Dell Children's Medical Center Pediatric Guideline

Title: Pediatric Opioid, Benzodiazepine, and Alpha Agonist Weaning Guideline

Purpose

To outline the recommended dosing conversion from opioid, benzodiazepine, and alpha-agonist continuous infusions to methadone, lorazepam, and clonidine and recommended weaning plan.

Personnel Affected

Authorized Prescribing Practitioners, Pharmacists, and Registered Nurses

Guidelines

OPIOIDS AND BENZODIAZEPINES

Duration of Methadone and Lorazepam Wean Based on Duration of Infusion

≤ 3 days: No taper necessary

4 days: Discontinue infusion without a wean or wean infusion over 24-36 hours. Monitor for symptoms of withdrawal. If symptoms occur, begin "short course" weaning plan.

5-13 days: Start a "short course" methadone/lorazepam wean. Start methadone and lorazepam 1-2 days prior to discontinuing infusions. Decrease opioid and benzodiazepine infusions by 25% with the 2nd dose of methadone and lorazepam, respectively. Continue to decrease infusions by 25% (of starting rate) every 6 hours. Alternate timing of methadone and lorazepam doses. Wean methadone and lorazepam daily until off. See below.

≥ 14 days: Start a "long course" methadone/lorazepam wean. Follow same protocol as for the "short course" wean; however wean doses every other day until off. Alternate methadone and lorazepam weaning steps daily. See Below.

Conversion from Infusions to Methadone and Lorazepam

*May begin as IV doses if NPO, however enteral administration is preferred

*PO designates enteral route, NG/NJ are acceptable

Opioid conversion plan:

Calculate starting methadone dose:

Fentanyl: Multiply current fentanyl drip rate (mcg/kg/h) X 0.05 = _____ mg/kg/dose methadone q6h (max initial dose 0.2 mg/kg/dose q6h AND max 10 mg q6h)

Morphine: Current morphine drip rate (mg/kg/h) = _____ mg/kg/dose methadone q6h (max initial dose 0.2 mg/kg/dose q6h AND max 10 mg q6h)

Benzodiazepine conversion plan:

Calculate starting lorazepam dose:

Midazolam: Multiply current midazolam drip rate (mg/kg/h) X 0.5 = _____ mg/kg lorazepam q6h (max initial dose 0.2 mg/kg/dose q6h AND max 4 mg q6h)

Weaning Methadone and Lorazepam

Once stable on methadone and/or lorazepam for 24 h with no withdrawal symptoms, wean methadone and lorazepam as follows.

Methadone

Short Course Methadone Wean (wean every day)

Step 1- Starting dose of methadone PO q6h x4 doses (see above calculation)
Step 2- Wean to 80% of starting dose PO q6h x4 doses
Step 3- Wean to 80% of starting dose PO q8h x3 doses
Step 4- Wean to 80% of starting dose PO q12h x2 doses
Step 5- Wean to 80% of starting dose PO q24h x1 dose
Step 6- If each dose is ≤0.1 mg/kg, discontinue methadone. If not, wean methadone dose by ~20% (of starting dose) each day until ≤0.1 mg/kg/dose Q24h x1 dose (last step may be an ~10% wean). Then discontinue methadone.

Long Course Methadone Wean (wean every *other* day)

Step 1- Starting dose of methadone PO q6h x8 doses (see above calculation)
Step 2- Wean to 80% of starting dose PO q6h x8 doses
Step 3- Wean to 80% of starting dose PO q8h x6 doses
Step 4- Wean to 80% of starting dose PO q12h x4 doses
Step 5- Wean to 80% of starting dose PO q24h x2 doses
Step 6- If each dose is ≤0.1 mg/kg, discontinue methadone. If not, wean methadone dose by ~20% (of starting dose) every other day until ≤0.1 mg/kg/dose Q24h x2 doses (last step may be an ~10% wean). Then discontinue methadone.

