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Opioid Use Disorders and Treatment in Pregnancy

Wednesday, May 13, 2015
Anne Johnston, MD
Hendrew Jones, PhD
Carl Seashore, MD

Behavioral Health is Essential To Health
Prevention Works
Treatment is Effective
People Recover
Agenda

- Introduction/Opening Remarks
  Sharon Amatetti, MPA
- Opioid Use, Dependency and Treatment in Pregnancy
  Hendree Jones, PhD
- Working with Mothers and Infants: Post-Delivery
  Carl Seashore, MD
- Working with Mothers and Infants: Post-Discharge
  Anne Johnston, MD
- Discussion

Sponsored by the SAMHSA Women’s Coordinating Committee in observance of National Women’s Health Week

Acknowledgements

- Study patients and infants
- National Institute on Drug Abuse
  - R01 DAs: 015764, 015738, 017513, 015778, 018410, 018417, 015741, 15832
- Maternal Opioid Treatment: Human Experimental Research (MOTHER) Site PIs and investigative teams

Disclosures

- Discussing methadone and buprenorphine, labeled by the US Food and Drug Administration (FDA) as Category C for use in pregnancy for the treatment of maternal opioid dependence: “Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.”
- Pregnant women with opioid use disorders can be effectively treated with methadone or buprenorphine. Both these medications should not be considered “off-label” use in the treatment of pregnant patients with opioid use disorder [Jones et al., Am J Obstet Gynecol. 2014]
- Reckitt-Benckiser Pharmaceuticals for donated active placebo tablets and reimbursement for time and travel in 2011.
Objectives

1. Participants will review the historical and current contexts of opioid use by pregnant women

2. Participants will compare and contrast the risks and benefits of methadone and buprenorphine given during pregnancy for the fetus, child, and mother

3. Participants will identify treatment components for comprehensive treatment programs that provide medication-assisted treatment

Outline

♦ Context of Opioid Use during Pregnancy
  - Historical
  - Current
♦ Pharmacotherapy for Pregnant Women with Opioid Use Disorders
  - Methadone
  - Buprenorphine
♦ Treatment Components for Medication-assisted Treatment
♦ UNC Horizons: Women-centered comprehensive care focusing on mother and child

Historical Context of Opioid Use during Pregnancy

Substance use during pregnancy in the USA has been a long-standing important health issue. In the 1800s:

• 66–75% of individuals with opium use disorders were women
• Women’s most common opium source was medical prescriptions to treat pain
• Physicians recognized neonatal opioid withdrawal and the need to treat in utero opium exposure with morphine in order to prevent morbidity and mortality

Following the 1914 Harrison Narcotic Act, the treatment of substance use disorders was segregated from mainstream medical practice

National Survey on Drug Use and Health 2011-2012 Past Month Use

- The two most common drugs used by non-pregnant women have been alcohol and tobacco
- This same statement is true for pregnant women
- Among pregnant women in the United States, approximately 18% smoked cigarettes, 9.4% drank alcohol, and 5% used illicit drugs in the past month

Among pregnant women, approximately .2% used heroin, and .9% used pain relievers non-medically in the past month

Credit: Still from The Dividend, 1916. public domain (Kandel, Substance and shadow, 1996. Earle, Medical Standards, 1888.)
Current Context of Opioid Use during Pregnancy

- Neonatal Abstinence Syndrome (NAS) often results when a pregnant woman uses opioids (e.g., heroin, oxycodone) during pregnancy.
- Defined by alterations in the:
  - **Central nervous system**
    - high-pitched crying, irritability
    - exaggerated reflexes, tremors and tight muscles
    - sleep disturbances
  - **Autonomic nervous system**
    - sweating, fever, yawning, and sneezing
  - **Gastrointestinal distress**
    - poor feeding, vomiting and loose stools
  - **Signs of respiratory distress**
    - nasal stuffiness and rapid breathing

  - NAS is not Fetal Alcohol Syndrome (FAS)
  - NAS is treatable
  - There are no known long-term consequences from having NAS or being treated for NAS

(Finnegan et al., Addict Dis. 1975; Desmond & Wilson, Addict Dis. 1975)

In the US, it is estimated that:
- 100 million people have chronic pain
- 22 million are living with addiction, and of those individuals
  - 7 million misuse prescription medications

Current Context of Opioid Use during Pregnancy

- A retrospective, serial, cross-sectional analysis of a nationally representative sample of newborns with NAS.
- Clinical conditions were identified using ICD-9-CM diagnosis codes.
-NAS and maternal opiate use were described as an annual frequency per 1000 hospital births.

Weighted National Estimates of the Rates of Maternal Opiate Use per 1000 Hospital Births

- Low Birthweight, Respiratory Diagnoses, and Medicaid Coverage in 2009
- Low Birthweight, Respiratory Diagnoses, and Medicaid Coverage in 2009

Percentage of US Population Estimated to Have the Disorder

- Chronic Pain
- Addiction
- Opioid Addiction
- Diabetes
- Depression
Why are more individuals, including pregnant women, using opioids?

