SUBJECT: Pentobarbital Treatment Guideline **PAGE:** 1 of 3
REVIEWED/UPDATED: New **EFFECTIVE: 9/1/2024**

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PURPOSE:
Severe TBI with elevated ICP refractory to standard maximal medical therapy poses a difficult treatment problem. The UAMS TBI Goal-Directed Therapy Guideline outlines tiers of therapies for sustained (>15 minutes) ICP ≥22 mmHg, of which barbiturate coma is included as a fourth (and final) tier therapy. This guideline will outline the specific indications, goals, and prerequisites of barbiturate coma as a salvage therapy.

RATIONALE:
Studies evaluating the use of pentobarbital as a prophylactic therapy in severe TBI have shown no significant improvement in outcome, although barbiturates have been shown to successfully reduce ICP. The most recent Brain Trauma Foundation Guidelines for the management of severe TBI (4th Ed.) recommend high-dose barbiturate administration for elevated ICP refractory to maximum standard medical and surgical treatments.

DEFINITIONS:
Burst suppression – in severe TBI, considered 2-3 bursts/minute
Refractory intracranial hypertension – sustained (>15min) intracranial hypertension (ICP ≥22 mmHg) despite maximal medical therapy including Tier 1, 2 and 3 treatment exhaustion (e.g., Na >160, pCO2 optimized, HOB max elevation, max sedation)

Prerequisites for Barbituate Initiation:
1. ***Sustained*** (>15 min) ICP >22 mmHg ***REFRACTORY*** to maximal medical therapy
2. Provider has reviewed all treatments and determined that they are optimized and exhausted
3. Repeat CTH (if able to obtain) shows no surgically treatable lesions
4. Surgical intervention has been performed or ruled out
5. ACS and Neurosurgery Attending - to - Attending conversation has occurred and all parties agree to proceed as other treatments have been exhausted
6. Goals of Care conversation has been held with family and Palliative Care Consult ordered if appropriate

Pentobarbital Initiation:
1. Continuous EEG monitoring:
    - consult Neurology to initiate EEG
    - specify pentobarbital protocol in order
        - when burst suppression needed, SICU Attending must call Epilepsy Attending on-call to closely monitor and interpret EEG
2. Pentobarbital loading dose: 10 mg/kg IV bolus (from bag) infused over 30 min
3. Pentobarbital Infusion:
    a) Starting dose: 1mg/kg/hr
    b) Dosing range: 0.5-5 mg/kg/hr
    c) All dose adjustments must be ordered by provider (no nursing titration permitted)
4. Sedative/Analgesia/Paralytic infusions:
    a) Target RASS -5 or Riker 1
    b) Continue at current doses

Pentobarbital Therapeutic Goals:

- The *Primary Goal* of pentobarbital is to achieve ICP control
- Infusion rate should be titrated to the lowest effective dose
- Burst suppression should only be pursued if ICP control is not achieved at lower doses
- If burst suppression is achieved and ICP remains refractory, further increases in pentobarbital should be avoided

Non-Responder to Treatment:

- "non-responder" is defined as goal burst suppression reached without ICP control:
  - ICP 25-35 for 4 hours
  - ICP 36-40 for 1 hour
  - ICP >40 for 15 minutes
- If patient is a non-responder, consider discontinuing pentobarbital

Pentobarbital Discontinuation:

If

1) Burst suppression for 72 hours

And

2) ICP controlled <22mmHg for 48 hours

Then:

- Pentobarbital infusion wean:
  - Reduce the infusion dose by 50% every 12 hours
  - Turn off the infusion when the dose is ≤ 0.5 mg/kg/hr

- If ICPs become uncontrolled within 12 hours of infusion discontinuation, resume at prior goal infusion rate and continue for at least 48 hours prior to attempting to wean again.

Responder with Failure of Treatment:

- Failure of ICP to normalize after multiple failed weaning attempts
- Severe side effects requiring treatment discontinuation (liver failure, severe hypotension, etc)
- Failure of ICP to remain <22 in 7 days without pentobarbital

Additional Monitoring:

- Check LFTs prior to initiation and every 72 hours during treatment
- Monitor for signs of propylene glycol toxicity: acute renal dysfunction, osmolar gap > 10, anion gap metabolic acidosis
- Consider post-infusion pentobarbital level to determine reliability of neurological exam
  - Must be <5mcg/ml to be considered nontherapeutic
  - Send-out lab run weekly on Saturdays

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