

HYPERTENSION

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Cardiovascular Disease (CVD)

- Leading cause of death in most parts of world
- ~ 32% in OPT die of CVD
- Risk factors: HTN, DM, HLD, obesity, smoking
- Atherosclerosis is main cause of CVD events
- 1 billion worldwide with HTN, 7 mil deaths/yr
- ~ 1/4th of pop in OPT have HTN (age 35-60)
- Direct correlation between elevated BP and: stroke, MI, CKD, angina, CHF, death

Hypertension: Definition

- Elevation in blood pressure
- Systolic Vs. Diastolic pressure
- Effect of age on BP
- JNC 7 Definition (≥ 18 yr)

| Classification | Systolic (mmHg) | | Diastolic BP (mmHg) |
|------------------|-----------------|-----|---------------------|
| Normal | < 120 | and | < 80 |
| Pre-hypertension | 120-139 | or | 80-89 |
| Stage I HTN | 140-159 | or | 90-99 |
| Stage II HTN | ≥ 160 | or | ≥ 100 |

Hypertension: Types

- Primary (Essential)
 - 90% of cases
 - Unknown cause- genetics?
 - Incurable, goal is control
- Secondary- has an identifiable cause
 - < 10%
 - Conditions: CKD, Cushing syndrome, aortic coarctation, OSA, pheochromocytoma, aldosteronism, thyroid/parathyroid disorder, renal artery stenosis

Hypertension: Types

- Substances: cocaine, methamphetamines, corticosteroids, calcineurin inhibitors, decongestants, ergot alkaloids, oral contraception, etc.
- White Coat Hypertension

Pathophysiology

- Cardiac output (CO) and Total Peripheral Resistance (TPR)
 - $MAP = CO \times TPR$
 - $CO = HR \times SV$
 - $MAP = DBP + 1/3 (SBP-DBP)$
- What increases CO?
 - Increased cardiac pre-load (fluid up, Na, etc.)
 - Frank Starling Law
 - SNS, RAAS via increasing HR, aldosterone and angiotensin II production

Pathophysiology

- What increases TPR?
 - RAAS activation
 - Sympathetic activation
 - Endothelial factors
 - Hyperinsulinemia (metabolic syndrome)

Clinical Presentation & Diagnosis

- *Silent Killer*
- Average of ≥ 2 BP readings per visit over ≥ 2 separate visits
- 24-h BP monitoring
- Rule out secondary causes, evaluate for target organ damage, test for co-morbidities
- Co-morbidities: DM, obesity (BMI > 30 kg/m²), HLD, tobacco use, physical inactivity
- Other risk factors: family history of CVD, Age (≥ 55 for men, ≥ 65 for women)

Clinical Presentation & Diagnosis

- Target organ damage:
 - Eyes: retinopathy
 - Heart: angina, MI, LVH, CHF
 - Brain: stroke
 - Kidneys: CKD
 - Vascular: PAD
- Labs: lipid panel, HbA1C, Cr, UA or ACR, other labs for secondary causes

Treatment of Hypertension

- Reduces risk for MI, stroke, CKD, CHF, death
- For every 20 mmHg increase in SBP, or 10 mmHg increase in DPP, mortality doubles from ischemic heart disease and stroke
- Pharmacotherapy and lifestyle modifications are utilized

Treatment of Hypertension Lifestyle Modification

- Weight loss
- Physical activity: 3-4x/wk, 40 min
- Sodium reduction: <2400 mg/d
- DASH diet (Dietary Approaches to Stop HTN)
 - high in fruits, vegetables, low-fat dairy, whole grains, fish, poultry, nuts
 - Low in sweets, saturated and unsaturated fats, red meat
- Moderate alcohol intake

Treatment of Hypertension Pharmacotherapy (JNC 7)

| BP CLASSIFICATION | SBP* MMHg | DBP* MMHg | LIFESTYLE MODIFICATION | INITIAL DRUG THERAPY | |
|----------------------|--------------|---------------|------------------------|---|--|
| | | | | WITHOUT COMPELLING INDICATION | WITH COMPELLING INDICATIONS (SEE TABLE 8) |
| NORMAL | <120 | and <80 | Encourage | | |
| PREHYPERTENSION | 120-139 | or 80-89 | Yes | No antihypertensive drug indicated. | Drug(s) for compelling indications. ³ |
| STAGE 1 HYPERTENSION | 140-159 | or 90-99 | Yes | Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination. | Drug(s) for the compelling indications. ² Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed. |
| STAGE 2 HYPERTENSION | ≥ 160 | or ≥ 100 | Yes | Two-drug combination for most ¹ (usually thiazide-type diuretic and ACEI or ARB or BB or CCB). | |

Treatment of Hypertension

Pharmacotherapy (JNC 7): Compelling Indications

- Heart failure
 - Asymptomatic with ventricular dysfunction: BBs, ACEIs or ARBs
 - Symptomatic or end-stage: ACEIs, BBs, ARBs, aldosterone blockers, loop diuretic
- Ischemic heart disease
 - BBs and CCBs beneficial in stable angina
 - BBs and ACEIs beneficial in ACS (unstable angina/MI) and post-MI

