Neonatal Abstinence Syndrome

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https://www.youtube.com/watch?v=tk2hOYUpKVI&feature=youtu.be
Dramatic Increases in Maternal Opioid Use and Neonatal Abstinence Syndrome

The use of opioids during pregnancy can result in a drug withdrawal syndrome in newborns called Neonatal Abstinence Syndrome (NAS), which causes lengthy and costly hospital stays. According to a new study, an estimated 21,732 babies were born with this syndrome in the United States in 2012, a 5-fold increase since 2000.

Every 25 minutes, a baby is born suffering from opioid withdrawal.

Average Length or Cost of Hospital Stay

<table>
<thead>
<tr>
<th>Newborns</th>
<th>With NAS</th>
<th>W/O NAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days</td>
<td>16.9</td>
<td>2.1</td>
</tr>
<tr>
<td>Cost ($66,700)</td>
<td>$3,500</td>
<td></td>
</tr>
</tbody>
</table>

NAS and Maternal Opioid Use on the Rise

30%, 68%, and 91% of NAS infants required pharmacologic treatment in separate studies

Mean length of hospital stay: 23 days

Mean hospital charge: $93,400 per infant

Total cost: $1.5 billion

Medicaid is most common payer ($1.2 billion)

Estimated cost for 25 newborns (HCMC)

$1,492,000
Drug Withdrawal

Withdrawal are a set of physical and emotional symptoms that occur with a decrease in the amount or abrupt discontinuation of drugs, nicotine, alcohol or prescription medications.

Withdrawal can happen after prolonged exposure to substances such as:
Caffeine
Nicotine
Prescription medications (anti depressants) SSRI
Opioid’s ; Methadone, fentanyl, oxycodone, heroin etc
Benzodiazepines; Valium, Ativan, Xanax, etc
Alcohol
2016 HCMC had

- 44 opiate exposed newborns were born here in 2016 (total births 2021) Illicit or prescribed
- 25 of those newborns needed Medical management with morphine, some with additional phenobarbital
- Of the 25 medically managed NAS kiddos there were 746 NBICU days with an average length of stay of 31 days.
- 746 NBICU days average $2000.00/day
Neonatal Abstinence Syndrome
Newborn Withdrawal

Newborn Withdrawal

Neonatal abstinence syndrome occurs after baby is born and the umbilical cord is cut. The steady supply of medications or substances is abruptly stopped.

Symptoms present 48-72 hours after birth.
Babies are NOT born addicted!!!
What are symptoms of withdrawal?

Baby unable to stop crying
Jitteriness and tremors.
Feeding problems and poor weight gain.
Fast breathing.
Difficulty sleeping.
Tense arms and legs.
Vomiting, diarrhea and skin breakdown from diaper changes or frequent stools.
Gabapentin

- Street name; Morontin or gabbies
- Prescribed as anti-epileptic, neuropathic pain, nerve pain. Off label use bipolar, insomnia, and hyperemesis in pregnancy.

Gabapentin may provide a euphoric “high” that may be similar to that produced by marijuana, bringing an increase in sociability and inducing feelings of calm to recreational users.
Gabapentin withdrawal case study

Maternal – 31 year old, parapalegic
Gabapentin 600 mg TID prescribed since MVA at age 20 and sustained a C6-7 incomplete transection injury to spinal cord. Medications prescribed for neuropathic pain and prescriptions continued during pregnancy. Baclofen 30 mg QID, oxybutynin 10 MG/day

Newborn
Symptoms associated with drug withdrawal by 24 hours of life including;
- sneezing
- irritability
- jitteriness
- and loose stools.

The overall clinical picture raised initial concerns for possible withdrawal syndrome from prolonged in utero gabapentin exposure.

- Treatment started at 36 hours with Lorazepam, at 0.5 mg/kg every 6 hours, after withdrawal scores ranged from 15 to 19
- Scores remained elevated, and needed an escalated dose of Ativan on day of life 5 (.15 mg/kg every 6 hours)
- Day 6 team started gabapentin at 2.5 mg/kg every 12, increased on day 7 to 5 mg/kg. Which showed improvement in Finnegan scores once Gabapentin treatment started.
- Day 8 started weaning lorazepam. Lorazepam discontinued on day 10.
- Able to nipple all feedings by day of life 24

Pediatric Neurology 53 (2015) 445-447 Neonatal Gabapentin withdrawal Syndrome Melisa Carrasco MD, PhD, Sanajai C Rao DO, Cynthia F Bearer MD, PhD, Sripriya Sundararajan MBBS, MD
# Scoring tools

