Neurobiology of Neonatal Opiate Withdrawal (NOW) Identifying the Newborn Exposed Prenatally to Drugs

Maureen Shogan, MN, RNC
Deaconess Hospital
Spokane, WA
Maureen.shogan@gmail.com

Objectives

- Differentiate opiate (methadone, heroin, hydrocodone, oxycodone) withdrawal from prenatal exposure to buprenorphine (Subutex®).
- State the implication of amount of nicotine ingested in pregnancy on Neonatal Withdrawal from opiates.
- Discuss potential misinterpretations of the Finnegan Neonatal Abstinence scoring tool and definitions for scorer.
- Describe variations in pharmacologic and nursing interventions that improve care for the newborn experiencing withdrawal from opiates.
- Describe evidenced-based protocols for the management of infants exposed prenatally, that may reduce the symptoms of neonatal abstinence.

Tolerance, dependence and addiction

- Tolerance
- Dependence
- Cannot function normally without presence of the substance - manifested as a physical disturbance when the substance is removed (withdrawal)
- Addiction

Neonatal Drug Withdrawal 2012

Prescription Opiates effects on neonate
- NAS scoring
- Discharge at 3 days if no abstinence from maternal hydrocodone
- Discharge 5-7 days if no abstinence from maternal methadone

http://aappolicy.aappublications.org/cgi/reprint/pediatrics;101/6/1079.pdf
Neurobiology of NAS: Symptomatology and Management
Nourishing the Neonate Phoenix 10/8/2015 Maureen Shogan, MN, RNC

Opioid Abuse, Dependence, and Addiction in Pregnancy

Past month Non medical Use of Psychotherapeutic Drugs among persons 12 and older

Pain Killer prescriptions per 100 people

US motor vehicle traffic, poisoning and drug poisoning death rates 1980 - 2010

Number of Drug Overdose Deaths Involving Selected Drugs in Arizona 2003 - 2014
Prescription Monitoring Program interconnect

Opioid Prescriptions During Pregnancy

Rates of Opioid Prescriptions in Pregnancy 2000-07

Percentage of Drugs prescribed in AZ in 2014

Opioid Prescriptions women 15-44

Heroin Use Rising Trend

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maureen.shogan@gmail.com  Spokane, WA
NAS in Arizona

- Rate of NAS increased 235% between 2008 and 2014.
- Rate increased 27% between 2013 and 2014
- White, non Hispanic = 52% of opiate exposure cases
- Hispanics composed 28%
- Newborns exposed to cocaine dropped 76% between 08 and 14. (39% drop seen between 2013 and 2014)

Myth or Reality?
All newborns prenatally exposed to opiates will experience some degree of withdrawal symptoms

Myth or Reality?
Newborns exhibit worse withdrawal when their mothers smoke cigarettes
Relationship of Smoking and Newborn opioid withdrawal

- 131 moms
- Methadone or buprenorphine
- Self report nicotine previous 30 days
- Daily use
  - Below average 5.8
  - Average 13.6
  - Above Average 21

Jones, H.H. et al., 2013 Drug and Alcohol Dependence

Myth or Reality?

The higher the maternal dose of methadone, the worse the newborn experiences withdrawal.


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Myth or Reality?

The timing of appearance of neonatal withdrawal symptoms is dependent upon the drug, drug half life, mom’s last use and genetics.

Hydrocodone

- Analgesic
- Used for mod to severe
- Onset 10-30 minutes
- Duration

Oxycodone

- Fills receptor sites
- Dose
- Used for moderate to severe (10) pain
- Mixed with acetaminophen or aspirin
- 1.5x more potent than morphine

OxyContin

- Controlled released
- Long acting
- Dose

- Times as potent as MSContin
- Pure
- Older formulation

OxyNEO

- When mixed with water
- Released in US 8/10
- OP slightly larger, new formulation

Agonist Opiates

- Agonist
  - Morphine, hydrocodone, oxycodone activate mu and kappa receptor sites

- Agonist/antagonist
  - Nubaine activated kappa and block or have minimal effect on mu receptor sites

Methadone

- Peak effect 60 - 90 minutes

- Long acting - ½ life of 8 - 59 hours*

- Oral liquid to prevent diversion

- Used for heroin / Oxy/Hydro withdrawal

- Highly regulated by Federal government

- Also prescribed for pain

- Fast metabolizers and slow metabolizers

Myth or Reality?

