PHARMACY TO DOSE
THE CRITICAL CARE PODCAST

Hypertensive Crises

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I. Diagnosis
   a. Hypertensive (HTN) emergency
      i. SBP > 180 mm Hg or DBP > 120 mm Hg with new or worsening end-organ damage
   b. HTN urgency
      i. No signs/symptoms of new or worsening end-organ damage
   c. Be sure to conduct a thorough history and complete diagnostic testing in the patient work-up
      i. Ensure BP taken in both arms using validated devices and the results should be reproducible

II. Clinical Presentation
   a. Varies based on the specific end-organ damage
   b. Most commonly affected organs: brain, heart, and kidneys
      i. Neuro – headache, visual disturbances, changed in mental status, focal motor deficits
      ii. Cardiac – chest/back pain, SOB, orthopnea, elevated JVP, nausea/vomiting
      iii. Renal – change in urine color, reduction in urine volume

III. Common Causes
   a. Non-adherence
      i. Risk factor: pre-existing hypertension prescribed 2+ anti-HTN medications
   b. Medication/dietary changes
   c. Illicit medications – amphetamine/cocaine (generally cause acute not chronic hypertension)
   d. Drug-induced – NSAIDs, corticosteroids, immunosuppressants, stimulants
   e. Withdrawal symptoms – alcohol withdrawal, clonidine/beta blocker withdrawal
   f. Disease-specific – pregnancy, spinal cord injury, and sleep apnea
   g. Hospitalized patients - fluid overload, pain, urinary retention, and holding anti-HTN meds

IV. HTN Urgency
   a. Conservative approach with no specific initial blood pressure lowering goal
   b. Preferred PO anti-HTN – "reinstitute/intensify oral anti-HTN therapy and arrange follow-up"

Labetalol – $Alpha_1/Beta_{1/2}$ blocker	200-400mg PO	Onset: 20-120 minutes Peak: 2-4 hrs
Captopril – ACE-I	25-50mg PO	Onset: 15 minutes Peak: 1-1.5 hrs
Clonidine – $Alpha_2$ agonist	0.1-0.2 mg PO	Onset: 30-60 minutes Peak: 2-4 hrs
Nitroglycerin – Venous vasodilator with dose-dependent afterload reduction	0.4mg Sublingual tablet/spray 1/2" 2% ointment	Sublingual/spray Onset: 1-3 mins; Peak: 4-15 mins Transdermal Onset: 15-30 mins; Peak: ~60 mins

c. Avoid using IV medications because we don't need to quickly lower BP
    i. Lower slowly over first 24-48 hours using oral agents

V. HTN Emergency
a. Initial BP Goals
    i. Ultimately depends on target end-organ damage but generally:
        1. Reduce MAP by 25% in 1st hour
        2. Maintain DBP >/= 100 mm Hg
    ii. Aortic dissection/ischemic & hemorrhagic stroke/eclampsia are exceptions to this rule
b. Autoregulation
    i. Initial BP goals meant to avoid overcorrection
    ii. Maintain cerebral perfusion and prevent ischemia
        1. End organs adapt in the setting of chronic hypertension
c. Treatment
    i. IV push v. continuous IV infusions
        1. IV push – easily accessible, not as titratable, continued treatment can be time-consuming for RNs
        2. Continuous IV infusion – fairly quick onset, more titratable, possibly longer half-life, larger volume load from the IV infusion, may require PCU/ICU admission
    ii. Switch to IV infusion once you've reached the maximum dose of the IV push medication
        1. Treatment failure doesn't occur after one dose, ensure dose escalation occurs

VI. End-Organ damage with different treatment goals
a. Acute aortic dissection
    i. SBP < 120 mm Hg AND HR < 60 bpm within first hour (ideally within 20 mins)
    ii. Vasodilator + Beta blockers typically indicated for treatment
        1. Start Beta blocker first to avoid reflex tachycardia from vasodilator therapy
        2. Reduce pulsatile load and aortic stress
b. Acute ischemic stroke (AIS)
    i. BP goals:
        1. To receive thrombolytic treatment: < 185/110 mm Hg
        2. Post-thrombolytic treatment: < 180/105 mm Hg
        3. No thrombolytic treatment: < 220/120 mm Hg
            a. If treatment needed, reduce BP by no more than 10-15%
    ii. Lowering BP may reduce cerebral blood flow and worsen ischemia
c. Intracranial hemorrhage
    i. BP goal: If SBP 150-220 mm Hg, decrease SBP < 140-150 mm Hg in 1st hour
        1. Alternatively, some experts recommend goal SBP < 140 mm Hg
d. Pre-eclampsia/eclampsia
    i. Diagnosis: BP > 160/110 mm Hg in setting of pre-eclampsia or eclampsia
        1. Not necessary to have symptoms or end-organ damage in pregnancy

ii. BP goals: Reduce MAP by 15-25 % in 1st hour
1. SBP: 140-150 mm Hg; DBP: 90-100 mm Hg
iii. Common teatment options: IV labetalol/hydralazine and PO nifedipine

