Hypertensive Crisis

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Disclosures

- Nothing to Disclose
Outline

- Definitions
- Evaluation
- Goals of treatment
- Initial drug therapy
- Special Cases
- Oral drug therapy
Definitions

- Hypertensive Crisis
  - Hypertensive Emergency
  - Hypertensive Urgency
Hypertensive Crisis:

Arbitrarily defined as a severe elevation of blood pressure (i.e., DBP > 120 mmHg) which, if not treated promptly, will result in high morbidity and mortality.
Definitions

- **Hypertensive Emergency:**
  Severe elevation in blood pressure in the presence of acute or ongoing end-organ damage.

- **Hypertensive Urgency:**
  Severe elevation of blood pressure in the absence of target-organ involvement.
Hypertensive Emergencies

Key Points

- The diagnosis of hypertensive emergency is based more on the clinical state of the patient rather than on the absolute level of blood pressure per se.

- Sometimes the absolute level of blood pressure (i.e., >250/150 mm Hg), or the rate of rise of BP may constitute an emergency because of the risk of developing a poor outcome i.e. evolving aortic dissection.
Epidemiology

- Affects 1-2% of hypertensive adults per year
- Vast majority have pre-existing hypertension
- In US, more likely in
  - Elderly
  - African-American
  - Men
  - Parallels essential hypertension risk in US

Risk factors for hypertensive crisis
(Switzerland)

Table 2 | Variables associated with hypertensive crisis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bivariable analysis</th>
<th>Multivariable analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>Age (HR per year increase)</td>
<td>1.04 (1.00–1.08)</td>
<td>0.05</td>
</tr>
<tr>
<td>Sex (HR for female vs. male sex)</td>
<td>6.15 (1.69–22.37)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Stage of hypertension (HR for stage 2 vs. stage 1)</td>
<td>2.17 (0.73–6.47)</td>
<td>0.16</td>
</tr>
<tr>
<td>Grade of obesity (HR per grade increase)</td>
<td>1.68 (1.01–2.79)</td>
<td>0.046</td>
</tr>
<tr>
<td>Hypertensive heart disease (HR for presence vs. absence)</td>
<td>3.82 (1.28–11.40)</td>
<td>0.02</td>
</tr>
<tr>
<td>Coronary artery disease (HR for presence vs. absence)</td>
<td>4.43 (1.36–14.44)</td>
<td>0.01</td>
</tr>
<tr>
<td>Previous stroke (HR for presence vs. absence)</td>
<td>4.39 (1.21–15.97)</td>
<td>0.03</td>
</tr>
<tr>
<td>Thyroid disease (HR for presence vs. absence)</td>
<td>3.09 (1.01–9.48)</td>
<td>0.048</td>
</tr>
<tr>
<td>Depression (HR for presence vs. absence)</td>
<td>2.36 (0.77–7.21)</td>
<td>0.13</td>
</tr>
<tr>
<td>Somatoform disorder (HR for presence vs. absence)</td>
<td>4.55 (1.39–14.87)</td>
<td>0.01</td>
</tr>
<tr>
<td>Number of antihypertensive drugs (HR per number of drug increase)</td>
<td>1.45 (1.07–1.97)</td>
<td>0.02</td>
</tr>
<tr>
<td>Nonadherence to medication (HR for nonadherence vs. adherence)</td>
<td>8.51 (2.34–30.95)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

CI, confidence interval; HR, hazard ratio.
*Adjustment for age and sex.