There is less withdrawal in the newborn exposed prenatally to buprenorphine (Subutex®) than to methadone.

Buprenorphine (Subutex®) agonist - antagonist

- Strong affinity
- Displaces oxycodone, hydrocodone, methadone
- Not displaced by other opiates
- Slow dissociation from mu receptors
- Dosing


Figure 14-9.

Buprenorphine

- Half life of 24 to 60 hours
- Sublingual – moderate bioavailability
- Respiratory depression less likely
- No disruption in cognitive or motor
- IV – good bioavailability
- IV - Suboxone (naloxone and buprenorphine) initiates withdrawal
  - Least likely to be abused by crushing/shooting up.
- Not FDA approved for use in pregnancy.

Effects level off, as dose increases

- No increase in
  - Euphoria
  - Analgesia
  - Respiratory depression

Prenatal Exposure to methadone versus buprenorphine (Subutex®)

- 73 methadone exposed
- Maternal smoking 99%
- Peak NAS score 11.0
- Treated for NAS 57%

- 58 buprenorphine exposed
- Maternal smoking 95%
- Peak NAS score 12.8
- Treated for NAS 47%

Jones, HE et al (2010) NAS after methadone or buprenorphine exposure. NAS 761, 2030

Subutex® (monotherapy)

Poor GI bioavailability
- Fair sublingual bioavailability
- Dose 8 - 16mg
- Equal to 60mg methadone
- Dose for pain relief
  - 0.3 – 0.6 mg IM/IV
Neurobiology of NAS: Symptomatology and Management
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Multi-center Data: Birth Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Methadone N= 73</th>
<th>Buprenorphine N= 58</th>
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</thead>
<tbody>
<tr>
<td>% Treated</td>
<td>57%</td>
<td>47%</td>
</tr>
<tr>
<td>Birth Weight (gm)*</td>
<td>2878</td>
<td>3093</td>
</tr>
<tr>
<td>Length (cm)*</td>
<td>47.8</td>
<td>49.8</td>
</tr>
<tr>
<td>LOS baby (Days)</td>
<td>17.5</td>
<td>10</td>
</tr>
<tr>
<td>Length of treatment</td>
<td>9.9</td>
<td>4.1</td>
</tr>
<tr>
<td>Total amount of MS</td>
<td>10.4</td>
<td>1.1mg</td>
</tr>
<tr>
<td>NAS Peak Score</td>
<td>12.8</td>
<td>11</td>
</tr>
</tbody>
</table>


Onset & Duration of Withdrawal Symptoms

- Methadone
  - Median time to TX: 36 hours
  - Duration: up to 30 days

- Buprenorphine
  - Median time to TX: 72 hours
  - Duration: up to 28 days

- SSRI
  - Median time to TX: 36 hours
  - Duration: 2-6 days


Symptoms of NAS

- Chronically stimulated receptors now lack the opioids
- Adenyl cyclase activity increases
- Norepinephrine increases
- Storage center of dopamine releases less
- Decreased serotonin
- Increased production of acetylcholine

Physical Signs of Withdrawal

- Serotonin, norepinephrine & dopamine
  - Alertness
  - Stress
  - Insomnia

Frontal Cortex

Serotonin

Dopamine

Physical Dependence and Withdrawal
Myth or Reality?

Some signs of neonatal abstinence syndrome (NAS) may be attributed to other medical conditions, while others are ONLY seen with NAS.

Initial response to Opioid

Response to chronic opioid exposure

Locus ceruleus response to withdrawal of chronic opioid exposure

Prenatal Exposure to Opiates

- Sleep deprivation
- Excessive Crying, irritability
- Increased muscle
- Increased respiratory rate
Prenatal Exposure to Opiates
(Hydrocodone, oxycodone, methadone, buprenorphine)

- Increased need to suck
- Tremors
- Frantic movement indicated by _________________
- GI cramp – diarrhea

Neonatal Abstinence Scoring

- Finnegan 1975
- Opiate withdrawal
- Within 2 hours of delivery
- Score every 2 hours when score 8 or over
- Score every 4 hours when score 7 or less
- Score all behaviors within time period

Neonatal Abstinence Scoring (NAS)

- Low scores indicate lower risk
- Higher scores indicate a greater risk for NAS
- Duration and severity

Decreased NAS in Preterm

- Less cumulative
- Decreased transmission across the placenta
- Decreased morphine clearance
- Decreased excretion
- Decreased fatty tissues
- Decreased receptor sensitivity

Myth or Reality?

