Hypertension

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Disclosure Statement

Dr. Firnhaber has nothing to disclose.

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Learning Objectives

1. Recognize the initial drug therapy and the compelling indications for alternative drug therapy in hypertension.
2. Cite the common causes for refractory hypertension.
3. Identify the frequent causes and therapy for secondary hypertension.
BP and Cardiovascular Risk

- HTN is an independent risk factor for ischemic cardiovascular events.
- Risk of vascular death increases progressively and linearly from a “normal” pressure of 115/75 mm Hg.
- For every 20 mm Hg systolic or 10 mm Hg diastolic increase in blood pressure, the risk of major cardiovascular events and stroke *doubles.*
JNC-8 Recommendations

• In the general population < 60 years, and population ≥ 18 years with CKD, and population ≥ 18 years with diabetes:
  – Initiate treatment at SBP > 140 or DBP > 90
  – Treat to goal SBP < 140 and DBP < 90

• In the general population ≥ 60 years:
  – Initiate treatment at SBP > 150 or DBP > 90
  – Treat to goal SBP < 150 and DBP < 90
JNC-8 Recommendations

- In the general non-black population, including those with diabetes, initial treatment should include:
  - A thiazide-type diuretic, or CCB, or ACEI, or ARB

- In the general black population, including those with diabetes, initial treatment should include:
  - A thiazide-type diuretic, or CCB
JNC-8 Recommendations

• In the population > 18 years with CKD, initial (or add-on) treatment should include an ACEI or ARB to improve kidney outcomes.
• Do not use an ACEI and an ARB together in the same patient.

• The main objective of hypertension treatment is to attain and maintain goal BP.
  – Add and titrate as necessary to meet this objective.
ASH/ISH Recommendations

• In patients > 18 years, initiate treatment at BP ≥ 140/90
• In patients ≥ 80 years, initiate treatment at BP ≥ 150/90
• Initial therapy:
  – Non-black < 60 ACEI or ARB
  – Non-black ≥ 60 CCB or thiazide
  – Black CCB or thiazide
• If initial BP > 160/100, initiate with 2 drugs
  – CCB or thiazide *plus* ACEI or ARB
1. Which one of the following is a preferred first-line agent for managing hypertension in patients with stable ischemic heart disease?

A. A thiazide diuretic  
B. An angiotensin receptor blocker  
C. A β-blocker  
D. A long-acting calcium channel blocker  
E. A long-acting nitrate
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A. A thiazide diuretic
B. An angiotensin receptor blocker
C. A β-blocker
D. A long-acting calcium channel blocker
E. A long-acting nitrate

- A: 18%
- B: 39%
- C: 36%
- D: 7%
- E: 1%
Hypertension in IHD

• American Heart Association guidelines recommend β-blockers and/or ACEIs for hypertensive patients with stable ischemic heart disease.

• ACEIs are recommended in patients already on β-blocker therapy (especially following myocardial infarction), in diabetics, and in patients with left ventricular dysfunction.
Hypertension in IHD

- Long-acting CCBs may be used in patients who do not tolerate β-blockers; short-acting CCBs should be avoided because they increase mortality.
- Although ARBs have indications similar to those of ACEIs, the AHA recommends using them only in patients who do not tolerate ACEIs.
- Long-acting nitrates are used for their anti-anginal properties and have little role in the management of hypertension.
## Compelling Indications for Individual Drug Classes (JNC-7)

<table>
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<th>Compelling indication</th>
<th>Diuretic</th>
<th>BB</th>
<th>ACEI</th>
<th>ARB</th>
<th>CCB</th>
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ASH/ISH: Other Major Conditions

Hypertension *plus*:

- **Diabetes:** ACEI or ARB
- **CKD:** ACEI or ARB
- **Clinical CAD:** β-blocker *plus* ACEI or ARB
- **Stroke history:** ACEI or ARB
- **CHF:** β-blocker *plus* ACEI or ARB, *plus* diuretic, *plus* spironolactone, *regardless of BP*
HTN Treatment in Minority Populations

• African-American patients exhibit “somewhat reduced BP responses” to monotherapy with:
  – ACE-inhibitors
  – ARBs
  – β-blockers
  when compared with diuretics or CCBs

• ACE-inhibitor-induced angioedema occurs 2-4 times more frequently in African-American patients with HTN than in other groups.
2. A 48-year-old female presents as a new patient. BP 172/110 in both arms; CV exam unremarkable. BMI: 24.4; she takes no medications. BMP: Cr 0.68 mg/dL, K 3.3 mEq/dL.
If the patient’s hypertension should prove refractory to treatment, which one of the following tests is most likely to reveal the cause of her secondary hypertension?

