Using IV Nicardipine for Blood Pressure Treatment in a Stroke Unit Setting

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Hypertensive Crisis: Emergency vs Urgency

- Hypertensive emergency\(^1,2\)
  - Evidence of end-organ damage
    - Kidney
    - Retina
    - Heart
    - Brain
    - About 500,000 cases annually in US due to high prevalence of HTN

- Hypertensive urgency\(^1,2\)
  - No evidence of end-organ damage
  - BP reduction over several hours to days
  - Usually treated with oral antihypertensives


End-Organ Damage Characterizes Hypertensive Emergencies

Using Nicardipine in the Stroke Unit: Improving Patient Flow

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Pathophysiologic Principles at Work in the Hypertensive Milieu

Acute Hypertension—Pathophysiology

Circulating and local factors acting on endothelium and vascular smooth muscle

BP = SVR × CO

Abrupt ↑ BP Abrupt ↑ SVR

SVR = systemic vascular resistance; CO = cardiac output; SV = stroke volume; HR = heart rate

Cerebral Autoregulation Is Central to Treatment of Hypertensive Crises

Cerebral Blood Flow

Patients with chronic hypertension autoregulate cerebral blood flow around higher set points

Patients with cerebral ischemia lose their ability to autoregulate ischemia

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Hypertension Can Drive Elevated Intracranial Pressure

Vascular Smooth Muscle Contraction Is Calcium Dependent

BP Goals in Ischemic Stroke

- Usually no need to treat unless BP > 220 or > 120 mm Hg
- TPA patients have different parameters
  - 180-185 systolic; 105-110 diastolic
- Do not want a sudden drop
- New guidelines suggest that it is OK to begin BP medications after 24 hours
  - Rule out a high-grade proximal stenosis
  - Typically begin with oral agents if BP > 160/100

Class 1 C recommendations
Predictors of Outcome

- Hematoma volume
- GCS
- Intraventricular hemorrhage
- Age
- ICH location (deep)
- Increased cerebral edema (midline shift, herniation)


Hematoma Expansion

- 72% have some hematoma expansion over the first 24 hours
- 38% have significant (>33%) expansion over 24 hours
- In 26% of these cases, the enlargement is within 1 hour


Approaches to Prevent or Reduce ICH Expansion

- Controlling blood pressure
  - Under study
- Using recombinant factor 7 (all patients)
  - 1 positive and 1 negative study
  - Clear biologic effect; unclear benefit
- Correct coagulopathy immediately
  - Factor 7; PCC (prothrombin concentrate complex); transfuse platelets
- If all fail—consider emergency surgery
- Prognosis poor without intervention
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<table>
<thead>
<tr>
<th>SBP and MAP Levels (mm Hg)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP &gt;200 or MAP &gt;150</td>
<td>Consider aggressive reduction of BP with continuous IV infusion, with frequent BP monitoring every 5 min</td>
</tr>
<tr>
<td>SBP &gt;180 or MAP &gt;130</td>
<td>Consider monitoring ICP and reducing BP using intermittent or continuous IV medications to keep CPP &gt;60–80 mm Hg</td>
</tr>
<tr>
<td>SBP &gt;180 or MAP &gt;130</td>
<td>Consider a modest reduction of BP (eg, MAP of 110 mm Hg or target BP of 160/90 mm Hg) using intermittent or continuous IV medications to control BP, and clinically reexamine the patient every 15 min</td>
</tr>
</tbody>
</table>

Understanding Cerebral Hemodynamics

- CPP = MABP – ICP
  - If an agent reduces MABP but does not decrease ICP, then CPP will fall in some cases
  - If MABP falls and ICP rises, CPP can fall dramatically
  - Depends on ability of cerebral autoregulation to compensate

IV Medications That May Be Considered for Control of Elevated BP in Patients With ICH (2007 AHA Guidelines)

<table>
<thead>
<tr>
<th>Drug</th>
<th>IV Bolus Dose</th>
<th>Continuous Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>5–20 mg q 15 min (max. 300 mg/d)</td>
<td>2 mg/min</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>NA</td>
<td>5–15 mg/h</td>
</tr>
<tr>
<td>Esmolol</td>
<td>250 µg/kg IV P loading dose</td>
<td>25–300 µg · kg⁻¹ · min⁻¹</td>
</tr>
<tr>
<td>Enalapril</td>
<td>1.25–5 mg IV P q 6 h²</td>
<td>NA</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>5–20 mg IV P q 30 min</td>
<td>1.5–5 µg · kg⁻¹ · min⁻¹</td>
</tr>
<tr>
<td>Nipride</td>
<td>NA</td>
<td>0.1–10 µg · kg⁻¹ · min⁻¹</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>NA</td>
<td>20–400 µg/min</td>
</tr>
</tbody>
</table>

AHA = American Heart Association; ICH = intracerebral hemorrhage; IVP = intravenous push; IV P = intravenous push; NA = not applicable.

