

Management of Hypertensive Emergency

Introduction

1. Hypertensive emergency is characterized by systolic blood pressure (SBP) > 180 mmHg or diastolic blood pressure (DBP) > 120 mmHg with evidence of target organ damage.
2. Rapid blood pressure lowering with intravenous antihypertensives is warranted to prevent further organ damage.
3. Patients presenting with intracranial hemorrhage, aortic dissection, preeclampsia, or pheochromocytoma crisis should achieve target blood pressure within one hour of presentation.
4. Current literature lacks evidence of mortality benefit with any one antihypertensive drug. Selection of a medication should consider target organ(s) affected, underlying disease states, and time to target blood pressure.

Treatment in Selected Co-Morbidities

Condition	BP Goal	Preferred Agents
Acute aortic dissection	SBP < 120 mmHg within 20 min	Esmolol Labetalol Nicardipine Nitroprusside
Eclampsia or Preeclampsia	SBP < 140 mmHg within 1 hour	Nicardipine Labetalol Hydralazine
Pheochromocytoma (catecholamine excess)	SBP < 140 mmHg within 1 hour	Nicardipine Phentolamine*
Intracranial hemorrhage	SBP < 160 mmHg within 6 hours	Nicardipine Labetalol
Acute ischemic stroke	<i>Pre-alteplase:</i> < 185/110 mmHg <i>Post-alteplase:</i> < 180/105 for 24 hours No thrombolytic: SBP reduced 15% in 24 hours**	Nicardipine Labetalol

*Phentolamine currently unavailable due to nationwide shortage

**Permissive hypertension may be reasonable; maintain SBP < 220 mmHg or DBP < 120 mmHg

Pharmacology: Intravenous Antihypertensives

First-line Agents

Medication	Class	Onset	Duration	Dosing	Clinical Pearls
Nicardipine	Ca channel blocker	IV: 5-10 min	IV: 2-6 hours	<i>Initial:</i> 5 mg/hr <i>Titration:</i> 2.5 mg/hr every 15 min <i>Maximum:</i> 15 mg/hr	No dose adjustments in elderly patients
Esmolol	Beta-blocker	IV: 1-2 min	IV: 10-20 min	<i>Bolus:</i> 500-1,000 mcg/kg <i>Initial:</i> 50 mcg/kg/min <i>Titration:</i> repeat bolus dose, then increase by 50 mcg/kg/min every 10 min <i>Maximum:</i> 200 mcg/kg/min	Contraindications: • Bradycardia • Decompensated HF
Labetalol	Beta-blocker Alpha-1 antagonist	IV: 2-5 min Peak: 5-15 min	IV: 2-6 hours Peak: 18 hours	<i>Bolus:</i> 10-20 mg IV push every 10 min <i>IV infusion:</i> 0.5 – 10 mg/min titrated 1-2 mg/min every 2 hours <i>Maximum:</i> 300 mg total	Precaution: • Second-/third-degree heart block • Bradycardia • Heart failure

Second-line Agents

Phentolamine*	Non-selective alpha antagonist	IV: Seconds	IV: 15 min	<i>Initial:</i> 5 mg IV push May repeat every 10 min PRN	Useful in catecholamine excess and clonidine withdrawal
Nitroglycerin	NO-dependent vasodilator	IV: 2-5 min	IV: 5-10 min	<u>ACS:</u> <i>Initial:</i> 5 mcg/min <i>Titration:</i> 5 mcg/min every 3-5 min <i>Maximum:</i> 20 mcg/min <u>Pulmonary edema:</u> <i>Initial:</i> 100-200 mcg/min <i>Titration:</i> 50 mcg/min every 3-5 min <i>Maximum:</i> 400 mcg/min	Indicated in ACS or pulmonary edema Use caution in volume-depleted patients
Sodium nitroprusside	NO-dependent vasodilator	IV: Seconds	IV: 1-2 min	<i>Initial:</i> 0.3-0.5 mcg/kg/min <i>Titration:</i> 0.5 mcg/kg/min every 1 min <i>Maximum:</i> 10 mcg/kg/min	Requires intra-arterial BP monitoring Tachyphylaxis and cyanide toxicity with prolonged use - Limit treatment duration
Hydralazine	Direct vasodilator	IV: 10 min IM: 20 min	IV: 1-4 hours IM: 2-6 hours	<i>Initial:</i> 10-20 mg IV push Repeat every 4-6 hours PRN	Not available as an IV infusion
Enalaprilat	ACE inhibitor	IV: 15-30 min	IV: 12-24 hours	<i>Initial:</i> 1.25 mg IV over 5 min <i>Titration:</i> increase by 5 mg every 6 hours as needed	Slow onset (~15 min) Contraindications: • Pregnancy • MI • Bilateral renal stenosis