Lorazepam

Short Course Lorazepam Wean (wean every day)

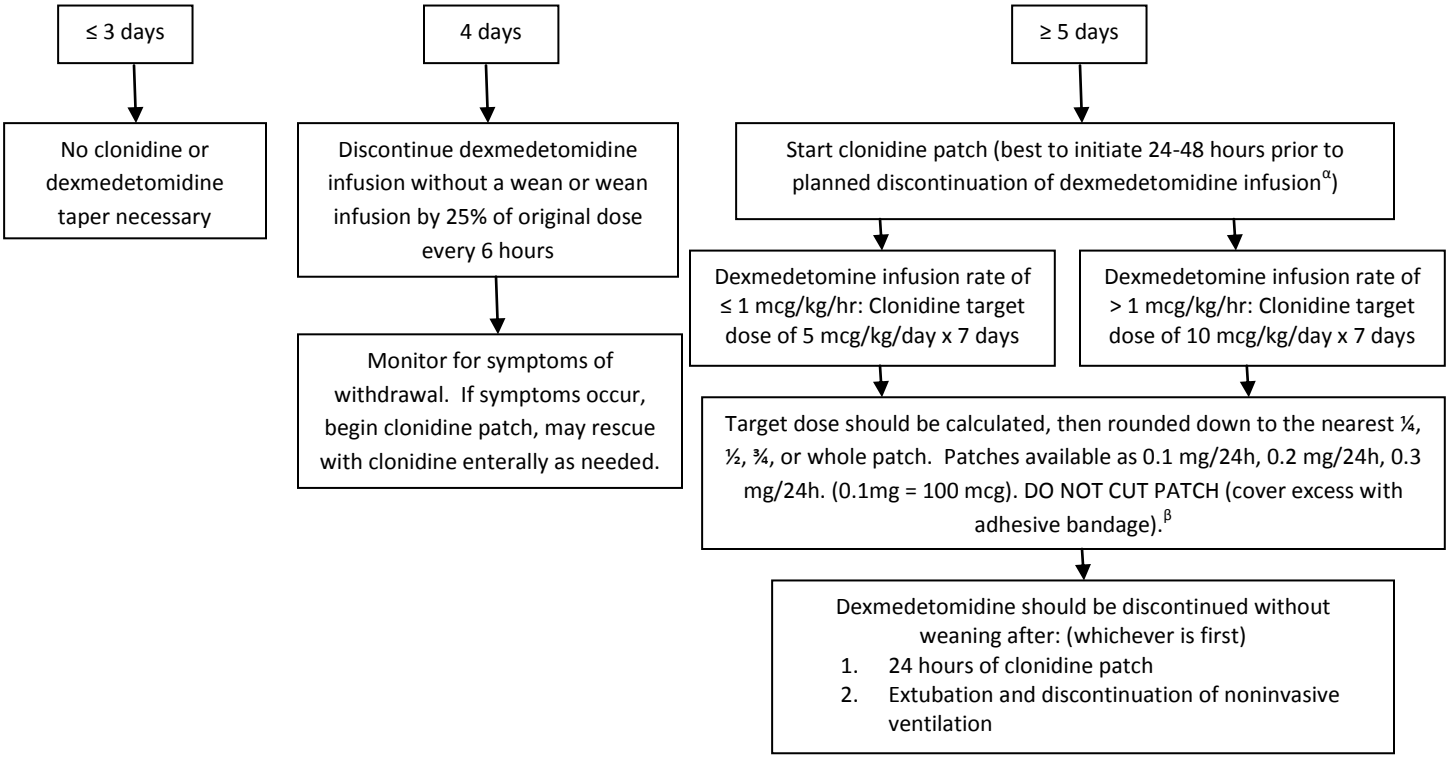
Step 1- Starting dose of lorazepam PO q6h x4 doses (see above calculation)
Step 2- Wean to 80% of starting dose PO q6h x4 doses
Step 3- Wean to 80% of starting dose PO q8h x3 doses
Step 4- Wean to 80% of starting dose PO q12h x2 doses
Step 5- If each dose is ≤0.05 mg/kg, discontinue lorazepam. If not, wean lorazepam dose by ~20% (of starting dose) each day until ≤0.05 mg/kg/dose Q12h x2 doses (last step may be an ~10% wean). Then discontinue lorazepam.