- There has been an increase in the access to these medications
- Pain became the 5th vital sign in the early 21st century
- Federal prosecutors allege in documents filed in U.S. District Court that Chris and Jeff George from Florida dramatically increased the numbers of pain clinics in Florida and routed opioid pain medications to Kentucky, Ohio and South Carolina.

Summary of Historical and Current Context

- Although less frequent than alcohol and tobacco use, opioid misuse during pregnancy is nonetheless a serious and growing issue.
- This increase in use of opioids by pregnant women appears to be driving an increase in the incidence of neonatal opioid withdrawal.
- Opioid use by pregnant women is often complicated by polydrug use, and often occurs intertwined with complex personal, interpersonal, family, social, and environmental factors that can contribute to adverse consequences.
- Women have unique needs for addiction treatment and multi-faceted interventions are needed to help prevent and treat opioid-dependence among women during pregnancy and their infants.

Pharmacotherapy for Opioid Dependence

- Prevention of erratic maternal opioid levels lessens fetal exposure to repeated withdrawal episodes.
- Reduces maternal craving and fetal exposure to illicit drugs.
- With drug abstinence, other behavior changes can follow which decrease risks to mother fetus of infection from HIV, hepatitis and sexually transmitted infections.
- Reduces the incidence of obstetrical and fetal complications and improves outcomes.

Current Context of Opioid Use during Pregnancy

Issues facing drug-using pregnant women and their children

- Exposure to violence and trauma
- Generational drug use
- Lack of formal education
- Lack of job acquisition and maintenance skills
- Gender inequality/male-focused society
- Legal involvement
- Multiple drug exposures
- Limited parenting skills and resources
- History of child abuse and neglect
- Multiple psychiatric issues
- Unstable housing
- Lack of positive and supportive relationships
- Food insecurity and lack of nutrition

These factors with or without drug use can influence mother and child outcomes.
NIDA’s 13 Principles of Effective Treatment:

1) Addiction is a complex but treatable disease that affects brain function and behavior.
2) No single treatment is appropriate for everyone.
3) Treatment needs to be readily available.
4) Effective treatment attends to multiple needs of the individual, not just drug abuse.
5) Remaining in treatment for an adequate period of time is critical.
6) Behavioral therapies—including individual, family, or group counseling—are the most commonly used forms of drug use treatment.
7) Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies.
8) An individual’s treatment and services plan must be assessed continually and modified as necessary to ensure that it meets his or her changing needs.
9) Many drug-addicted individuals also have other mental disorders.
10) Medically assisted detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug abuse.
11) Treatment does not need to be voluntary to be effective.
12) Drug use during treatment must be monitored continuously, as lapses occur.
13) Treatment programs should test patients for infectious diseases and provide targeted risk-reduction counseling, linking patients to treatment if necessary.

Role of Medication-assisted Withdrawal

With opioid medications we are not replacing one addiction for another. Opioid medications are long-acting medication that help with:

- CRAVING
  - An individual’s cravings are controlled
- COMPULSION
  - Individual is no longer compulsively using opioids
- CONTROL
  - Medication-assisted treatment gives back control to the individual
- CONSEQUENCES
  - Medication assisted treatment helps the individual focus on rebuilding her life

- An individual receiving opioid pharmacotherapy must be monitored by a medical team that evaluates adequacy of medication dosage and general health and well-being of the individual.

Maintenance v. Medication-assisted Withdrawal

- WHO 2014 Guidelines: “Pregnant women dependent on opioids should be encouraged to use opioid maintenance treatment whenever available rather than to attempt opioid detoxification. Opioid maintenance treatment in this context refers to either methadone maintenance treatment or buprenorphine maintenance treatment.”
- Guidance regarding maintenance versus medication-assisted withdrawal has traditionally been based largely on good clinical judgment
- Medication followed by no medication treatment has frequently been found to be unsuccessful, with relatively high attrition and a rapid return to illicit opioid use
- Maintenance medication facilitates retention of patients and reduces substance use compared to no medication
- Biggest concern with opioid agonist medication during pregnancy is the potential for occurrence of neonatal abstinence syndrome (NAS) – a treatable condition

Methadone: Dosing during Pregnancy

- In the 1970s, a positive relationship between maternal methadone dose and NAS severity was reported
- Recommendations to maintain pregnant women on methadone doses between 20 to 40 mg
- 3 decades of research shows an inconsistent relationship between maternal methadone dose and NAS severity
- The latest systematic review and meta-analysis concluded that the “Severity of the neonatal abstinence syndrome does not appear to differ according to whether mothers are on high- or low-dose methadone maintenance therapy.”