*Because of the risk of precipitous blood pressure lowering, the enalapril first test dose should be 0.625 mg.


AHA = American Heart Association; CPP = cerebral perfusion pressure; ICH = intracerebral hemorrhage; MAP = mean arterial pressure; SBP = systolic blood pressure.
AHA/ASA guideline: BP management in acute hemorrhagic stroke

SBP >200 mm Hg or MAP >150 mm Hg
• Consider aggressive ↓BP with continuous IV infusion
  – Monitor BP q5 min

SBP >180 mm Hg or MAP >130 mm Hg; ICP evident or suspected
• Monitor ICP
  – Administer intermittent or continuous IV antihypertensive treatment to keep cerebral perfusion pressure 60-80 mm Hg

SBP >180 mm Hg or MAP >130 mm Hg and no ↑ICP
• Administer intermittent or continuous IV antihypertensive treatment to achieve modest ↓BP (eg, target BP 160/90 mm Hg or MAP 110 mm Hg)
  – Reexamine patient q15 min

These are all Class IIb level C recommendations

ICP = intracranial pressure

Nicardipine
• Selective arteriolar vasodilator1,2
• Calcium ion channel inhibitor2
• Onset of action: 5-10 minutes3
• Duration: 15-30 minutes; may exceed 4 hours3
• Adverse effects: tachycardia, headache, flushing, and local phlebitis3
  – No significant effect on ICP4
• Special indications/contraindications
  – Appropriate in most hypertensive emergencies except acute heart failure1-3
  – Use with caution in coronary ischemia3
• Only IV CCB indicated for short-term treatment of HTN5; maintains or increases cardiac output6; as effective as sodium nitroprusside with fewer dose adjustments6; not associated with coronary steal7


Use of IV Nicardipine in a Stroke Unit for Acute Blood Pressure Control

• Many patients require acute BP control but are otherwise stable
• They often do not need all of the services of an NICU
• Can these patients be treated safely in a Stroke Unit setting?
• We performed a prospective open-label study to answer this question
Inclusion Criteria

• Enrolled patients with:
  – Ischemic stroke
  – ICH
  – SAH
  – CVT
  – Hypertensive urgency, crisis
  – Pre or post IV TPA therapy

• Who required BP control with an IV agent

Exclusion Criteria

• Need for ICU care due to unstable vital signs or other conditions (intubation)
• Contraindications to IV Nicardipine therapy
• Need for arterial catheters

Treatment Paradigm

• Trained Stroke Unit nurses on the use of IV Nicardipine
• Used non-invasive blood pressure monitoring and multi-channel telemetry
• Began IV Nicardipine at dose of 5 mg/hr
• Titrated as needed to achieve desired BP
  – Goal determined by treating physician
PRIMARY ENDPOINT: Achievement of desired blood pressure
SAFETY ENDPOINT: 1) symptomatic hypotension, 2) transfer to NICU due to inability to control BP, 3) other complication due to nicardipine infusion
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Study Population
- 12 patients enrolled to date (plan = 20)
- 6 male/ 6 female
- Age range 41 - 85 yrs
- Disease: 5 ICH 4 Ischemic 3 HTN Urg
- Location: 9-NICU 2-ED 1-MICU

Results
- # dose adjustments: 1-15
- Treatment time: 1 – 64 hours
- % who achieved target BP: 100%
- % with symptomatic hypotension: 0%
- % requiring ICU transfer: 0%
- % with side effects: 0%

Conclusions
- Blood pressure control is possible using IV Nicardipine in a Stroke Unit type setting for patients with a variety of cerebrovascular disorders
- There were no serious hypotensive events or other serious side effects
- Most patients could be controlled with a modest number of dose adjustments
Limitations

- These were selected patients in a specific stroke unit setting
- Nurses had special training and back-up of experienced nurses
- Study is ongoing with a relatively small number of patients