Neuroscience NICU

Neonatal Opioid Withdrawal Guidelines

(Last Revised April 2019)

This guideline provides recommendations regarding assessment and treatment of neonatal opioid withdrawal syndrome. Evidence to support one pharmacological regimen over others is limited; this recommendation is based upon the available evidence, including a meta-analysis suggesting that buprenorphine is the optimal treatment for neonatal abstinence syndrome.[1] These recommendations only include management of newborns with in-utero exposure to opioids. Several other drugs may result in neonatal withdrawal symptoms; however, those infants are less likely to benefit from opioid administration, as outlined in this guideline. Ultimately, the final decision for care of the infant will be determined by the primary medical team.

Initial Assessment

- All neonates with known prenatal exposure to opioids must be monitored for withdrawal in the NICU
- Urine and either meconium or cord drug screening should be performed as soon after delivery as possible
- Duration of monitoring should be based on the pharmacokinetics of the drug being used (if known):
  - 72 hours for drugs with short duration of action (e.g. heroin, morphine, fentanyl, oxycodone)
  - 4-7 days for drugs with long duration of action (e.g. methadone, buprenorphine), if multiple drugs being abused (delayed onset has been seen when opioids used with barbiturates or benzodiazepines), or drug not known
- Finnegan scores[2] should be performed within the first 2 hours of life and then 30 minutes after each feeding (every 3-4 hours) when the infant is awake
- Pharmacologic therapy is indicated when non-pharmacologic management has been optimized and the infant has three consecutive Finnegan scores ≥8 **OR** two consecutive scores >12.

Non-Pharmacologic Management

- Non-pharmacologic supportive therapy should be initiated as the first line of treatment for NAS. This may include any/all of the following (see Koala Care sheet):
  - Minimizing light and noise
  - Slow and gentle handling
  - Swaddling or kangaroo care
  - Music therapy
  - Infant massage
  - Allowing periods of rest and sleep
  - Provision of adequate nutrition to establish weight gain
- Infants with NAS are at high risk for severe diaper dermatitis, so should receive early and aggressive management for any irritation or breakdown in the diaper area

Feeding and Nutrition

- Breastfeeding and expressed breast milk should be encouraged if mother enrolled in stable methadone/ buprenorphine program and not contraindicated for other reasons (HIV, illicit drug use, polydrug use, etc)
  - Although minimal amounts of methadone/buprenorphine pass through breast milk, mothers who are taking hydrocodone or oxycodone should be warned of sedative effects on the infant as these drugs are seen in high concentrations in breast milk and clearance is reduced in some neonates
- Feedings may need to be provided frequently and in smaller volumes or with a higher caloric content.

- If formula feeding, infants should receive sensitive formula (e.g. Similac Sensitive or Enfamil Gentlease)
- If infant requires pharmacologic management, may require increased calories – many infants will increase intake to compensate for calorie use, but others may require hypercaloric feeds