(Review in Cleary et al., Addiction, 2010)
Methadone: Dosing during Pregnancy

Split Dosing

- **Maternal Results**
  - Increase drug negative urines during treatment
  - Increased adherence with treatment
  - Decrease withdrawal symptoms in mother
  - No change in maternal heart rate, vagal tone or skin conductance

- **Fetal Results**
  - Minimizes the reduction in breathing
  - Minimizes the reduction in movement
  - Fetal movement-fetal heart rate coupling less suppressed

(DePetrillo et al., 1995; Swift et al., 1989; Wittmann et al., 1991; Jansson et al., 2009; McCarthy)

Credit: “Human Fetus” by ddpavumba; “Smiling Pregnant Female Holding Her Tummy” by imagerymajestic

Methadone: NAS

**Methadone-associated NAS**

- NAS signs: 55-90%
- Requiring medication: ~ 60%
- NAS appears: 45 to 72 hrs
- NAS peaks: 40 to 120 hrs

- Most common medication for treatment is morphine
- Most common assessment tool is a “modified” Finnegan scale
- No current standard uniform protocol for treatment

Credit: “Sleeping Asian Baby” by NeleS5

Methadone: Breastfeeding

**Breastfeeding in Methadone-Stabilized Mothers**

- Methadone detected in breast milk in very low levels
- Methadone concentrations in breast milk are unrelated to maternal methadone dose
- The amount of methadone ingested by the infant is low
- The amount of methadone ingested by the infant remains low even 6 months later
- Several studies show relationships between breastfeeding and reduced NAS severity and duration
- Hepatitis C is not a contraindication for breastfeeding
- Contraindications: HIV+, unstable recovery

(D’Apollito, 2013; AAP 2012; McQueen et al., 2011; Jansson et al., 2007; Jansson et al., 2010)

Credit: “Mother is Breast Feeding For Her Baby” by Jongphong

Methadone: Child Development

Research focusing on the effects of prenatal exposure to methadone has been inconsistent

- Long-term effects on physical growth have not been demonstrated
- Although some research has shown that methadone-exposed school-age children to be less interactive, more aggressive, and showing poorer achievement than children not so exposed, other research has failed to show any differences in either cognitive or social development
- The issue is confounded by the fact that children exposed to methadone in utero may experience a nutritional, family, and parenting history quite different than children not so exposed
- 2014 meta-analysis showed “no significant impairments for cognitive, psychomotor or observed behavioural outcomes for chronic intra-uterine exposed infants and pre-school children compared to non-exposed infants and children.”

(Salotrichov et al., BMC Psychiatry 2014; Behrke et al., Pediatrics, 2013; Field et al., Curr Neuropsych, 2006)

Credit: “Lady Doctor Measuring Girls Height” by David Castillo
Methadone: Summary

50 years of documented benefits of methadone during pregnancy

- Induction is relatively simple
- Adequate doses are needed to prevent withdrawal and other opioid use
- Indicators of fetal well-being are less compromised with split-dosing
- NAS is worse with heavier smoking
- Breastfeeding is compatible with methadone

Buprenorphine

- A derivative of the opioid alkaloid thebaine
- Schedule III opioid
- μ-opioid receptor partial agonist
- Primarily antagonistic actions on κ-opioid and δ-opioid receptors
- Half-life estimated to fall in the range of 24-60 hours

Buprenorphine and Pregnancy

- Since 1995, over 40 published reports of prenatal exposure to buprenorphine maintenance
- Approximately 750 babies prenatally exposed to buprenorphine (number of cases per report ranged from 1 to 159; Median=14)
- Dose range 0.4 to 32 mg
- 88% reported concomitant drug use

Buprenorphine: Maternal Outcomes

- Research with buprenorphine not as extensive as with methadone
- Well-tolerated and generally safe
- In contrast to the research with methadone, little research has compared buprenorphine to an untreated control group
- Rather, buprenorphine has been compared in both retrospective and prospective studies to methadone
- Majority of research would suggest that maternal outcomes are not in any way different than for methadone
### Buprenorphine: Fetal Outcomes

#### Figure 3: Non-Reactive Non-Stress Test

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-Test</th>
<th>Post-Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>p &lt; .01</td>
<td>p &gt; .05</td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Figure 4: Biophysical Profile Score

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-Test</th>
<th>Post-Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
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<td></td>
</tr>
<tr>
<td>Methadone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Salisbury et al., Addiction, 2012)

### Buprenorphine: NAS

- Incidence rate for NAS is estimated to be 50% – about the same as for methadone
- NAS onset approximately 48 hours
- Peaking within approximately 72-96 hours
- Exceptions to this onset history have been the few neonates with NAS onset of 8-10 days postnatal age
  - such a protracted withdrawal syndrome may be due to withdrawal from concomitant drug exposure (e.g., benzodiazepines) rather than a direct effect of buprenorphine withdrawal
- Correlation between buprenorphine dose and NAS severity has been inconsistent
- Time of first dose of NAS treatment medication has been shown to be later with buprenorphine than methadone (71 hrs vs 34 hrs, respectively)

(Reviews in Jones et al., Drugs, 2012 and Addiction, 2012; Gaalema et al., DAD, 2013)

### Buprenorphine: Breastfeeding

- Buprenorphine is found in breast milk 2 hours post-maternal dosing
- Concentration of buprenorphine in breast milk is low
- Amount of buprenorphine or norbuprenorphine the infant receives via breast milk is only 1%
- Most recent guidelines: “the amounts of buprenorphine in human milk are small and unlikely to have negative effects on the developing infant”
- “The advantages of breast feeding prevail despite the risks of an infant opiate intoxication caused by methadone or buprenorphine.”

