Newborn Critical Care Center (NCCC) Clinical Guidelines

Opioid Weaning and Conversion Guidelines

BACKGROUND

Preventing and minimizing pain in a neonate in the neonatal critical care center is a primary goal for the clinician. This is achieved by providing adequate and safe analgesia and sedation by using both pharmacologic and non-pharmacologic measures. Pharmacologic treatment typically includes medications in the opioid and benzodiazepine drug classes. If these medications cannot be safely discontinued within a few days, physical dependence can develop with infants presenting with signs and symptoms of withdrawal with attempting weaning or cessation of pharmacologic therapy. As a result, more children have been treated for actual or potential withdrawal symptoms as a comorbidity of hospitalization.[1]

Neonatal Abstinence Syndrome is a generalized multisystem disorder, which predominantly involves the central and autonomic nervous systems, as well as the gastrointestinal tract. Symptoms may include:

Neurological	Gastrointestinal	Autonomic
• Irritability • Increased wakefulness • High-pitched cry • Tremor • Increased muscle tone • Hyperactive deep tendon reflexes • Frequent yawning and sneezing • Seizures (2-11%)	• Vomiting/diarrhea • Dehydration • Poor weight gain • Poor feeding • Uncoordinated and constant sucking	• Diaphoresis • Nasal stuffiness • Fever • Mottling • Temperature instability • Piloerection • Mild elevations in respiratory rate and blood pressure

Infants who undergo complex surgery, who require prolonged intensive care, or who are supported with extracorporeal membrane oxygenation (ECMO) therapy are among those at greatest risk of acquired drug dependency.

Patients develop tolerance to fentanyl faster than morphine. Continuous or scheduled dosing of fentanyl for 5 days or more necessitates weaning rather than abrupt discontinuation. Higher doses over shorter duration can also potentiate withdrawal. **The most successful method for weaning fentanyl is to steadily reduce the dosage by 10-20% of the original dose daily based on the length of exposure.[2]** Successful weaning can be accomplished more rapidly with fewer side effects when steadily vs intermittently decreasing dosing. Intermittent weaning appears to be associated with increased tolerance, higher incidence and severity of withdrawal symptoms, and longer lengths of stay.[2] In some situations, it may be preferable to convert the infant to an oral agent to facilitate narcotic weaning.

Weaning may be complicated in cases where the infant is receiving a continuous infusion or scheduled opioid for pain concurrently with a benzodiazepine for sedation and physical dependence both medications is probable.[2] **It may be reasonable to wean off the benzodiazepine first given the risks of propylene glycol toxicity and the long-term cognitive and developmental problems in children younger than 3 years.[3] However, concurrent weaning of both benzodiazepines and opioids should be avoided.[2]**

PURPOSE

- To aid in the weaning of opioids in order to prevent Neonatal Abstinence Syndrome as defined by 2 consecutive NAS (Finnegan) scores of ≥ 12 OR 3 consecutive NAS (Finnegan) scores of ≥ 8
- Infants who have received > 3 days of continuous or scheduled opioids are at risk of developing withdrawal symptoms, which can cause a deterioration in clinical status. Use routine scoring and weaning protocol for the following infants:
  - Infants who have received continuous or around the clock opioid medication for > 3 days
  - Infants who have received > 3 doses per day for > 5 days

Notes:

- Infants with cumulative exposure to opioids below the above threshold can undergo a rapid taper over a 24 to 48 hour period.
- Signs and symptoms of withdrawal may develop within 24 hours of discontinuation or during the course of a rapid taper of an opioid. If this happens, infant may require rescue dosing and a weaning strategy must be implemented.
- Preterm infants have been described as being at lower risk of drug withdrawal with less severe and/or prolonged courses. This may be related to developmental immaturity of the CNS, however the clinical evaluation of the severity of symptoms may be more difficult because scoring tools (Finnegan) were developed in term infants.