Treatment of Hypertension

Pharmacotherapy (JNC 7): Compelling Indications

- Diabetes: BP goal < 130/80 mmHg
 - Thiazide diuretics, BBs, ACEIs, ARBs, CCBs reduce CVD and stroke
 - ACEIs and ARBs slow nephropathy
- CKD: goal BP < 130/80 mmHg
 - ACEIs, ARBs, slows progression of diabetic and non-diabetic CKD
- Pregnant or likely to become pregnant
 - Methyldopa, BBs, vasodilators are preferred
 - C/I: ACEIs/ARBs due to teratogenicity

Pharmacotherapy Diuretics

- Thiazides: HCTZ, chlorthalidone, metolazone
 - 1st line if no compelling indications according to JNC7
 - Multiple mechanisms proposed
 - Very effective in controlling BP as part of 2-agent Rx
 - CV morbidity and mortality benefit
 - AHA considers ACEIs, ARBs, and CCBs preferred over thiazides
 - Most studies with chlorthalidone, likely class effect

Pharmacotherapy Diuretics

- Not considered effective if GFR < 30 mL/min, switch to loop diuretic
- Common AEs: Hypo-Mg, Hypo-K, dyslipidemia, hyperglycemia, hyperuricemia, sexual dysfunction
- Associated with higher rates of DMII than other BP Rx
- Limit doses to minimize AE (HCTZ 50 mg, chlorthal 25 mg)
- Usual doses: HCTZ 12.5-25 mg/d, Chlorthalidone 6.25-25 mg/d
- QD dosing

Pharmacotherapy Diuretics

- Loop Diuretics- furosemide, ethacrynic acid, torsemide, bumetanide
 - Potent diuretics
 - Same AE as Thiazides except:
 - No metabolic effects
 - Universal depletion of electrolytes (Na, Ca, K, Mg)
 - Usual dose: furosemide 20-80 mg PO in two divided doses for HTN
 - Loop diuretics have no ceiling effect- very large doses or continuous IV infusion may be required

Pharmacotherapy Diuretics

- Loops & Thiazides: monitor closely populations with gout, arrhythmias, electrolyte imbalance, digoxin level, DM & HLD with thiazides
- K-Sparing Diuretics- triamterene, amiloride
 - Little effect on BP; weak diuretics
 - Primarily used to balance K loss 2/2 thiazide
 - Often in combination with thiazide or loop diuretics
 - Hyperkalemia (esp. if with ACEI/ARB, CKD, K supplements)
 - Needs close follow-up on K after initiation or dose change
 - Usual dose: amiloride 5-10 mg/d in 1 or 2 doses

Pharmacotherapy Diuretics

- Aldosterone Antagonists- spironolactone, eplerenone
 - Not true diuretics- modulate vascular tone
 - K-sparing effect- ideal with thiazide and loop diuretics
 - AEs: same as with K-sparing diuretics, gynecomastia
 - Usual dose: spironolactone 25-50 mg/d in 1-2 doses
- All diuretics are best given in AM

Pharmacotherapy ACE Inhibitors (ACEIs)

- Lisinopril, enalapril, captopril, benazepril..
- Per JNC 7, first line in compelling indications: CKD, DM, LVH/CHF, post-MI
- Target RAAS activation post-MI and in HF pts.
- Very effective in reducing BP; all equally effective at equipotent doses
- CV/renal benefits thought to be class effect
- Usual dose: lisinopril 10-40 mg/d, enalapril 5-40 mg/d
- QD dosing for most

Pharmacotherapy ACE Inhibitors (ACEIs)

- AEs:
 - Hyper-K: rarely a reason to D/C, monitor periodically
 - Orthostatic HoTN
 - Dry cough: switch to ARBs
 - Decreased GFR: monitor periodically, titrate slowly especially in vulnerable pts, hold if GFR rises >30%, challenge at lower dose or slower titration
 - Rare angioedema
 - Do not rechallenge
 - Consider ARBs; cross-reactivity <10%
 - Teratogenic, C/I in pregnancy

Pharmacotherapy Angiotensin-Receptor Blockers (ARBs)

- Losartan, telmisartan, valsartan, candesartan, irbesartan..
- Equivalent in efficacy and outcomes to ACEIs, but with fewer AEs (less cough, angioedema)
- Same precautions/AEs apply as ACEIs
- Usual dose: losartan 50-100 mg/d, valsartan 80-320 mg/d
- QD dosing for most

Pharmacotherapy Renin Inhibitors

- Aliskiren is first and only agent
- Direct Renin blocker
- No outcome data, unclear role
- Same precautions as ACEIs/ARBs

Pharmacotherapy Calcium Channel Blockers (CCBs)

- DHP Vs. NDHP
- Ex: diltiazem, verapamil, amlodipine, felodipine, nifedipine (LA)
- IR nifedipine may precipitate reflex tachycardia
- Reduction in CVD events in pts with non-compelling indications
- Compelling indications: second line in CAD, DM
- NDHP ideal if pt suffers from SVTs

Pharmacotherapy

Calcium Channel Blockers (CCBs)

