).

**Dosing:**
Most agents can be dosed once daily.

Because of the risk for hypotension (seen most common after the first few doses), initial dose should be reduced by 50% in those patients who are taking a diuretic, or are volume depleted, or in frail elderly patients.

All ACEIs require dosage adjustment for renal impairment, except for fosinopril.

All ACEIs are available as generic products.

(Microdex, 2013 & Lexi-Comp, 2013).
Side Effects:

Angioedema is a rare (<1%) but serious side effect that can occur at any time during treatment, but most often after the first dose.

Patients should be made aware of symptoms before initiating treatment: lip and tongue swelling, difficulty breathing, edema around the larynx.

Angioedema may require urgent treatment with epinephrine, steroids, antihistamines, and/or intubation.

African Americans and smokers are at higher risk.

ACEI are contraindicated in any patient who has a history of angioedema.

An ARB can be used with caution in patients with a history of ACEI-angioedema due to low cross-reactivity.

(Microdex, 2013 & Lexi-Comp, 2013).

Side Effects:

Persistent dry, unproductive cough is seen in up to 20% of patients, and usually develops during the first few months of treatment. The cough results from an increase in bradykinin, as ACE itself is the enzyme normally responsible for bradykinin degradation.

The ACEI cough may necessitate a change in therapy if patients find it bothersome and if it affects compliance.

Upon discontinuation of the ACEI, the cough should resolve in 1-4 weeks. Other causes for cough should be excluded anytime a patient develops a cough while receiving an ACEI.

(Microdex, 2013 & Lexi-Comp, 2013).

Side Effects:

Hyperkalemia (increased potassium levels) are usually seen due to decreased aldosterone, but hyperkalemia can occur.

Risk factors for hyperkalemia exists in those with:

- Chronic kidney disease
- Diabetes mellitus
- Concomitant drug therapy with potassium supplements, potassium-sparing diuretics, ARBs, or DRI.
Potassium levels should be monitored within 4 weeks of initiating treatment or increasing the dose and should be monitored extremely close in those patients with risk factors for hyperkalemia.

(Microdex, 2013 & Lexi-Comp, 2013).

**Side Effects:**

**Declined renal function** occurs due to small increases in serum creatinine (<1mg/dL) and decreases in glomerular filtration rate. These changes are due to the loss of vasoconstriction usually exerted by angiotensin II on the efferent arteriole of the kidney.

*Note: If kidney function greatly worsens, the ACE inhibitor should be stopped or the dose reduced.*

Acute kidney failure occurs in <1% of patients; those with preexisting renal disease are at increased risk.

Concomitant use with NSAIDs may cause a further decline in renal function; NSAIDS also can elevate BP and decrease the effectiveness of ACE inhibitors.

(Microdex, 2013 & Lexi-Comp, 2013).

**Drug Therapy: DRI (Aliskiren)**

DRI is the newest agent approved for hypertension (monotherapy or combination therapy).

It directly inhibits renin and inhibits the conversion of angiotensinogen to angiotensin I. Unlike ACEIs and ARBs, which indirectly increase levels of PRA, aliskiren directly inhibits renin.

These reductions occur whether or not aliskiren is used as monotherapy or concomitantly with other antihypertensive agents. It is unknown if aliskiren has an effect on other RAAS components.

Adverse effects include rash, diarrhea, increased CK, cough, angioedema and orthostatic hypotension.

(Microdex, 2013 & Lexi-Comp, 2013)

*Note! DRI has a Pregnancy Category C rating in the 1st trimester and a Category D rating in the 2nd trimester.*

**Drug Therapy: DRI (Aliskiren):**

The dose is 150 mg orally once daily; may increase to 300 mg/day based on clinical response.
Contraindications are similar to ACEI/ARB, such as history of angioedema; bilateral renal artery stenosis; pregnancy, renal failure.

Since aliskirin is a minor substrate for CYP3A4; we expect slightly increased aliskiren levels with known inhibitors, such as ketoconazole.

DRI is available as brand only, in 150mg and 300mg tablets.

