Hypertensive Crises

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Definitions

• Hypertensive Crises (Acute)
  – Hypertensive Emergency:
    • Marked HTN associated with Target Organ Damage/Dysfunction (TOD)
  – Hypertensive Urgency:
    • Marked HTN NOT associated with TOD
Definitions (old terminology)

• Malignant HTN
  – Marked HTN with papilledema (Grade 4 KW hypertensive retinopathy)
  – Renal involvement called malignant nephrosclerosis

• Accelerated HTN
  – Same as malignant hypertension but without papilledema (Grade <4 KW)
  – Prognosis of both is similar

Historical Aspects

• “Malignant Hypertension”
  – Coined in 1928
  – Prognosis similar to most cancers
  – 50% of those affected dead in 5/12 after diagnosis

  – 1950’s: 1yr survival after Dx of hypertensive emergency 20-30%
  – 1985: 1yr survival 90-95%
Definitions

• Hypertensive encephalopathy
  – the presence of signs of cerebral edema caused by breakthrough hyperperfusion from loss of cerebral autoregulation

Hypertensive encephalopathy

• Signs include:
  – Somnolence
  – Decreased LOC
  – Seizures
  – Focal neurologic deficits

• Diagnosis of exclusion
Autoregulation

- Chronic HTN shifts curve to right
  - Allows hypertensive patients to maintain normal perfusion and avoid excessive blood flow at higher levels of BP
• Sudden lowering of BP into a range that would be considered ‘normal’ can be out of the autoregulatory capacity of the hypertensive individual and precipitate ischemia

Secondary Causes

• Consensus until recently was that a secondary cause of hypertension was very common in individuals with hypertensive crises
  – Renovascular HTN was thought to be most common
• But now, medication non-adherence is thought to be the most common cause
• Basically, anything that can raise BP can cause a hypertensive crisis (even essential HTN)
End Organ Damage

- Hypertensive encephalopathy
- Cerebral Infarction
- Subarachnoid Hemorrhage
- Intracranial Hemorrhage
- Eclampsia
- Retinopathy
- Aortic Dissection
- Myocardial ischemia and infarction
- Acute LV dysfunction
- Pulmonary Edema
- Renal Insufficiency
- Microangiopathic hemolytic anemia
- Bleeding

Objective End Organ Damage
Hypertensive Emergency Trial n=183

- Encephalopathy 4%
- Retinal Hemorrhage 5%
- Renal Insufficiency (Cr >200) 7%
- Myocardial Ischemia 8%
- Papilledema 13%
- CHF 16%
- Hematuria 19%
Stages of CHRONIC HTN

- Stage 1: SBP>140 DBP>90
- Stage 2: SBP>160 DBP>100
- Stage 3: SBP>180 DBP>110
- **Stage 4:** SBP>210 DBP>120

Stage 3 and 4 CHRONIC

- **Non-urgent:** reduce BP in 1 week
- **MYTH:** You can’t send someone home from hospital with high blood pressure

[Image of a man presenting]
Hypertensive Urgency ACUTE

- Aka. Acute Stage 4 HTN
- (hypertension.ca definition: DBP>130)
- Reduce BP within **hours (24-48)**
- **ORAL MEDICATIONS**
  - Short admission to hospital **CAN BE** reasonable for frequent vitals and monitoring for development of TOD
- **BUT,** **MAY ALSO BE DONE AS OUTPATIENT IF CLOSE FOLLOW UP AVAILABLE**

Hypertensive Emergency

- Reduce BP **immediately**
  - Reduce MAP by 20-25%
  - Or
  - Reduce MAP to 110-120
  - *Whichever is higher*

Achieve target BP in 2-4 hours

**IV MEDICATIONS**
Initial Management

- ABCs
  - Confirm BP in both arms
- Assess target organ involvement
  - Clinically
  - Laboratory/Imaging
- Frequent monitoring of vital signs
- Initiate treatment

History

- PMHx of HTN and any medications including illicit drugs
- Previous TOD
- Other Medical Problems:
  - Thyroid
  - SLE/Vasculitis
  - Cushings
  - Renal Disease
  - Pregnancy
- Presence of:
  - Chest pain (MI, dissection)
  - Back Pain (dissection)
  - Neurologic Phenomena
  - Dyspnea (CHF)
Target Organ Involvement

• Clinical:
  – Detailed neurologic examination including fundoscopy
  – Complete cardiac exam
    • Acute AI, ischemic MR, S3
  – Volume assessment
    • JVP
    • Peripheral edema
    • Lung crackles

HTN Retinopathy (Keith-Wagner)

• Grade I
  – Mild arteriolar narrowing and sclerosis
• Grade II
  – Definite focal narrowing and AV nicking
  – Moderate to marked sclerosis of the arterioles
• Grade III
  – Retinal hemorrhages, exudates and cotton wool spots
• Grade IV
  – Severe grade III + papilledema
Target Organ Involvement

