

## West Virginia University Healthcare Vasospasm Guidelines

Cerebral infarction associated with delayed ischemic neurological deficits (DINDs) secondary to vasospasm is one of the main causes of mortality and poor neurological outcome after aneurysmal subarachnoid hemorrhage (SAH). Current recommended therapies include nimodipine as prophylaxis and “Triple-H” therapy as treatment. Triple-H therapy consists of using a combination of hypertension, hypervolemia, and hemodilution to try to perfuse ischemic areas of the brain. However, this therapy not only is associated with significant complications such as pulmonary edema, myocardial ischemia, and brain edema but also is shown to have increased rates of complications with no beneficial effects in prior studies.

WVU has adopted the Montreal Protocol to manage patients with SAH to treat patients with symptomatic vasospasm. This includes using milrinone, a phosphodiesterase III inhibitor with both inotropic and vasodilatory effects, to reverse cerebral vasospasm. The Montreal Protocol was validated by a single center prospective study that had 88 patients enrolled, including patients diagnosed with DINDs secondary to cerebral vasospasm after aneurysmal SAH. Norepinephrine was also used to maintain baseline blood pressure or to maintain MAP > 90 mmHg if no improvement after milrinone infusion. A total of 43 patients (48.9%) were able to return to all their previous activities, and 66 patients (75%) had a good outcome (mRS ≤ 2). No patients had serious adverse events like pulmonary edema, cardiac arrhythmias, myocardial ischemia, or severe hypotension. Older age and a higher Hunt and Hess grade were associated with worse outcomes. A total of 60 patients (68.2%) required norepinephrine to achieve baseline blood pressure or to maintain a MAP > 90 mmHg. Overall, the protocol was successful in treating symptomatic vasospasms.

Along with milrinone and triple-H therapy, intrathecal nicardipine is considered a potential therapy for treatment of cerebral vasospasm. Nicardipine reduces calcium dependent vascular smooth muscle contraction, however administering nicardipine intravenously is limited by hypotension. Since most patients already have an EVD in place from the SAH, this provides the opportunity for easy access to administer nicardipine intraventricularly. Intrathecal nicardipine is indicated when other modalities fail in patients with cerebral vasospasms due to SAH. Several reports demonstrate that administering intrathecal nicardipine is both safe and efficacious for cerebral vasospasms. WVUH’s implementation of the protocol is outlined below.

### The Vasospasm Protocol Interventions

#### **Triple-H therapy:**

- Hypertension with vasopressor therapy (**goal SBP >160 mmHg**)
- Hypervolemia with Plasmalyte or normal saline
- Hemodilution with Plasmalyte or normal saline
- Baseline ECHO, EKG, and troponin

#### **Milrinone:**

- Start milrinone at 0.5 mcg/kg/min
- Monitor Transcutaneous Doppler studies (TCDs) and CT vasospasm regularly
- If nurse evaluation finds new deficit or change in neuro status, titrate up by 0.25 mcg/kg/min upon confirmation with NCCU team to a max rate of 1.25 mcg/kg/min

- Hypotension is common with milrinone therapy, therefore vasopressor therapy may be indicated to **maintain a MAP of >90 mmHg**
  - Norepinephrine 0.03 mcg/kg/min titrated to MAP >90 mmHg

#### **Intrathecal nicardipine:**

- Inclusion:
  - Patients with aneurysmal subarachnoid hemorrhage (aSAH)-induced vasospasm
  - Patients not responding to triple-H therapy and/or milrinone therapy
- Exclusion:
  - Patient's EVD cannot be clamped secondary to increased ICPs
- Dose:
  - Nicardipine 4 mg in 2 mL of preservative free (PF) saline intrathecally Q12h
    - Flush with 2 ml PF saline
  - Withdraw 4 mL CSF prior to administration
  - Clamp drain for 30 minutes following administration
  - Administer for five days or discontinue when patient's clinical status improves
- Monitoring:
  - Monitor TCDs, angiography and/or clinical exam
  - Daily CSF and ICP during clamping

#### **References:**

1. Lannes M, Teitelbaum J, et al. Milrinone and Homeostasis to Treat Cerebral Vasospasm Associated with Subarachnoid Hemorrhage: The Montreal Neurological Hospital Protocol. *Neurocritical Care*. 2012;16: 354-62.
2. Lee KH, Lukovits T, et al. "Triple-H" Therapy for Cerebral Vasospasm Following Subarachnoid Hemorrhage. *Neurocritical Care*. 2006;04: 68-76.
3. Ehtisham A, Taylor S, Use of Intrathecal Nicardipine for Aneurysmal Subarachnoid Hemorrhage-Induced Cerebral Vasospasm. *Southern Medical Association*. 2009;102(2): 150-3.
4. Webb A, Martin K, et al. The Effect of Intraventricular Administration of Nicardipine on Mean Cerebral Blood Flow Velocity Measured by Transcranial Doppler in the Treatment of Vasospasm Following Aneurysmal Subarachnoid Hemorrhage. *Neurocritical Care*. 2010;12: 159-64.