*Note! High fat food decreases AUC and Cmax by 71% and 85%, respectively, and ~25% of oral dose is excreted unchanged in urine, t1/2 ~ 24 hours.*

(Microdex, 2013 & Lexi-Comp, 2013)

**Drug Therapy: ARBs:**

ARBs directly block angiotensin II AT₁ receptors resulting in:

- Vasodilatation (leading to decreased blood pressure)
- Decreased aldosterone secretion, which leads to:
  - Less sodium and water reabsorption
  - Less potassium excretion
  - Lower blood pressure

ARBs do not block degradation of bradykinin, unlike ACEI which increase bradykinin. Thus, the likelihood of drug-induced cough is minimal.

(Microdex, 2013 & Lexi-Comp, 2013)

**Drug Therapy: ARBs**

Most ARBs can be dosed once daily, preferably in the morning.

- Consider lower initial doses (~50% normal dose) for volume-depleted (dehydrated) patients.
- Caution needed and the serum creatinine should be monitored in patients with a history of renal impairment.
- Losartan requires a dosage adjustment for hepatic impairment, but caution may need to be used with other ARBs in liver failure.

All agents can be taken without regards to meals.

Losartan and eprosartan are available as generic products, as well as valsartan plus HCTZ.

(Microdex, 2013 & Lexi-Comp, 2013)
Drug Therapy: ARBs

Common side effects include dizziness, hypotension, fatigue, diarrhea, abdominal pain and abnormal renal function tests.

Rare, but potentially severe side effects include hyperkalemia, hypotension, renal failure and neutropenia.

Patients receiving ARBs should be monitored for blood pressure, changes in kidney and liver function and an increase in serum potassium.

(Microdex, 2013 & Lexi-Comp, 2013)

Note! ARBs are much less likely than ACE Inhibitors to cause cough and angioedema.

Summary of RAAS Drugs in Hypertension

ACEI and ARB are preferred drugs as initial therapy in patient with hypertension who also have the following conditions:

- Heart failure (BB concurrently in most patients)
- Post MI (BB concurrently in most patients)
- Patients at high risk for coronary artery disease
- Diabetes
- Chronic kidney disease (with stable renal function)
- Recurrent stroke prevention

(Saseen et al., 2011 & Chobanian et al., 2003)
## RAAS Drugs + Diuretic Combinations

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<tr>
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<th>Brand Name</th>
<th>Available Doses</th>
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<td>Accuretic®</td>
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**Diuretics**

Diuretics decrease plasma and stroke volume, which decreases cardiac output and BP.

A more sustained effect of decreasing peripheral vascular resistance is responsible for the chronic antihypertensive effects of diuretics.

Potassium-sparing diuretics, such as triamterene, provide an additive effect when used in combination with a thiazide. They can also attenuate the loss of potassium and magnesium with diuretic use.

Aldosterone antagonists, such as spironolactone and eplerenone, are not routinely used for hypertension, but have a role in patients with HF.

(Saseen et al., 2011)

**Diuretics**

Patients with hypertension should be initiated on a thiazide diuretic, such as HCTZ or chlorthalidone unless a compelling indication exists for a different agent.

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<td>Irbesartan/HCTZ</td>
<td>Avalide®</td>
<td>75/12.5, 150/12.5, 300/12.5</td>
</tr>
<tr>
<td>Losartan/HCTZ</td>
<td>Hyzaar®</td>
<td>50/12.5, 100/25</td>
</tr>
<tr>
<td>Olmesartan/HCTZ</td>
<td>Benicar HCT®</td>
<td>20/12.5, 40/12.5, 40/25</td>
</tr>
<tr>
<td>Telmisartan/HCTZ</td>
<td>Micardis HCT®</td>
<td>40/12.5, 80/12.5</td>
</tr>
<tr>
<td>Valsartan/HCTZ</td>
<td>Diovan HCT®</td>
<td>80/12.5, 160/12.5</td>
</tr>
</tbody>
</table>

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**Renin Inhibitor/HCTZ**

<table>
<thead>
<tr>
<th>Combination</th>
<th>Brand Name</th>
<th>Available Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aliskiren/HCTZ</td>
<td>Tekturna HCT®</td>
<td>150/12.5, 150/25, 300/12.5, 300/25</td>
</tr>
</tbody>
</table>
Patients unable to achieve adequate blood pressure control may be started on combination therapy. For example, the use of a thiazide diuretic in combination with a drug that acts on the RAAS, yields synergistic antihypertensive effects.

