A toddler recovering from surgery for complex congenital heart disease and iatrogenic drug dependence: "He looks so comfortable – should I wean his opioids by 50%?"

Presenters: Allison M. Fernandez, MD
All Children's Hospital JHM
Johns Hopkins Medicine
St. Petersburg, FL

Constance L. Monitto, MD
Charlotte Bloomberg Children's Center
Johns Hopkins University School of Medicine
Baltimore, MD

Goals:

1. Review risk factors for iatrogenic drug dependence, tolerance, and withdrawal
2. Identify assessment methods to diagnose withdrawal
3. Discuss medication weaning strategies
4. Consider confounding variables that impact the management of weaning in children with complex medical illnesses

Case Introduction:

You are consulted by the Pediatric Intensive Care Unit (PICU) to assist in iatrogenic opioid weaning for a one-month old, 5 kg male born with hypoplastic left heart syndrome. Since birth the baby has had a very complicated medical history. He underwent Stage 1 Norwood repair 15 days ago, and post-operatively required ECMO for 5 days. He has been sedated with hydromorphone and midazolam drips for the past 15 days and a dexmedetomidine drip for the past 8 days. During the course of the last 3 days he has been weaned off the dexmedetomidine.

The PICU has consulted you as they will need assistance with opioid weaning once the infant is extubated. From a cardiac standpoint the baby is doing fair. He is on a milrinone drip, lasix three times a day, and enalapril. Upon further review of his medical record, you note that the highest doses of the hydromorphone and midazolam drips were 60 mcg/kg/hr and 0.1 mg/kg/hr, respectively. The intensivist halved the hydromorphone and midazolam infusions yesterday in the hopes of getting him extubated today. He is alert, opens his eyes, and is passing his CPAP trials. According to the PICU team he is ready to be extubated and his pain score is zero. He remains NPO.

- **Is this child at risk for opioid withdrawal?**
- **How do opioid tolerance, physical dependence, and addiction differ?**
- **What are the causes of opioid tolerance?**
- **Are there strategies to decrease the development of tolerance?**

- **Is this child receiving other medications that can cause withdrawal?**

Case history, continued:

The infant tolerates extubation and you transition his hydromorphone drip to basal/bolus hydromorphone nurse-controlled analgesia (NCA), and plan to wean the continuous (basal) infusion by 25% every other day. After two days the bedside nurse tells you that she thinks the baby is withdrawing.

- **How will you assess opioid withdrawal in this infant?**
- **Are there validated assessment tools?**

Case history, continued:

You come to the bedside and find that the infant is extremely irritable. He has been having WAT-1 scores $\geq$ 3 overnight. You look at his medical record and find that his WAT scores have been elevated because of the following symptoms: hypotension, fever, sweating, and inconsolability. You talk to the primary team who feel that the baby has been doing well medically and his ECHO from one day ago was stable.

- **What changes in management might you consider?**

Case history, continued:

The following day you are again called by the PICU to come and evaluate the infant. You go to the room and note that he is not looking well. His WAT-1 scores have ranged between 3 and 6 overnight. A dopamine drip has been started, and the nurse tells you that increasing the hydromorphone basal infusion has not helped his symptoms.

- **What are your concerns now?**
- **How do you proceed with the opioid management?**

Case history, continued:

The following day you go to see the baby and find that he had emergency cardiac surgery overnight. A repeat ECHO had demonstrated a patch dehiscence and congestive heart failure. This morning he is hemodynamically stable, has just been extubated, and is doing well. His WAT scores have been < 3, and he has required only a few NCA bolus doses overnight. He will remain NPO at present awaiting a swallowing study.

- **Is the baby ready to resume opioid weaning?**
- **Since he remains NPO, how might you transition him off his intravenous opioid infusion?**
- **How will you determine his overall medication consumption?**
- **If changing medications, what role will cross-tolerance play in your recommendations?**

Case history, continued:

Over the next few days the infant remains stable, tolerating a conversion from hydromorphone to methadone. His WAT scores have remained < 3. The primary team has started ND feeds, which they are slowly advancing, but he is not tolerating the feeds very well. The PICU team is having trouble maintaining intravenous access and requests that you convert the methadone from intravenous to oral dosing. You do so but on the second day the baby starts to have symptoms of withdrawal. His WAT scores range from 1-4 and he has required several prn doses of morphine.

- **What are your concerns and considerations when transitioning from intravenous to enteral medications?**
- **Are there any adjunctive medications that you could use to "smooth" the weaning process?**

References

Anand K, Willson D, Berger J, Harrison R, Meert K, Zimmerman J, Carcillo J, Newth C, Prodhan P, Dean J, and Nicholson C. Tolerance and withdrawal from prolonged opioid use in critically ill children. Pediatrics 2010; 125(5):e1208-1225.

Galinkin J, Koh JL. Recognition and management of iatrogenically induced opioid dependence and withdrawal in children. Pediatrics 2014; 133(1):152-155.