- Usual dosing: amlodipine 2.5-10 mg QD, diltiazem CD/XR/XT 120-420 QD (also available BID as SR)
- AEs (DHPs): dizziness, flushing, HA, peripheral edema, GI, gingival hyperplasia
- AEs (NDHP): bradycardia, AV block, acute HF, anorexia, nausea, peripheral edema, constipation
- CYP450 inhibition (verap>dilt)
- Caution with β Bs, avoid giving both IV

Pharmacotherapy

Beta-Blockers

- Metoprolol, atenolol, carvedilol, propranolol, labetalol, acebutolol
- JNC7 lists as acceptable option for non-compelling indications but JNC8 opposes
 - Less reduction in CV events than ACEI, ARB, CCB, diuretics
 - Meta-analysis published in 2005 showing increased risk of stroke from β Bs
- Compelling indications: first line in CAD, post-MI, CHF/LVH (bisoprolol, carvedilol, metoprolol succinate)

Pharmacotherapy

Beta-Blockers

- Generally, cardioselective agents preferred
 - Cardioselectivity is lost at higher doses
- Avoid β Bs with +ISA, esp. post-MI, i.e. acebutolol
- Avoid non-selective β Bs with asthma, COPD, PVD, or DM, i.e. propranolol, timolol, pindolol
- Avoid abrupt D/C; taper over 1-2 wks
 - Reflex tachycardia, cardiac ischemia

Pharmacotherapy

Beta-Blockers

- Usual doses: atenolol 25-100 mg QD, metoprolol tartrate 50-200 mg BID, metoprolol succinate 50-200 mg QD, carvedilol 6.25-25 mg BID
- AEs: bradycardia, heart block, AHF, possible erectile dysfunction
- Atenolol renally excreted and needs adjustment

Pharmacotherapy

Other Agents

- α 1-Blockers
 - Prazosin, terazosin, doxazosin
 - Inferior to thiazide-type diuretics in preventing CV events in HTN patients
 - Higher incidence of CHF Vs. chlorthalidone
 - Reserved for use in addition to first line, i.e. BPH
 - Syncope, dizziness, orthostatsis
- Central α 2-Agonists
 - Clonidine, methyl dopa, guanfacine, etc.
 - Orthostasis, sedation, dry mouth
 - Clonidine- resistant HTN, caution with rebound HTN, D/C β B days before clonidine

Pharmacotherapy

Other Agents

- Direct vasodilators
 - Hydralazine, minoxidil
 - Can cause reflex tachycardia and peripheral edema, use with β Bs and diuretics
- Reserpine
 - Rarely used, numerous AEs
 - Depletes NE from sympathetic nerve endings

Pharmacotherapy
Misc.

- IV options for scheduled dosing
 - Enalaprilat- Q6h
 - Metoprolol- Q6h
- Hypertensive emergencies ($\geq 180/120$ WITH organ damage/impending damage)
 - Reduce BP slowly, 25% within minutes to first hour, then to 160/100 within the next 2-6h, then goal within 24-48h
 - Nitroprusside continuous infusion is DOC

Pharmacotherapy
Misc.

- Hypertensive Urgency ($\geq 180/120$ WITHOUT organ damage/impending damage)
 - Can treat with fast acting oral agents, i.e. captopril, clonidine
 - Goal BP is 120-140 within hours to a day
 - Rebound HTN often fits in this category

Monitoring

- F/U every 2-4 wks until stable and depending on regimen, severity, co-morbidities
- When stable, F/U can be annual or semi-annual
- Monitor for effectiveness, safety, compliance/convenience
- Minimize pill #
- Labs: depends on agent, may include electrolytes, BUN, Cr, uric acid, others to assess target-organ damage progression and co-morbidities

JNC 8

| Criteria/JNC | JNC 7 | JNC 8* |
|----------------------------|------------------------------------|---|
| Evidence | RCT, observational, expert opinion | RCT and expert opinion |
| Focus | Comprehensive | Drug treatment only |
| Definition of HTN | $>140/90$ | $>140/90$ |
| Staging | Pre, Stage 1, Stage 2 | None |
| Treatment Threshold | 140/90 non-DM 130/80 DM & CKD | 140/90 < 60 y/o 150/90 ≥ 60 y/o |

*Non-black patients

JNC 8

| Criteria/JNC | JNC 7 | JNC 8 |
|------------------------------------|---|---|
| Thiazide Diuretics | Initial Rx unless compelling indication | Equal to ACEIs, ARBs, CCBs as initial Rx |
| β-Blockers | Included in initial options for gen. pop. | Not recommended anymore 2/2 stroke risk |
| CKD | Initial: ACEI/ARB | Initial OR add-on Rx should include ACEI/ARB |
| DM | Initial: ACEI/ARB | Does not differentiate Treat as general pop. |
| CHF, Post-MI, CAD | Addressed | Not addressed, defer to JNC 7 or other guidelines |

Remember..

- Guidelines should not replace clinical judgment
- Guidelines change constantly- what you practice today may be proven wrong tomorrow
- JNC is only one of several other guidelines on HTN, but JNC 8 is closer to most than JNC 7