## Modified Finnegan Neonatal Abstinence Score Sheet

<table>
<thead>
<tr>
<th>System</th>
<th>Signs and Symptoms</th>
<th>Score</th>
<th>AM</th>
<th>PM</th>
<th>Currents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Nervous System Dysfunction</td>
<td>Frequent crying or grunting</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rubbing face or head against object</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rapid or shallow breathing</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Excessive highpitched cry, baby cry</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autonomic Nervous System Dysfunction</td>
<td>Dilated pupils</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poor muscle tone</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Narrowing of the eyes</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Palmar hyperextension</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild tremors when distressed</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nystagmus on eyes when disturbed</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyperactive Moro reflex</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased muscle tone</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized Nervous System Dysfunction</td>
<td>Stiff arms or legs</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inability to move extremities</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Increased reflexes</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Respiration rate &gt; 60/min</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Respiration rate &lt; 10/min</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Respiratory rate &gt; 10/min with intercostal recession</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Continuous crying</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poor feeding (milk/diluted milk/fruit juice)</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nasal flaring</td>
<td>2</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Tachypnea (2 times normal breathing rate)</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diaphoresis</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Loose stools (or, occasionally, vomit)</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Watery stools (water, milk, or purée)</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
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© Western Australian Centre for Evidence-Based Midwifery & Maternity Health, January 2007 (ENP07 D1MRA). All guidelines should be used in conjunction with the Disclaimer.
Non pharmacologic Comfort measures

- Loud noises increase their distress.
  - Turn down TVs and music
  - Limit loud voices
  - Dim overhead lights
- Routine is very important
- Babies will respond more positively when caregivers use soft voices and speak and move slowly.
Comfort techniques

- Mom’s not using street drugs and are HIV negative we want you to breastfeed. If taking methadone, there will be a small amount of methadone in your breastmilk, this will not hurt your baby and may help your baby withdrawal easier.

- Wrapping baby snug in a blanket.

- Feeding baby small amounts more often.
Breastfeeding is encouraged and breast practices!
Smoking and NAS

OLS and Poisson regression analyses were used to test average daily number of cigarettes smoked in the past 30 days at α = .05, adjusting for both Medication Condition and Site. Below-average cigarette smoking was defined as 6 cigarettes/day (-1 SD), average cigarette smoking as 14 cigarettes/day (Mean), and above-average cigarette smoking as 21 cigarettes/day (+1 SD). Jones et al., JAD, 2013.
Comparing Medication Assisted Treatment

- The Buprenorphine exposed babies; Required 89% less morphine to treat NAS
- Spent 43% less times in the hospital
- Spent 58% less time in the hospital being medicated for NAS
- Both medications in the context of comprehensive care produces similar maternal treatment and delivery outcomes

Jones et al., N Engl J Med. 2010
<table>
<thead>
<tr>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better retention in care</td>
<td>89% less morphine to treat neonatal abstinence syndrome,</td>
</tr>
<tr>
<td>Less slips/or relapse</td>
<td>a 43% shorter hospital stay</td>
</tr>
<tr>
<td></td>
<td>58% shorter duration of medical treatment for neonatal abstinence syndrome</td>
</tr>
<tr>
<td></td>
<td>More illicit use of opiates</td>
</tr>
</tbody>
</table>
746 NBCIU days average $2000.00/day  = $1492,000
So there are trade-offs depending on which side of the umbilical cord you work.
Only qualified doctors with the necessary DEA (Drug Enforcement Agency) identification number are able to start in-office treatment and provide prescriptions for ongoing medication. CSAT (Center for Substance Abuse Treatment) will maintain a database to help patients locate qualified doctors.

- **Complete at least 8 hours of approved training on the treatment and management of opioid-dependent patients**

- First year waivered physicians can prescribe to **30** patients concurrently (including both detoxification and maintenance) during their first year

- After the first year, they may treat up to **100** patients concurrently in each subsequent year. Minnesota currently has approximately **120** Buprenorphine waivered prescribers.
New Legislation

- August 5th Patient cap raised to 275 for addiction Medicine physicians
- July CARA act signed into law
  - Opens prescribing to ANP’s and PA’s
Management of NAS

- Baby will need to stay in the hospital a minimum of 3-5 days after birth.
- Baby watched for signs of withdrawal. Inpatient nurses will use a scoring system such as Finnegan’s.
- If baby does need medicine for withdrawal, we will then treat your baby in the Neonatal Intensive Care Unit (NICU).
- Additional risk factors are likely to make for a longer hospitalization such as you smoking cigarettes, or taking benzodiazepines such as Ativan, Clonazepam, Xanax, and Valium, Gabapentin during your pregnancy.
Medical management of Neonatal Opiate Withdrawal

If 3 scores are >8 or 2 >12: Begin oral morphine 0.07mg/kg/dose q 3 hours
Maximum dose of morphine 0.2mg/kg/dose q 3 hours

Wean with scores less than 6 by 0.02mg/kg/dose of Morphine

Rescue dosing is sometimes used. This is an extra dose of Morphine

If weaning fails or you reach maximum dose of Morphine, consider adding clonidine or phenobarbital.

