Treatment of Iatrogenic Opiate Withdrawal in the NICU

*East Bay Newborn Specialists Guideline*

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**Background:**

Neonates and young infant patients often require prolonged treatment with opiates for analgesia and sedation following surgical procedures. Drug withdrawal when the opiate is discontinued is significantly correlated with both the dose and duration of opiate exposure. It has been reported that children receiving fentanyl for more than 5 days have a greater than 50% chance of experiencing withdrawal and that the risk for withdrawal increases to 100% when receiving an infusion for 9 days or longer. Continuous opiate infusions can be gradually weaned, or a long acting opiate such as methadone can be used. The benefit of using methadone includes its oral bioavailability and long half-life (15-60 hrs. in children) that allows for long dosing intervals. A tapering protocol using methadone provides a standardized practice for weaning, consistent dosing calculations, attention to withdrawal symptoms, and potentially fewer days of opiate use. **Because of the risk of accumulation and potential toxicity, the methadone-dosing interval should be increased after 48 hours of therapy.**

Our guideline is intended for neonatal patients who have received a continuous infusion of fentanyl or morphine for greater than 7 days and do not have ongoing painful stimuli or a condition that requires continuation or escalation of opioid dose to adequately manage pain before weaning.

**Risks of opiate withdrawal associated with duration of exposure:**

- Low risk: < 5 days
- Moderate risk: 5-9 days
- High risk: ≥ 10 days or cumulative fentanyl dose of 1500 -2499 micrograms/kg of fentanyl or opioid equivalent
- Very high risk: ≥ 28 days or a cumulative fentanyl dose of greater than or equal to 2,500 micrograms μg/kg or opioid equivalent

**Opiate weaning schedule:**

*If patient received either a morphine or fentanyl continuous infusion of greater than 7 days without weaning the dose:*

- Use the current 1-hr dose of morphine or fentanyl to convert an equal dose of methadone
- Using patient’s weight, calculate total hourly fentanyl dose received (micrograms/hr to mg/hr), and convert to the total daily fentanyl or morphine dose (mg/day)
- Include bolus doses of morphine or fentanyl received by the patient in addition to a continuous drip

Convert to an equivalent dose of PO methadone from IV fentanyl or morphine using a conversion of:
IV fentanyl 0.001 mg
PO methadone 0.1 mg

IV morphine 0.1 mg
PO methadone 0.1 mg

If patient received routine po morphine of greater than 7 days without weaning the dose:

Use the current daily dose of morphine to convert to an equal dose of methadone
Convert to an equivalent dose of PO methadone from PO morphine using a conversion of:

PO morphine 0.3 mg
PO methadone 0.1 mg

Tapering steps:

Use current hourly dose of morphine or fentanyl to convert to an equivalent dose of methadone

- Day 1-2 Give determined methadone dose orally every 6 hrs X 48 hrs.
  - Simultaneously, reduce the morphine or fentanyl drip infusion as follows:
    - After 2nd dose of methadone, decrease opiate infusion to 50% of initial dose (dose just prior to starting the wean)
    - After 3rd dose of methadone, decrease opiate infusion to 25% of initial dose
    - After the 4th methadone dose, discontinue opiate infusion.
    - Note: if patient has received 4 weeks or more of an opiate infusion, then decrease opiate infusion to 75% of initial dose after the 2nd dose of methadone. After 4th dose of methadone, decrease opiate infusion to 50% of initial dose. After 6th dose of methadone, decrease opiate infusion to 25% of current dose. After 8th methadone dose, discontinue opiate infusion.
- Day 3-4 give original daily dose every 8 hrs X 48 hrs
- Day 5-6 decrease to 80% original daily dose and give orally every 8 hrs X 48 hrs
- Day 7-8 give 80% original daily dose orally every 12 hrs X 48 hrs
- Day 9-10 decrease to 60% original daily dose and give orally every 12 hrs X 48 hrs
- Day 11-13 give 60% original daily dose orally every 24 hrs x 48 hrs
- Day 14-15 give 40% original daily dose orally every 24 hrs x 48 hrs
- Day 16-17 give 20% original daily dose orally every 24 hrs x 48 hrs
- Day 18 - discontinue methadone

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**Example**: A 5 kg child receiving a continuous morphine drip at 0.05mg/kg/hr (0.25mg/hr)

Conversion: \[
\frac{\text{morphine} \ 0.1\text{mg/kg}}{\text{methadone} \ 0.1\text{mg/kg}} = \frac{0.25\text{mg/hr}}{X}
\]

\[X = 0.25\text{mg}\]

Day 1-2, give methadone .25mg PO every 6 hrs X 48 hrs
   Daily dose = 1.0mg

   After 2\textsuperscript{nd} dose of 0.25 mg methadone, decrease morphine drip to 0.025mg/kg/hr
   After 3\textsuperscript{rd} dose of 0.25mg methadone, decrease morphine drip to 0.01 mg/kg/hr
   After 4\textsuperscript{th} dose of 0.25 mg methadone, discontinue morphine drip

Day 3-4, give methadone 0.25mg PO every 8 hrs X 48 hrs
   Daily dose = 0.8mg

Day 5-6, give methadone 0.20 mg PO every 8 hrs X 48 hrs
   Daily dose = 0.6mg

Day 7-8, give methadone 0.20 mg PO every 12 hrs X 48 hrs
   Daily dose = 0.4mg

Day 9-10, give methadone 0.15 mg PO every 12 hrs X 48 hrs
   Daily dose = 0.2mg

Day 11-13, give methadone 0.15mg PO every 24 hrs X 48 hrs

Day 14-15, give methadone 0.1mg PO every 24 hrs x 48 hrs

Day 16-17 give methadone 0.05mg PO 20% every 24 hrs x 48 hrs

Day 18 - discontinue methadone

**Note:**
- Breakthrough withdrawal symptoms/pain may require prn doses of morphine sulfate 0.05 mg/kg/dose IV/PO
- If converting from IV methadone to PO methadone, convert by using a IV: PO methadone ratio of 1:2
- Enteral dosing of methadone is preferred.

**The tapering schedule should be individualized according to the patient’s individual responses and WAT (Withdrawal Assessment Tool) scores.** WAT scores must be documented in the nurse’s flow sheet every 4 hours.

- WAT score under 3 indicates that the patient can continue with opiate weaning.
- WAT score of 3 or above indicates that the patient may be experiencing withdrawal symptoms and may not be ready for opiate weaning.
References:

Galinkin, J et al. Recognition and Management of Iatrogenically Induced Opioid Dependence and Withdrawal in Children. Pediatrics 2014; 133;152


University of Minnesota Amplatz Children’s Hospital Opiate Weaning Guideline