Long Course Lorazepam Wean (wean every *other* day)

Step 1- Starting dose of lorazepam PO q6h x8 doses (see above calculation)
Step 2- Wean to 80% of starting dose PO q6h x8 doses
Step 3- Wean to 80% of starting dose PO q8h x6 doses
Step 4- Wean to 80% of starting dose PO q12h x4 doses
Step 5- If each dose is ≤0.05 mg/kg, discontinue lorazepam. If not, wean lorazepam dose by ~20% (of starting dose) every other day until ≤0.05 mg/kg/dose Q12h x4 doses (last step may be an ~10% wean). Then discontinue lorazepam.

ALPHA AGONISTS

Clonidine Management Based on Duration of Dexmedetomidine Infusion



[α]Clonidine patch may take 2-3 days to reach steady state concentrations
[β]If patch must be removed or falls off at any point, request a replacement patch from pharmacy to complete duration of therapy.

MANAGEMENT OF EXCESSIVE SEDATION AND WITHDRAWAL BASED ON PHARMACEUTICAL CLASS

Methadone and/or Lorazepam ONLY

Excessive Sedation

- If excessive sedation is apparent on clinical assessment after beginning methadone and/or lorazepam, hold the next dose x1, then proceed to the next step on the weaning plan.

Withdrawal Symptoms

- Opioid withdrawal symptoms include: Gastrointestinal (diarrhea, vomiting, feeding intolerance), central nervous system (tremors, seizures, agitation, insomnia, yawning, sneezing), and sympathetic hyperactivity / autonomic dysfunction (tachycardia, diaphoresis, hypertension, tachypnea, nasal stuffiness, hyperpyrexia)

- Benzodiazepine withdrawal symptoms include: Central nervous system (agitation, restlessness, irritability, delirium, hallucinations, seizures) and sympathetic hyperactivity (tachycardia, hypertension, tachypnea, hyperpyrexia)

- Management:
  1. If WAT-1 score ≥3*and assessment consistent with withdrawal, give morphine 0.05-0.1 mg/kg (max 5 mg) IV x1. Reassess WAT-1 score in 1 hour.
  2. If WAT-1 score still ≥3* and assessment consistent with withdrawal, give lorazepam 0.05-0.1 mg/kg (max 4 mg) IV x1. Reassess WAT-1 score in 1 hour.
  3. If WAT-1 score still ≥3* and assessment consistent with withdrawal, give morphine 0.05-0.1 mg/kg (max 5 mg) IV x1. Reassess WAT-1 score in 1 hour.
  4. If patient requiring greater than 3 rescue doses of morphine and/or lorazepam in a 12 hour period, resume previous dosage on the weaning plan (or increasing dose 20% if on Step 1). Resume wean when WAT-1 score <3 OR withdrawal symptoms have been resolved x24 hours.

  - *Physician may choose higher WAT-1 score if patient has preexisting condition such as baseline hypertonia. See “DCMC WAT-1 Guidelines”.