• Laboratory/Investigations
  – CBC, Lytes, Urea, Cr, CK, TnT
  – EKG
  – CXR
  – U/A
  – CT/MRI head (if indicated)
  – CT Chest (if indicated)

PO DRUG THERAPY
Oral Therapy

• If you are using PO meds, there is no urgency to bring down the BP
• USE ANYTHING REASONABLE
• Fast Acting:
  – sl captopril 25mg
  – sl nifedipine 30mg (if no Hx IHD)
• Others:
  – ACE-I, DHP-CaCB, labetalol, hydralazine, LASIX

IV Drug Therapy
### Intravenous Vasodilators for Hypertensive Emergencies

<table>
<thead>
<tr>
<th>Agent</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitroprusside</td>
<td>Immediate</td>
<td>1-2 min</td>
<td>Potent Titratable</td>
<td>Cyanide, Thiocyanate</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>2-5 min</td>
<td>3-5 min</td>
<td>Coronary Perfusion</td>
<td>Tolerance, Variable Efficacy</td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>&lt;5 min</td>
<td>5-10 min</td>
<td>Renal Perfusion</td>
<td>Increased IOP (Attn: Glaucoma)</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>10-20 min</td>
<td>3-8 hrs</td>
<td>Eclampsia</td>
<td>Tachycardia, Headache</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>5-15 min</td>
<td>1-4 hrs</td>
<td>CNS Protection (prevents cerebral spasm)</td>
<td>Avoid in CHF or Cardiac Ischemia</td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>15-30 min</td>
<td>6 hr</td>
<td>CHF, Acute LV Failure</td>
<td>Avoid in MI</td>
</tr>
</tbody>
</table>

### Intravenous Antiadrenergics for Hypertensive Emergencies

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</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>5-10 min</td>
<td>3-6 hrs</td>
<td>Combines Beta Blockade With Vasodilation</td>
<td>Beta Blocker Effects Heart Block, Acute CHF</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>1-2 min</td>
<td>3-10 min</td>
<td>Catecholamine Excess</td>
<td>Tachycardia</td>
</tr>
</tbody>
</table>
Nitroprusside

Advantages
• Immediate onset
• Short duration of action
• Potent

Limitations
• Arterial line recommended
• ICU-level care required

Nitroprusside Adverse Effects

• Excessive Hypotension
• Redistribution of Flow
  – Intrapulmonary Shunt
  – Coronary Steal
  – Reduced Renal Blood Flow
• Platelet Dysfunction (decr. TXA2 activity)
• Toxicity
  – Cyanide
• Sodium Thiosulfate can be used as a sulfur donor to metabolize cyanide into thiocyanate
Signs Of Cyanide Toxicity

- **Increased** mixed venous saturation
- Increased metabolic acidosis
- Loss of consciousness and abnormal breathing patterns
- Death may be very rapid
- Tolerance is a hint of early cyanide toxicity

Nitroglycerin

- Coronary vasodilator
- Direct venodilator (variable arterial effects)
- Side effects: headaches and tachycardia
- Methemoglobinemia

- Clues: N PaO2, cyanosis, variable SpO2
Labetalol

- Combined alpha & beta blocker
- Half-life 4-6 hours
- Beta blockade blunts reflex tachycardia from alpha blockade
- Myocardial depression
- Caution in patients with reactive airway disease

Nicardipine

- Only IV Dihydropyridine CaCB
- Slow onset and offset
- May accumulate
- Variable duration of hypertensive effect
Dopamine Receptor Agonists

Actions of Dopaminergic Agonists

<table>
<thead>
<tr>
<th></th>
<th>Dopamine</th>
<th>Fenoldopam</th>
</tr>
</thead>
<tbody>
<tr>
<td>DA₁ (vasodilation)</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>α (vasoconstriction)</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>β₁ (inotropic, chronotropic)</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>β₂ (vasodilation)</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

+++ = Major action
++  = Moderate action
+   = Minimal action
-   = No action

Fenoldopam: Pharmacokinetics

- t₁/₂ (~ 5 min)
- No alteration in pharmacokinetics over 48 hr infusion
- Rapid elimination upon discontinuation
Fenoldopam: Potential Benefits

- Rapid, predictable, dose-dependent blood pressure decrease (without overshoot)
- Short $t_{1/2}$, rapid attainment of steady state titration
- No dosing adjustment for pre-existing renal or hepatic impairment
- Increases renal blood flow and maintains GFR

Phentolamine

- IV non-selective alpha blocker
- Use is restricted to high catecholamine states
  - esp. Pheochromocytoma
  - Cocaine/sympathomimetics
  - Tyramine crisis
Hydralazine

- Arterial vasodilator
- Reflex tachycardia
- Drug induced SLE
- Very useful in pre-eclampsia/eclampsia

Enalaprilat

- Only IV ACE-I available
- **DO NOT USE IN AMI SETTING**
- Very useful in CHF given with furosemide
Esmolol

- Very short half-life: 9 minutes
- Very cardioselective
- Immediate effect
- Can be used to test out airway reactivity or future tolerability of beta blockade

