

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

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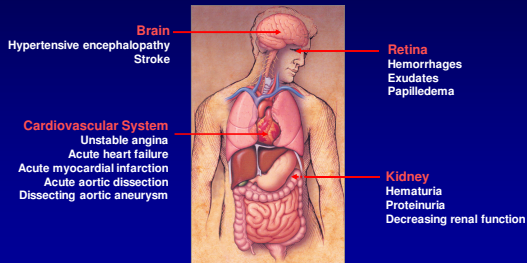
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Hypertensive Crisis: Emergency vs Urgency

- 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

1. Mansoor GA, Frishman WH. *Heart Dis.* 2002;4:358-371.
2. Varon J, Mark PE. *Chest.* 2000;118:214-227.

End-Organ Damage Characterizes Hypertensive Emergencies



Adapted from Varon J, Mark PE. *Chest.* 2000;118:214-227.

Pathophysiologic Principles at Work in the Hypertensive Milieu

Acute Hypertension—Pathophysiology

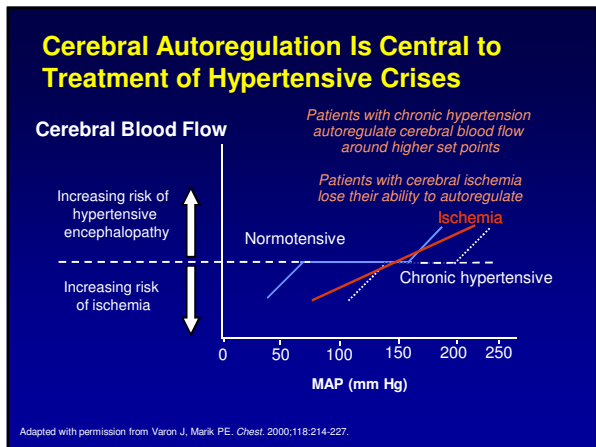
Circulating and local factors acting on endothelium and vascular smooth muscle

BP = SVR X CO

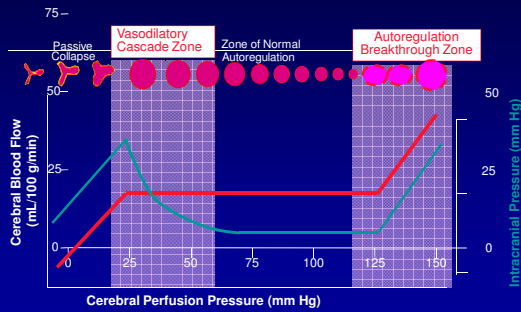
Abrupt ↑ BP **Abrupt ↑ SVR** (SV x HR)

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

Adapted from Hoffman BB. In: Brunton LL, et al, eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 11th ed. New York, NY: The McGraw-Hill Companies Inc; 2006:845-868.

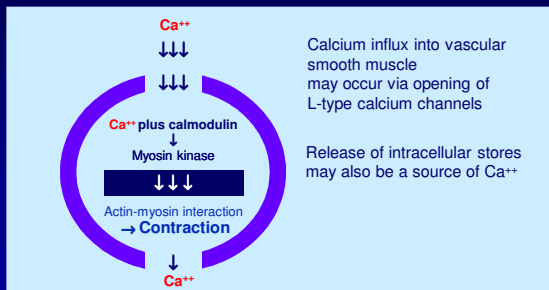


Hypertension Can Drive Elevated Intracranial Pressure



Courtesy of Stephan A. Mayer, MD.

Vascular Smooth Muscle Contraction Is Calcium Dependent



Adapted with permission from Frishman WH, et al. *Curr Probl Cardiol*. 1987;12:285-346.

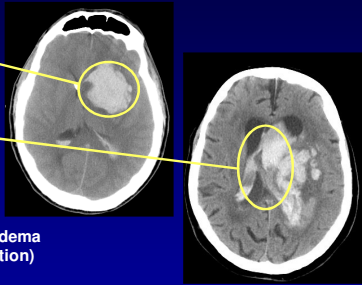
BP Goals in Ischemic Stroke

- 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

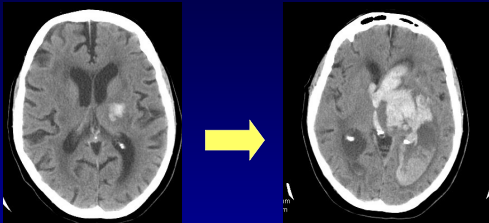
Predictors of Outcome

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



Manno EM, et al. *Mayo Clin Proc.* 2005;80:420-433; Garibi J, et al. *Br J Neurosurg.* 2002;16:355-361; Flaherty ML, et al. *Neurology.* 2006; 66:1182-1186.

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

Davis SM, et al. *Neurology.* 2006;66:1175-1181; Brott T, et al. *Stroke.* 1997;28:1-5.

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

VBWG

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 Broderick J et al. Stroke. 2007;38:2001-23.

Nicardipine

- Selective arteriolar vasodilator^{1,2}
- 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 HTN²; maintains or increases cardiac output²; as effective as sodium nitroprusside with fewer dose adjustments²; not associated with coronary steal²

1. Rose JC, et al. Neurocrit Care. 2004;1:287-299. 2. Cardene I.V. (nicardipine hydrochloride). Prescribing information. Fremont, Calif: PDI BioPharma Inc; 2006. 3. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. US Dept of HHS; NIH publication No. 04-5230; 2004:55. 4. Nishiyama T, et al. Can J Anesth. 2000;47:1196-1201. 5. Neural JM, et al. Am J Hypertens. 1994;7:623-628.

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 a 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

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