Franck L, Harris S, Soetenga D, Amling J and Curley M. The Withdrawal Assessment Tool-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.

Ista E, van Dijk M, de Hoog M, Tibboel D and Duivenvoorden H. Construction of the Sophia Observation withdrawal Symptoms-scale (SOS) for critically ill children. Intensive Care Med 2009; 35:1075-1081.

Franck L, Scoppettuolo L, Wypij D and Curley M. Validity and generalizability of the Withdrawal Assessment Tool-1 (WAT-1) for monitoring iatrogenic withdrawal syndrome in pediatric patients. Pain 2012; 153:142-148.

Ista E, de Hoog M, Tibboel D, Duivenvoorden HJ and van Dijk M. Psychometric evaluation of the Sophia Observation withdrawal symptoms scale in critically ill children. Pediatr Crit Care Med 2013; 14(8):761-769.

Siddappa R, Fletcher J, Heard A, Kielma D, Cimino M, Heard C. Methadone dosage for prevention of opioid withdrawal in children. Paediatr Anaesth 2003; 13:805-810.

American Academy of Pain Medicine; American Pain Society; American Society of Addiction Medicine. Definitions Related to the Use of Opioids for the Treatment of Pain. Glenview, IL, and Chevy Chase, MD: American Academy of Pain Medicine, American Pain Society, American Society of Addiction Medicine; 2001.

Anand KJ, Clark AE, Willson DF, Berger J, Meert KL, Zimmerman JJ, Harrison R, Carcillo JA, Newth CJ, Bisping S, Holubkov R, Dean JM, Nicholson CE; Eunice Kennedy Shriver National Institute of Child Health; Human Development (NICHD) Collaborative Pediatric Critical Care Research Network (CPCCRN). Opioid analgesia in mechanically ventilated children: results from the multicenter Measuring Opioid Tolerance Induced by Fentanyl study. Pediatr Crit Care Med. 2013; 14(1):27-36.

Weber MD, Thammasitboon S and Rosen DA. Acute discontinuation syndrome from dexmedetomidine after protracted use in a pediatric patient. Paediatr Anaesth 2008; 18: 87–88

Darnell C, Steiner J, Szmuk P and Sheeran P. Withdrawal from multiple sedative agent therapy in an infant: is dexmedetomidine the cause or the cure? Pediatr Crit Care Med 2010; 11: e1–e3.

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; 28:2122–2132.

Hudak M, Tan R and the Committee on drugs and the committee on fetus and newborn. Neonatal Drug Withdrawal. Pediatrics 2012; 129(2): e540 -e560.

Ira J. Chasnoff, MD Prenatal Substance Exposure: Maternal Screening and Neonatal identification and management. NeoReviews 2003; 4(9): e228 -e235.

Giby K, Vaillancourt R Varughese N, Vadeboncoeur C, and Pouliot A. Use of Methadone for Opioid Weaning in Children: Prescribing Practices and Trends. Can J Hosp Pharm. 2014; 67(2):149-56.

Costello JM, Clapper TC, Wypij D. Minimizing complications associated with percutaneous central venous catheter placement in children: recent advances. Pediatr Crit Care Med. 2013; 14(3):273-83.

Tobias JD, Schleien CL, Haun SE. Methadone as treatment for iatrogenic narcotic dependency in pediatric intensive care unit patients. Crit Care Med. 1990; 18(11):1292-3.

Meyer MM, Berens RJ. Efficacy of an enteral 10-day methadone wean to prevent opioid withdrawal in fentanyl-tolerant pediatric intensive care unit patients. Pediatr Crit Care Med. 2001; 2(4):329-33.

Jeffries SA, McGloin R, Pitfield AF, Carr RR. Use of methadone for prevention of opioid withdrawal in critically ill children. Can J Hosp Pharm 2012; 65(1):12-8.

Yaster M, Kost-Byerly S, Berde C, Billet C. The management of opioid and benzodiazepine dependence in infants, children, and adolescents. Pediatrics 1996; 98(1):135-40.

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 Oct;1(2):119-23.

Agthe A, Kim G, Mathias K, Hendrix C, Chavez-Valdez R, Jansson L, Lewis T, Yaster M, Gauda E. Clonidine as an Adjunct Therapy to Opioids for Neonatal Abstinence Syndrome: A Randomized, Controlled Trial. Pediatrics 2009;123:e849–e856.

Xie H, Cao Y, Gauda E, Agthe A, Hendrix C, and Lee H. Clonidine clearance matures rapidly during the early postnatal period: a population pharmacokinetic analysis in newborns with neonatal abstinence syndrome. Journal of Clinical Pharmacology, 2011; 51:502-511

Tobias JD. Dexmedetomidine: applications in pediatric critical care and pediatric anesthesiology. Pediatr Crit Care Med. 2007; 8(2):115–131

Tobias JD. Dexmedetomidine to treat opioid withdrawal in infants following prolonged sedation in the pediatric ICU. J Opioid Manag. 2006; 2(4):201–205