Diversity and HTN: Approaches to optimal BP control in African Americans

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Improving People's Lives
through innovations in personalized health care
Do Racial Differences Really Exist in HTN?

- Hypertension is very complex

- Hypertension is polygenic phenotype (many different gene products contribute to elevated BP—from gene products that influence electrolyte metabolism, CNS reflexes, VSMC growth, etc.)

- Very difficult to separate the impact of race on BP separate from the impact of culture, geography, and socioeconomic status

- Despite these realities, some differences do exist and are measurable
Racial Differences in Hypertension: 
Renal/Fluid Balance

- Whites excrete a water load more rapidly than blacks
  Alan B. Weder, MD,* et al. 
  *Hypertension 2009 April 53 (4):715-718

- Ethnic Differences in Renal Responses to Furosemide

- Determinants of salt sensitivity in black and white normotensive and hypertensive women. Wright JT Jr, et
Racial Differences in Hypertension: 
*Vascular Mechanisms*


Racial Differences in Hypertension

- Available data seem to suggest that, compared to Whites, African Americans with hypertension on average:
  - Are more salt sensitive
  - Have higher large vessel tone
  - Are less sensitive to the vasodilating effects of N.O.
Racial Differences in Hypertensive-End Organ Damage

Chronic high blood pressure (hypertension) left untreated can lead to:

- Stroke
- Blood vessel damage (arteriosclerosis)
- Heart attack or heart failure
- Kidney failure

ADAM
Target Organ Damage in Hypertension:  
*Left Ventricular Hypertrophy*

LVH is an independent risk factor for CHF, MI, stroke, and death in hypertensive patients.

Compared to Whites with similar BP levels, African Americans have higher incidence of LVH.
Target Organ Damage in Hypertension:  
Congestive Heart Failure


  - 497 Black, 8199 Non Black pts with HTN and no CHF
  - Treated with Losartan and Atenolol
  - Odds Ratio for Incident (“On Treatment”) Heart Failure Blacks vs Non-Blacks: 2.30
Target Organ Damage in Hypertension: 
*Kidney Failure*

- Rate of ESRD from 2-5 times higher in Black vs White Hypertensives
- Among ESRD pts under age 50, death rate of Blacks>Whites
Target Organ Damage in Hypertension: Stroke

Compared to Whites with the same BP, Blacks are significantly more likely to suffer a stroke.

Post stroke mortality in Blacks is significantly worse than in Whites.
Racial Differences in Hypertensive-End Organ Damage

For the same level of BP, Compared to Whites, Blacks are More likely to suffer from:

- LVH
- CHF
- Stroke
- ESRD
Is the Hypertension Suffered by Blacks a more “Malignant” variety?
Changes in BP Classification

<table>
<thead>
<tr>
<th>JNC 6 Category</th>
<th>JNC 7 Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>Normal</td>
</tr>
<tr>
<td>Normal</td>
<td>Prehypertension</td>
</tr>
<tr>
<td>Borderline</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Stage 1</td>
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<tr>
<td>Stage 1</td>
<td>Stage 2</td>
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<tr>
<td>Stage 2</td>
<td></td>
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<tr>
<td>Stage 3</td>
<td></td>
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</tbody>
</table>

SBP/DBP

Optimal: < 120/80
Normal: 120–129/80–84
Borderline: 130–139/85–89
Hypertension: ≥ 140/90
Stage 1: 140–159/90–99
Stage 2: 160–179/100–109
Stage 3: ≥ 180/110

Hypertension 2003;289:2560-2572.
“Pre-Hypertension”

- 130/80-139/89 (non-diabetics)


- Individuals with “pre-hypertension” twice as likely to develop HTN as those with lower BPs
Pre-Hypertension

- Identified as a group to be targeted with aggressive lifestyle changes, (? Drug therapy?)

Epidemiology

- Benefits of lowering BP:
  - 50% reduction in risk of developing CHF
  - 35-40% reduction in risk of stroke
  - 20-25% reduction in risk of MI
Hypertension Management in African Americans

- Significant number of patients still without adequate BP control
  - 1991-1994: 27% of patients with HTN were controlled
  - 1999-2000: 34% of patients with HTN were controlled
  - The numbers for African Americans are worse
# Impact of a 5 mmHg Reduction

<table>
<thead>
<tr>
<th></th>
<th>Overall Reduction</th>
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</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>14%</td>
</tr>
<tr>
<td>Coronary Heart Disease</td>
<td>9%</td>
</tr>
<tr>
<td>All Cause Mortality</td>
<td>7%</td>
</tr>
<tr>
<td>Lifestyle intervention</td>
<td>BP lowering</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Weight reduction</strong></td>
<td>5–20 mm Hg/10 kg</td>
</tr>
<tr>
<td>Maintain normal body weight</td>
<td></td>
</tr>
<tr>
<td><strong>DASH eating plan</strong></td>
<td>8–14 mm Hg</td>
</tr>
<tr>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat.</td>
<td></td>
</tr>
<tr>
<td><strong>Na restriction</strong></td>
<td>2–8 mm Hg</td>
</tr>
<tr>
<td>Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).</td>
<td></td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td>4–9 mm Hg</td>
</tr>
<tr>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week).</td>
<td></td>
</tr>
<tr>
<td><strong>Reduce EtOH intake</strong></td>
<td>2–4 mm Hg</td>
</tr>
<tr>
<td>Limit consumption to no more than 2 drinks (eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter-weight persons.</td>
<td></td>
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</tbody>
</table>