Pharmacologic Management

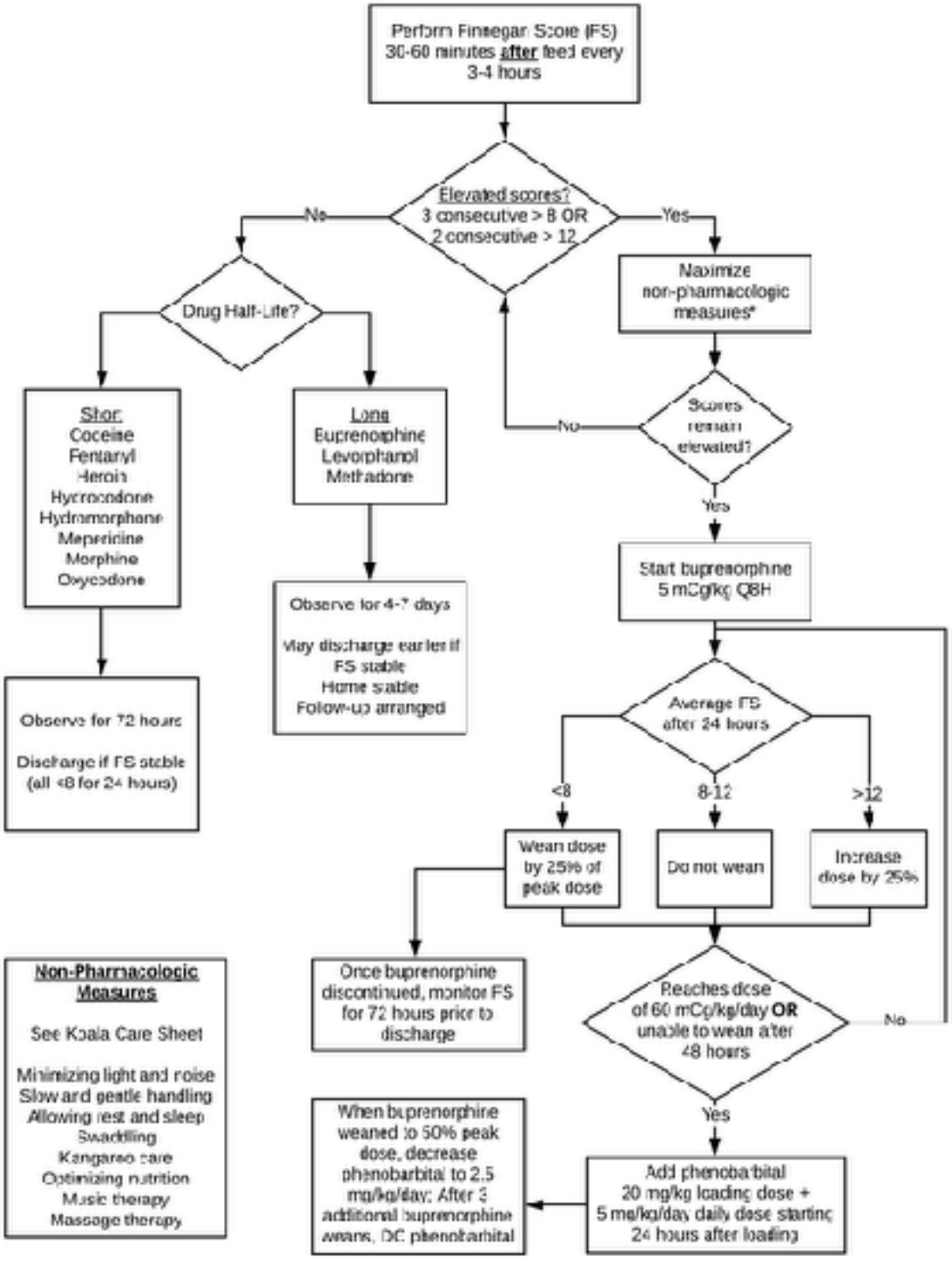
- Many reviews have been published assessing pharmacologic management of NOWS,[3-5] including a meta-analysis concluding that buprenorphine is the optimal treatment for withdrawal from opioids[1]
  - The optimal treatment for infants withdrawing from sedatives or hypnotics is unknown.[5]
  - In cases of polysubstance abuse, it is reasonable to follow these guidelines but these infants may benefit from quicker initiation of phenobarbital
- Buprenorphine has been shown in several recent studies to result in shorter treatment duration and length of stay over other opioid medications[6] (see evidence table below)
- Because of these findings and the early trends seen in the initial pilot at UNMC, these guidelines use buprenorphine as the primary drug of choice
  - Initial dose: 15 μg/kg/day (appropriate range 13.2-15.9 μg/kg/day)
  - See dosing algorithm for further management
- If a maximum dose of buprenorphine is reached, or the infant reaches a steady dose but is unable to wean after 48-72 hours, phenobarbital (20 mg/kg loading dose then 5 mg/kg/day daily) may be added
  - See algorithm for weaning parameters
- Every attempt should be made to wean infants off of opioids prior to discharge, as outpatient pharmacotherapy for NOWS has been associated with >3 times longer therapy and a significant increase in ED visits after discharge[7]
  - If an infant is discharged on opioids, ensure that the reason is well documented in the progress note prior to prescribing the medication (Epic Smartphrase at UNMC: ".pedsopioid" and at CHMC: ".rxopiate")

