Hypertension: A Focus on JNC 7

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Objectives

• Upon completion of this lecture, the participant will be able to:
  – Identify the various classifications of prehypertension, Stage I and Stage 2 hypertension
  – Discuss nonpharmacologic treatment options for the patient with hypertension
  – Discuss pharmacologic treatment options for the patient with hypertension

CVD Is the Most Common Health Problem in the United States

More than 60 million Americans (>20%) have some form of cardiovascular disease
CVD disease mortality trends for males and females (United States: 1979-2004). Source: NCHS and NHLBI.

Evolution in Understanding Cardiovascular Disease: Total Risk Perspective

Cardiovascular Disease is an interplay of Risk Factors

Hypertension and Dyslipidemia Contribute to Atherogenesis

Partners in Healthcare Education, LLC 2009
Impact of Elevated SBP and Total Cholesterol on CHD Mortality in MRFIT

<table>
<thead>
<tr>
<th>Cholesterol Quintile (mg/dL)</th>
<th>SBP Quintile (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>160-181</td>
<td>140-159</td>
</tr>
<tr>
<td>150-159</td>
<td>130-139</td>
</tr>
<tr>
<td>140-149</td>
<td>120-129</td>
</tr>
<tr>
<td>130-139</td>
<td>110-119</td>
</tr>
<tr>
<td>120-129</td>
<td>100-109</td>
</tr>
<tr>
<td>110-119</td>
<td>90-99</td>
</tr>
</tbody>
</table>

MRFIT = Multiple Risk Factor Intervention Trial. Adapted from Neaton JD et al. Arch Intern Med.

Hypertension and Dyslipidemia: A Significantly Undertreated Syndrome

27 Million Affected by Both Hypertension and Dyslipidemia

- 14.7 million undiagnosed
- 9 million diagnosed with both
- 3 million treated for both
- 300,000 at both goals (~ 1%)

Impact of Hypertension

- 50 million individuals in the United States have hypertension
- 277,000 deaths annually in US due to hypertension

Adapted from American Heart Association and CDC; NHANES III (1988-1994).
Hypertension Remains One of the Most Important Multipliers of CV Risk

BP >140/90 mm Hg is associated with:

- 277,000 deaths in 2003

BP, blood pressure; CHF, congestive heart failure; MI, myocardial infarction.

It is currently estimated that...

- 90% of normotensive 55 year olds will develop hypertension at some point in his/her lifetime

Hypertension: Controlled or Not?

Prevalence (%)

Controlled on medication
Uncontrolled on medication
Diagnosed

Adapted from NHANES III Morning Examination Subset: Hypertension (June 1998);
Statistics of Interest

- 53% of patients with hypertension are being treated with medications
- Of those treated, 29% have their blood pressure < 140/90

Physiology of the Renin Angiotensin System

RAAS and Adipose Tissue
- All components of the RAAS system are expressed in adipose tissue, especially the visceral adipose tissue\textsuperscript{1,2,3}
- Visceral adipose tissue of patients with insulin resistance and Type 2 diabetes is dysfunctional and is a source of chronic low-grade inflammation\textsuperscript{4}

RAAS and Endothelial Dysfunction
- Growing body of evidence
  - Promotion of endothelial dysfunction
  - Microalbuminuria\textsuperscript{1,2}
- RAAS Inhibition (ACE, ARB and Direct Renin Inhibitor)
  - Decreased incidence of new onset Type 2 diabetes
  - Improvement in CVD outcomes\textsuperscript{3}
Today –
The Hypertensive Patient Exhibits...

• More insulin resistance
• More hyperinsulinemia
• Dyslipidemia
• Microalbuminuria
• Obesity

...as compared to nonhypertensive patients!


Blocking the RAAS has been shown to be beneficial in...

Cardiovascular Disease
Hypertension
Diabetes

JNC VII:
Messages to Clinicians

JAMA. 2003;289:2560-2572.
New Messages JNC VII

• The risk of CVD, beginning at 115/75 mm Hg, **doubles** with each increment of 20/10 mm Hg.