(Atkinson et al., 1990; Marquet et al., 1997; Johnson, et al., 2001; Grimm et al., 2005; Lindemalm et al., 2009; Jansson et al., 2009; Müller et al., 2011)

### Buprenorphine: Child Development

- Research on the neonatal consequences of prenatal exposure to buprenorphine is quite limited
- Not enough births have been followed for a sufficient period of time to collect convincing data regarding factors such as cognitive and social development
- Same issue of confounding parental and family factors in teasing apart developmental effect

(Reviews in Jones et al., Drugs, 2012 and Addiction, 2012)
MOTHER: Sites

**Lead Site** Johns Hopkins University PI: H. Jones
Brown University PI: B. Lester
Thomas Jefferson University PI: K. Kaltenbach
University of Vermont PI: S. Heil
University of Vienna PI: G. Fischer
University of Toronto PI: B. Lester
Wayne State University PI: S. Stine

**Coordinating Center** University of Maryland PI: A. Arria

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MOTHER: Buprenorphine v. Methadone

**MOTHER: Sites**

Compared with methadone-exposed neonates, buprenorphine-exposed neonates:
- Required 89% less morphine to treat NAS
- Spent 43% less time in the hospital
- Spent 58% less time in the hospital being medicated for NAS

**MOTHER: Buprenorphine v. Methadone**

Incidence of NAS signs

- All neonates in each medication condition had at least one total NAS score greater than 0 at some point during the observation period
- Three individual signs were observed significantly more often in the buprenorphine than in the methadone condition: sneezing, loose stools, and nasal stuffiness
- There were no signs that were observed significantly more often in the methadone condition than in the buprenorphine condition

**Notes:**
- Significant results are encircled. Site was a blocking factor in all analyses. The O'Brien-Fleming spending function resulted in \( \alpha = .0091 \) for the inferential tests of the Medication Condition effect for the 5 primary outcome measures at the conclusion of the trial.
- Notes: Bonferroni’s principle was used to set familywise \( \alpha = .003125 \) (nominal \( \alpha = .05/16 \)) for the secondary outcome measures.
Severity of NAS Signs

- Methadone-exposed neonates had higher mean NAS total score, and higher mean scores for hyperactive Moro reflex, disturbed tremors, undisturbed tremors, failure to thrive, and excessive irritability (all p ≤ 0.04).
- Buprenorphine-exposed neonates had higher mean scores on sneezing.

NAS: Factors

Other factors that contribute to severity of NAS in neonates exposed to opioid agonists in utero:

- Genetics
- Other Substances: Cigarette smoking, Benzodiazepines, SSRIs
- Hospital Protocols: The NAS assessment and medication initiation and weaning protocols, Not breastfeeding, Rooming in or separating mother and baby

Summary: Buprenorphine

- MOTHER provided the first RCT data to support the safety and efficacy of methadone.
- Maternal outcomes are similar between medications.
- Pain management and breastfeeding recommendations are similar between medications.
- In terms of NAS severity, buprenorphine can be a front-line medication option for managing opioid-dependence for pregnant women who are new to treatment or maintained on buprenorphine pre-pregnancy.
- NAS, its treatment and elucidating factors that exacerbate and minimize it, remains a significant clinical issue for prenatally opioid-exposed neonates.
- Currently there is great variation in terms of medications and use of tools.

Smoking and Neonatal Abstinence Syndrome (NAS)

Self-reported past 30-day daily average number of cigarettes smoked, measured at study entry, was used to predict neonatal and maternal outcomes in 131 pregnant participants in the MOTHER study.

RESULTS

Higher average daily number of cigarettes smoked in the past 30 days was related to increasing:

- Total amount of morphine needed to treat NAS
- Number of days neonate was medicated for NAS
- Neonatal length of hospital stay

Related to decreasing:

- Neonatal weight at birth

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).
Buprenorphine v. Methadone

<table>
<thead>
<tr>
<th>Benefits and Risks of Pharmacotherapy</th>
<th>Methadone</th>
<th>Buprenorphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Availability</td>
<td>Methadone clinic</td>
<td>Doctor's office with an “X number”</td>
</tr>
<tr>
<td>Frequency of dosing</td>
<td>daily</td>
<td>daily</td>
</tr>
<tr>
<td>Abuse liability</td>
<td>abused</td>
<td>abused</td>
</tr>
<tr>
<td>Cost</td>
<td>$</td>
<td>$$</td>
</tr>
<tr>
<td>Reduced HIV drug risk behaviors</td>
<td>$6</td>
<td>$6</td>
</tr>
<tr>
<td>Greater birthweight than no treatment</td>
<td>$6</td>
<td>$6</td>
</tr>
<tr>
<td>Recommended for pregnancy</td>
<td>$6</td>
<td>$6</td>
</tr>
<tr>
<td>Independent replication of results</td>
<td>$0</td>
<td>$0</td>
</tr>
<tr>
<td>Fetal behavior</td>
<td>(with split dosing)</td>
<td>$6</td>
</tr>
<tr>
<td>Neonatal Abstinence Syndrome</td>
<td>$4</td>
<td>$4</td>
</tr>
</tbody>
</table>

