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7th EMIRATES FAMILY MEDICINE SOCIETY CONGRESS 2024

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Severe Asymptomatic Hypertension

How worried should I be?

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Learning Objectives

1. Describe the diagnosis of severe asymptomatic hypertension.
2. Review treatment options for severe asymptomatic hypertension.
3. Differentiate treatment options that decrease cardiovascular morbidity from those that increase risk of adverse outcomes.

Monday morning, your first patient

54-year-old man with history of hypertension, variably controlled, and hyperlipidemia. His medications include: lisinopril/HCTZ 20/12.5 mg daily, and atorvastatin 40 mg daily.

His BP at check-in: 192/108; he reports home readings that are “good” but can’t recall specific numbers. Repeat BP is unchanged.

Other that feeling “a little on edge” he is asymptomatic.

What should you do?

Definitions

- Hypertensive *urgencies* are situations associated with severe BP elevation in otherwise stable patients without acute or impending change in target organ damage or dysfunction.
- Many of these patients have withdrawn from or are noncompliant with antihypertensive therapy and do not have clinical or laboratory evidence of acute target organ damage.
- This is now termed **Severe Asymptomatic Hypertension.**

Definitions

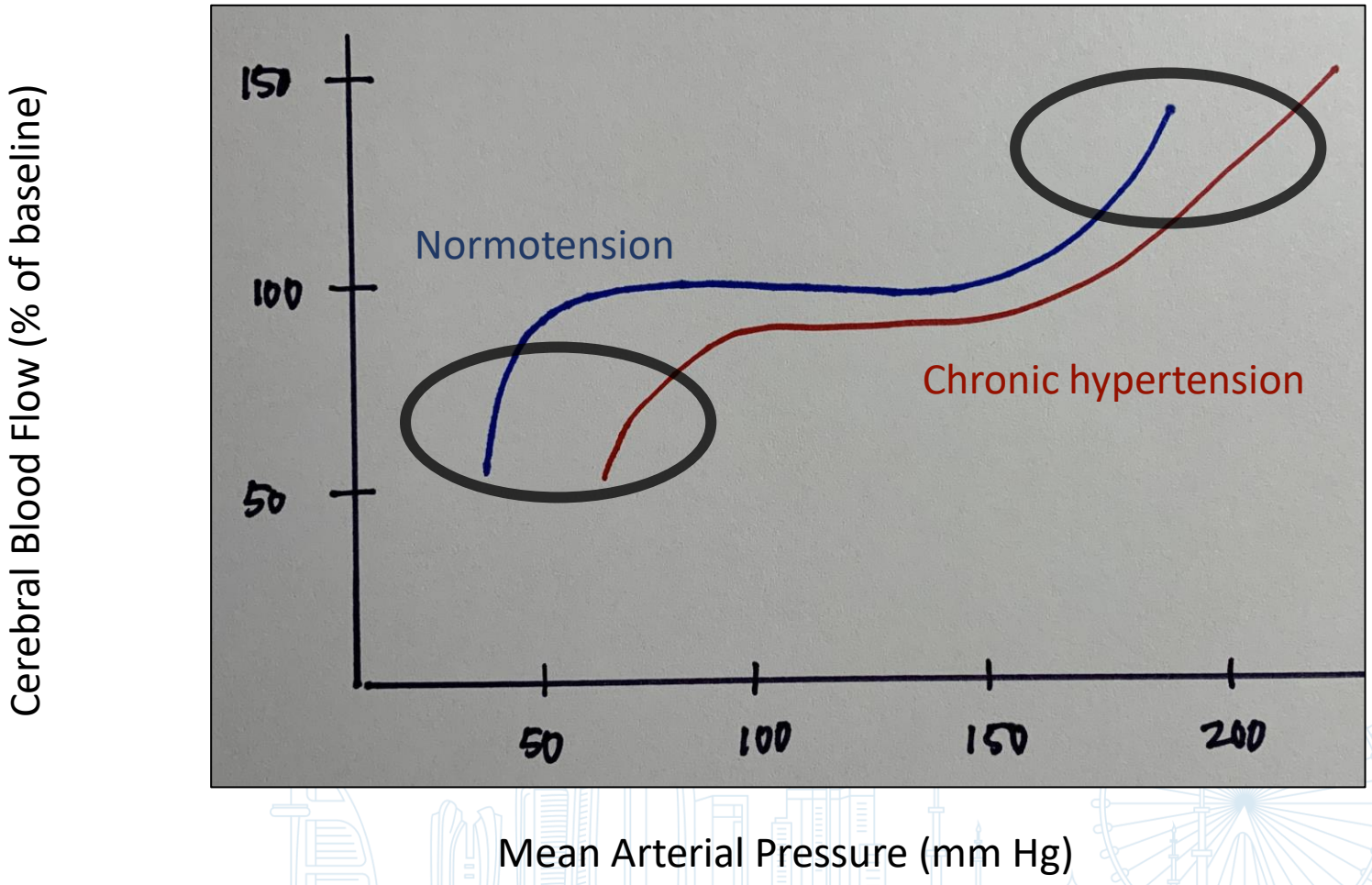
- Hypertensive *emergencies* are defined as severe elevations in BP (>180/120 mm Hg) associated with evidence of new or worsening *target organ damage.*
- The actual BP level may not be as important as the rate of BP rise; patients with chronic hypertension can often tolerate higher BP levels than previously normotensive individuals.

