Clinical Management of Neonatal Abstinence Syndrome

Tricia L. Romesberg, DNP, MSN, ARNP, CNNP
Timeline

1804: Morphine isolated
1817: Marketed as analgesic
1827: Commercial production

1853: Hypodermic needle developed

1874: Heroin synthesized
1898: Commercial production

1875: First reported case of neonatal withdrawal

1903: Morphine treatment for neonates reported

1892: Series of 12 infants, 9 died. Paregoric was tried

1937: Methadone developed
1964: Methadone maintenance treatment

1967: Buprenorphine developed
1996: Buprenorphine use in France
2002: FDA approval for opioid dependence

Opioid analgesic medications:
- Vicodine (1984)
- OxyContin (1989)
- Percocet (1999)

1971: Methadone withdrawal in 5 neonates

1997: First reported case of buprenorphine withdrawal
2001: Series of buprenorphine withdrawal in 13 infants

2002: First reported case of NAS due to oxycontin
2012: Epidemic of NAS
Incidence of NAS

• Healthcare Cost and Utilization Project (HCUP), 1999-2013
  ▫ State Inpatient Databases for 28 states

• NAS increased 300% from 1.5 per 1,000 births to 6.0 per 1,000 births

• Florida
  ▫ 2000: 0.4
  ▫ 2005: 0.9
  ▫ 2010: 4.9
  ▫ 2013: 6.3

• $1.5 billion in NAS related annual hospital charges in 2012
  ▫ Medicaid programs responsible for approximately 80%
Upstream and Downstream

- **The Spectrum of Prevention**
  - **Primary**: efforts to reduce the incidence of in-utero opioid exposure
  - **Secondary**: efforts to treat known in-utero exposure using evidence-based interventions to reduce disease severity
  - **Tertiary**: efforts to promote long-term health outcomes for children with a known in-utero opioid exposure
Evidence Based Management of NAS

Use of a stringent protocol to treat NAS, regardless of the initial opioid chosen, reduces the duration of opioid exposure and length of hospital stay.

Evidence Based Management of NAS

- Neonatology
- Nursing
- NNP/PAs
- Pharmacy
- Lactation
- Education
- Social Work
Toxicology Confirmation

Cord, urine, and meconium analysis:
• noninvasive
• inexpensive
• reproducible
• a fully automated procedure

Positive results are helpful for confirmation of symptoms, but are not used for guiding daily clinical management.

Positive results are useful when filing a report with DCF, and may present strong evidence for future custody issues.
# Drugs of Abuse