A. 24-hour urine catecholamine level
B. Plasma aldosterone/renin ratio
C. MRA of the renal arteries
D. Echocardiography
E. Sleep study (polysomnography)
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C. MRA of the renal arteries  
D. Echocardiography  
E. Sleep study (polysomnography)
Secondary Hypertension

- Primary hyperaldosteronism is the most common cause of secondary hypertension in the middle-aged population.
- Diagnosis is based on the aldosterone/renin ratio. Plasma renin activity is variable and may be misleading.
- Unprovoked hypokalemia further supports the diagnosis, although is not present in the majority of cases.
Secondary Hypertension

Other considerations include:

• Coarctation of the aorta (more common in younger patients)
  – Echocardiogram
• Sleep apnea
• Pheochromocytoma
• Hypercortisolism
• Hyperthyroidism
• Renal parenchymal disease (children)
Renal Artery Stenosis

• Most common cause:
  – Age < 30: fibromuscular disease
  – Age > 30: atherosclerotic disease

• May present with:
  – Accelerated or resistant HTN, renal dysfunction, flash pulmonary edema

• Diagnosis:
  – MRA of renal arteries (or CT angiogram)
  – Elevated renin level alone is not diagnostic
3. A 54-year-old male with type 2 diabetes has a BP of 148/94 and creatinine of 1.25 mg/dL. One month after starting lisinopril 20mg/d, his BP is 128/80 and creatinine is 1.5 mg/dL. A repeat creatinine 1 week later is unchanged. What should you do?

A. Continue lisinopril at the same dosage  
B. Reduce the lisinopril dosage to 10 mg  
C. Discontinue lisinopril  
D. Change lisinopril to chlorthalidone  
E. Change lisinopril to losartan
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93% A. Continue lisinopril at the same dosage
4% B. Reduce the lisinopril dosage to 10 mg
0% C. Discontinue lisinopril
1% D. Change lisinopril to chlorthalidone
2% E. Change lisinopril to losartan
Treatment-Induced Decline in Renal Function

• A 20-30% increase in creatinine, which then stabilizes, represents a *hemodynamic* change, and *not* a structural change.

• Slight rise in creatinine serves as an indirect indicator that intraglomerular (IG) pressure has been reduced.

• ACEI/ARB also dilate efferent arteriole, exaggerating decline in IG pressure.
Treatment-Induced Decline in Renal Function

• Renal dysfunction associated with antihypertensive treatment is *independent* of the agent used.

• If creatinine increases by *more than 30%*, agent should be discontinued and other causes of renal dysfunction should be evaluated.
4. For which one of the following conditions is a thiazide diuretic an appropriate option for antihypertensive therapy?

A. Gout
B. Bipolar disorder treated with lithium
C. Diabetes
D. Chronic renal insufficiency, with a serum creatinine level of 2.6 mg/dL
4. For which one of the following conditions is a thiazide diuretic an appropriate option for antihypertensive therapy?

A. Gout
B. Bipolar disorder treated with lithium
C. Diabetes
D. Chronic renal insufficiency, with a serum creatinine level of 2.6 mg/dL

- A: 9%
- B: 8%
- C: 65%
- D: 18%
Thiazide Diuretics in HTN

• Advocated as initial treatment since 1977 (JNC-1)
• JNC-7: “thiazide diuretic should be used in drug treatment for most, either alone or combined with drugs from other classes”
• JNC-8: one of several options for initial treatment
Thiazide Diuretics in HTN

• *Reduce* excretion of:
  – Calcium (may slow bone demineralization)
  – Uric acid (increasing likelihood of gout)
  – Lithium (increasing risk of lithium toxicity)

• *Increase* excretion of:
  – Potassium (average decrease of 0.3-0.4 mmol/L; dietary salt restriction can minimize thiazide-induced K loss)
  – Magnesium (complicates correction of hypo-K)
Thiazide Diuretics in HTN

- Average increase in glucose attributed to thiazide use: 3-5 mg/dL
- Presence of diabetes is *not* a contraindication to use of thiazides

- Typically considered ineffective when GFR < 30-40 mL/min
  - Exception is metolazone, which is not useful as monotherapy but improves diuresis when used in conjunction with loop diuretic
Does It Matter Which Thiazide?