Program Components for Women

- Considers the needs of women in all aspects of program design and delivery, including location, staffing, program development, program content, and program materials
- Provides safe and comfortable environments in which women develop supportive relationships that allow them to address their recovery needs
- Services need to include:
  - Outreach and engagement
  - Screening
  - Detoxification
  - Crisis intervention
  - Assessment
  - Treatment planning
  - Case management
  - Substance use counseling and education
  - Trauma specific and informed services
  - Medical and mental health care
  - Pharmacotherapy
  - Drug monitoring
  - Continuing care

UNC Horizons Program

Where women and their children find... **Help**

... **Hope**

... **Healing**

UNC Horizons’ mission is to provide world class empowering and transformative interdisciplinary care to women and their children affected by substance use disorders

Program should be accredited by an outside body like CARF or JHACO
Last year we treated 233 women, including 57 women with 66 children in our residential program and 45 women in our prenatal clinic.

- 100% are covered by Medicaid or are uninsured
- 33% have less than a high-school education
- ~40% pregnant at intake
- ~90% have at least one child under 18 (majority under 2)
- Over 50% of those women with children have had recent Child Protective Services (CPS) involvement

Who We Serve:

- Her boyfriend uses opioids and alcohol
- He is violent
- She lost custody of her children ages 2 and 4
- Baby tested positive for opioids
- She wants to keep him
- Has no car
- Lives on friend’s couch
- 11th grade education
- Exotic dancer
- Multiple legal issues
- Sexually abused as a child
- Raped as an adult
- Baby tested positive for opioids
- She wants to keep him
- Has no car
- Lives on friend’s couch
- 11th grade education
- Exotic dancer
- Multiple legal issues
- Sexually abused as a child
- Raped as an adult

Model of Care:

- Trauma and Addiction Treatment
- Childcare and Transportation
- Medical Care OB/GYN Psychiatry
- Parenting Education and Early Intervention
- Vocational Rehabilitation
- Residential and Outpatient Care

Substance Abuse Comprehensive Outpatient Treatment

Substance Abuse Intensive Outpatient Treatment

Elements Common to both services:

- Multiple evidence-based practices
- Childcare ◆ Transportation
- Psychiatry ◆ OB/GYN care
- Case management ◆ Peer support
- Individual counseling ◆ Group counseling
- Parenting ◆ Urine drug screening
- Crisis contingency planning
- Disease management
**UNC Horizons Program**

**Residential Programs**
- Up to a one-year program with 6-month aftercare
- Apartments in 2 Chapel Hill complexes
- Transitional apartments
- Services:
  - Childcare services
  - Case management
  - Individual counseling
  - Urine drug screens
  - Disease management
  - Transportation
  - Peer-support
  - Parenting/ Family therapy
  - Crisis contingency plans

**Goals:**
- Recovery and self-care related to addiction and trauma
- Employment
- Parenting

**Success: Infants and Children**

Child Protective Service Involvement:
- Outpatient women and children who complete the program: 75% of families had positive changes (e.g., closed cases, children reunited)
- Residential women and children who complete the program: 100% of families with cases had positive changes (regained custody, cases closed)

**Early Intervention and Therapeutic Services for Children**
- All children receive age-appropriate mental health and social/emotional assessments; and individual, group, and/or family therapy as needed
- All children screened for speech and language, occupational therapy, physical therapy, dental, hearing and vision and referred for developmental evaluations
- About 90% of the residential children ages 0-5 qualify for and receive early intervention services

**Comparisons of Birth Outcomes**

NC data were derived from 2013 NC State Center for Vital Statistics: http://www.nchsc.state.nc.us/nchsvitals/ncbirths.cfm
Opioid addiction is a treatable illness
Pregnant women with opioid use disorders have medication options from which to choose as a part of a comprehensive treatment program
Women-centered treatment programs that focus on the needs of the women, her fetus, and her family offer the promise of addressing the multiple and complex needs of women with opioid use disorders.

Credit: “balanced stones” by Pakhnyushchyy.
Resources

- http://www.youtube.com/watch?v=3HsmuxtsBZ8
- DRMC Neonatal Abstinence Syndrome
- http://pcmch.on.ca/LinkClick.aspx?fileticket=JTt9IpgEbN0%3D&tabid=40
- http://www.uvm.edu/medicine/vchip/documents/VCHIP_SNEONATAL_GUIDELINES.pdf
- http://pediatrics.aappublications.org/content/101/6/1079.full
- http://store.samhsa.gov/product/Methadone-Treatment-for-Pregnant-Women/SMA09-4124

Disclosures

I have no financial disclosures (I am a pediatrician)

I will discuss off-label use of medications (I am a pediatrician)

Goals

- Recognize that neonatal abstinence syndrome is an important public health problem
- Understand when and why infants may be at risk for neonatal abstinence syndrome
- Understand the approach to treatment of infants at risk for and exhibiting symptoms of neonatal abstinence syndrome
Background

“During the past decade, narcotic addiction in the United States has reached epidemic proportions.”