<table>
<thead>
<tr>
<th>Opioids</th>
<th>CNS Stimulants</th>
<th>CNS Depressants</th>
<th>Hallucinogens</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agonists</strong></td>
<td></td>
<td></td>
<td><strong>Indolealkylamines</strong> (LSD, psilocin, psilocybin, DMT, DET)</td>
</tr>
<tr>
<td>Morphine</td>
<td>Amphetamines</td>
<td>Alcohol</td>
<td><strong>Phenylethylamines</strong> (mescaline, peyote)</td>
</tr>
<tr>
<td>Codeine</td>
<td>Dextroamphetamine (Dexedrine)</td>
<td>Barbiturates</td>
<td><strong>Phencyclidines</strong> (MCA, MDMA, MDMA, MDEA)</td>
</tr>
<tr>
<td>Methadone</td>
<td>Methamphetamine</td>
<td>Benzodiazepines</td>
<td><strong>Inhalants</strong></td>
</tr>
<tr>
<td>Meperidine (Demerol)</td>
<td>Amphetamine sulfate</td>
<td>Other sedative-hypnotics</td>
<td><strong>Solvents and aerosols</strong> (glues, gasoline, paint thinner, cleaning solutions, nail polish remover, Freon)</td>
</tr>
<tr>
<td><strong>Oxycodone</strong> (Percodan, OxyR, Percolone, Roxicodone, Percocet, OxyContin)</td>
<td>Amphetamine congeners</td>
<td>Methaqualone (Qualude)</td>
<td><strong>Nitrites</strong></td>
</tr>
<tr>
<td>Propoxyphene (Darvon)</td>
<td>Benzphetamine (Didrex)</td>
<td>Glutethimide (Doriden)</td>
<td><strong>Nitrous oxide</strong></td>
</tr>
<tr>
<td>Hydromorphone (Dilaudid)</td>
<td>Diethylpropion (Tanautea)</td>
<td>Chlora hydrate</td>
<td><strong>Cannabinoids</strong></td>
</tr>
<tr>
<td>Hydrocodone (Lortab, Vicodin)</td>
<td>Fenfluramine</td>
<td>Cannabinoids</td>
<td><strong>Marijuana</strong></td>
</tr>
<tr>
<td>Fentanyl (Sublimaze)</td>
<td>Phendimetrazine (Adipost, Bontril, Prelu-2)</td>
<td>Marijuana</td>
<td><strong>Hashish</strong></td>
</tr>
<tr>
<td>Tramadol (Ultram, Ultracet)</td>
<td>Phentermine (Adipex-P, Zantryl)</td>
<td>Cocaine</td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>Methylphenidate (Ritalin, Concerta)</td>
<td>Methylphenidate (Ritalin, Concerta)</td>
<td></td>
</tr>
<tr>
<td><strong>Antagonists</strong></td>
<td></td>
<td></td>
<td><strong>Pemoline (Cylert)</strong></td>
</tr>
<tr>
<td>Naloxone (Narcan)</td>
<td></td>
<td></td>
<td><strong>Phenylpropanolamine</strong></td>
</tr>
<tr>
<td>Naltreone (ReVia)</td>
<td></td>
<td></td>
<td><strong>Phencyclidines</strong></td>
</tr>
<tr>
<td>Mixed Agonist-Antagonists</td>
<td></td>
<td></td>
<td><strong>Nicotine</strong></td>
</tr>
<tr>
<td>Pentazocine (Talwin)</td>
<td></td>
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<tr>
<td>Buprenorphine (Buprenex)</td>
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</tbody>
</table>

Pharmacokinetics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset, h</th>
<th>Frequency, %</th>
<th>Duration, d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin</td>
<td>24–48</td>
<td>40–80^27</td>
<td>8–10</td>
</tr>
<tr>
<td>Methadone</td>
<td>48–72</td>
<td>13–94^57</td>
<td>Up to 30 or more</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>36–60</td>
<td>22–67^46,48</td>
<td>Up to 28 or more</td>
</tr>
<tr>
<td>Prescription opioid medications</td>
<td>36–72</td>
<td>5–20^56,60</td>
<td>10–30</td>
</tr>
<tr>
<td><strong>Nonopiods</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRIs</td>
<td>24–48</td>
<td>20–30^64</td>
<td>2–6</td>
</tr>
<tr>
<td>TCAs</td>
<td>24–48</td>
<td>20–50^64</td>
<td>2–6</td>
</tr>
<tr>
<td>Methamphetamines</td>
<td>24</td>
<td>2–49^101</td>
<td>7–10</td>
</tr>
<tr>
<td>Inhalants</td>
<td>24–48</td>
<td>48^70</td>
<td>2–7</td>
</tr>
</tbody>
</table>

Pharmacokinetics

- Opiates are capable of increased permeability across the placenta –
  - low molecular weights
  - water soluble
  - lipophilic

- The combination of cocaine or heroin with methadone further increases the permeability of methadone across the placenta.

- Onset/duration/severity of NAS depends on drug types, amounts, half-lives, receptor-binding capacities, receptor affinities, placental transferability, time of last dose, duration of exposure, total accumulation of the exposure, and polysubstance drug use.
Symptoms of NAS

Central Nervous System
Irritability/Restlessness
Tremors
High-pitched cry
Hyperreflexia
Sleep disturbance
Yawning
Seizures

Gastrointestinal System
Poor feeding
Excessive sucking
Suck-swallow incoordination
Vomiting/Diarrhea
Poor weight gain
Dehydration

Autonomic Nervous System
Fever
Excessive sweating
Mottling
Tachypnea
Nasal congestion/Sneezing
Finnegan Tool

• The tool most commonly used to objectify symptoms with a scoring system.

• Pharmacologic management based on Finnegan scoring.

• Begin Finnegan scoring within 24 hours of birth for term infants with suspected or proven NAS.

• Scoring is most applicable to infants tolerating full feeds, without respiratory distress, and not experiencing pain or discomfort due to diagnoses independent of NAS.