Proper technique for measuring BP

- An appropriately sized automated electronic arm cuff device should be used.
- Initially, a measurement should be obtained in both arms, and the higher blood pressure should be used (significant differences between arms occur in aortic coarctation, subclavian artery stenosis).
- The patient should have an empty bladder and remain seated with legs uncrossed for five minutes before the measurement.
- The measurement should occur at the level of the heart with the arm resting on a table.
- Postural blood pressure should be obtained in older adults.
- A minimum of two readings should be obtained one to two minutes apart and averaged.

Cerebral autoregulation as a model

- In the context of SAH, flow autoregulation is a critical point.
- Autoregulation is best studied in the brain, although the same principles are applicable to most end organs.



Cerebral autoregulation as a model

- In chronic severe HTN, cerebral blood flow is maintained at similar levels as in normal persons, but its autoregulatory curve is *shifted to the right*.
  - Allows patients to tolerate higher BP levels without cerebral edema, *but*
  - Predisposes to cerebral hypoperfusion at substantively *higher* BP than in normotensive persons
- The *lower limit* of autoregulation occurs at BP levels approximately 25% lower than baseline.
- Symptoms of cerebral hypoperfusion develop when cerebral blood flow falls by more than ~30%.

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA

Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults

ACC/AHA Class I recommendations: hypertensive emergency

For adults *with* a compelling condition (i.e., aortic dissection, severe preeclampsia or eclampsia, or pheochromocytoma crisis), SBP should be reduced to less than 140 mm Hg during the first hour and to less than 120 mm Hg in aortic dissection.

Class I; LOE C-EO

For adults *without* a compelling condition, SBP should be reduced by no more than 25% within the first hour; then, if stable, to 160/100 mm Hg within the next 2 to 6 hours; and then cautiously to normal during the following 24 to 48 hours.

Class I; LOE C-EO

ACC/AHA Class I recommendations: hypertensive emergency

Acute ischemic stroke

- In adults with an acute ischemic stroke, BP should be less than 185/110 mm Hg before administration of IV tPA and should be maintained below 180/105 mm Hg for at least the first 24 hours after initiating drug therapy Class I; LOE B-NR

Acute ischemic stroke: specifics

Acute ischemic stroke

Early initiation or resumption of antihypertensive treatment after acute ischemic stroke is indicated only in specific situations:

1) patients treated with tPA , and

2) patients with SBP >220 mm Hg or DBP >120 mm Hg.

For the latter group, it should be kept in mind that *cerebral autoregulation in the ischemic penumbra of the stroke is grossly abnormal* and that systemic perfusion pressure is needed for blood flow and oxygen delivery.

2017 ACC/AHA algorithm

SBP > 180 mm Hg and/or DBP >120 mm Hg

Target organ damage (new/progressive/worsening)?

[YES]

Diagnosis: hypertensive emergency

Admit to ICU [Class I]

2017 ACC/AHA algorithm

[YES]

Diagnosis: hypertensive emergency

Admit to ICU [Class I]

IF: Aortic dissection, or

Severe preeclampsia or eclampsia, or

Pheochromocytoma crisis

Reduce SBP to < 140 mm Hg during 1st hour;

if aortic dissection, reduce SBP to < 120 mm Hg [Class I]

2017 ACC/AHA algorithm

[YES]

Diagnosis: hypertensive emergency

Admit to ICU [Class I]

IF NOT: Aortic dissection, or

Severe preeclampsia or eclampsia, or

Pheochromocytoma crisis

Reduce BP by max 25% over first hour, then to 160/100-110 over next 2-6 hours, then to normal over next 24-48 hours

2017 ACC/AHA algorithm

SBP > 180 mm Hg and/or DBP >120 mm Hg

Target organ damage (new/progressive/worsening)?