Antihypertensive Efficacy of Hydrochlorothiazide as Evaluated by Ambulatory Blood Pressure Monitoring

Systematic review of all the randomized trials that assessed 24-hour BP with HCTZ in comparison with other antihypertensive drugs

J Am Coll Cardiol 2011;57:590–600
Findings

• Decrease in 24-hour BP with HCTZ dose 12.5 to 25 mg: systolic 6.5 mm Hg, diastolic 4.5 mm Hg

• This reduction was statistically inferior to:
  – ACEI  (mean BP reduction 12.9/7.7 mm Hg)
  – ARBs  (mean BP reduction 13.3/7.8 mm Hg)
  – β-blockers (mean BP reduction 11.2/8.5 mm Hg)
  – CCBs  (mean BP reduction 11.0/8.1 mm Hg)
HCTZ Dose Titration

• There was no significant difference in systolic or diastolic 24-hour BP reduction between HCTZ 12.5 mg (5.7/3.3 mm Hg) and HCTZ 25 mg (7.6/5.4 mm Hg)

• With HCTZ 50 mg, the reduction in 24-hour BP was significantly higher (12.0/5.4 mm Hg) and was comparable to that of other agents
HCTZ Dose Titration

• All biochemical adverse effects such as hypokalemia, hyponatremia, hyperuricemia, insulin resistance, and visceral fat accumulation are dose dependent and become clinically more significant with daily doses exceeding 25 mg.

• An additional concern is the risk of sudden cardiac death that has been shown to increase in a dose dependent fashion with HCTZ doses exceeding 25 mg daily.
Messerli Conclusion

“HCTZ in its commonly used dose of 12.5 to 25 mg daily lowers BP significantly less well than do all other drug classes as measured in head-to-head studies by ABP monitoring.

Because of such paltry antihypertensive efficacy and the lack of outcome data at these doses, physicians should refrain from prescribing HCTZ as initial antihypertensive therapy.”
Other Thiazide Options

• Chlorthalidone: 12.5-25 mg daily; maximum dose 50 mg daily
• Indapamide (Lozol): 1.25-2.5 mg daily; maximum dose 5 mg daily
5. 54-year-old male presents for f/u of HTN. Despite careful adherence, his BP averages 150/90 mm HG. Recent labs are normal: CBC, BMP, UA. Medications: chlorthalidone 12.5 mg/d, carvedilol 25 mg bid, amlodipine 10 mg/d and lisinopril 40 mg/d.

Which one of the following medication changes would be most reasonable?

A. Adding isosorbide mononitrate
B. Substituting furosemide for chlorthalidone
C. Substituting losartan for lisinopril
D. Adding spironolactone
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78% ▶ D. Adding spironolactone
Resistant Hypertension

Spironolactone is an appropriate choice for treating resistant HTN, even when hyperaldosteronism is not present.

- Nitrates have some effect on BP but are recommended only for patients with CAD
- No benefit to switching ACEI to ARB
- A longer-acting diuretic such as chlorthalidone is also recommended for treating hypertension, particularly in resistant cases with normal renal function
Resistant Hypertension

- Persistent HTN despite ≥ 3 drugs
- Most common cause: poor adherence
- Suboptimal therapy
  - Typically inadequate diuresis
  - Move to loop diuretic
  - Add spironolactone
  - Consider vasodilating β-blocker (carvedilol, labetalol, nebivolol)
  - Consider clonidine, hydralazine, α-blocker
Resistant Hypertension

- Exogenous drugs
  - Caffeine (energy drinks, supplements)
  - Alcohol, nicotine
  - Cocaine
  - NSAIDs
  - OCPs
  - Steroids, erythropoietin
  - Herbal agents

- Secondary HTN
References


References


References


Systolic Hypertension in the Elderly

In the SHEP (Systolic Hypertension in the Elderly Program) study, treatment with chlorthalidone resulted in reduction of:

- Stroke incidence: 36%
- Coronary heart disease: 27%
- CHF: 55%
Answers

1. C
2. B
3. A
4. C
5. D