DEPARTMENT: Trauma Services	POLICY TITLE: Pentobarbital Coma for Refractory ICP
Page 1 of 5	POLICY DATED: 01/2016
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PURPOSE:
To provide a guideline for therapy intended as a Tier 3 treatment for Traumatic Brain Injury patients with refractory ICP not controlled by Tier 1 or Tier 2 interventions.

RATIONALE:
High-dose barbiturate therapy is used in patients with traumatic brain injuries when intracranial hypertension is refractory while on maximum medical treatment involving Tier 1 and Tier 2 interventions to lower intracranial pressure. By lowering intracranial pressure, decreasing the cerebral metabolic usage of oxygen by altering vascular tone and suppressing metabolism, high-dose barbiturate therapy can have a beneficial response on intracranial pressure and overall cerebral perfusion.

PROTOCOL:

1. **Prerequisites**

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

2. **Patient Assessment Parameters**

- Ventilatory status is secured by mechanical ventilation.
- Central line in place
- Arterial line in place
- ICP monitor in place
- CVP (central venous pressure) between 5 and 10 mm Hg or SVV (stroke volume variation) less than 13%.
- Cerebral perfusion pressure (CPP) is greater than 60 mmHg and/or is optimal for patient per neurosurgery recommendations. May utilize vasopressors as needed to achieve optimal CPP.
- BIS bedside monitor and/or continuous EEG monitor in place attached and continuously monitoring

3. **Dosing- *Discontinue any current sedation, paralytic or narcotic continuous infusions. May continue or switch infusions to scheduled IVP or PRN dose. See below for guide to titrate propofol.***

- Loading dose:
    1. 10mg/kg bolus over 30 minutes (obtain a serum pentobarbital and phenobarbital level one hour after administration; therapeutic pentobarbital serum level 2.5-4 mg/dl, may increase to 6 mg/dl if needed, therapeutic phenobarbital serum level 15-40mcg/ml)
- Maintenance dose:
    1. 5mg/kg/hr continuous infusion x 3 hours
    2. Decrease infusion rate to 1mg/kg/hr, may titrate for a max dosage of 5mg/hr
- If patient is on high dose propofol at time of induction of barbiturate therapy, titrate as follows:
    1. When starting loading dose of pentobarbital, decrease propofol infusion by half
    2. Continue to decrease propofol drip again by half every 15 mins after initiation of pentobarbital loading dose until propofol weaned off.
- Titrate infusion rate using BIS monitoring as primary monitor, then EEG if available, using the below titration:
    1. BIS monitor
        - Maintain BIS between 10 and 20
        - Continue for the duration of the infusion
    2. EEG burst suppression
        - EEG burst suppression goal (2-5 bursts/min) Infusion rates likely to be between 1-5mg/kg/hr
        - Continue burst suppression for at least 48 hours, if ICP <20 and CPP >60 then initiate weaning
- When increasing pentobarbital for BIS maintenance between 10 and 20 or EEG burst suppression goal (2-5 bursts/min), bolus with the target dose. (Ex. If increasing from 1mg/kg/hr to 1.5mg/kg/hr, administer a 1.5mg/kg bolus then increase continuous rate to 1.5mg/kg/hr.)
- Once ICP <20 for 72 hours or 10 days post injury, contact the physician (neurosurgeon/trauma surgeon). If orders received to wean, titrate pentobarbital by 0.5mg/kg/hr increment every 8hrs while monitoring the effects on ICP and hemodynamic monitors.

4. **Goals**

- A reduction of ICP within 10 minutes
- ICP $\leq$20 for at least 48 hours
- Resolution of cerebral edema
- Maintain CPP >60 mm Hg

5. **Failure of Treatment**

- ICP 25-35 for 4 hours, 36-40 for 1 hours, or over 40 for 5 minutes once pentobarbital infusion at max dose for hemodynamic stability

- No decrease of ICP, wean pentobarbital after 24 hours
- Brain death/herniation
- Side effects requiring discontinuation of treatment (ex. hypotension, sepsis, etc.)
- Patients should not be maintained on this therapy for more than 10 days post injury.

6. **Monitoring**

- Ventriculostomy or ICP
- Continuous EEG or BIS monitoring
- Arterial line for invasive blood pressure monitoring and arterial blood gas
- Use PA catheter or Flotrac (Vigileo) to continuously monitor patients hemodynamics
- Obtain serum pentobarbital and phenobarbital level one hour after loading dose administered
    a. Therapeutic pentobarbital serum level 2.5-4 mg/dl, may increase to 6 mg/dl if needed
    b. Therapeutic phenobarbital serum level 15-40mcg/ml
- Daily CBC, CMP, serum pentobarbital level, serum phenobarbital level and CXR
- If significant increase in ICP, obtain a STAT CT scan of the head.
- If concern for decrease in cerebral brain flow, obtain a STAT CTA of the head.

7. **Nursing Assessments- *These patients should be staffed 1:1.***

- Document ICP, EVD drainage (if in place), BIS and pupil assessment every hour
- Monitor EEG for burst suppression. Goal is 10-12 seconds of burst suppression as seen on EEG. Monitor BIS monitor for score between 10-20.
- Maintain CPP >60
- Document central venous pressure (CVP) and cardiac output/index (CO/CI) every hour
- Place post pyloric feeding tube
- Maintain normothermia
- SCD's in place.

8. **Potential Side Effects**

- Hypotension
    a) Treat hypotension with volume first in the hypovolemic setting, then norepinephrine or phenylephrine
    b) Use PA catheter or Flotrac (Vigileo) to monitor patients hemodynamics
    c) Avoid dopamine as it increases $CMRO_2$
- Feeding intolerance
    a) Monitor Frequently for signs of feeding intolerance as there are risks of decreased gastrointestinal motility and feeding intolerance

b) Enteral feeds are not currently contraindicated
c) Post pyloric feedings are poorly tolerated if high residuals noted with gastric feedings
d) Prokinetics have not shown benefit in improving tolerance of enteral feeds
e) Consider early total parenteral nutrition (TPN) at onset of ileus
f) Continue TPN throughout duration of pentobarbital therapy and until ileus resolves
g) Ileus may persist up to 7days after discontinuation of pentobarbital

- Hypokalemia
  a) Check BMP daily and replete as necessary to maintain K>4.0
  b) Respiratory complications
  c) Expect apnea, maintain full vent support
  d) Daily ABG to monitor for hypoxemia and ARDS
  e) Daily CXR to monitor for developing pulmonary processes
- Infections
  a) Daily CBC
  b) Culture and treat as indicated
- Renal Dysfunction
  a) Monitor urine output
  b) Prevent hypovolemia
  c) Daily BMP to monitor renal function
  d) Minimize exposure to nephrotoxins
- Hepatic dysfunction
  a) Periodic check of LFT's

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.
- ❖ Palliative care consult recommended to assist in defining goals of care and potential end of life issues.
- ❖ Mandatory Neurology consult.
- ❖ All cases to be reviewed by Trauma Committee.

These guidelines are designed for the general use of most critically ill trauma patients, but may need to be adapted to meet the special needs of a specific patient as determined by the patient's care giver.

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