[NO]

Diagnosis: markedly elevated BP

Reinstitute/intensify oral antihypertensive drug therapy and arrange follow up

Prevalence of emergency vs. urgency

- Systematic review of eight studies, representing 1970 hypertensive emergencies and 4983 hypertensive urgencies in ED setting
- The prevalence of hypertensive emergencies and hypertensive urgencies was 0.3% and 0.9%, respectively

- SBP at presentation did not differ between hypertensive emergencies and hypertensive urgencies (1.4 mmHg; [-0.8 to 3.6])
- DBP was slightly higher in hypertensive emergency patients (2.3 mmHg; CI [0.3 – 4.3]

Journal of Hypertension 2020, 38:1203–1210

Acute hypertension-mediated organ damage

- Acute pulmonary edema/heart failure was the most common aHMOD (32%), followed by:
  - Ischemic stroke (29%)
  - Acute coronary syndrome (18%)
  - Hemorrhagic stroke (11%)
  - Acute aortic syndrome (2%) and
  - Hypertensive encephalopathy (2%)

Acute hypertension-mediated organ damage

- The main symptoms hypertensive *emergency* patients were:
  - Neurological symptoms (35%)
  - Dyspnea (31%)
- Hypertensive *urgency* patients more commonly presented with:
  - Headache (22%)
  - ‘Nonspecific symptoms’ (48%)

- Prevalence of ‘nonspecific symptoms’ in hypertensive emergency patients was 24%

SAH: risk of MACE

Retrospective outpatient study (n = 58,535)

- Mean SBP = 183 mm Hg (10% of patients >200 mm Hg) and mean DBP = 96 mm Hg (6% of patients >120 mm Hg)
- From OP setting, 426 patients (0.7%) referred to the hospital (387 to ED; 39 directly admitted); remainder were sent home.
- Outcomes: MACE at <7d, 8-30d, and 6m.

- Overall rate of MACE <1% in both groups; no significant differences at any time point.

JAMA Intern Med. 2016;176(7):981-988.

Acute treatment of SAH in ED

- 21 patients with SAH in the ED setting
- Discharged with ambulatory BP monitors after receiving acute antihypertensive treatment in ED (captopril: 10 patients; captopril + additional drug: 5; clonidine: 7; other drug: 4)
- Patients were instructed to *continue* their usual antihypertensive regimen after discharge from the ED.

Journal of Clinical Hypertension. 2016;18(8):796-800

Acute treatment of SAH in ED

BP *decreased* from **199**±16**/101**±17 mm Hg to **154**±34**/83**±23 mm Hg after 5 hours

but then *rose* to **174**±25**/94**±17 mm Hg after 19 hours.

- In 17 (of 21) patients, SBP was ≥180 mm Hg after 6.7±5.3 hours.
- Two patients treated with clonidine developed hypotension at home (87/48, 87/39 at 2 hours post-discharge from ED.

Journal of Clinical Hypertension. 2016;18(8):796-800

Resistant hypertension

Persistent BP elevation despite three or more antihypertensive medications, *assuming*:

- *Reasonable doses*
- *At least one medication is a diuretic*

- Inadequate diuresis is a common reason for persistent BP elevation.

Significance of resistant hypertension

Retrospective study of >400,000 patients

Compared with patients *without* RH, those *with* RH had:

- 32% increased risk of developing ESRD
- 24% increased risk of an ischemic heart event
- 46% increased risk of heart failure
- 14% increased risk of stroke
- 6% increased risk of death.

Kidney Int. 2015;88:622–632.

Lifestyle factors

- Excess body fat ranks among the most important factors responsible for the increasing prevalence of hypertension.
- Higher dietary sodium intake is incontrovertibly linked to increases in arterial BP. However, *relatively large interindividual variations* exist in "salt sensitivity" of BP.
- Alcohol intake has been linked to increases in BP and the risk for developing hypertension.
- Both reduced physical activity and lower physical fitness are independent risk factors for hypertension.

Hypertension. 2018;72:e53-e90.

Drugs: NSAIDs

- NSAIDs increase BP by reducing the production of prostaglandins E_2 and I_2, leading to reduced vasodilation and reduced sodium excretion.
  - *NSAIDs are one of the most common offending agents affecting BP control.*
  - All nontopical NSAIDs in doses adequate to reduce inflammation and pain can affect BP levels in both normotensive and hypertensive individuals.
- BP effects from the use of NSAIDs vary by type; selective COX-2 inhibitors (e.g.: celecoxib) have less BP effect than traditional NSAIDs.
- Low-dose aspirin does not have COX-2-inhibiting or BP-increasing effects.

Hypertension. 2018;72:e53-e90.