Hypertensive Emergency

**Key Points**

- **CNS Emergencies**
  - Hypertensive encephalopathy
  - Intracerebral or subarachnoid hemorrhage
  - Thrombotic brain infarction with severe HTN

- **Cardiac Emergencies**
  - Acute CHF
  - Acute coronary insufficiency
  - Aortic dissection
  - Post vascular surgery HTN

- **Renal Emergencies**
  - Severe HTN with rapidly progressive renal failure
  - Rapidly rising BP with rapidly progressive glomerulonephritis
Hypertensive Emergencies

http://www.the-hospitalist.org/details/article/764887/How_Should_Hypertensive_Emergencies_Be_Managed.html
Patient evaluation

- Medical history
- Physical examination
- Laboratory evaluation
  - serum
  - urine
- Medication profile
- Illicit drug use
- Fundoscopy
- EKG, CXR, head CT, echo
Medical history

- HTN, CVD, CAD
- Cancer
- Endocrine: thyroid, aldosterone/ PRA
- Renal disease

Physical examination

- Vitals: regression to the mean? White coat?
  - BP both arms, orthostatic, intra arterial
  - HR, RR, edema
  - fever, neurological, etc
INTERPRETATION
The large round area of bleeding is a burst arterial aneurysm that has bled posteriorly into the retinochoroidal space, and anteriorly into the vitreoretinal space. A compact blood clot has formed posterior to the bleeding, from which a sharply delineated band of hemoglobin has been released. The blood vessels present around the aneurysm have been covered by the anterior bleeding. A portion of this blood dripped down between the retina and the vitreous body, and formed the second larger level bleeding, as described above. The sharp margin of the preretinal bleeding shows that the posterior vitreous body has been lifted only at this location.

DIAGNOSIS
Retinal bleeding, secondary to poorly controlled hypertension

http://medweb.unibe.ch/OcularFund/
Laboratory evaluation

- Urinalysis: protein, RBC, casts
- Lytes, BUN, creatinine
- Cardiac enzymes - CKMB, troponins
- CBC with smear - schistocytes, LDH
- Toxicology screen
- EKG, echo, angiography, X-ray
- Thyroid, cortisol
- LFTs
Endothelial damage

Myointimal proliferation and scarring, decreased diameter of this vessel has serious implications for the individual. There is reduced flow to the target area as well as potential shearing of blood cells which may cause a hemolytic anemia

http://www.vh.org/adult/provider/emergencymedicine/Hypertension/HypertensionTitle.html (4/29/03)
Medication profile

- Antihypertensives
- Antipsychotics + SSRI, MAOIs
- Alternative therapies
- Abuse: cocaine, amphetamines, bath salts
Goals of Therapy

- **Time frame**: consider risk level
- **Autoregulatory curve shifted to right**
- **BP goal**
  - **Urgency**: gradual; DBP to 110 in 24-48 hours
  - **Emergency**: DBP <110 in 30-60 min
  - Aortic dissection: 5 to 10 min
- **Drug selection**: what is ideal?
- **Route**
Autoregulation

http://web.squ.edu.om/med-Lib/MED_CD/E_CDs/anesthesia/site/content/v03/030626r00.htm
Be cautious but aggressive

Distinguish from situations where rapid BP reduction is not necessary or may be even hazardous

Treatment may be necessary based on a presumptive diagnosis (i.e., before results of laboratory tests are done)

Select an agent that allows for “titration” of BP
Ideal Medication for Hypertensive Emergency

- Effective
- Short onset of action
- Short half-life (titrable)
- IV
- No toxicity
Actual Medications that you should probably use

- Nicardipine
- Clevidipine
- Labetalol
- Esmolol
# Nicardipine

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Start:</strong> 5 mg/hr</td>
<td>5-15 min</td>
<td>1-4 hrs</td>
<td>CNS/coronary Protection</td>
<td>Variable duration, tachycardia</td>
</tr>
<tr>
<td>Titration: increase 2.5 mg/hr every 5 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Max:</strong> 15 mg/hr</td>
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</tr>
</tbody>
</table>
Nicardipine: Characteristics

- Dihydropyridine
- Water soluble and light stable (allows for IV infusion)
- Slow onset and offset
- Arterial catheter not mandatory
- May accumulate
- Metabolized by the liver
- Variable duration of hypertensive effect
## Clevidipine

