Blood Pressure Management in ICH, SAH, AIS

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Andrew Russman, D.O.
Staff, Cerebrovascular Center

As a result of this presentation, the participant will be able to:

• Evaluate the recommendations for blood pressure management in intracerebral hemorrhage, subarachnoid hemorrhage, and acute ischemic stroke.

• Apply current guidelines in blood pressure management.
Disclosures

• None
Guidelines for Early Management of AIS

• Systemic hypotension should be avoided and, if present, corrected to limit further cellular damage.

• In patients with markedly elevated blood pressure who do not receive fibrinolysis a reasonable goal is to lower blood pressure by 15% during the first 24 hours after onset of stroke. The level of blood pressure that would mandate such treatment is not known, but consensus exists that medications should be withheld unless the systolic blood pressure is >220 mm Hg or the diastolic blood pressure is >120 mm Hg. (Class I, Level C)
Optimal BP After AIS?

• Prospective study of 1121 patients admitted within 24h from stroke onset and followed up for 12 months.

• Death due to neurological damage from brain edema is associated with high initial BP-values.

Guidelines for Early Management of AIS

• The usefulness of drug-induced hypertension in patients with acute ischemic stroke is not well established. Induced hypertension should be performed in the setting of clinical trials. (Class IIb, Level B)

Guidelines for Early Management of AIS

• Evidence from one clinical trial indicates that initiation of antihypertensive therapy within 24 hours of stroke is relatively safe. Restarting antihypertensive medications is reasonable after the first 24 hours for patients who have preexisting hypertension and are neurologically stable unless a specific contraindication to restarting treatment is known. (Class I, Level B)

How should we manage blood pressure in the first 24 hours after stroke? (Carefully?)

- INWEST study
- IV nimodipine (1 or 2 mg/h) vs. placebo
- Stopped after 295 patients (600 planned) due to neurological worsening
- Nimodipine produced a statistically significant reduction in BP in both dose strategies
- Multivariate analysis showed an OR of 10.16 for death or dependency with \( \geq 20\% \) reduction in the high-dose group

How should we manage blood pressure in the first 24 hours after stroke? (Carefully?)

- Prospective registry of 481 AIS patients, including 235 patient who received first doses of antihypertensives within 24 hours of stroke onset

**TABLE 3. Independent Predictors of Early Complete Recovery Using Logistic Regression Analysis**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Mathew score &gt;74</td>
<td>331.3</td>
<td>45.2–2428.2</td>
</tr>
<tr>
<td>Lack of hypertension</td>
<td>1.9</td>
<td>1.1–3.1</td>
</tr>
<tr>
<td>No brain edema on CT scan</td>
<td>4.2</td>
<td>2.1–2.8</td>
</tr>
<tr>
<td>20% to 30% drop in MAP, day 2</td>
<td>2.9</td>
<td>1.3–6.3</td>
</tr>
</tbody>
</table>

Drop in MAP was compared with “no blood pressure decline.”

Case Scenario #1

- 65M college professor with DM, HTN, CAD
- LKW 98 minutes prior to your clinical evaluation
- Sudden onset left hemiparesis without sensory loss.
- BP 225/105
- Exam shows NIHSS=7 (left facial weakness, left arm and leg weakness, dysarthria).
- NCCT shows no evidence for acute/prior infarct or hemorrhage.
- CTA shows no evidence for large vessel occlusion.
- BP 203/101 after Labetalol 20mg IV
Uncontrolled BP before and during tPA infusion

• ECASS II, tPA Survey and SITS- International Stroke thrombolysis register have shown deleterious effects of uncontrolled hypertension before tPA bolus and during alteplase infusion in terms of increasing the risk of sICH

• SITS registry analysis of 30,000 patients has demonstrated that history of hypertension and pretreatment systolic BP > 146 mmHg independently increased odds for symptomatic ICH by 40 and 60%, respectively.
Treatment Approach to HTN Management in Thrombolysis Candidates