If a baby has moderate-severe undisturbed tremors, they will also get a score for disturbed moderate – severe tremors.

Myth or Reality?

The difference between mild tremors and moderate tremors is the length of time the tremors are sustained.
Myth or Reality?
Excoriation is scored when the baby’s bottom is red or there is loss of skin.

Myth or Reality?
Morphine or methadone may be used for newborns experiencing opiate, methamphetamine, or cocaine withdrawal.

Myth or Reality?
Newborns withdraw from stimulants in the same way they withdraw from opiates.

Myth or Reality?
Phenobarbital and Clonidine are used first to treat newborns with experiencing opiate withdrawal.

Myth or Reality?
Babies who are older in chronologic age should be scored differently on the NAS.
Myth or Reality?

Mother’s should not breast feed or give their baby breast milk when their baby is experiencing withdrawal symptoms.

Use of Breast milk  AAP  9/13

- Methadone
- Do not suddenly withdraw breast milk

Can moms taking buprenorphine breast feed?

- Remember Bioavailability?
- How is drug best absorbed into blood stream?
- Breast milk is processed in the GI tract.
- How available is buprenorphine to the newborn in the GI tract?

Prenatal Exposure to Drugs

- Environmentally sensitive
- Unable to attend
- Parental over stimulation
- Lack of understanding
- Respect for the baby


Promote Stability

Parents
- Teach signs of stress and stability
- Interpret their baby’s cues
- Provide a parent friendly area
- Promote and Facilitate Skin to Skin

Minimize Noise

Monitor and muffle sounds
Walk softly and without commotion
- Prepare articles away from bedside
- Protected sleep area
- Avoid visiting with your colleague

Promote Stability

Positioning
- Provide boundaries
- Swaddling
- Sucking to self calm
- ALWAYS respond to cries

Skin to Skin - Kangaroo Care

- Infants Slept Longer
- Moms felt positive about their contribution
- Hiles, 2011

Minimize Motoric stress

- Limp extremities
- Extension of extremities
- Provide Flexion to minimize extension
Promote Flexion for High Tone Babies

Meet metabolic demands and Promote growth

- Breast feed ad lib
- Demand feeding
- Frequent feeds
- High calorie formula
- Partially hydrolyzed protein formula - gas.

Inpatient Pathway for the Evaluation/Treatment of Infants with NAS

General
- Behavioral infant attachment is important. Breastfeeding is encouraged when appropriate.
- Caloric needs may be as high as 150-250 cal/kg/day.
- Frequent small volumes of hypocaloric (12-25 cal/kg) feeding may help minimize hunger and improve growth.
- Hypocaloric formula may improve feeding intolerance.

Encourage breastfeeding for mothers engaged in the following
- Stabilized Methadone maintenance or Suboxone (buprenorphine) regardless of dose
- Substance abuse treatment program who have the endorsement of their counselor/treatment provider
- Plans to continue in substance abuse treatment in the postpartum period
- Positive maternal/some neonatology testing at delivery, except for prescribed medications
- History of adverse outcomes

Breastfeeding is discouraged or contraindicated in the following
- No maternal care


Music Therapy

- Mom’s singing lullaby to baby improved
- HR
- Sucking
- Feeding behaviors
- Ocean sounds improved
- Quiet alert
- O2 sats
- Loewy (2013)

Massage Therapy

- Better weight gain
- Decreased stress cues
- Better neurodevelopmental outcome 2 yrs


- Maguire, D., Cline, G.J., Parnell, L & Tai, C. (2013). Validation for the Finnegan Neonatal abstinence syndrome Tool-Short Form, Advances on Neonatal Care, 13(4), 430-7. USFl