*JAMA. 2003;289:2560-2577.*

CV Disease Risk Doubles with Each 20/10 mm Hg BP Increment*

<table>
<thead>
<tr>
<th>SBP/DBP (mm Hg)</th>
<th>CV disease risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>115/75</td>
<td>1</td>
</tr>
<tr>
<td>135/85</td>
<td>2</td>
</tr>
<tr>
<td>155/95</td>
<td>3</td>
</tr>
<tr>
<td>175/105</td>
<td>4</td>
</tr>
</tbody>
</table>

*Individuals aged 40-70 years, starting at BP 115/75 mm Hg.
CV, cardiovascular; SBP, systolic blood pressure; DBP, diastolic blood pressure.

• 2 readings; separated apart
• Patient should not ingest caffeine or smoke for 30 minutes before readings
• Patient should sit for 5 minutes with arm at heart level before blood pressure is checked
JNC 7: New Blood Pressure Classification

<table>
<thead>
<tr>
<th>Blood Pressure Classification</th>
<th>SBP* DBP* (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 and &lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120-139 or 80-89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140-159 or 90-99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160 or ≥100</td>
</tr>
</tbody>
</table>

*Treatment determined by highest BP category (SBP or DBP).


Prehypertension

- Individuals with a systolic BP of 120-139 mm HG or a diastolic BP or 80-89 mm HG should be considered as prehypertensive and lifestyle modification initiated.

*JAMA*. 2003;289:2560-2577.

Most Cases of Hypertension

- Primary hypertension
  - Also called essential
  - Responsible for 90-95% of all hypertension diagnoses
Consider Secondary Causes of HTN

- Sleep apnea
- Drug-induced or drug related
  - Including OTC medications
- Chronic kidney disease
  - Polycystic kidneys
- Renal artery stenosis
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing’s disease
- Pheochromocytoma
- Coarctation of the Aorta
- Thyroid or parathyroid disease

JAMA. 2003;289:2560-2577.

What about White-Coat Hypertension?

- Patient involvement in the measurement of his/her blood pressure is recommended, particularly for those individuals whose blood pressure is normal out of the office but consistently elevated in the office
- The office blood pressure of elders is 5 mm Hg higher than their ambulatory blood pressure
- Older the individual, the greater the discrepancy between home and office blood pressures
- No longer considered a benign condition

JAMA. 2003;289:2560-2577.

Initial Work-up

- History and review of systems
  - Medications and risk factors
- Consider home blood pressure readings with validated blood pressure cuff
- Laboratory workup: CBC, BUN, Creatinine, Glucose, Lipids, GFR, urine - protein
- EKG and/or Echocardiogram, if indicated

Treatment of Hypertension

How Helpful is control of BP?
In stage 1 HTN, combined with additional CVD risk factors, achieving a sustained 12 mmHg reduction in SBP over 10 years will prevent 1 death for every 11 patients treated.

Other Implications of Treatment
- Controlled hypertension reduces:
  - CHF by 50%
  - MI’s by 25%
  - CVA’s by 35%
**Treatment Goals**

- < 140/90 mm Hg for those with no complications
- < 130/80 mm Hg for those with diabetes or CRF (per ADA and NKF)

**JNC 7: Algorithm for Treatment of Hypertension**

- Prehypertension (SBP 120-139 mm Hg or DBP 80-89 mm Hg)
- Not at Goal BP (<140/90 mm Hg, or <130/80 mm Hg for patients with diabetes or chronic kidney disease)

**Without Compelling Indications**

- Stage 1 Hypertension (SBP 140-159 or DBP 90-99 mm Hg)
  - Thiazide-type diuretics for most; may consider ACEI, ARB, BB, CCB, or combination.

- Stage 2 Hypertension (SBP ≥ 160 or DBP ≥ 100 mm Hg)
  - 2-drug combinations for most (usually thiazide-type diuretics and ACEI or ARB or BB or CCB).

**With Compelling Indications**

- Drug(s) for compelling indications other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.

**LIFESTYLE MODIFICATIONS**

If not at goal BP, optimize dosages or add additional drugs until goal BP is achieved. Consider consultation with hypertension specialist.

**INITIAL DRUG CHOICES**

- Prehypertension
  - If not at goal BP, optimize dosages or add additional drugs until goal BP is achieved. Consider consultation with hypertension specialist.

