Rationale: Pentobarbital and other barbiturates have been shown in human and animal studies to have neuroprotective effects on patients with traumatic brain injury. This effect appears to be related to their hemodynamic actions. Pentobarbital has been demonstrated to reduce cerebral blood flow (CBF) and cerebral metabolic rate of oxygen (CMRO₂) and thus, a reduction in intracranial pressure (ICP). This occurs in a dose-dependent fashion. Studies with pentobarbital as a prophylactic therapy have repeatedly shown no improvement in outcome. However, there is literature supporting its use in reducing ICP in patients with refractory intracranial hypertension. This has led to its use as a potential salvage therapy for patients with refractory intracranial hypertension.

Prerequisites
1. Meets criteria for refractory intracranial hypertension
   - ICP parameters
     21-29 for at least 30 minutes
     30-39 for at least 15 minutes
     40 or more for greater than 1 minute
   - Metabolic parameters
     Na 145-155 target (but less than 160)
     Serum osmolarity between 320 and 330
2. Repeat head CT shows no surgically treatable lesions
3. Neurosurgery evaluation recommends nonsurgical treatment

Dosing
1. 10 mg/kg bolus over 30 minutes
2. 5 mg/kg/hr continuous infusion x 3 hours
3. Decrease infusion rate to 1 mg/kg/hr
4. Titrate infusion rate based electroencephalogram (EEG) burst suppression

EEG burst suppression goal (2-5 bursts/min)
Infusion rates likely to be between 1-5 mg/kg/hr
5. Continue burst suppression for at least 72 hours
6. After 72 hours, wean as tolerated to maintain ICP <20

Goals
- ICP ≤20 for at least 48 hours
- Resolution of cerebral edema

Failure of treatment
- ICP 21-35 for 4 hours, 36-40 for 1 hour, or over 40 for 5 minutes
- Failure of ICP to return to normal (<20) in 7 days without pentobarbital
- Brain death/hemiation
- Side effects requiring discontinuation of treatment (e.g. hypotension, sepsis, etc)

Monitoring
✓ Ventriculostomy or ICP monitor
Continuous EEG (requires WIZ order for continuous EEG consult)
Arterial line for invasive blood pressure monitoring and arterial blood gas (ABG)
Pulmonary artery (PA) catheter or hemodynamic transesophageal echocardiography (hdTEE) for invasive cardiac monitoring and guide resuscitation
Daily CBC, BMP, CXR
LFTs periodically
Pentobarbital drug levels not indicated

Potential Side Effects
- Hypotension
  - Treat hypotension with volume first, then norepinephrine or phenylephrine
  - Use PA catheter or hdTEE to guide fluid resuscitation
  - Avoid dopamine as it increases CMRO₂
- Feeding Intolerance
  - Monitor frequently for signs of feeding intolerance as there are risks of decreased gastrointestinal motility and feeding intolerance
  - Enteral feeds are not currently contraindicated
  - Postpyloric feedings are poorly tolerated if high residuals noted with gastric feedings
  - Prokinetics have not shown benefit in improving tolerance of enteral feeds
  - Consider early total parenteral nutrition (TPN) at onset of ileus
  - Continue TPN throughout duration of pentobarbital therapy and until ileus resolves
  - Ileus may persist up to 7 days after discontinuation of pentobarbital
- Hypokalemia
  - Check BMP daily and replete as necessary to maintain K≥4.0
- Respiratory complications
  - Expect apnea, maintain full vent support
  - Daily ABG to monitor for hypoxemia and ARDS
  - Daily CXR to monitor for developing pulmonary processes
- Infections
  - Daily CBC
  - Culture and treat as indicated
- Renal dysfunction
  - Monitor urine output
  - Prevent hypovolemia
  - Daily BMP to monitor renal function
  - Minimize exposure to nephrotoxins
- Hepatic dysfunction
  - Periodic check of LFTs

Other considerations
- Educate family on indications for pentobarbital therapy, goals for therapy, what to expect, indicators of treatment failure, side effects and alternatives to pentobarbital therapy
- Engage in family discussion of treatment options and goals of care prior to initiation of pentobarbital therapy. Strongly consider having neurosurgery team present for discussion
- Consider palliative care consult prior to initiation of therapy to assist in defining goals of care and potential end of life issues
References:


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