-Finnegan, et al, 1975


Background-Opiate explosion

Prescription Painkiller Overdoses

A growing epidemic, especially among women.

July 2013

48,000 women died of prescription painkiller overdose from 1999-2010.

-400% increase from prescription painkiller overdoses among women compared to 200% among men.

Background-NAS

Recent data illustrating the geographic distribution of NAS in the US.

Almost 22,000 babies: 2012

Cost: $1.5 Billion (hospital)

~80% Medicaid

More complications

Has not peaked

Background-Treatment Team

NAS can occur in babies whose mothers are using prescribed or illicit opiates of any kind, including those on opiate replacement therapy as Dr. Jones outlined.

A TEAM is required to care for these families
• (ideally) Engage all players before delivery for planning
• Early testing in mother during gestation in addition to mother AND baby at delivery is key
• Evidence-based protocols exist for L&D and Newborn
• Pain management plan for mother

Recognition-Prevention?

Screening Protocols can involve nurses and mothers
• Educating mother about NAS symptoms is empowering
• Help her (and family) help the baby
• Emphasize Non-pharmacologic treatments
• Support mom’s desire to breastfeed
• Model soothing techniques

Recognition-Parent Scoring

Date and Time

Excessive crying

Less than 5 minutes

More than 5 minutes

Sleepiness

Sleeps:

less than 1 hr after feeding

less than 2 hrs after feeding

less than 3 hrs after feeding

Tremors/Jitteriness

Mild tremors when disturbed

Moderate/severe tremors when disturbed

Mild tremors when UNDISTURBED

Moderate/severe tremors when UNDISTURBED

Sweating

Present

Not present

Yawning

More than 3 times in the past 4 hours

0-3 in the past 4 hours

Sneezing

More than 3 times in the past 4 hours

0-3 times in the past 4 hours

Stuffy nose

Present

Not present

Poor Feeding (not feeding often or not sucking well)

Yes

No

Spit up

Yes, more than 2 times during or after a feeding

Yes, projectile vomiting

No, none or less than 2 times

Loose/Watery Stool

More liquid than normal or any type of stool with a water ring on the diaper

No

Recognition-Tools

Use a standard screening tool for at-risk infants
• Finnegan is most widely used
  • MOTHER study (NEJM, 2010) used modified Finnegan
  • Lipsitz, Neonatal Withdrawal Inventory, etc
• Vermont Oxford Network
• PQCNC project underway
Management

Initiate non-pharmacologic treatment for at-risk infants

- Finnegan noted this in 1975 and it is true today
- Skin-to-skin, breastfeeding (if not illicit use)
- Swaddling, teaching parents soothing/coping
- Minimize external stimuli - lights, TV, visitors, noise

Pharmacologic treatment if symptoms/scores warrant

- Morphine oral solution is standard first-line treatment
- Dosing regimens vary; use protocol approach
- Range 0.24 mg/kg per day to 1.3 mg/kg per day (AAP)
- Weight-based vs Symptom-based (MOTHER)
- Methadone used in some centers

Abdel-Latif et al, Pediatrics, 2006
Management

Pharmacologic treatment if symptoms/scores warrant(2)
- Escalate/Wean dosage based on scoring
- Clonidine as an adjuvant therapy (first-line use rare)
- Transition to Methadone for home care?
  - Depends on PCP, social supports
  - Continue non-pharm interventions!!

Management

Referral and Long-Term Follow-up for exposed infants
- Early Intervention, CDSA, other local resources
- Early childhood development, ongoing “eyes” in home
- MAT programs-mom’s treatment does not end in L+D
  - We are fortunate with Horizons at UNC
  - Finding an appropriate PCP for baby

Management

Referral and Long-Term Follow-up for exposed infants
- DSS involvement
- This can and should be seen as supportive not punitive
  - Active illicit use should escalate involvement
  - Often past history with DSS precludes acceptance
- Preschool as child gets older

Improvement!

PQCNC.org
References


Effects of Breast Milk on the Severity and Outcome of Neonatal Abstinence Syndrome Among Infants of Drug-Dependent Mothers. Mohamed E. Abdel-Latif, MRCPCH, MPH, MEpi, Jason Pinner, MRCPCH, Sara Clews, RN, Fiona Cooke, RN, Kei Lui, FRACP, MD, Julee Oei, FRACP. Pediatrics 2006;117;e1163

References


Effects of Breast Milk on the Severity and Outcome of Neonatal Abstinence Syndrome Among Infants of Drug-Dependent Mothers. Mohamed E. Abdel-Latif, MRCPCH, MPH, MEpi, Jason Pinner, MRCPCH, Sara Clews, RN, Fiona Cooke, RN, Kei Lui, FRACP, MD, Julee Oei, FRACP. Pediatrics 2006;117;e1163

Pain as a 5th Vital Sign

Measuring Pain as the 5th Vital Sign Does Not Improve Quality of Pain Management
Richard A. Mularski, MD, MSHS,1,2 Foy White-Chu, MD,3 Devorah Overbay, MS, RN,4 Lois Miller, PhD, RN,4 Steven M. Asch, MD, MPH,1,2 and Linda Ganzini, MD, MPH1,6