Clonidine ONLY

Excessive Sedation

- If excessive sedation due to dexmedetomidine or clonidine is apparent on clinical assessment after beginning clonidine, perform the following in a stepwise manner:
  1. Discontinue dexmedetomidine infusion, if still infusing
  2. Remove clonidine patch (Note: it may take time for concentrations to decline)
  3. Reduce the dosing of or discontinue concomitant sedation

Withdrawal Symptoms

- Alpha-agonist withdrawal symptoms include: rebound hypertension, tachycardia, agitation, insomnia

- If withdrawal due to dexmedetomidine or clonidine is apparent on clinical assessment, perform the following in a stepwise manner:
  1. Give clonidine enterally 2 mcg/kg x1 (up to Q6h PRN) [If clonidine is being used frequently, wean clonidine by 25% of dosing daily until off.]
  2. Start clonidine doses as recommended above based on dexmedetomidine infusion rate, if not on clonidine
  3. If already on clonidine and greater than 2 rescue doses needed in a 12 hour period, increase clonidine patch dose by 25%
  4. If withdrawal symptoms not controlled, restart dexmedetomidine infusion

Methadone, Lorazepam, and Clonidine

Excessive Sedation

- If excessive sedation is apparent on clinical assessment after beginning methadone, lorazepam, and/or clonidine, hold the next dose of methadone and/or lorazepam x1, then proceed to the next step on the weaning plan. If excessive sedation continues, refer to the stepwise "Clonidine ONLY Excessive Sedation" management above.

Withdrawal Symptoms

- There is considerable overlap in the withdrawal symptoms of opioids, benzodiazepines, and alpha agonists (see the symptoms associated with each above).

- Management:
  1. If symptoms isolated to rebound hypertension and tachycardia, refer to the "Clonidine ONLY Withdrawal Symptoms" management above.
  2. For other symptoms of withdrawal, refer to the "Methadone and/or Lorazepam ONLY Withdrawal Symptoms" management above.

References

1. Bowens CD, et al. A trial of methadone tapering schedules in pediatric intensive care unit patients exposed to prolonged sedative infusions. Pediatr Crit Care Med. 2011;12(5):504-511.
2. Franck LS, Harris SK, Soetenga DJ, Amling JK, Curley MAQ. The withdrawal assessment tool – version 1 (WAT-1): an assessment instrument for monitoring opioid and benzodiazepine withdrawal symptoms in pediatric patients. Pediatr Crit Care Med. 2008;9(6):573-580.
3. Franck LS, Scoppettuolo LA, Wypij D, Curley MAQ. Validity and generalizability of the withdrawal assessment tool-1 (WAT-1) for monitoring iatrogenic withdrawal syndrome in pediatric patients. Pain. 2012;153:142-148.
4. Johnson PN, Boyles KA, Miller JL. Selection of the initial methadone regimen for the management of iatrogenic opioid abstinence syndrome in critically ill children. Pharmacotherapy. 2012;32(2):148-157.
5. Kanwalijeet JS, et al. Tolerance and withdrawal from prolonged opioid use in critically ill children. Pediatrics. 2010;125:e1208-e1225.
6. Lugo RA, et al. Enteral methadone to expedite fentanyl discontinuation and prevent opioid abstinence syndrome in the PICU. Pharmacotherapy. 2001;21(12):1566-1573.
7. Robertson RC, Darsey E, Fortenberry JD, Pettignano R, Hartley G. Evaluation of an opiate-weaning protocol using methadone in pediatric intensive care unit patients. Pediatr Crit Care Med. 2000;1:119-123.
8. Tobias JD. Tolerance, withdrawal, and physical dependency after long-term sedation and analgesia of children in the pediatric intensive care unit. Crit Care Med. 2000;12:2122-2132.
9. Sica DA. Transdermal clonidine: therapeutic considerations. J Clin Hypertens. 2005;7:558–562.
10. Burbano NH, et al. Discontinuation of prolonged infusions of DEX in critically ill children with heart disease. Intensive Care Med (2012) 38:300–307.
11. Gupta P, et al. Safety and efficacy of prolonged DEX use in critically ill children with heart disease. Pediatr Crit Care Med 2012; 13:660–666.
12. Kukoyi AT, Coker SA, Lewis LD, Nierenberg DW. Two cases of acute DEX withdrawal syndrome following prolonged infusion in the intensive care unit: Report of cases and review of the literature. Human and Experimental Toxicology 2013. 32(1) 107–110

Updated August 2014