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start: 1-2 mg/hr</td>
<td>2-4 min</td>
<td>5-15 min</td>
<td>CNS/coronary Protection</td>
<td>Lipid vehicle = 2 kcal/ml, tachycardia</td>
</tr>
<tr>
<td>Titration: double every 90 s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max: 16 mg /hr</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Clevidipine: Characteristics

- Third generation dihydropyridine
- Water insoluble 20% phospholipid emulsion
- Ultrashort acting
- Metabolized via ubiquitous plasma esterase so liver/kidney independent
- Mostly used post operatively
- FDA approval in 2008
Clevidipine trial: Velocity

- Open label, uncontrolled trial
- Demonstrated safety and efficacy for hypertensive crisis

Figure 2. Kaplan-Meier curves demonstrating probability of attaining initial systolic blood pressure target range within 30 minutes (modified intention-to-treat population: patients with or without end-organ injury, and all patients).

### Labetalol

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Load: 20 mg</td>
<td>2-5 min</td>
<td>2-6 hours</td>
<td>Safe in pregnancy</td>
<td>bradycardia</td>
</tr>
<tr>
<td>Start: 2 mg/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titration: increase 1 mg/min every 10 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max: 10 mg /min</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Labetalol: Characteristics

- Combined selective alpha1 – nonselective beta blocker
- Alpha:Beta ratio 1:7
- Reduces afterload so cardiac output maintained despite β blockade
- Metabolized by the liver
- First choice in pregnancy
## Esmolol

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Load: 500 mcg/kg</td>
<td>1 min</td>
<td>10-20 min</td>
<td>Ultrashort acting</td>
<td>Bradycardia</td>
</tr>
<tr>
<td>Start: 25 mcg/kg/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titration: increase 50 mcg/kg/min every 4 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max: 300 mcg/kg/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Esmolol: Characteristics

- Cardioselective beta blocker
- Metabolized via red cell esterase so liver/kidney independent
- Ideal for patients with tachyarrhythmias
- Bolus should be re-given prior to uptitrations
Actual Medications that you should probably NOT use for hypertensive crisis unless there are special circumstances

- Sodium nitroprusside
- Hydralazine
- Nifedipine immediate release – oral or sublingual
- Nitroglycerin gtt (unless for pulmonary edema)
- Fenoldopam
- Diltiazem
- Phentolamine
# Sodium Nitroprusside

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start: 1 mcg/kg/min</td>
<td>3 sec</td>
<td>1-2 min</td>
<td>Ultrashort acting</td>
<td>Tachyphylaxis, cyanide toxicity</td>
</tr>
<tr>
<td>Titration: increase 0.25 mcg/kg/min every 2 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max: 4 mcg /kg/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sodium Nitroprusside Characteristics

Advantages

- Immediate onset
- Short duration of action
- Potent

Limitations

- Light sensitive
- Arterial catheter usually recommended
- ICU-level care usually required
Sodium Nitroprusside Characteristics

• Excessive Hypotension
• Tachyphylaxis (hyperdynamic response)
• Redistribution of Flow
  • Intrapulmonary Shunt
  • Coronary Steal
  • Reduced Renal Blood Flow
• Platelet Dysfunction
• Toxicity
  • Cyanide
  • Thiocyanate
Metabolism of Sodium Nitroprusside

Tinker JH, Michenfelder JD. Anesthesiology 1976;45:340-354

Thiocyanate (SCN$^-$)

Thiosulfate

Hepatic Rhodanase

Thiocyanate (SCN$^-$)

CN$^-$

Non-enzymatic

Renal Excretion

Cytochrome Oxidases

Inactive Cytochromes

Cyanmethemoglobin

Methemoglobin

Oxyhemoglobin

TOXICITY

Tinker JH, Michenfelder JD. Anesthesiology 1976;45:340-354
Signs Of Cyanide Toxicity

- Increased mixed venous saturation
- Increased metabolic acidosis
- Loss of consciousness and abnormal breathing patterns
- Death may be very rapid
Additional Costs Often Associated With Nitroprusside Infusions