Categories

- Aorta
- Cardiac
- Catecholamine Excess
- Obstetric
- Renal
- Neurologic
- Hemorrhagic

“ACORN”
Specific Types

• Aortic Dissection
  – Aortic Dissection can be a **CAUSE OR RESULT** of marked hypertension
  – BP targets:
    • SBP <120 (ideally 100-120 or lowest tolerable)
    • HR<60
    • Time to achievement: <20 minutes

Aortic Dissection

• 1. IV Labetalol
  – If SBP remains >100 with good mentation and renal function or HR <50 add nitroprusside

• 2. IV Nitroprusside
  – **DO NOT USE** without beta blockade since vasodilation alone induces reflex activation of the SNS leading to enhanced ventricular contraction and increased aortic shear stress

• IV Enalaprilat or IV CaCBs may also be effective in lowering blood pressure **IN COMBINATION WITH A BETA BLOCKER**
• **DO NOT USE HYDRALAZINE**; increases shear stress
Cardiac Crises

• Myocardial infarction/ischemia
• Pulmonary Edema

• **BP CONTROL IS SECONDARY** to the primary problem; *i.e.: open the infarct related artery and treat pain, diurese and oxygenate those in pulmonary edema*

Cardiac Crises

• Drugs:
  – Nitroglycerine
  – Nitroprusside
  – Nicardipine
  – Enalaprilat
Cardiac Crises

• BP goals:
  – Ischemia/infarction: that which improves the ischemia
  – Pulmonary edema: that which improves the failure

Hemorrhagic Crises

• Defined as bleeding unresponsive to local measures associated with makedly elevate BP
  – Common Sites:
    • Nose
    • Kidney/bladder
    • Surgical sites
Obstetrical Crises

• Risks of BP transmitted to fetus
• Risk of pre-ecampsia/eclampsia
• HELLP
• AFLP
• Abruptio placentae
• Preterm Labor
• IUGR

Obstetrical Crises

• Drugs of Choice:
  – Methyldopa (IV/po)
  – Labetalol (IV/po)
  – Hydralazine (IV/po)
  – Nifedipine (po)

• Contraindicated:
  – ACE-I/ARB
  – Nitroprusside
Obstetrical Crises

- BP targets:
  - $<140/90$
- Treatment of choice is delivery if severe complications encountered

Catecholamine Crises

1. Pheochromocytoma
2. MAO inhibitor crisis
3. Cocaine and other sympathomimetics
4. Clonidine Withdrawal
Pheochromocytoma

• Principles:
  – Alpha blockers first then Beta blockers
    • Beta blockade can lead to unopposed alpha activity and further increases in BP

• Alpha Blockers:
  – po- phenoxybenzamine (alpha-1,2), terazosin, prazosin, doxazosin (alpha-1)
  – IV phentolamine (alpha-1,2)

Tyramine Crisis

• MAO inhibitor + tyramine (such as fermented cheeses, smoked, red wine, champagne, and avocados)

• Mechanism:
  – MAO inhibitor-induced decrease in intestinal tyramine metabolism
  – followed by increased tyramine absorption
  – subsequent tyramine-induced release of endogenous catecholamines
Clonidine Withdrawal

- Usually as a result of missed doses
- Responds quickly to reinstatement of clonidine
- Usually a single dose is all that is necessary

Cocaine/Sympathomimetics

- Treatment starts with IV alpha blocker (phentolamine) and beta blockers can be added if necessary
- Never use Beta blocker as monotherapy!
  - Leads to unopposed alpha stimulation
- Benzodiazepines also play a role
Renal Crises

- Renal insufficiency can be a cause or a result of marked hypertension
- Causes:
  - Renal Parenchymal Disease
  - Acute GN
  - RAS
  - Renin secreting tumors
  - Cyclosporine use in kidney transplant patients
- Microscopic hematuria w/o RBC casts can be seen with all hypertensive crises
  - Large amounts of RBCs and/or RBC cast should prompt further renal and/or urologic investigation

Renal Crises

- Drug Treatment
  - Nitroprusside has longest track record
  - IV Fenoldopam
    - Dopamine agonist
  - ACE-I for Scleroderma Renal Crisis
Other

• Spinal Cord Injury and Trauma:
  – Leads to secondary sympathetic overdrive
    • Ie. Transection, GBS

• Endocrine:
  – Cushings
  – Hyperaldosteronism
  – Hyperthyroidism

Neurologic Crises

• As a cause for HTN:
  – Cushings Response: (Incr. ICP)
    • HTN
    • Bradycardia
    • Low respiratory rate
  – Very important to reduce BP cautiously
Neurologic Crises

- As a result of HTN:
  - Ischemic infarction
  - Subarachnoid hemorrhage
  - Intracerebral/pontine/cerebellar infarction

Post-operative Hypertension

- Classically ~2h post op
- Short lived
  - Usually requires treatment for <6hrs
- Most feared complication is bleeding from operative site
- Caused by sympathetic stimulation and catecholamine surge
- Use whatever, labetalol po works great