Diuretics can be associated with hypokalemia, hypomagnesemia and hyperuricemia (dose-related).

(Microdex, 2013 & Lexi-Comp, 2013)

**Calcium Channel Blockers (CCBs)**

Both CCB classes, dihydropyridine (e.g. amlodipine) and nondihydropyridine (e.g. verapamil and diltiazem) are efficacious to treat hypertension, and both classes are useful in hypertensive patients with coronary artery disease and diabetes.

*Note! Verapamil and diltiazem are uniquely beneficial in patients with atrial fibrillation.*

(Julius et al., 2004, Saseen et al., 2011, Chobanian et al., 2003 & ALLHAT, 2002)

*Did You Know?*

*The Valsartan Antihypertensive Long-Term Use Evaluation (VALUE) study showed no difference in the primary outcome of first CV event in high-risk patients between valsartan and amlodipine.*

**Calcium Channel Blockers (CCBs)**

Note that dihydropyridines are more potent peripheral vasodilators than nondihydropyridines and may cause more reflex tachycardia, headache, gingival hyperplasia and edema.

Extended-release or sustained-release CCBs are preferred for shorter-acting agents, such as nifedipine, verapamil and diltiazem.

Long-acting dihydropyridine CCBs are effective in elderly patients with isolated systolic hypertension.

(Johnson et al., 2004 & Staessen et al., 1997)

**Test Yourself**

Which CCBs are most suitable for elderly patients with isolated systolic hypertension?

A. Short-acting CCBs
B. Sustained-release CCBs
C. CCBs are not suitable for use in the elderly

The correct answer is: B.

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Beta Adrenergic Blockers (BBs)

BBs are appropriate for compelling indications, such as post-MI, coronary disease, atrial fibrillation (for rate control) and heart failure.

Cardioselective BBs, such as atenolol, metoprolol are preferred over non-selective agents, such as propranolol, for treating hypertension.

Cardioselective agents are also safer than non-selective agents in patients with asthma or diabetes.

(Sasseen et al., 2011, Chobanian et al., 2003 & ALLHAT, 2002)

Note! Nevibolol also produces an endothelium-derived nitric oxide-dependent vasodilation and decreases systemic vascular resistance.

Beta Adrenergic Blockers

At higher doses, these cardioselective agents lose their selectivity for beta 1-receptors and block 2-receptors too.

Abruptly stopping BBs can exacerbate angina or MI in patients with coronary disease. Abrupt cessation may also lead to rebound hypertension.

BBs should be tapered gradually over 1 to 2 weeks before discontinuation.

Atenolol and nadolol are renally excreted and may accumulate in patients with renal failure.

(Sasseen et al., 2011, Chobanian et al., 2003 & ALLHAT, 2002)

Alpha-1 Adrenergic Blockers

Terazosin, and doxazosin are selective alpha 1-receptor blockers. They cause peripheral vasodilation and lower BP.

Alpha 1-blockers should be considered alternative agents to be used in combination with other first-line antihypertensives.

These drugs do provide symptomatic relief in men with benign prostatic hyperplasia.

(Sasseen et al., 2011, Chobanian et al., 2003 & ALLHAT, 2002)
Did You Know?

In the ALLHAT study, the doxazosin arm was stopped prematurely because episodes of stroke and heart failure, were increased, relative to chlorthalidone.

Central Alpha-2 Blockers

Clonidine, guanabenz, guanfacine, and methyldopa reduce sympathetic outflow from the vasomotor center in the brain and increase vagal tone. These agents decrease heart rate, cardiac output, total peripheral resistance and renin activity.

Abrupt cessation of central 2-agonists may lead to rebound hypertension.

Methyldopa is a first-line agent during pregnancy, but has been associated with hemolytic anemia.

Clonidine can be given as a transdermal patch to improve adherence.

(Sasseen et al., 2011, Chobanian et al., 2003 & ALLHAT, 2002)

Direct Acting Vasodilators

Hydralazine directly relaxes arteriolar smooth muscle, resulting in vasodilation and decreased BP. Hydralazine can increase in heart rate, cardiac output, and renin release. Thus, these drugs are often given with a diuretic to decrease fluid retention and a BB to decrease reflex tachycardia.