• Patient otherwise eligible for acute reperfusion therapy except that BP is >185/110 mm Hg:
  – Labetalol 10–20 mg IV over 1–2 minutes, may repeat 1 time; or
  – Nicardipine 5 mg/h IV, titrate up by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h; when desired BP reached, adjust to maintain proper BP limits; or
  – Other agents (hydralazine, enalaprilat, etc) may be considered when appropriate

• If BP is not maintained at or below 185/110 mm Hg, do not administer rtPA
Treatment Approach to HTN Management in Thrombolysis Candidates

• Management of BP during and after rtPA or other acute reperfusion therapy to maintain BP at or below 180/105 mm Hg:
  – Monitor BP every 15 minutes for 2 hours from the start of rtPA therapy, then every 30 minutes for 6 hours, and then every hour for 16 hours
  – If systolic BP >180–230 mm Hg or diastolic BP >105–120 mm Hg:
    – Labetalol 10 mg IV followed by continuous IV infusion 2–8 mg/min; or
    – Nicardipine 5 mg/h IV, titrate up to desired effect by 2.5 mg/h every 5–15 minutes, maximum 15 mg/h
  – If BP not controlled or diastolic BP >140 mm Hg, consider IV sodium nitroprusside
Guidelines for Early Management of ICH

• For ICH patients presenting with SBP between 150 and 220 mmHg and without contraindication to acute BP treatment, acute lowering of SBP to 140 mm Hg is safe *(Class I; Level of Evidence A)* and can be effective for improving functional outcome *(Class Ila; Level of Evidence B)*. (Revised from the previous guideline)

• For ICH patients presenting with SBP >220 mm Hg, it may be reasonable to consider aggressive reduction of BP with a continuous intravenous infusion and frequent BP monitoring *(Class Iib; Level of Evidence C)*. (New recommendation)
INTERACT2 Trial – Game Changer?

- Randomized controlled trial of 2839 patients with spontaneous ICH
- SBP<140 vs SBP <180 within 6 hours of onset x 7 days
- Primary outcome mRS 0-2 vs 3-6 at 90 days with pre-specified ordinal analysis
- Secondary outcomes: safety, QOL
- SBP<140 (mRS 3-6): 52% vs. SBP<180 (mRS 3-6): 55.6%, P=0.06
- Ordinal analysis showed statistically significant benefit for SBP<160 target (P=0.04)
- No difference in adverse events
- Improved QOL (P=0.002) in intensive (SBP<140 target) group

INTERACT2 Controversy

- No differences in ICH volume between groups
- 2/3 of patients enrolled in China
- Most commonly used drug (urapidil) not available in North America
- 83% deep, small ICH (median volume 11 ml)
- 72% of patients had HTN
- No data on ICP
- Studied 140 vs. 180 (rather than AHA <160)
  - 6 h post randomization median SBP 153 in liberal group vs. 139 in intensive group
- ATACH -2 (<140 vs. <180 with nicardipine)
  - (748/1280 subjects randomized as of 4/11/15)

Case Scenario #2

• 64 year old male with HTN and left thalamic ICH
• Intubated, PBD#2, sedated with propofol, versed and fentanyl and BP 76/37 MAP 51
• CTA showed no evidence for large vessel occlusion
• TEE no PFO, EF 60%, no LAA thrombus, mild aortic arch atheroma.
How safe is intensive BP lowering after ICH?
• Intensive BP lowering appears beneficial across a wide range of baseline SBP levels, and target SBP level of 130–139 mm Hg is likely to provide maximum benefit in acute ICH.

• Dropping BP too low might be detrimental—Though this may be confounded since pre-terminal ICH can directly lower BP

Treatment Approach to HTN Management in Acute ICH

- SBP $\leq$ 140 mm Hg and MAP $\geq$ 65 mm Hg
  - Nicardipine infusion (5-15 mg/h IV) or labetolol (20 mg IV push or infusion 2 mg/min)
  - Avoid nitroprusside and nitroglycerin due to risk of labile BP and increased ICP
Up to 14% of aSAH patients may experience rebleeding within 2 hours of the initial hemorrhage.