**Therapeutic Lifestyle Changes**
### Lifestyle Modifications to Manage Hypertension

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Systolic Diastolic Chgs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Reduction</td>
<td>BMI 18.5-24.9 Diet rich in fruits vegetables and low fat with reduced saturated and total fat</td>
<td>5-20mm/10 kg wt loss</td>
</tr>
<tr>
<td>Adopt DASH eating</td>
<td>2-4g Na Brisk exercise 30&quot; day most days of week</td>
<td>2-8 mm Hg</td>
</tr>
<tr>
<td>Dietary Sodium</td>
<td>2 drinks day max 24 oz beer; 10 oz wine; 2 oz 100 proof whiskey</td>
<td>2-4 mm Hg</td>
</tr>
<tr>
<td>Physical Inactivity</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
How Successful Is It?

- Combination of the DASH diet and a dietary sodium reduction to 1600 mg/day is as effective as 1 medication

Alcohol Intake

- Limit alcohol intake to < 30 mL or 1 ounce of ethanol/day
  - Translation: 2 ounces of whiskey
  - 10 ounces of wine
  - 24 ounces of beer
- Excessive amounts increases treatment resistance
- Also increases risk of a CVA
  ** Women: ½ this amount

Electrolytes

- Diets high in potassium, calcium and magnesium are associated with a lower blood pressure
- JNC VII recommends an adequate dietary intake of these but does not recommend supplementing from an outside source to lower blood pressure
Additional Recommendations

- Omega-3 fatty acids may lower blood pressure
- Caffeine may increase it but tolerance often develops
  - Most studies do not support a relationship between hypertension and caffeine
- Smoking: discontinuation is important
- Exercise: 30 minutes daily recommended

Pharmacologic Treatments

New Messages JNC VII

- Thiazide diuretics should be used in drug treatment for patients with uncomplicated hypertension.
  
  *JAMA. 2003;289:2560-2577.*
Thiazide Diuretics

- **Dosing:**
  - Start @ 12.5 mg of HCTZ
  - Increase to 25 mg at 6 weeks
- **Benefits**
  - 55% reduction in CHF
  - 37% reduction in CVA
  - 27% reduction in cardiac events
- If not adequately controlled, add additional agents

Diuretic Precautions

- Electrolyte imbalances
- Syncope/presyncope when combined with ACE/ARB
- Hemoconcentration
- Decrease in urate excretion
- Worsening of insulin resistance at higher doses
- Fatigue

Angiotensin Converting Enzyme (ACE) Inhibitors

- Increased nitrous oxide at vessel for vasodilatation
- Improved glucose disposal
- Reduction in LV geometry changes
- Reduction in inflammation
- Stabilization of fibrous cap of lipid lesion
- Decreased proteinuria
- Improves endothelial function
- Reduced mortality in patients with CHF
- Decreases post-MI mortality

ACE Inhibitor Trials

ACE Inhibitors Precautions

- Hyperkalemia
- Increase in creatinine
- May improve insulin sensitivity
- Decrease in serum Na+ may result in syncope and dizziness when used with diuretics

Product inserts accessed 04-20-2008

Effects on Hypoglycemia

- Several studies have shown the ability of ACE inhibition to improve glycemic control – even decrease the risk of hypoglycemia in patients using sulfonylureas.

ACE Inhibitors Are Highly Effective..

But…

Long Term Effect of Enalapril (20mg) on Plasma ACE and Angiotensin II

If you block the receptor site, you don’t have to worry about the angiotension levels…

AT1
Angiotensin Receptor Blockers

Angiotension Receptor Blockers (ARB’s)

- Utilized since April 1995
- Blocks uptake at receptor site
- Angiotension II produced in locations other than in the lungs
- BP decreased by reducing vascular tone and enhancing NA+ and water clearance

Metabolic Effects of ARB’s

- Angiotensin II Receptor Blockers
  - Metabolically neutral
  - No impact on lipids
  - No impact on insulin
  - No impact on K+
  - Lowers uric acid levels
  - Minimal side effect profile

Product Inserts accessed 04-20-2008
ACE vs ARB ONTARGET Trial

1. Assess the effects of ACE VS ARB in terms of efficacy
2. Assess if the combination ACE & ARB was superior

Results:
- Telmisartan was found to be "noninferior" to ramipril in patients with vascular disease or high risk diabetes
- Combination of these two agents was associated with more adverse events without an increase in benefit.