Working with Mothers and Infants Post-Discharge

ANNE JOHNSTON, MD
Neonatal Perinatal Medicine
Associate Professor of Pediatrics
University of Vermont

May 13, 2015
OBJECTIVES

- Neonatal antenatal approach to the pregnant opioid-dependent woman at the University of Vermont
- The choice of methadone for inpatient and outpatient treatment
- UVM outcomes

UVM Children’s Hospital
Antenatal Visit With Neonatology

- Schedule 1 - 2 visits with NeoMed Clinic staff
- Written information (Care Notebook)
- http://www.uvm.edu/medicine/vchip/?Page=ICONcarenotebook.html
- Promote breastfeeding

"I swear to tell the truth, the whole truth, and nothing but the truth, from my perspective."
UVM Children’s Hospital NeoMed Experience

- Alleviation of fear
  - Care Notebook
  - You are not alone...
  - Ask them for their stories
- Respect
  - Introductions to others on the team
  - “Tell me about yourself”
  - “What are your dreams/goals”
- Recognition of strengths
  - Hearts

UVM Children’s Hospital
Why methadone for treatment of neonatal abstinence syndrome?

- Decreased frequency of dosing
- Less respiratory depression
- Less need for adjustment of dose

UVM Children’s Hospital
Benefits/risks of newborn outpatient treatment program with methadone

**Benefits**
- Length of stay reduced
- Slow wean of methadone reduces symptoms of withdrawal
- Allows for more breastfeeding success
- Empowers family

**Risks**
- Safety concerns - overdose to baby, use by others
- Long half-life may lead to “overmedication” in hospital
- Often prolonged course - are we treating normal baby instability with methadone?

UVM Children’s Hospital
Inpatient treatment with methadone

- Initial dose 0.3 mg q12h to 0.6 mg q12h depending upon severity of symptoms
- Watch for lethargy!!!
- Stable dose for at least 48 hours prior to discharge
- Extensive family teaching regarding measurement of methadone dose
UVM Children’s Hospital
Administration of methadone

Infrastructure: what works in Vermont

• Clinic staff with ability to “track infants down”
• Close relationships with obstetrics, substance abuse treatment providers, WIC, child protective services and home health nursing
• Single pharmacy to dispense methadone

NeoMed Clinic Staff

- Nurse Clinician
- Medical Assistant
- Nurse Practitioner
- Neonatal Fellow
- Neonatologist

UVM Children’s Hospital NeoMed

- First NeoMed clinic visit within 1 week of discharge
- Infants requiring medication for NAS are seen at least every 2 weeks
- Infants not requiring treatment follow up monthly for the first 4 months, then every 2-4 months until 12-18 months
- Bayley III Scales at 8-10 months
- Hepatitis C antibody at 18 months for exposed infants
- Multidisciplinary approach involving primary care provider, home health, early intervention, CHARM team, and maternal substance abuse provider
UVM Children’s Hospital
NeoMed clinic visits for infants on methadone

- 1st visit within 1 week to 10 days (usually no weaning before 1st visit)
- Must bring methadone to clinic visit, document amount remaining
- Caregiver demonstrates with syringe and air how much methadone they are administering
- Have caregiver demonstrate other doses
- Review storage, need for additional syringes, who is measuring and administering medicine

UVM Children’s Hospital
Agree on methadone weaning plan

- Review symptoms of “withdrawal” if any
- “Usual weans”
  - 0.02 mg every Monday and Thursday OR
  - 0.02 mg every Monday
- Provide written schedule for the weaning
- If any change in weaning schedule – first discuss with clinic

UVM Children’s Hospital
Sample methadone weaning schedule

<table>
<thead>
<tr>
<th>Day of the week</th>
<th>Date</th>
<th>Med</th>
<th>Dose (mg)</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday</td>
<td>2/4/13</td>
<td>Methadone dose</td>
<td>0.24</td>
<td>2/day</td>
</tr>
<tr>
<td>Thursday</td>
<td>2/7/13</td>
<td>Methadone dose</td>
<td>0.22</td>
<td>2/day</td>
</tr>
<tr>
<td>Monday</td>
<td>2/11/13</td>
<td>Methadone dose</td>
<td>0.2</td>
<td>2/day</td>
</tr>
<tr>
<td>Thursday</td>
<td>2/14/13</td>
<td>Methadone dose</td>
<td>0.18</td>
<td>2/day</td>
</tr>
<tr>
<td>Monday</td>
<td>2/18/13</td>
<td>Methadone dose</td>
<td>0.16</td>
<td>2/day</td>
</tr>
<tr>
<td>Thursday</td>
<td>2/21/13</td>
<td>Methadone dose</td>
<td>0.14</td>
<td>2/day</td>
</tr>
<tr>
<td>Monday</td>
<td>2/25/13</td>
<td>Methadone dose</td>
<td>0.12</td>
<td>2/day</td>
</tr>
<tr>
<td>Thursday</td>
<td>3/1/13</td>
<td>Methadone dose</td>
<td>0.1</td>
<td>2/day</td>
</tr>
</tbody>
</table>