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Overview of Evidence

Author (Title), Year	Design	Purpose	Outcome
Anderson (INTERACT), 2008	RCT (N=404)	Comparison of BP goals (SBP \leq 140 vs SBP \leq 180) in patients with acute ICH	<ul style="list-style-type: none"> • Mean hematoma expansion was smaller in the intensive group (13.7% vs 36.3%) • No difference in death or disability at 3 months (48% vs 49%) • <u>Limitation</u>: included patients with SBP \geq 150 mmHg, over 30% of patients were treated with oral antihypertensive therapy
Quereshi (ATACH-2), 2016	RCT (N=1,000)	Comparison of BP goals (SBP 110-139 vs SBP 179-140) in patients with acute ICH	<ul style="list-style-type: none"> • All patients received nicardipine infusion • No difference between death or disability at 3 months (38.7% vs 37.7%) • Increased renal adverse events within 24 hours in the intensive group (9.0% vs 4.0%) • <u>Limitation</u>: mean SBP differed by only 10 mmHg between groups 2 hours post-randomization (129 mmHg vs 141 mmHg)
Peacock (CLUE), 2011	RCT (N=226)	Nicardipine IV infusion versus labetalol IV bolus for management of hypertensive emergency	<ul style="list-style-type: none"> • Patients receiving nicardipine were more likely to reach target BP within 30 min (91.7% vs 82.5%) • Rescue antihypertensive use did not differ significantly between groups within first 6 hours • <u>Limitation</u>: only 63.3% of patients had evidence of target organ damage at randomization
Yang, 2004	Prospective cohort (N=40)	Nitroprusside IV versus nicardipine IV for hypertensive emergency with pulmonary edema	<ul style="list-style-type: none"> • No significant difference between blood pressure readings across groups at any time point • No adverse events reported in either group • <u>Limitation</u>: nicardipine dosing started at 3 mcg/kg/min (12.5 mg/hr in a 70 kg patient)

Conclusions

1. Selection of a first-line antihypertensive should consider compelling indications and acute blood pressure goals, as robust literature comparing long-term outcomes across drug classes is lacking for most indications.
2. Nicardipine may provide more consistent blood pressure control than labetalol. This is particularly important in patients with acute stroke, as large fluctuations in blood pressure are believed to negatively impact cerebral perfusion.
3. Aggressive lowering of SBP less than 140 mmHg in patients with acute ICH has not been shown to improve long-term outcomes and may negatively impact renal perfusion.
4. Nicardipine has been shown to provide similar blood pressure control to nitroprusside. In patients with acute ICH, nitroprusside use within 24-hours of presentation was associated with higher in-hospital mortality.

References

1. Whelton, et al. 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. *J Amer Heart Assoc* 2018;71(6):e13-e115.
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4. Quereshi, et al. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. *New Engl J Med* 2016;375(11):1033-43.
5. Peacock WF, et al. CLUE: a randomized comparative effectiveness trial of IV nicardipine versus labetalol use in the emergency department. *Critical Care* 2011;15(R157):1-8.
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