Golisano Children's Hospital of Southwest Florida- NICU
Lee Health, Fort Myers, Florida

Management of the Infant with Neonatal Abstinence Syndrome

GOAL:
To safely and judiciously achieve an acceptable newborn physiologic state using pharmacologic and non-pharmacologic therapy. This is achieved through a strong emphasis on the use of non-pharmacologic soothing maneuvers, and encouragement/ facilitation of family participation. Pharmacologic treatment is utilized when, with a treatment strategy that seeks to minimize the total exposure to opioid therapy.

MANAGEMENT:

1. **Non-pharmacologic** soothing strategies are critical to this phase and include a quiet minimally stimulating environment without excessive sound and light exposure, swaddling and containment, soothing/ comforting interaction with the baby by staff, including nursing, occupational therapy, "cuddler" volunteers. Staff should strongly encourage parental involvement, and empathetically support a collaborative partnership with the family.
2. **Pharmacologic treatment:**
   - Evidence-based assessment of optimal treatment regimens is difficult, with no compelling recommendation for any specific regimen. Treatment is a necessary evil, and we should recognize that post-natal opioid exposure continues to increase the risk for neuronal apoptosis, as well as perpetuating an ongoing stimulation of *u* opioid receptors.
     - Our unit employs Morphine sulfate as the first-line pharmacologic therapy.
     - We utilize a milliliter dosing titrated to effect rather than a calculated mg/kg dosing schedule. Morphine concentration is standardized for all newborn areas within Lee Health at 0.4 mg/ml.
   - **Adjunctive non-opioid pharmacologic** treatment (e.g. Phenobarbital or Clonidine) is a way to minimize post-natal exposure to opioids. If the alternative is continued stimulation of μ opioid receptors by increasing Morphine dosing, the addition of a non-opioid agent is preferable. Using an alternative therapy that is not reinforcing the physiology of opioid dependence, provides the infant additional days to habituate to the lower dosage of opioids.
     - Phenobarbital may adversely affect neurodevelopment, and is delivered in 10% EtOH, adding to this risk. Long-term exposure to this drug should also be minimized.
     - Clonidine is a centrally acting alpha-2-adrenergic agonist, and decreases sympathetic outflow, acting to diminish some of the autonomic-mediated symptoms of NAS.

SCORING

FNAST: the Finnegan score is validated only for the term infant in the first month of life.

- Not for the infant who is acutely transitioning, or with active medical conditions
- Not for the preterm infant
- May not be the optimal scoring tool for the older newborn, e.g. 2-4 weeks of age

When scoring, the nurse should focus on maintaining an unbiased, objective assessment of scoring criteria (high inter-rater reliability), without regard for the above confounders. The physician/ NNP will adjust for these variables in the management of each patient.

PHARMACOLOGIC TREATMENT

Initiation of treatment is based upon three consecutive scores of 8 or greater. *By physician order*, treatment may also be initiated by >=2 high score (e.g. greater than 12-15). Adjustments in treatment dosage are an individualized titration process.

- **Acute escalation phase**: Initial rapid, incremental increase in treatment dosing to reach a state of control of neonatal abstinence syndrome symptoms, achieving score less than 8, using the lowest effective dosage of narcotic for treatment. In this phase, Morphine is the initial drug of treatment, and should be advanced aggressively to achieve effect.
- **Maintenance phase**: A 1-day period of control, where the immediate period when acceptable scores are reached following initiation of treatment.
- **Weaning phase**: Once control is established, we seek to wean a newborn who is opioid-dependent off of all narcotic therapy. This is a "controlled withdrawal," and the newborn will experience a necessary degree of discomfort as his dosage is decreased. Anticipate an inherent tension between over and under treatment.

1. **Acute Escalation phase**: Infant is newly diagnosed, order set is implemented, and over the ensuing 48-72 hours, the infant is rapidly treated with escalating doses of Morphine sulfate (0.4 mg/ml standard

concentration) in 0.1 ml/feed increments every 3 hours. The NAS Order Set will allow the nurse to rapidly increase dosing, based upon FNAST scores, up to 0.5 ml.