Buprenorphine Evidence Table

Author (year)	Study Design	N*	Buprenorphine Dose	Comparison	Results
Kraft (2008)[8]	RCT	13	13.2 μg/kg/day divided Q8H, advance by 20% to max 39 μg/kg/day	Opium	No significant diff in treatment failure, seizures, days of treatment (10 days less in buprenorphine group), or hospital stay (11 days less in buprenorphine group)
Kraft (2011)[9]	RCT	12	15.9 μg/kg/day divided Q8H, advance by 25% to max 60 μg/kg/day	Morphine	Significantly shorter length of treatment (by 15 days) and length of stay (by 10 days) in buprenorphine group
Hall (2016)[10]	Retrospective cohort	38	13.2 μg/kg/day divided Q8H, advance by 0.8 μg/kg/dose to max 39 μg/kg/day	Methadone	Significantly shorter length of treatment (by 4 days) and length of stay (by 4 days) in buprenorphine group
Kraft (2017)[11]	RCT	33	15.9 μg/kg/day divided Q8H, advance by 25% to max 60 μg/kg/day	Morphine	Significantly shorter length of treatment (by 13 days) and length of stay (by 12 days) in buprenorphine group
Hall (2018)[12]	Retrospective cohort	174	13.5 μg/kg/day divided Q8H, advance by 1.5 μg/kg/dose to max 22.5 μg/kg/day	Morphine	Significantly shorter length of treatment (by 3 days) and length of stay (by 3 days) in buprenorphine group

*N refers to only the number treated with buprenorphine in each study

Neonatal Opioid Withdrawal Syndrome
Evaluation & Treatment



References

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7. Maalouf FI, Cooper WO, Slaughter JC, Dudley J, Patrick SW. Outpatient Pharmacotherapy for Neonatal Abstinence Syndrome. J Pediatr 2018;199:151-7 e1.

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9. Kraft WK, Dysart K, Greenspan JS, Gibson E, Kaltenbach K, Ehrlich ME. Revised dose schema of sublingual buprenorphine in the treatment of the neonatal opioid abstinence syndrome. Addiction 2011;106:574-80.

10. Hall ES, Isemann BT, Wexelblatt SL, et al. A Cohort Comparison of Buprenorphine versus Methadone Treatment for Neonatal Abstinence Syndrome. The Journal of Pediatrics 2016;170:39-44.e1.

11. Kraft WK, Adeniyi-Jones SC, Chervoneva I, et al. Buprenorphine for the Treatment of the Neonatal Abstinence Syndrome. New England Journal of Medicine 2017;376:2341-8.

12. Hall ES, Rice WR, Folger AT, Wexelblatt SL. Comparison of Neonatal Abstinence Syndrome Treatment with Sublingual Buprenorphine versus Conventional Opioids. Am J Perinatol 2018;35:405-12.

Koala Care

Environmental and Handling Guidelines

GOALS:

1. Maintain a consistent low-stimulus environment that will be conducive to a successful weaning treatment plan

2. Support frequent parent involvement and education to develop a safe and quiet atmosphere for the infant

- ✓ Draw window shades (filtered light) with low ambient lighting
- ✓ Noise will be kept to a minimum - all conversations will be quiet, and non-essential conversations will be discouraged
- ✓ Because Koala babies often have trouble falling asleep, it is important to let them sleep undisturbed while minimizing noise and visitors
- ✓ No non-essential foot traffic into the room will be allowed - visiting will be limited to the family members giving care to the baby
- ✓ Use of swings will be encouraged
- ✓ Infant massage will be encouraged - parents can be educated and encouraged in these techniques
- ✓ Develop and maintain a consistent routine - a developmental and feeding care plan will be posted at the bedside
- ✓ Handle me slowly and gently to reduce stimuli
- ✓ Swaddle me tightly (to prevent hypertonic and erratic movement)

✓ Provide me with music or rhythmic sounds
✓ Small frequent feedings are best
✓ Remember: when burping me, rub my back instead of patting
✓ Cuddle me! I love to snuggle!