VII. Other end-organ damage
a. Acute coronary syndrome
i. Labetalol may be used in patients with acute cocaine ingestion
1. May be due to its non-selective alpha/beta blockade
b. Acute decompensated heart failure – nitrates are a cornerstone of treatment
i. Risk of cyanide toxicity in treatment with sodium nitroprusside
1. Nitroprusside contains cyanide and cyanide is metabolized via thiosulfate to inactive less toxic metabolite, thiocyanate
a. Thiocyanate is excreted via kidneys
b. Cyanide is metabolized to thiocyanate via liver
i. Higher risk when higher rate (> 4 mcg/kg/min) used with concomitant organ dysfunction (renal/hepatic dysfunction)
1. Generally safe to use for up to 24 hrs

VIII. Head-to-head studies comparing anti-HTN treatment
a. Lacking prospective randomized controlled trials (outside of stroke-specific literature)
i. Smaller studies comparing labetalol and nicardipine have similar outcomes
1. Although faster BP target achievement and less BP variability with nicardipine
b. Treatment based on end-organ injury, availability, cost, experience, and patient-specific

IX. Oral medication transition
a. Ultimately still unknown
i. Risk of hypotension largest in first 6 hours following treatment
b. Start within 6-12 hours and once we've met blood pressure reduction goals

X. Take-home points
a. Management is very different between HTN emergency and urgency
b. Non-adherence is a common cause of HTN crises, education for patients and providers is key

Medication	Preload	Afterload	Cardiac Output
Labetalol	←→	↓	↓
Hydralazine	←→	↓	↑
Esmolol	←→	←→	↓
Nicardipine	←→	↓	↑
Clevidipine	←→	↓	↑
Nitroglycerin	↓↓	↓	←→
Sodium Nitroprusside	↓	↓↓	←→
Enalaprilat	←→	↓	↑

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Drug Info	Dosing and PK	Additional Info
Labetalol – $Alpha_1/Beta_{1/2}$ blocker IV push and continuous IV infusion	10-20mg IV bolus; double dose up to max of 80mg to reach goal BP Infusion rate: 0.5-10mg/min Onset: 2-5 mins; Peak 5-15 mins; Duration: 3-6 hrs	Beta:alpha ratio 7:1 A drug of choice in pregnancy (eclampsia) Contraindicated in ADHF, heart block, asthma/COPD exacerbation Risk of hypotension with IV infusion
Hydralazine – Direct arterial vasodilator IV push	5-20mg IV q4-6h; Max dose 40mg Onset: 10-80 mins Duration: 3-12 hrs	A drug of choice in pregnancy (eclampsia) Variable onset and duration of action Unpredictable BP response May worsen ischemia (reflex tachycardia) Avoid use in CAD and AIS Can be given IM (longer onset)
Esmolol – $Beta_1$ blocker continuous IV infusion	25-300 mcg/kg/min +/- 500 mcg/kg IV bolus Onset: 1-2 mins Duration 10-20 mins	Metabolized by RBC esterases Associated with large fluid load Avoid in ADHF, heart block, asthma/COPD exac. Caution w/ acute aortic regurgitation
Nicardipine – DHP calcium channel blocker and vasodilator continuous IV infusion	2.5-15 mg/hr Onset: 2-10 mins Duration: 4-6 hrs	Reflex tachycardia can cause ischemia Large fluid load (can be concentrated if given via central line) Unique benefits in cerebrovascular disease
Clevidipine – DHP calcium channel blocker and vasodilator continuous IV infusion	1-6 mg/hr rapidly titrated to 32 mg/hr (acute max dose) Long-term max: 21 mg/hr Onset: 2-4 mins Duration: 5-15 mins	Metabolized by RBC esterases Titrate every 90 seconds to effect Lipid emulsion, monitor triglycerides Contraindicated if allergic to soy or eggs Max dose d/t lipids in IV infusion $$$
Nitroglycerin - Venous vasodilator with dose-dependent afterload reduction IV infusion	5-200 mcg/min Onset: 2-5 mins Duration: 5-20 mins	Predominant venous vasodilation Tachyphylaxis can occur rapidly Headaches can be rate-limiting Avoid use if volume depleted or if taking phosphodiesterase inhibitors
Sodium Nitroprusside – Direct vasodilator with arteriole and venous dilation IV infusion	0.25-10 mcg/kg/min Onset: 1-2 mins Duration: 2-5 mins	Contraindicated in pregnancy Risk of cyanide toxicity (hepatic/renal impairment) & methemoglobinemia May increase ICP, use caution Protect from light Tachyphylaxis can occur $$$
Enalaprilat – ACE inhibitor IV push	1.25mg IV q6h Max: 5mg IV q6h Onset: 15-30 mins Duration: 12-24 hrs	Last line treatment in HTN emergencies Only able to be titrated q12h Caution in renal dysfunction Contraindicated in pregnancy