• Record scores every 3-4 hours.
Finnegan Tool

- Scoring should be performed after feedings when infant is awake.

- The score should represent the status of the infant at the time of the assessment and during the preceding time period.

- Scoring should routinely be done by nurses trained to use the Finnegan tool.

- Dual scoring should be utilized as needed to confirm trending of scores.
Non-pharmacologic measures

- minimizing sound and light

- holding and rocking
  - Cuddler priority

- swaddling

- management of skin integrity related to:
  - perianal breakdown as a result of frequent/loose stools
  - excoriation of extremities from excessive friction caused by agitation
  - sucking blisters on hands and fingers
  - scratches to face

- physical/occupational therapy and developmental follow-up
Feeding

- Enfamil Gentlease or Similac Sensitive to minimize gastric discomfort and improve feeding intolerance

- Caloric requirements of 150-250 cal/kg/day to achieve optimal growth

- Frequent small volumes to minimize hunger and improve growth

- Breast feeding and breast milk – recommendations vary with:
  - maternal history and availability
  - types of drug exposure - confirmed and suspected
  - current maternal drug use - confirmed and suspected
  - outpatient expectations and anticipatory planning
  - social situation
  - clinician beliefs and opinions
Pharmacologic Management
Oral Morphine

• Medications will be initiated, increased, decreased, or discontinued based on Finnegan scoring.

• Start oral Morphine when 2 consecutive scores are $\geq 12$, or 3 consecutive scores are $\geq 8$.

• Starting dose is based on highest score:
  - Scores 8-10 $\rightarrow$ starting dose = 0.05 mg/kg/dose
  - Scores 11-13 $\rightarrow$ starting dose = 0.08 mg/kg/dose
  - Scores 14-16 $\rightarrow$ starting dose = 0.11 mg/kg/dose
  - Scores $>16$ $\rightarrow$ starting dose = 0.15 mg/kg/dose
Pharmacologic Management
Oral Phenobarbital

• Phenobarbital may be considered when maximum Morphine dose of 1.3 mg/kg/day is reached or 3 consecutive Morphine wean attempts have been unsuccessful.

• Phenobarbital levels are not indicated in the absence of seizures.

• Recommendations for outpatient weaning of Phenobarbital should be included in the discharge summary for the infant’s Primary Care Provider (PCP).
Management Plan for NAS

Start Finneganscoring within 24 hours of birth
Monitor score every 3–4 hours

2 Consecutive scores ≥ 12
or 3 consecutive scores ≥ 8

Yes

Is the mother on opioids?

No

Continue to monitor scores at
every 3–4 h intervals.
When scores consistently ≤ 8,
observe for 3–5 days more

Yes

Are the scores increasing?

No

Start phenobarbital: 16 mg/kg
Maintenance dose: 5 mg/kg/day
in two divided doses
Change the dose every 24–48 h
Increase/decrease the dose
by 10% or 1 mg
Monitor phenobarbital level
Add other medications, if levels
are high

Yes

Start morphine 0.05 mg/kg/dose
Increase/decrease the dose
by 10% or 0.05 mg
Change the dose every 24–48 h
Rescue dose: if scores are ≥ 12
for 2 consecutive times
Maximum dose: 1.3 mg/kg/day
Add phenobarbital/clonidine if
maximum dose reached

For scores consistently ≥ 12: increase the dose
For scores between 9 and 11: no change in the dose
For scores consistently ≤ 8: decrease the dose

Discharge Plan
Pediatrician follow-up in 2 days
Home visiting referral
Anticipatory guidance

When the infant is off morphine for 2 days,
when scores consistently ≤ 8 h for 2 days, and
when the infant is cleared medically and socially.
Discharge Criteria

- infant has not received Morphine for 48 hours;
- scores are consistently <8 for 48 hours; and,
- the infant is cleared medically and socially.
Tricia L. Romesberg, DNP, MSN, ARNP, CNNP
Neonatal Nurse Practitioner

Nemours Children's Hospital
13535 Nemours Parkway
Orlando, FL 32827
Office: (407) 567-3317
Voalte: (407) 567-5638
iPhone: (407) 280-2860
Cell: (505) 301-8845

Thank you.
References