INSTRUCTIONS FOR SCORING (PLEASE SEE REFERENCE SECTION)

- Document all analgesics or sedatives administered
- Observe infant between scoring intervals for any of the signs of withdrawal listed in Table 1
- Complete NAS assessment every 4 hours during weaning of opioids and for 48-72 hours after they have been discontinued
- If any score is ≥ 8, change scoring interval to every 2 hours until score decreases to < 8
- Record “0” for any sign that is not seen during the interval
- Scores for individual signs may be subtracted from the total if the sign is expected to occur independently of withdrawal, due to a pre-existing condition. The decision to adjust a score should be made only after conferring with the provider.
- Review NAS scores by choosing the “View Flowsheet” tab (left side) inside the patient’s chart then choose the “Neonatal Abstinence” tab (top).
- The sum of the scores can be seen in the Neonatal Abstinence Scale Score row. When hovering over an entry, you will see “calculated.” If this is not present, the score has been manually adjusted.
- If the adjusted score is < 8 for 24 hours, consider weaning (based on the ORIGINAL dose). Weaning should occur only once every 24-48 hours.
- If the adjusted score is ≥ 8 for three intervals, or ≥ 12 for two intervals, consider increasing dose by 10% of the original dose.
- Reassess within two hours of any change in opioid dose.

- Non-pharmacologic techniques are used as adjunct therapy to comfort the neonate and manage withdrawal manifestations, which include swaddling, rocking, minimal sensory or environmental stimulation and maintaining temperature stability

INSTRUCTIONS FOR WEANING CONTINUOUS INFUSIONS

GENERAL WEANING GUIDELINES *Always wean based on ORIGINAL dose*	
Fentanyl continuous dosing for 2 weeks or less:	Wean by 20% per day over 5 days
Fentanyl continuous dosing for > 2 weeks:	Wean by 10% per day over 10 days

CONVERTING FENTANYL TO ORAL MORPHINE

(See Appendix A)

Cautions:

1. Narcotic conversion is an inexact process and requires careful monitoring of the infant to determine if adjustments in dosage are needed. Monitor clinical exam, vital signs, NAS and PIPP scores to assess clinical response. Excess narcotic administration or narcotic withdrawal can complicate the infant's clinical course and lengthen hospitalization.
2. ***Do not attempt to convert narcotics and wean on the same day***
3. For calculations use the weight on the fentanyl order **NOT** current weight
4. IV morphine and PO morphine are **NOT** equivalent
    - IV morphine dose x 3 = PO morphine dose
5. **When transitioning from fentanyl to PO morphine please do the following:**
    - 30 minutes after 1st dose of PO morphine decrease fentanyl infusion rate by half
    - 30 minutes after the 2nd dose of PO morphine discontinue fentanyl infusion
6. When converting to oral morphine, you may calculate a dose that is significantly higher than the normal dosing range. This may be due to the infant receiving higher doses of fentanyl than typical. Monitor clinical status closely.
7. Morphine may decrease GI motility to a greater extent than fentanyl.

INSTRUCTIONS FOR WEANING ORAL MORPHINE

- Decrease dose by 10-20% of the original (converted) dose every 24 hours (if scores < 8)
    - Use 20% of the original dose if total opioid exposure is 2 weeks or less
    - Use 10% of the original dose if total opioid exposure is > 2 weeks
    - Continue the same frequency (goal steady, consistent weaning)
- Once the morphine dose is between 0.03 - 0.05 mg/kg/dose, it may be discontinued

DISCHARGE

- Discharge from the hospital should be delayed until infant is free of withdrawal signs and symptoms for a period of 24 to 48 hours after complete cessation of opioids

References:

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5. Lewis T, Erte BL, Ezell T, and Gauda E. Pharmacoepidemiology of opiate use in the Neonatal ICU: Increasing cumulative doses and iatrogenic opiate withdrawal. Journal of Opioid Medicine (2015) 11(4): 305–312 Osborn DA, Jeffery HE, Cole MJ. Sedatives for opiate withdrawal in newborn infants. *Cochrane Database of Systematic Reviews* 2010, issue 10. Art. No.: CD002053. DOI 10.1002/14651858.CD002053.pub3.
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7. Wexelblatt, SL, McAllister, JM, Nathan, AT, Hall, ES. Opioid neonatal abstinence syndrome: An overview. *Clinical Pharmacology & Therapeutics*. 2018;103(6):979-981. doi:10.1002/cpt.958

Reviewed April 2019 – Croop / Trembath / Brown (RPh)

APPENDIX A

Example: *A 2 kg infant is receiving an IV fentanyl infusion at 3 mcg/kg/hr*
Convert this to Q4 hour oral morphine.

Conversion Calculations Fentanyl infusion to Oral Morphine

DIRECTIONS	EXPLANATION	EXAMPLE
Multiply fentanyl dose (mcg/kg/hr) by fentanyl infusion order weight (kg) to get hourly fentanyl dose	***Use weight that is on fentanyl order, not current weight***	Fentanyl 3 mcg/kg/hr x 2 kg = 6 mcg/hr fentanyl
Multiply hourly fentanyl dose (mcg/hr) by 50 to convert to Q4 hour **IV** morphine (mcgs)	*Intravenous fentanyl is 50-100 times more potent than IV morphine*	6 mcg x 50 = 300 mcg IV morphine Q 4 hours
Divide by 1000 to convert from mcg to mg of **IV** morphine		300 mcg IV morphine ÷ 1000 = 0.3 mg IV morphine Q 4 hours
Multiply Q4 hours IV dose by 3 for Q4 hour **ORAL** dosing	*Oral morphine is 1/3 to 1/6 as potent as IV morphine*	0.3 mg x 3 = 0.9 mg PO morphine Q 4 hours
Multiply Q4 hour **ORAL** morphine dose by 0.75	*Calculating 75% of the total converted dose allows for incomplete cross-tolerance between narcotics. Tolerance developed to one narcotic is not exactly the same as for a different drug.*	0.9 x 0.75 = 0.68 mg PO morphine Q 4 hours * * *Reminder – this is the total dose,* ***not*** *a weight-based dose*

APPENDIX B

NEONATAL ABSTINENCE SCORING SYSTEM

SYSTEM	SIGNS AND SYMPTOMS	SCORE	AM					PM						COMMENTS
CENTRAL NERVOUS SYSTEM DISTURBANCES	Continuous High Pitched (or other) Cry	2												Daily Weight:
	Continuous High Pitched (or other) Cry	3												
	Sleeps <1 Hour After Feeding	3												
	Sleeps <2 Hours After Feeding	2												
	Sleeps <3 Hours After Feeding	1												
	Hyperactive Moro Reflex	2												
	Markedly Hyperactive Moro Reflex	3												
	Mild Tremors Disturbed	1												
	Moderate-Severe Tremors Disturbed	2												
	Mild Tremors Undisturbed	3												
	Moderate-Severe Tremors Undisturbed	4												
	Increased Muscle Tone	2												
	Excoriation (Specific Area)	1												
	Myoclonic Jerks	3												
	Generalized Convulsions	5												
METABOLIC/VASOMOTOR/RESPIRATORY DISTURBANCES	Sweating	1												
	Fever 100.4°-101°F (38°-38.3°C)	1												
	Fever > 101°F (38.3°C)	2												
	Frequent Yawning (>3-4 times/interval)	1												
	Mottling	1												
	Nasal Stuffiness	1												
	Sneezing (>3-4 times/interval)	1												
	Nasal Flaring	2												
	Respiratory Rate >60/min	1												
	Respiratory Rate > 60/min with Retractions	2												
GASTRO-INTESTIONAL DISTURBANCES	Excessive Sucking	1												
	Poor Feeding	2												
	Regurgitation	2												
	Projectile Vomiting	3												
	Loose Stools	2												
	Watery Stools	3												
	TOTAL SCORE													
	INITIALS OF SCORER													