Beta Blockers

- Decreased contractility
- Decreased heart rate
- Decreased myocardial oxygen demand
Beta Adrenergic Receptors

- 3 receptors are found in human cardiac myocytes that are coupled to a positive inotropic response and cell growth.
  - $\text{Beta}_1$
  - $\text{Beta}_2$
  - $\text{Alpha}_1$


Calcium Channel Blockers

- Effectively treat systolic hypertension
- May be superior to other antihypertensives for stroke prevention
- Effective in patients with:
  - Comorbid conditions (Raynauds, migraine)$^1$
- Particularly effective in
  - Elderly and African American’s$^2$

The Calcium Blockers

Dihydropyridines
- Studies of DPH’s effects on proteinuria have produced conflicting results
- NKF recommends that in patients who have diabetes and kidney disease, DPH’s should only be used in combination with an ACE or ARB

Nondihydropyridines
- Regression of proteinuria
- Combination of Verapamil + ACE, reduction in proteinuria can be greater than achievable with verapamil alone.
- NKF now recommends adding a NDH to treat hypertension with an ACE inhibitor or an ARB to slow the progression of kidney disease.


Alpha Blockers

- Block postsynaptic Alpha1 Receptors
- Results in vasodilatation
- Relatively inexpensive
- Fair tolerability; May cause postural effects
- Additive agent for older men to decrease BPH symptomatology
- Add on agent only
- Should never be used as monotherapy due to increased risk of stroke and CHF

Centrally Acting Blockers

Centrally Acting Agents
- Stimulates central alpha₂ receptors which results in:
  - Inhibiting efferent sympathetic activity
- Additive agents
- Should be used 3rd or 4th line
  - Examples: Clonidine (catapress, catapress TTS); methyldopa
- Caution: sedation, orthostatic hypotension

[Link](http://jama.ama-assn.org/cgi/content/full/289.19.2560v1) Assessed 5-1-08

Direct Vasodilators
Direct Vasodilators

- Direct smooth muscle vasodilatation primarily arteriolar
- Two agents
  - Apresoline (Hydralazine)
  - Minoxidil

**Precautions include:** tachycardia, significant peripheral edema and hair growth

Agents to reduce heart rate may be needed


http://jama.ama-assn.org/cgi/content/full/289.19.2560v1

Assessed 5-1-08

Aldosterone Agonists

- Spironolactone (Aldactone)
- HCTZ / spironolactone (Aldactazide)
- Eplerenone (Inspra)

Aldosterone Antagonists
Aldosterone as a Therapeutic Target

- Aldosterone promotes:
  - Retention of sodium
  - Loss of magnesium and potassium
  - Sympathetic activation
  - Parasympathetic inhibition
  - Baroreceptor dysfunction
  - Impaired arterial compliance


Aldosterone Antagonists

- May be recommended in the following individuals:
  - Post MI
  - NYHA Class III or IV
  - Ejection fraction of < 35%
  - Serum creatinine of < 2.5 mg/dl
  - K+ < 5.0 mmol/L


Precautions

- Must monitor electrolytes
- Must obtain baseline renal function
- Should discontinue the K+ supplement
- Should limit to use in severe heart failure and post MI patients

New Classes/Agents

Direct Renin Inhibitor

Direct Renin Inhibition
Inhibits the Entire Renin System¹-⁴

<table>
<thead>
<tr>
<th>Class</th>
<th>PRA</th>
<th>Ang I</th>
<th>Ang II</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>ARB</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Direct Renin Inhibitor (DRI)</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

Increased peptide levels have not been shown to overcome the blood-pressure-lowering effect of these agents.