The magnitude of blood pressure control to reduce the risk of rebleeding has not been established, but a decrease to a systolic blood pressure of <160 mm Hg is reasonable (Class IIa, Level of Evidence C).
What is the Optimal SBP to Reduce aSAH Re-bleeding?

**TABLE 3.** Comparison of Systolic Arterial BP in the Rebleed and the Non-Rebleed Groups With Various Cutoff Points

<table>
<thead>
<tr>
<th>BP, mm Hg</th>
<th>Rebleed Group (n=37)</th>
<th>Non-Rebleed Group (n=236)</th>
<th>P</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤120</td>
<td>35</td>
<td>221</td>
<td>&gt;0.9999</td>
<td>1.2 (0.3–5.4)</td>
</tr>
<tr>
<td>≤140</td>
<td>31</td>
<td>168</td>
<td>0.1090</td>
<td>2.1 (0.8–5.2)</td>
</tr>
<tr>
<td>≤160</td>
<td>26</td>
<td>100</td>
<td>0.0016</td>
<td>3.1 (1.5–6.8)</td>
</tr>
<tr>
<td>≤180</td>
<td>20</td>
<td>41</td>
<td>&lt;0.0001</td>
<td>5.6 (2.7–11.6)</td>
</tr>
<tr>
<td>≤200</td>
<td>6</td>
<td>5</td>
<td>0.0012</td>
<td>8.9 (2.6–31.0)</td>
</tr>
</tbody>
</table>
Hypotension in Anesthetized Patients During Microsurgical Aneurysm Clipping

• In univariate analysis, ΔMAP>50% was associated with poor outcome.

• After adjusting for age and World Federation of Neurological Surgeons grade, the association with poor outcome was no longer statistically significant [odds ratio (OR) 1.018; 95% CI 0.996–1.041].

• Minimizing the degree and duration of intraoperative hypotension during aneurysm surgery is probably indicated (Class IIa, Level of Evidence B).

Guidelines for Early Management of Aneurysmal SAH

- When DCI is diagnosed, the initial treatment is the induction of hemodynamic augmentation to improve cerebral perfusion.

- Oral nimodipine should be administered to all patients with aSAH (Class I, Level of Evidence A). It should be noted that this agent has been shown to improve neurologic outcomes but not cerebral vasospasm. The value of other calcium antagonists, whether administered orally or intravenously, remains uncertain.

- Induction of hypertension is recommended for patients with DCI, unless their blood pressure is elevated at baseline or their cardiac status precludes it (Class I, Level of Evidence B).

Hemodynamic Augmentation After Delayed Cerebral Ischemia in aSAH

• Although no RCTs of this intervention have been performed, but rapid improvement of many patients with this therapy and their worsening when it is stopped prematurely are convincing proof of efficacy.

• Mechanism of benefit may include increased MAPs which may increase CBF in the setting of autoregulatory dysfunction; or a direct transluminal pressure effect that leads to arterial dilation.

• Hemodynamic augmentation has consisted of hemodilution (a common occurrence in this population), hypervolemia, and hypertensive therapy. Accumulating literature has shifted the focus from triple-H therapy to the maintenance of euvolemia and induced hypertension.

Hemodynamic Augmentation After Delayed Cerebral Ischemia in aSAH – Hypertension and CBF

Figure 2 Mean CBF (ml/100 g/min) difference between start of intervention and follow-up within 24 hours.
Summary

- For AIS, patients who are not thrombolytic candidates should have SBP<220 target, and cautious BP lowering for those with large vessel occlusion.

- For ICH, while intensive BP lowering to target SBP<140, we should avoid hypotension.

- For SAH, hemodynamic augmentation via euvolemic hypertension is reasonable for treatment of delayed cerebral ischemia.

- Nicardipine is likely more efficacious than labetolol, and safer than nitroprusside among patients with controlled hypertension after acute stroke.