Hydralazine has been associated with drug-induced lupus-like syndrome.

(Sasseen et al., 2011, Chobanian et al., 2003 & ALLHAT, 2002)

Did You Know?

Minoxidil is also in this class, but used less often.

Patient Counseling

Nurses and APRNs play an important role in collaborating with physicians to improve blood pressure control in patients with hypertension.

Nurses should educate patients about the consequences of uncontrolled or untreated disease, especially target organ damage and assure that patients understand the benefits of optimal blood pressure control.

Patients should also be made aware of the most likely potential side effects anytime a medication is initiated.

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Nurses can recommend the use of a portable digital blood pressure monitoring device that allows patients to take a more active role in managing their blood pressure and may improve medication compliance.

The nurse can further assist patients with identifying routine, daily activities that may aid in remembering drug administration, such as brushing one’s teeth; and counsel patients who will be filling prescriptions for blood pressure lowering medications about the effects of NSAIDs, pseudoephedrine, nicotine, alcohol and dietary supplements (e.g. Ginseng) on raising blood pressure.

**Case Study**

Miss B is a 39 year old female with a history of hypertension who presented to the ED with hypertension. On admission, she stated that her BPs at home have been “running a bit high.”

**History of present illness and brief physical exam:**

Miss B has some complaints of mild fluid retention (puffy eyes and hands), and presents with a BP of 176/98 (previously well-controlled at last few visits), Pulse of 80, and BMI: 28.

**Past medical and social history:**

Hypertension, tension-type headaches, Miss B is newly sexually-active with one male partner and has regular periods. She drinks 3-4 beers daily, exercises on the weekends, and smokes 1 pack of cigarettes daily and denies recreational drug use. She uses no natural products or supplements.

**Meds:**

HCTZ 25mg QD, no signs or symptoms of heart failure, ibuprofen 400mg PRN for headache.

**Q: What might you consider or do to help explain Miss B’s lack of adequate blood pressure control?**

**Answer:**

1. Verify Miss B’s adherence to hydrochlorothiazide.
2. Repeat Miss B’s blood pressure.
3. Ask if she recently smoked a cigarette.
4. Inquire about how much and how often she is taking ibuprofen.
5. Ask about Miss B’s sodium (salt intake) and caloric intake.

6. Ask if there any chance that she may be, or may become pregnant?

**Q: How might you counsel Miss B to improve her blood pressure control?**

**Answer:**

After probing the causes for her tension headaches, it is advisable for Miss B to discontinue ibuprofen and change to acetaminophen since ibuprofen can worsen BP control. The ibuprofen is also a likely reason for her puffy eyes and hands.

Advise her to increase exercise and/or activity level as tolerated to a more regular, sustained and aerobic form of exercise.

After taking a diet history, recommend reduction of intake of sodium (salt), saturated fats, sugars, red meat, and eat more fruits and vegetables, if necessary.

Assess Miss B’s readiness for change with respect to smoking cessation and alcohol intake reduction.

**Q: Would an ACEI or ARB be an appropriate choice for Miss B to improve her blood pressure control and what general counsel should she receive?**

**Answer:**

Both drug classes are contraindicated in pregnancy, so this may not be the best choice if Miss B is not using birth control. However, if she is unable to conceive (e.g. post-tubal ligation, using reliable birth control, etc.), then an ACEI would be acceptable.

If Miss B receives an ACEI, a once daily generic ACEI would be preferred (e.g. ramipril, lisinopril, others) and added onto her diuretic.

**Clinical Pearl:** Giving a single drug, combination product that is generically-available is a cost-effective strategy (e.g. lisinopril plus HCTZ).

Miss B should be cautioned about the development of a dry cough, and angioedema (swelling of the lips, tongue and/or face).

**Conclusion**

Hypertension is so prevalent that it is second only to diabetes as the most common predecessor for many life-threatening complications such as heart failure, end stage
renal disease, coronary artery disease (CAD) and stroke (Chobanian et al., 2003). Hypertension has become a national health crisis.

Given the seriousness and consequences of uncontrolled hypertension, it is essential that nurses are up to date on the most current guidelines related to hypertension and its therapies.

References


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