- Goal: to rapidly achieve an acceptable physiologic state that will allow the infant to feed, self-regulate and sleep in an acceptable fashion.
- Note that Morphine may be increased (by physician order) by greater than 0.1 ml increments for higher scores

  For infants with extreme withdrawal, initial scores may be excessive.
  - Initial Finnegan Score 13-16: 0.2 ml (0.08 mg) x 1 dose
  - Initial Finnegan Score 17-20: 0.3 ml (0.12 mg) x 1 dose
  - Initial Finnegan Score 21-24: 0.4 ml (0.16 mg) x 1 dose
  - Initial Finnegan Score 25 or greater: 0.5 ml (0.20 mg) x 1 dose
- The physician/NNP should consider beginning **adjunctive therapy** at a Morphine dosage of 0.5-0.7 ml/dose (~0.06-0.09 mg/kg/dose for a 3 kg baby). Dosing by physician order up to a maximum of 1-2 ml/ dose every 3 hours (~0.1-0.25 mg/kg/dose for 3 kg baby).

2. **Maintenance phase**: Infant has consistently achieved scores of less than 8.
   - Goal: to confirm that a therapeutic dosage of opioid medication has been attained, evidenced by FNAST scores <8.
3. **Weaning phase**: Once the infant has demonstrated control for 24-hours, may begin to wean Morphine doses. This is the most difficult period of management, and requires an ***INDIVIDUALIZED*** approach. Weaning is typically (but not always) by 0.05 ml (0.02 mg) increments (may wean once or more per day).
   a. Our primary approach is to wean the Morphine, and try not to increase the dosage. For equivocal scores, or scores that increase as the Morphine is weaned, we may adjust to longer intervals between weaning, with a high threshold for increasing ("ratchet weaning")- e.g. accept scores <12 before weaning.
   b. Adjunctive therapy should be used aggressively to facilitate Morphine weaning.
   c. By exception, if the infant is demonstrating ***unacceptable levels of withdrawal***, the Morphine dosage may be increased by 0.02-0.03 ml increments ("one step forward, ½ step backward").
   - With repetitive weaning, anticipate a period of acclimation. The more consecutive weans implemented, one may anticipate a subsequent longer period of acclimation, or a need to increase dosing of adjunctive therapy.
   - Family, cuddlers and nursing staff all must work together. **Encourage mother and/or cuddler to be available at the bedside**, and provide non-pharmacologic soothing.
   - Defining ***unacceptable levels of withdrawal*** is a joint collaboration between the infant's physician and nurse.
   d. Generally, this assessment is made during AM rounds by reviewing the previous 24-hour period, although shorter intervals for adjustment may be necessary based upon the severity of withdrawal symptoms.
   e. Based upon the FNAST scores (isolated spikes in scores, as well as "area under the curve" assessment), perceived effectiveness of non-pharmacologic strategies for comfort, the nurse, with input from the parents, OT/PT, and cuddlers, should report to the physician her general assessment of how well the infant is tolerating the weaning process.
   f. **Oftentimes in the older infant, we will accept higher score thresholds to trigger adjunctive therapy**.
      i. As the infant matures, FNAST scores that are considered "unacceptable" will be adjusted upward; e.g. A five-day old who is in the *escalation phase*, may have an upward adjustment in his dosage of Morphine for scores of 8 or greater, whereas a two-week old, or thirty-three day old infant, who is in the *weaning phase*, may remain on the same dosage of Morphine sulfate despite occasional scores of 12 or higher.
      ii. There may be a small subset of exceptionally affected babies that have sustained neurologic deficit/ intrinsic neurologic dysregulation due to severe opioid/ polydrug in utero exposure, with baseline hypertonicity, tremulousness, poor regulation w/ stimuli, that may persist beyond 3-4 weeks of chronologic age, with intermittent elevated scores, regardless of treatment. In this case, the baby may be weaned despite intermittent scores that remain in the 12 or greater range.
   g. **Feeds**: Morphine dosing is maintained at a consistent q 3-hour dosing interval, with a q 3-hour feeding schedule. However, for the older newborn (>42 wks corrected gestational age, or >2-

3 weeks chronologic age), based upon maturity of sleeping patterns, a "feeding on demand" schedule may be considered in discussion with the physician/ NNP.