When making decisions on weaning of morphine, doctors will consider what the nurses and the parents observe and daily exams into decision making.
Buprenorphine for NAS treatment

- 63 infants enrolled in study
- 33 received Morphine for NAS treatment
- 30 received Buprenorphine
- Mothers were on methadone at a mean dose of 135
<table>
<thead>
<tr>
<th>Buprenorphine</th>
<th>Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median duration of treatment 15 days</td>
<td>Median duration of treatment 28 days</td>
</tr>
<tr>
<td>Median Length of stay 21 days</td>
<td>Median length of stay 33 days</td>
</tr>
<tr>
<td>Adjunctive phenobarbital administered in 5/33 infants</td>
<td>Adjunctive phenobarbital 7/30 infants</td>
</tr>
</tbody>
</table>
- Probably no correlation unless comparing very low dose, less than 20 to 40 mg/d, to high dose, greater than 90mg/d.

- In a study by Jansoon et al in Pediatrics 2008 looking at methadone in breast milk during the first 30 days of life found no correlation between maternal methadone dose and maternal plasma level, the amount of methadone in breast milk, incidence of NAS, and infant plasma level for methadone

- The infant who clears the drug fastest appears to be at higher risk for NAS compared to infants who clear the drug more slowly
ACES

Death
Whole Life Perspective
Conception

Early Death
Disease, Disability, & Social Problems
Adoption of Health-risk Behaviors
Social, Emotional, & Cognitive Impairment
Adverse Childhood Experiences

Scientific Gaps
• **RESULTS:**
  - Sixty-six percent (n = 6015) of women reported > or = 1 ACE.
  - Teen pregnancy occurred in
    - 0 16%,
    - 1 21%,
    - 2 26%,
    - 3 29%,
    - 4 32%,
    - 5 40%,
    - 6 43%,
    - 7-8 53%

  - As the ACE score rises odds ratio rises for; family problems, financial problems, job problems, high stress and uncontrolled anger

  - The ACE score was associated with increased fetal death after first pregnancy. With each ACE score the

• **CONCLUSIONS:**
  - The relationship between ACEs and adolescent pregnancy is strong and graded. Moreover, the negative psychosocial sequelae and fetal deaths commonly attributed to adolescent pregnancy seem to result from underlying ACEs rather than adolescent pregnancy per se.
Mean length of hospital stay: 23 days

Mean hospital charge: $93,400 per infant

Total cost: $1.5 billion

Medicaid is most common payer ($1.2 billion)
Morphine Treatment for NAS

- Neonatal Morphine Solution
  - Concentration: 0.4mg/ml
  - Dosage range: 0.03-0.2mg/kg/dose every 3-24 hours

- Morphine is a pure mu receptor opioid agonist. Half-life range is 4-13 hours
  - CNS and respiratory depression
  - Sedation
  - Constipation
Clonidine

- Concentration: 20mcg/ml
- Dosage range: 1-3 mcg/kg/dose every 6 hours
- Clonidine is used as an adjunctive therapy with opiates.
- Clonidine is a central alpha 2 adrenergic receptor agonist. It reduces sympathetic outflow by decreasing central catecholamine release which is thought to palliate symptoms of autonomic over activity.
Clonidine Side Effects

- Bradycardia
- Hypotension
- Withdrawal Hypertension
Clonidine decreases the autonomic symptoms of NAS

1984 a pilot study, 7 infants, using Clonidine as a single agent for NAS

Agthe et al 2009 performed a randomized placebo controlled blinded study comparing Dilute Tincture of Opium and placebo and DTO and Clonidine

80 infants, 40 in each group

Primary outcome was the duration of opioid therapy
• The incidence of maternal opioid addiction is rising

• We cannot predict which newborns will require pharmacological treatment for opioid addiction based on the mother’s methadone dose

• BF or BM may decrease or obviate the need for NAS treatment

• AAP recommends treating opioid withdrawal with morphine or methadone

• There is more expert opinion than evidence based medicine in the treatment of NAS
Check your own bias

- Mother’s struggling with addiction and dependence already struggle with the disease of addiction.
- Lack family support, lack social support, housing problems, food insecurity, also financial struggles, and legal consequences.
- Any mother needs all the help they can get!
No mother needs additional guilt for their medical/genetic/ complications
The association between adverse childhood experiences and adolescent pregnancy, long-term psychosocial consequences, and fetal death.

Hillis SD¹, Anda RF, Dube SR, Felitti VJ, Marchbanks PA, Marks JS.
The Starfish Story

An old man was walking on the beach one morning after a storm. In the distance, he could see someone moving like a dancer. As he came closer, he saw that it was a young woman picking up starfish and gently throwing them into the ocean. “Young lady, why are you throwing starfish into the ocean?” “The sun is up, and the tide is going out, and if I do not throw them in they will die,” she said. “But young lady, do you not realize that there are many miles of beach and thousands of starfish? You cannot possibly make a difference.” The young woman listened politely, then bent down, picked up another starfish and threw it into the sea. “It made a difference for that one.”

Adapted from the original by Loren Eiseley

Life’s a Dance