Racial Differences in Responses to Different Drugs Have Been Documented. _But Are They Clinically Important?_

- Compared to Whites, Black hypertensives tend to be:
  - Less responsive to beta blockers
  - More responsive to CCBs
  - Very sensitive to diuretics
  - Less responsive to ACE inhibitors
But, remember, although racial differences in response to different antihypertensive classes have been reported, there is always . . . The Great Equalizer
Optimizing Drug Therapy for Hypertension in Blacks


“Thus, there is little justification to use racial profiling as a criterion for the avoidance of selected drug classes because of presumed lack of efficacy.”

- This could result in depriving African Americans of the important cardiovascular and renal therapeutic benefits of ACE inh/ARBs and beta blockers.
Optimizing Drug Therapy for Hypertension in Blacks

- Items for consideration in African American hypertensive patients:
  - Tend to be salt sensitive (diuretics)
  - Tend to have increased vascular tone (calcium channel blockers)
  - Are at particularly high risk for suffering LVH, CHF, renal failure, and strokes (think ACE inh/ARBs, diuretics)
Hypertension: Principles of Treatment

- Pharmacologic treatments

- Step 1: determine if HTN is accompanied by complications (end organ damage) or other cardiovascular risk factors (DM, CAD, etc.). **If so, controlling the BP is urgent**
Antihypertensive and Lipid-Lowering to Prevent Heart Attack Trial (ALLHAT)

- Randomized, double blind, multi-center, study
- Conducted between 1994-2002, average follow-up 4.9 years
- N=33,357
- Evaluate whether CCB, ACEI or Doxazosin would decrease fatal coronary heart disease, or non-fatal MI when compared to a diuretic

ALLHAT. JAMA. 2002 288(23):2981-97
ALLHAT: Endpoints

- Primary Endpoint
  - Fatal coronary heart disease or non-fatal MI

- Secondary Endpoints:
  - All cause mortality
  - Fatal and non-fatal stroke
  - Combined coronary heart disease
  - Combined cardiovascular disease

- Goal Blood Pressure: <140/90
ALLHAT: Inclusion

- Inclusion:
  - > 55 years old
  - Stage 1 or 2 HTN
  - With one risk factor:
    - Prior MI or stroke > 6 mo in past
    - LVH
    - Type 2 Diabetes
    - Smoker
    - HDL <35
    - Atherosclerotic cardiovascular disease
ALLHAT: Patients

- Average age = 67
- **Black 32%**
- Women 47%
- Baseline BP: 146/84
- Receiving antihypertensive treatment 90%
- Prior MI or Stroke: 23%
- Type 2 Diabetes: 36%
ALLHAT: Cumulative Event Rates for Fatal Coronary Heart Disease or Nonfatal MI
Optimizing Drug Therapy for Hypertension in Blacks: A Rational Approach

- Based on ALLHAT and JNC-7
  - Begin with a thiazide-type diuretic
  - If SBP>160, begin with two agents, one of which should be a thiazide-type diuretic
  - Combination pills are well tolerated and work well in African Americans
Hypertension: Principles of Treatment

- List and Take Into Account “Compelling Indications”:
  - CHF, LV systolic dysfunction
    Include ACE inh/ARB and a “CHF” beta blocker (carvedilol/toprol xl/bisoprolol)
  - Renal insufficiency
    Include ACE inh/ARB. Will need a diuretic to control BP
  - Diabetes
    Include ACE inh/ARB
Hypertension: Principles of Treatment

- CAD, history of MI
  Include a beta blocker and an ACE inh/ARB

- History of stroke
  Include ACE inhibitor
Case 1

- 72 year old African American woman
  - PMHx: CAD, LVEF=>65%, Diabetes x 15 years, mild renal insufficiency (creat 1.6 mg/dL), LVH on EKG
  - BP 168/60

End organ damage (LVH, CAD) and 2 “compelling indications” for specific antihypertensive drug classes. Her BP will probably not be controlled by a single agent

Rx: ACE inh or ARB for DM and renal protection
Diuretic will be necessary to control BP and volume
Beta blocker for CAD

Rx: ACE/HCTZ combination, beta blocker
Case 2

- 45 year old African American man
  - 1.5 ppd smoker, drinks two six packs of beer/wk, truncal obesity, fundoscopy normal, EKG normal, no diabetes or CHF
  - BP 150/94

No evidence of target organ damage or compelling indications. There is time for non-drug treatments first.

Tobacco cessation, reduce EtOH consumption, walk 30 min/day, follow up in 4-6 months
Summary

- Hypertension is a major risk factor for cardiovascular disease and death

- African Americans have the highest prevalence of hypertension among all racial ethnic groups in US

- African Americans seem to suffer disproportionately from complications of hypertension
Summary

- There are some documented differences in racial responses to antihypertensive drug classes.

- Thiazide diuretics are particularly effective, have been shown to reduce adverse outcomes, and can help override racial “unresponsiveness” to certain drugs.

- Compelling indications and end organ damage should be taken into account.