- Arterial blood gas measurements
- Lactate concentrations
- Cyanide / thiocyanate monitoring
- Invasive blood pressure monitoring
# Hydralazine

<table>
<thead>
<tr>
<th><strong>Dose</strong></th>
<th><strong>Onset</strong></th>
<th><strong>Duration</strong></th>
<th><strong>Advantages</strong></th>
<th><strong>Disadvantages</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus: 2.5 - 5 mg</td>
<td>5-15 min</td>
<td>3-10 h</td>
<td>Can be used in pregnancy</td>
<td>Unpredictable BP effect, long acting</td>
</tr>
</tbody>
</table>

Hydralazine: Characteristics

- Direct vasodilator
- Causes reflex sympathetic stimulation so contraindicated in CAD or dissection
- Unpredictable and long lasting
- Can be used in pregnancy but with caution
Overdoing it:
10 min versus 6 hours

http://web.squ.edu.om/med-Lib/MED_CD/E_CDs/anesthesia/site/content/v03/030626r00.htm
### Nifedipine immediate release

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg</td>
<td>5-10 min</td>
<td>6 h</td>
<td>Oral/sublingual</td>
<td>Unpredictable BP effect, long acting</td>
</tr>
</tbody>
</table>

Nifedipine: Characteristics

- Dihydropyridine calcium channel blocker
- Unpredictable and long lasting
- Due to sudden vasodilation cerebral, cardiac and renal ischemia has been reported with sometimes fatal outcomes
## Nitroglycerin gtt

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start: 10 mcg/min</td>
<td>2-5 min</td>
<td>10-20 min</td>
<td>Effective for pulmonary edema</td>
<td>Tachyphylaxis, Tachycardia, HA</td>
</tr>
<tr>
<td>Titration: increase 5 mcg/min every 5 min</td>
<td>Max: 100 mcg/min</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nitroglycerin gtt: Characteristics

- Primarily a venodilator
- Very effective for pulmonary edema
- Very effective for ACS
- Ineffective arteriolar vasodilator so NOT very effective for hypertension
Fenoldopam

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start: 0.1 mcg/kg/min</td>
<td>5-15 min</td>
<td>1-4 hr</td>
<td>Increased renal perfusion</td>
<td>Increased intraocular pressure,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Increase Na excretion</td>
</tr>
<tr>
<td>Titration: increase 0.05 mcg/kg/min every 15 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max: 0.3 mcg/kg/min</td>
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</tbody>
</table>

Physiologic Effects Fenoldopam

Systemic Vasodilation
- Metabolized by conjugation
- No P450 interaction

Coronary Vasodilation without “steal” (in animals)
- Reflex tachycardia

- ↑ RBF
- ↑ Na excretion
- ↑ H₂O excretion
- Maintains GFR during BP lowering

- Mesenteric vasodilation
- ↑ Mucosal PO₂ (in animals)

Does not cross BBB
Fenoldopam: Characteristics

- Vasodilation by peripheral dopamine-1 receptor
- Quickly metabolized
- Increase Na excretion and renal blood flow
- Excellent in patients with hypertensive crisis and volume overload (i.e. AKI/CKD patients)
- Caution if patients have had prior pressure natriuresis as Na excretion may result in hypotension
## Diltiazem

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus 0.25 mg/kg</td>
<td>1-3 min</td>
<td>1-3 hr</td>
<td>Rate control</td>
<td>bradycardia</td>
</tr>
<tr>
<td>Start: 5 mg/hr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Titratio: increase 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mg/hr every 10 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max: 15 mg/hr</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Diltiazem: Characteristics

- Non-dihydropyridine calcium channel blocker
- Effective for rate control in cases of tachyarrhythmias
- Not very effective for blood pressure
# Phentolamine

<table>
<thead>
<tr>
<th>Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolus: 1-5 mg</td>
<td>5 sec</td>
<td>15 min</td>
<td>Catecholamine crisis</td>
<td>angina</td>
</tr>
</tbody>
</table>