Aliskiren

- Dosage:
  - 150 mg or 300 mg once daily
- Indications:
  - Adults with hypertension
  - May be administered with any other antihypertensive

New Messages JNC VII

- Certain high risk conditions are compelling indications for the initial use of other antihypertensive drug classes.
  - Angiotensin-converting enzyme inhibitors
  - Angiotensin-receptor blockers
  - Beta blockers
  - Calcium channel blockers

JNC 7: Compelling Indications for Individual Antihypertensive Drug Classes

<table>
<thead>
<tr>
<th>Compelling Indication*</th>
<th>Recommended Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIURETI C BB ACEI ARB CCB Aldo ANT</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>•</td>
</tr>
<tr>
<td>Post-MI</td>
<td>•</td>
</tr>
<tr>
<td>High coronary disease risk</td>
<td>•</td>
</tr>
<tr>
<td>Diabetes</td>
<td>•</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>•</td>
</tr>
<tr>
<td>Recurrent stroke prevention</td>
<td>•</td>
</tr>
</tbody>
</table>

* Compelling indications for antihypertensive drugs are based on benefits from outcome studies or existing clinical guidelines; the compelling indication is managed parallel with the BP.

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; Aldo ANT = aldosterone antagonist; BB = beta-blocker; CCB = calcium channel blocker.

Adapted from NHBPEPCC. 2003. NIH Publication No. 03-5233.
Combination Therapy

When you put your hand in the cabinet...

JNC 7 (2003)  
Combination Therapy

- Most hypertensive patients will require two or more antihypertensive medications to achieve goal BP (<140/90 mm Hg or <130/80 mm Hg in patients with diabetes/renal disease)
- Initiating therapy with combination therapy should be considered when BP is >20/10 mm Hg above goal.

http://jama.ama-assn.org/cgi/content/full/289.19.2560v1
Assessed 5-1-08
**JNC 7 (2003)**

*Combination Therapy*

- "When BP is more than 20/10 mm Hg above goal, consideration should be given to initiating therapy with two drugs, either as separate prescriptions or in fixed-dose combinations."
- "Failure to titrate or combine medications, despite knowing the patient is not at goal BP, represents clinical inertia and must be overcome."

http://jama.ama-assn.org/cgi/content/full/289.19.2560v1

**Multiple Antihypertensive Agents Are Needed to Achieve Target BP**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Target BP (mm Hg)</th>
<th>No. of antihypertensive agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>UKPDS</td>
<td>DBP &lt;85</td>
<td>1</td>
</tr>
<tr>
<td>ABCD</td>
<td>DBP &lt;75</td>
<td>2</td>
</tr>
<tr>
<td>MDRD</td>
<td>MAP &lt;92</td>
<td>3</td>
</tr>
<tr>
<td>HOT</td>
<td>DBP &lt;80</td>
<td>4</td>
</tr>
<tr>
<td>AASK</td>
<td>MAP &lt;92</td>
<td></td>
</tr>
<tr>
<td>IDNT</td>
<td>SBP &lt;130/DBP &lt;80</td>
<td></td>
</tr>
</tbody>
</table>

DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.


**Hypertension Is More than a Number**
**Target Organ Damage**

- **Heart**
  - LVH, Angina, CHF, MI
- **Brain**
  - Stroke or TIA
  - Dementia
- **Chronic Kidney Disease**
- **Peripheral Vascular Disease**
- **Retinopathy**

*JAMA. 2003;289:2560-2577.*

**Pick the agent wisely**

- Benefits are not the same in antihypertensive therapy at the same commensurate blood pressure control.

*American Heart Association Scientific Sessions 2003; November 9-12, 2003, Orlando, Florida, USA.*

**Additional Considerations for the Patient with Hypertension**
New Messages JNC VII

• In presenting the NEW JNC VII, the committee recognizes that the responsible practitioner’s judgment remains paramount.

JAMA. 2003;289:2560-2577.

Summary

• Hypertension is highly prevalent and is a significant risk factor for CHD
• Current guidelines recognize the importance of assessing multiple cardiovascular risk factors in patients with hypertension
• Health-promoting lifestyle modifications are an important part of prevention and treatment of hypertension
• Antihypertensive therapy reduces CHD risk
• ≥2 antihypertensive agents are usually required to achieve BP goals in patients with hypertension

Thank You!
I Would Be Happy To Entertain Any Questions
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