VANDERBILT UNIVERSITY
MEDICAL CENTER
DIVISION OF ACUTE CARE SURGERY

Pentobarbital Treatment Guidelines for Severe Traumatic Brain Injury

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 ($CMRO_2$) 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. The latest guidelines from the Brain Trauma Foundation report a low-quality body of evidence to support the use of high-dose barbiturates to control elevated ICP refractory to maximum medical & surgical treatment. A systematic review published in 2012 reported that in the adult population, though barbiturates reduce ICP, there was no significant evidence that its use is associated with a decrease in death or disability. There is a small body of evidence in the pediatric population showing use of high-dose barbiturates helped to control ICP and was associated with improved long-term outcomes. It therefore continues to be used as a potential salvage therapy for patients with refractory intracranial hypertension. It is essential to ensure that families understand that this treatment is a salvage therapy for injuries associated with very high morbidity and mortality.

Prerequisites for Pentobarbital Initiation:

1. Meets criteria for refractory intracranial hypertension (RICH) after severe Traumatic Brain Injury
    a. Head of Bed maximally elevated
    b. Ventilation and pC02 optimized
    c. At maximal hyperosmolar therapy (Na >160 **and** Osmolality >330)
    d. Sedation to RASS -5:
        i. Propofol use exhausted for management of elevated ICP
        ii. Dosing up to 80 mcg/kg/min for at least 1 hour
    e. ICP parameters (***in the absence of acute agitation/external interventions/stimuli)*:**
        i. ICP 21-35 for 4 hours
        ii. ICP 36-40 for 1 hour
        iii. ICP >40 for 5 minutes
2. Repeat head CT shows no surgically treatable lesions
3. Neurosurgery Consultant without further surgical options and/or agrees with medical coma
4. Palliative care consulted and/or re-consulted upon pentobarbital initiation to help initiate or continue ongoing goals of care discussions & develop treatment boundaries related to pentobarbital, including discussion regarding non-responders and transitioning to comfort care.

Goal of Pentobarbital Treatment: ICP controlled <20 for at least 48 hours

Dosing of Pentobarbital:

1. Start pentobarbital load: 10 mg/kg intravenous bolus over 60 minutes followed by 5mg/kg/hr continuous infusion x 3 hours
2. Decrease PB infusion rate to 1mg/kg/hr and discontinue propofol infusion after completion of load
3. Titrate infusion rate (1-5 mg/kg/hr) to maintain burst suppression goal (2-5 bursts/min).
4. Continue burst suppression for at least 72 hours.
5. After 72 hours of treatment, if ICPs have been controlled for at least 48 hours, begin weaning pentobarbital.
    a. Reduce the dose by 50% every 12 hours until the infusion rate falls below 0.5mg/kg/hr, at which point it should be turned off.
    b. If ICPs become uncontrolled as defined by RICH criteria within the first 12 hours of the infusion being turned off, resume infusion rate which previously achieved goal burst suppression for at least another 48-hour period prior to attempting wean again.
        - If burst suppression is not achieved at previous rate, modify rate accordingly to achieve appropriate suppression.
        - Do not re-bolus pentobarbital if ICPs remain uncontrolled and a rate of 5 mg/kg/hr is achieved without burst suppression

Non-Responder to treatment defined as:

- *Once goal burst suppression is reached*, ICPs persistently uncontrolled at:
    1. 21-35 for 4 hours
    2. 36-40 for 1 hour
    3. >40 for 5 minutes
- Provider team must be notified of failure of therapy as soon as it occurs. Patient surrogate must be notified immediately of treatment failure and discontinuation of pentobarbital therapy.
- Continue to optimize ICPs through appropriate medical management after pentobarbital is discontinued.

PB-Responder with failure of treatment defined as:

1. Failure of ICPs to normalize after multiple failed weaning attempts
2. Failure of ICPs to return to <20 in 7 days without pentobarbital
3. Brain death/herniation
4. Severe side effects requiring discontinuation of treatment (hypotension, etc.)

Additional Monitoring:

1. Continuous EEG order *Do not delay initiation of pentobarbital load for EEG setup*
2. Continue monitoring & treatment with hyperosmolar therapy
3. Check LFTs prior to initiation of pentobarbital infusion and then every 72 hours during treatment.

4. Continue enteral feeding while patient is receiving pentobarbital. Monitor for intolerance but do not hold unless indicated.

Special Considerations

- **Determination of brain death should be based on cerebral brain flow study only.**
- **For transitioning to comfort care and potential DCD patients, send post-infusion pentobarbital level 72 hours after discontinuation of infusion to allow for adequate drug clearance prior to next phase of care.**
    - *How to order: Pentobarbital will need to be ordered as a MISC RFT, miscellaneous reference test, and the ordering provider will need to specify – "send pentobarbital level to Medtox laboratories" in the order. Otherwise, the test will get sent out to ARUP. Results will come back under the media tab as a scanned laboratory report.*
    - *Nurse reference for proper collection:* ***https://medtox.labcorp.com/tests/701768/pentobarbital-immunoassay-serum-plasma***

Toxicity

- If concern for pentobarbital toxicity, obtain BMP to determine anion gap and osmolar gap.
    - If patient has an anion-gap metabolic acidosis, increased osmolar gap, elevated lactate, and/or acute renal failure, toxicity should be considered.
        - May consider nephrology consultation for dialysis or consider use of fomepizole (consult toxicology and pharmacy for dosing).

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