Drugs: OCPs / ERT / HRT

- Oral contraceptives raise BP and induce HTN by increasing angiotensin biosynthesis.
- The Nurses' Health Study of >60,000 normotensive women followed up for 4 years found that women using OCPs had an 80% higher risk of developing HTN compared with women not using OCPs
  - Only 41.5 cases of hypertension per 10,000 person-years could be attributed to OCP use, and this number rapidly declined with cessation of therapy.
- (Postmenopausal) ERT and HRT appear to have a neutral effect on BP.

Hypertension. 2018;72:e53-e90.

Impact of OSA on resistant hypertension

- OSA is extremely common in patients with RH; prevalence is 70-90%, and when present, OSA is often severe.
- The high occurrence of OSA in patients with RH has been attributed to increased fluid retention and accompanying upper airway edema, as suggested by studies positively relating the presence and severity of OSA to aldosterone excess and high dietary sodium intake.
- The role of aldosterone in promoting OSA is additionally supported by studies demonstrating that *mineralocorticoid receptor antagonists reduce the severity of OSA in patients with RH*.

Hypertension. 2018;72:e53-e90.

Medication nonadherence

Medication nonadherence is highly prevalent in patients with *apparent* RH.

- 50% to 80% of hypertensive patients prescribed antihypertensive medications demonstrate suboptimal adherence.
- Consider:
  - Large pill burden
  - Dosing complexity
  - Expense
  - High frequency of adverse reactions with multidrug antihypertensive regimens
  - Poor patient-clinician relationship
  - Clinician inertia with reduced insistence on adherence when patients are consistently nonadherent.

Patients are less adherent than we'd like

- 25% of patients newly initiated on antihypertensive therapy fail to fill their initial prescription.
- During the first year of treatment, the average patient has possession of antihypertensive medications only 50% of the time
- 20% of patients have sufficiently high adherence to achieve the benefits observed in clinical trials.

Value Health. 2013;16:863–871.

And sometimes it's our fault

- During 2007 to 2010, only 49.6% of patients in a community-based practice network in the US with apparent treatment-resistant hypertension (aTRH) were prescribed an optimal antihypertensive regimen.
- While >90% of 84,193 patients with aTRH were prescribed a diuretic, in 42.1% of patients with aTRH, antihypertensive medications were prescribed at *<50% of their maximally recommended dose.*

Hypertension. 2013;62:691–697.

Sometimes rest is all you need

- In a study involving more than 500 patients presenting to an ED with severe hypertension, blood pressure fell to less than 180/110 mm Hg after 30 minutes of quiet rest (before medication administration) in approximately one third of the patients.

J Clin Hypertens (Greenwich) 2008;10:662-7.

Resistant hypertension: Strategies

- Diuretic
  - Switch to a more potent thiazide: chlorthalidone or indapamide
- RAAS blockade
  - Valsartan (Diovan) and irbesartan (Avapro) are typically more effective than losartan (Cozaar)
  - Add aldosterone antagonist (spironolactone or eplerenone)

Resistant hypertension: Strategies

- Add vasodilatory BB
  - Labetalol and carvedilol (Coreg) are alpha/beta blockers; nebivolol (Bistolic) increases nitric oxide levels
- CCB
  - Non-dihydropyridine CCBs (verapamil, diltiazem) are less potent vasodilators than dihydropyridine CCBs (all the -pine drugs)
- Next options:
  - Alpha blocker (doxazosin (Cardura), terazosin (Hytrin)
  - Hydralazine (multiple doses per day is a drawback)
  - Clonidine (consistent adherence is important)

Resistant hypertension: after the big three

- Top three:
  - Thiazide / thiazide-like diuretic
  - ACEI or ARB
  - CCB
- Fourth preferable drug
  - Spironolactone (clear superiority vs. bisoprolol and doxazosin)
- Fifth preferable drug is debated
  - Clonidine (recommended by this resource)

Current Hypertension Reports (2018) 20: 67

AHA: 5th drug

- The choice of a fifth drug (to add) depends on sympathetic drive as assessed in part by heart rate.
- In 2 post hoc analyses from large outcome trials, patients with heart rates >80 bpm had higher mortality.
- Thus, agents such as β-blockers or, if medically contraindicated, central α-2 agonists such as transdermal clonidine or guanfacine should be considered.

Take-home points

- Most patients without acute target-organ damage can be cared for as outpatients.
- Treatment with guideline-concordant long-acting medications should be started, reinstated, or adjusted, and follow-up should be scheduled within 1 to 7 days.
- Poorly-controlled hypertension is usually a multifactorial problem.
- Drug 4: aldosterone antagonist
- The choice of drug 5 depends on sympathetic drive as assessed in part by heart rate.

Thank you for your kind attention.