Phentolamine: Characteristics

- Pure alpha-adrenergic blocker
- Effective catecholamine crisis (pheochromocytoma, MAOI+tyramine)
- Can cause angina from alpha blockade
- Other medications are still effective for catecholamine crisis with less risk
Special Cases

- Post CVA
- Aortic dissection
- Sympathetic crisis
- Renal Artery Stenosis
- Pregnancy
Hypertension Post CVA

- Pressure rises to maintain cerebral BP
- Transient sympathetic activity
- HTN may not be harmful
- Lowering of BP may reduce cerebral flow and worsen ischemia
- Treat “rarely and carefully”, bleeding or DBP>120-130 or SBP>220
- Labetolol, nicardipine, fenoldopam,
- Impaired central autoregulation post CVA
Acute aortic dissection

- Aortic stress related to force of ventricular contraction
- Beta blocker (esmolol) drug of choice
- Vasodilator only in combo with BB
  - nicardipine, fenoldopam, nitroprusside
  - labetolol as monotherapy
- Surgical consult
Sympathetic crises

- Due to discontinuation of BB or clonidine
- Cocaine, “cheese effect”, pheochromocytoma
- Avoid beta blockers
- Nicardipine, verapamil, fenoldopam
- Phentolamine, nitroprusside second line
Renal artery stenosis

- HTN induced by perceived hypotension in kidney because of blockage
  - Abdominal bruits audible in 46%
- Stimulates RAS
- ACEI makes pharmacological sense
  - Would oppose the ANG II excess
  - Kicks crutch out from kidney
    - Acute renal failure
    - Hyperkalemia
- Fenoldopam?
Pregnancy

- Highest in first pregnancy, between 20 weeks gestation and 2 weeks post partum
- Preeclampsia
  - Pregnant with HTN
  - Proteinuria
  - Refer to immediate MD attention
- Eclampsia- convulsions, coma, death
- Magnesium infusions, delivery of baby, labetalol, hydralazine
Oral Medications

- Should be first line therapy for hypertensive urgency to provide slow long term decrease in BP
- Should be started for hypertensive emergency once BP is controlled by IV meds
- In most cases IV gtt can be weaned within 48 hours
Clonidine (Catapres)

- PO used acutely, 0.2mg x 1 then 0.1mg Q1H to max 0.8mg Onset 30min, duration 6-8h
- Good for urgency, not emergency
- Sedation common
- Rebound HTN problem
  - Taper off
  - Do not hold doses pre-op
  - Po to topical switch overlap
- Other routes: Epidural (Duraclon), topical (Catapress TTS)
- Should be third or fourth line agent long term but useful in the short term
Calcium Channel Blockers

- Amlodipine is a bad choice for hypertensive crisis
  - Half life of 30-50 hours
  - Takes days to get to maximal effect
  - Not titratable as an inpatient
  - Excellent choice for outpatient asymptomatic hypertension management because of the above effects

- Nifedipine XL is a better choice
  - Shorter half life 12-18 hours
  - Can change daily for BP control
  - Main disadvantage is cost as an outpatient
Other Oral Agents

- Beta-blockers are an excellent choices
- Avoid diuretics in the short term until patient is clearly volume overloaded as pressure natriuresis is common
- ACEI usually best started as an outpatient once renal function is clearly stable but can be used if CCB/B-blockade is not effective
Summary

- Hypertensive emergency versus urgency is defined by symptoms not absolute number
  - CNS, cardiac, renal
- Emergency requires rapid decrease in BP over hours as an inpatient
- Urgency requires treatment over days typically as an outpatient
- Over treatment based on numbers alone can result in morbidity and mortality due to autoregulation issues
- Choose medications that have quick onset and short duration to limit over treatment (nicardipine, clevidipine, esmolol, labetalol)
- Remember special cases
- Switch over to orals as soon as it is safe
Questions and my personal unrelated
Google Image find