Treatment Guidelines for Iatrogenic Opioid Withdrawal in the NICU

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Background:

Neonates and infants exposed to prolonged treatment with opiates may develop opioid dependence. This typically occurs in patients requiring continuous opioid infusions during acute illness. It has been reported that children receiving fentanyl infusions for >5 days have a 50% chance of experiencing withdrawal; when the duration of infusion is ≥ 9 days, the chance of withdrawal increases to 100%.

Methadone is commonly used for managing withdrawal symptoms due to its oral bioavailability and long half-life (15-25 hours in neonates and 15-60 hours in children). A standardized protocol for tapering methadone will allow for consistency among providers in weaning methadone doses, and will potentially decrease the total duration of opiate use.

The initial methadone dose should be determined by the potential risk for opiate withdrawal, which is based on duration of exposure. Empiric dosing may begin prior to discontinuation of continuous opioid infusion. Methadone will reach a steady state drug level at 48 hours. Due to potential accumulation and toxicity, the methadone-dosing interval should be lengthened after 48 hours of initiation.

The tapering schedule may be individualized according to the patient's response and NAS scores. Withdrawal is typically defined by a Finnegan score >8. **In addition to methadone therapy, it is vital to optimize non-pharmacological measures in the treatment of withdrawal.**

This guideline is intended for neonatal patients who have received prolonged exposure to fentanyl or morphine (defined as exposure for ≥ 5 days), who are ready to be weaned off opioid therapy and do not have a condition that requires continuation or escalation of opioid dosing.

Risk of opioid withdrawal associated with duration of exposure:

- < 5 days: current opioids may be stopped without weaning. No NAS scoring necessary.
- ≥5 to 9 days: initiate low dose methadone taper order panel and follow opioid infusion weaning guidelines.
- 10 to 28 days: initiate intermediate dose methadone taper order panel and follow opioid infusion weaning guidelines.
- >28 days: initiate high dose methadone taper order panel and follow opioid infusion weaning guidelines.

Tapering Dose guide:

Steps:

1. Order appropriate methadone taper (order panel) in Epic based on duration of exposure, as outlined above
2. Discontinue current (IV or Buccal) PRN opioids/benzos
3. Continue current continuous infusion of fentanyl/morphine; begin to taper the drip after the 2nd dose of methadone. Separate physician order must be written for drip taper.
4. Begin NAS scoring q 6 hours
5. PRN morphine rescue dosing may be ordered (indication NAS >8 unresponsive to non-pharmacologic interventions). PRN benzodiazepines should not be ordered to treat withdrawal symptoms or elevated NAS scores.

The Epic order panel (low, intermediate, high) for neonatal methadone dose taper will default to a 48hr duration for each step of the taper.

- For NAS scores consistently < 8 over the last 24 hours, the dose may be tapered early, by advancing to the next dose step.
- If NAS scores average 8, do not taper early and continue with planned wean.
- Some steps may need to be continued longer than the default 48 hours.
- NAS scores consistently > 8 indicate withdrawal, and rescue doses of morphine may be given (benzodiazepines should not be used).
- For NAS scores consistently >12, the methadone dose may need to be increased by 10%, or the previous step of the taper resumed. Do not increase the methadone dose without attending physician or fellow approval.

  Changes to the taper schedule should be discussed by the medical team (including input from pharmacy and bedside nursing) during daytime rounds.

Taper for ≥5 to 9 days of opioid infusion

	Methadone low dose	**# of Doses**
1	Methadone 0.1 mg/kg (_____mg) buccal q6hr	8
	➢ After dose # 2, MD to order decrease of opioid infusion rate by 50% of current dose	
	➢ After dose #3, MD to order decrease of opioid infusion rate by another 50% of current dose	
	➢ After dose #4, MD to order DC of opioid infusion	
2	Methadone 0.1 mg/kg (_____mg) buccal q8hr	6
3	Methadone 0.08 mg/kg (_____mg) buccal q8hr	6
4	Methadone 0.06 mg/kg (_____mg) buccal q8hr	6
5	Methadone 0.06 mg/kg (_____mg) buccal q12hr	4
6	Methadone 0.04 mg/kg (_____mg) buccal q12hr	4
7	Methadone 0.04 mg/kg (_____mg) buccal q24hr	2