4. **Adjunctive therapy: Addition of Clonidine or Phenobarbital**: Consider adjunctive therapy if FNAST scores are not controlled despite Morphine at 0.5-0.7 ml/dose (~0.06-0.09 mg/kg/dose) during the Acute Escalation phase; or FNAST scores that continue to rise after Weaning, or if the Weaning course stagnates:
    a. Clonidine is used adjunctively with Morphine. In newborns in the weaning phase of management, Clonidine may be considered for babies who are exhibiting strong autonomic symptoms (loose stools, diaphoresis, yawning, emesis, mottling).
        i. Starting dose of 0.5 mcg/kg/dose po every 6 hrs (2 mcg/kg/day). Recommended dosage range of 2-6 mcg/kg/day.
        ii. The baby should have monitoring of blood pressure.
        iii. Clonidine may be weaned once the infant is off Morphine. Wean by 25% per day over 3-4 days (e.g. increase dosing interval incrementally).
        iv. Clonidine should be discontinued prior to discharge, with careful monitoring of blood pressure for 48 hours off medication.
    b. Phenobarbital elixir: Start Phenobarbital adjunctively after Morphine and Clonidine have been initiated.
        i. The infant may be loaded w/ Phenobarbital (20-30 mg/kg total loading dose orally), and started on 5 mg/kg/day (divided twice per day) maintenance.
        ii. Once the infant is off Morphine, the Phenobarbital maintenance dosing may be discontinued immediately. Phenobarbital is slowly metabolized, and will continue to provide some additional support, even off all medications.
        iii. In addition, titrated against Phenobarbital levels (acceptable range of 20-40 ug/ml), a customized use of loading dose only, or "mini-loading doses" (5-10 mg/kg) may be used to "cut the edge" in a strategy to facilitate continued weaning of Morphine; or **after** Morphine, Clonidine and maintenance Phenobarbital have been discontinued, as a stop-gap to avoid restarting Morphine or Clonidine.
5. **Formula or breast**: In general, breast milk feeds are encouraged, and is a way for the mother to provide support to her infant, and facilitate bonding. It is uncertain if there is a clinically significant transference of medication to the breast milk, and the risk of illicit exposure must also be considered. Our present approach is to encourage breast milk feeds if the mother is committed to consistently providing this as a source of nourishment, AND she is not felt to be actively supplementing with illicit drugs. Formula feeds may be used as a more reliable food source, and the choice of lactose-based formulations versus Similac Sensitive (reduced lactose) or Enfamil Gentlease (partially hydrolyzed proteins and reduced lactose) remains unsubstantiated in the medical literature. We often use these alternative formulas empirically.
6. **Simethicone (Mylicon)**: Simethicone acts as a surface-active substance to theoretically decrease gas bubbles, and possibly decrease fussiness due to increased aerophagia or intestinal gas, and has been used to treat infantile colic. There is no medical literature to support efficacy of this medication for colic or for infants with NAS. It may be prescribed, by physician discretion, or on an empiric basis.

DISCHARGE

1. Patients may be considered for discharge when they are off Morphine and have acceptable scores for a 48-hour period.
2. If they were on adjunctive therapy, there should be a tailored longer period of observation.
    a. Clonidine may require a brief weaning period, with observation of acceptable blood pressures for 48 hours off therapy.
    b. Phenobarbital may be discontinued rapidly without weaning.
    c. It is not necessary to observe until all medication levels are undetectable. Rather, we observe for a long enough period to ensure that the family is capable of providing the non-pharmacologic soothing support to manage their infant through this final stage of continued withdrawal.
3. Social services will verify appropriateness of home discharge
4. Adequate follow-up includes a primary physician as well as neurodevelopmental follow-up.