Taper for ≥ 10 to 28 days of opioid infusion

Taper step #	**Methadone intermediate dose**	**# of Doses**
1	Methadone 0.15 mg/kg (_____mg) buccal q6hr	8
	➢ After dose # 2, MD to order decrease of opioid infusion rate by 50% of current dose	
	➢ After dose #3, MD to order decrease of opioid infusion rate by another 50% of current dose	
	➢ After dose #4, MD to order DC of opioid infusion	
2	Methadone 0.15 mg/kg (_____mg) buccal q8hr	6
3	Methadone 0.13 mg/kg (_____mg) buccal q8hr	6
4	Methadone 0.1 mg/kg (_____mg) buccal q8hr	6
5	Methadone 0.08 mg/kg (_____mg) buccal q8hr	6
6	Methadone 0.06 mg/kg (_____mg) buccal q8hr	6
7	Methadone 0.05 mg/kg (_____mg) buccal q8hr	6
8	Methadone 0.05 mg/kg (_____mg) buccal q12hr	4
9	Methadone 0.05 mg/kg (_____mg) buccal q24hr	2
10	Discontinue methadone and continue to score NAS x 72 hours	

Taper for >28 days of opioid infusion

Taper step #	Methadone high dose	# of Doses
1	Methadone 0.2 mg/kg (_____mg) buccal q6hr	8
	➢ After dose # 2, MD to order decrease of opioid drip rate by 25% of current dose	
	➢ After dose #4, MD to order decrease of opioid drip by 50% of current dose	
	➢ After dose #6, MD to order decrease of opioid drip by another 50% of current dose	
	➢ After dose #8, MD to order DC of opioid infusion	
2	Methadone 0.2 mg/kg (_____mg) buccal q8hr	6
3	Methadone 0.18 mg/kg (_____mg) buccal q8hr	6
4	Methadone 0.16 mg/kg (_____mg) buccal q8hr	6
5	Methadone 0.14 mg/kg (_____mg) buccal q8hr	6
6	Methadone 0.12 mg/kg (_____mg) buccal q8hr	6
7	Methadone 0.1 mg/kg (_____mg) buccal q8hr	6
8	Methadone 0.08 mg/kg (_____mg) buccal q8hr	6
9	Methadone 0.06 mg/kg (_____mg) buccal q8hr	6
10	Methadone 0.04 mg/kg (_____mg) buccal q12hr	4
11	Methadone 0.04 mg/kg (_____mg) buccal q24hr	2
12	Discontinue methadone and continue to score NAS x 72 hours	

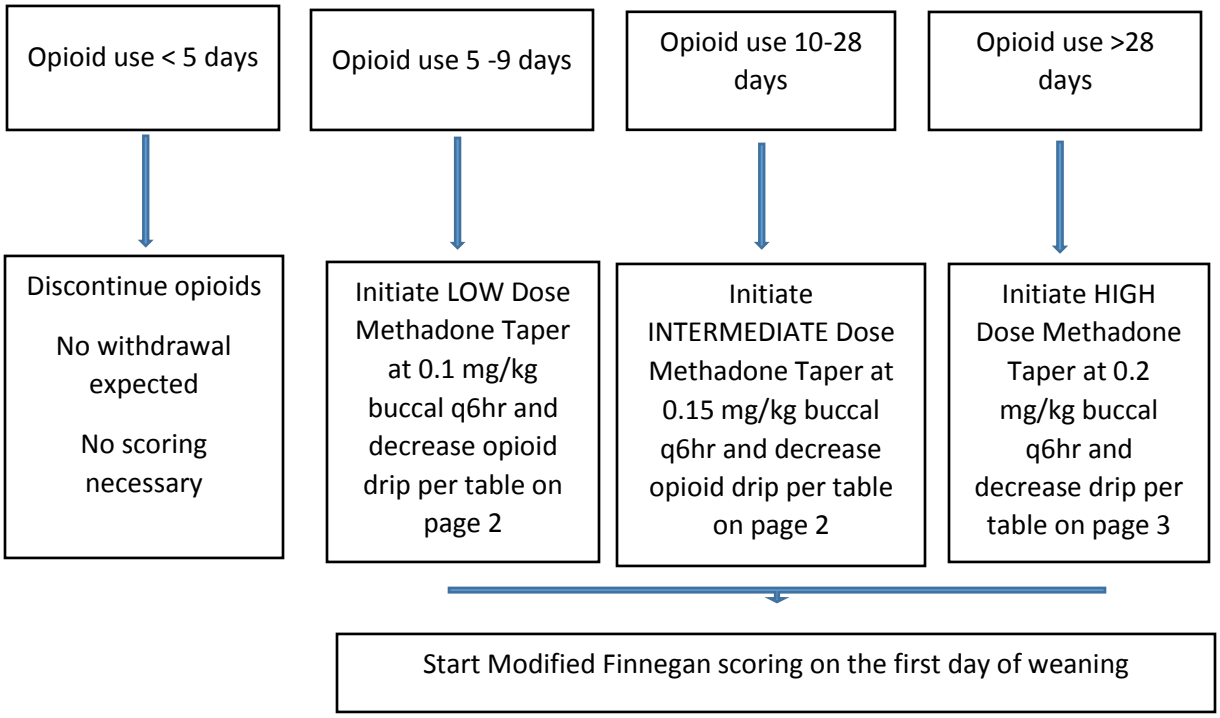
NAS scoring and withdrawal signs:

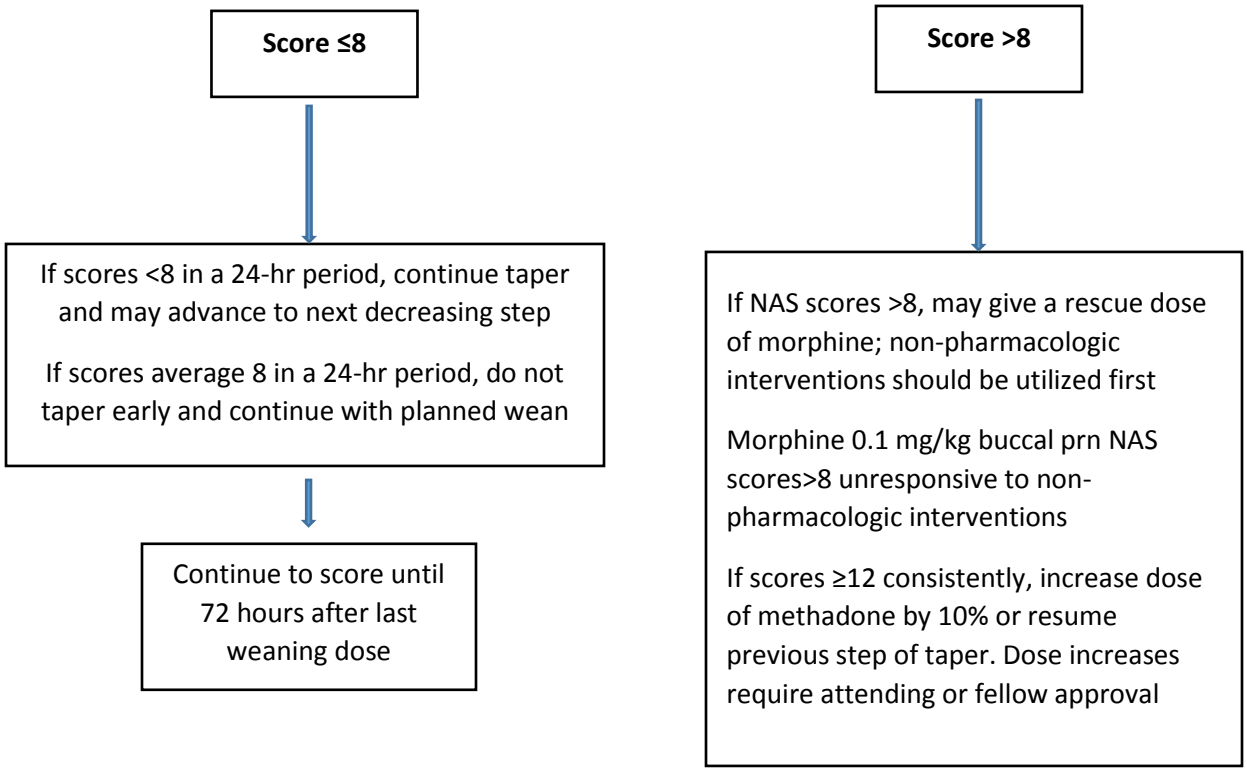
- The Modified Finnegan scoring system should be used to assess withdrawal.
- Q6 hour NAS Scoring should begin when the methadone taper is ordered.
- NAS scoring should continue for 72 hours after the taper is complete.

Withdrawal Signs:

Neurological	Gastrointestinal	Autonomic
• Irritability • Increased wakefulness • Tremors, seizures • Increased muscle tone • Hyperactive reflexes • Frequent yawning • Sneezing	• Poor feeding • Uncoordinated and constant sucking • Vomiting • Regurgitation • Loose/watery stools • Dehydration	• Sweating • Nasal stuffiness • Fever • Temperature instability • Tachypnea • Mottling of skin

Methadone Tapering Guidelines for Iatrogenic Opioid Exposure in the NICU





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