Instructions:
**Reminder to bring your baby’s methadone to each clinic visit**

UVM Children’s Hospital
Prescribing and dispensing methadone

- Use only one concentration (1 mg/mL)
- Use only one pharmacy
- Amount prescribed: 3 – 4 weeks
- We dispense in syringe connected to another syringe
- Recommend lock-box/lock-bag to store methadone
Total Opioid-exposed Newborns Followed at UVM Children’s Hospital (1,208 newborns)

UVM Children’s Hospital: Infants born to opioid dependent women with substance abuse on methadone or buprenorphine at delivery (N = 876)

Why did pharmacologic treatment for NAS decrease?

- Better use of non-pharmacologic treatment
- Less subjectivity in NAS scoring
  - Through participating in MOTHER study
  - Decreased assumption of need for treatment
- Over time, the proportion of buprenorphine-treated pregnant women increased
Mean Length of Hospital Stay

Infants treated with outpatient methadone (UVM Children's Hospital)

Infants treated with intravenous methadone (MOTHER STUDY)

UVM Children's Hospital
Mean Length of Infant Outpatient Treatment with Methadone

UVM Children's Hospital
Breastfeeding at discharge

University of Vermont Children's Hospital:
Bayley III Composite Scores at 7-14 months* (N=166)

<table>
<thead>
<tr>
<th></th>
<th>Cognitive</th>
<th>Language</th>
<th>Motor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>107.8</td>
<td>105.4</td>
<td>104.7</td>
</tr>
<tr>
<td>Percentile Rank</td>
<td>66.3</td>
<td>62.7</td>
<td>60.0</td>
</tr>
</tbody>
</table>

* Term infants born at UVM Children's Hospital
UVM Children’s Hospital
Deaths < 2 years of age
1,208 Opioid-exposed Newborns (2000 - 2014)

<table>
<thead>
<tr>
<th>#</th>
<th>Date of Death</th>
<th>Age @ Death</th>
<th>Cause of Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>05/2004</td>
<td>5 days</td>
<td>Shared sleeping</td>
</tr>
<tr>
<td>2</td>
<td>04/2006</td>
<td>4 months</td>
<td>SIDS</td>
</tr>
<tr>
<td>3</td>
<td>12/2008</td>
<td>6 months</td>
<td>Motor Vehicle Accident</td>
</tr>
<tr>
<td>4</td>
<td>01/2009</td>
<td>4 months</td>
<td>Shared sleeping</td>
</tr>
<tr>
<td>5</td>
<td>11/2009</td>
<td>5 months</td>
<td>Shared sleeping</td>
</tr>
<tr>
<td>6</td>
<td>03/2010</td>
<td>5 months</td>
<td>Hypoplastic Left Heart Syndrome</td>
</tr>
<tr>
<td>7</td>
<td>12/2010</td>
<td>6 weeks</td>
<td>Shared sleeping</td>
</tr>
<tr>
<td>8</td>
<td>05/2012</td>
<td>8 months</td>
<td>Motor Vehicle Accident</td>
</tr>
<tr>
<td>9</td>
<td>08/2013</td>
<td>3 months</td>
<td>Shared sleeping</td>
</tr>
<tr>
<td>10</td>
<td>09/2013</td>
<td>2 months</td>
<td>Shared sleeping</td>
</tr>
<tr>
<td>11</td>
<td>09/2013</td>
<td>19 days</td>
<td>Shared sleeping</td>
</tr>
<tr>
<td>12</td>
<td>11/2013</td>
<td>1 day</td>
<td>Extreme prematurity</td>
</tr>
<tr>
<td>13</td>
<td>04/2014</td>
<td>14 months</td>
<td>Head Injury (Non-accidental)</td>
</tr>
</tbody>
</table>

UVM Children’s Hospital
Outcomes

- Average length of treatment: 3.2 months (2014)
- No infant deaths from methadone overdose
- 1 infant who received prn doses – disconjugate gaze, slightly lethargic – resolved immediately when weaning schedule was adhered to
- 1 infant transitioned over to oral morphine due to parents’ inability to wean methadone at a certain level
- 1 infant required overnight hospitalization due to overdose by grandmother who had not been trained

UVM Children’s Hospital
Learn from our experience

- As a rule, parents do not use their infant’s methadone (they are usually on medication assisted treatment themselves)
- Beware of “prn dosing” of methadone by family
- If family cannot demonstrate the dose consistently - they may be altering the dose at their discretion
- If a spill occurs - have them take a picture with their cell phone
- Always ensure that caregiver has been trained in accurate methadone measurement
- Need to have close relationship with child protective services and be available for foster parent training

Vermont Experience: Overall

- CHARM Team: Children and Recovering Mothers
- Monthly multidisciplinary meetings with multiple agencies: impaneled
- High risk factors:
  - Increased distance to treatment center
  - Discontinuation of methadone / buprenorphine
  - Actively using partner
  - Abusive relationship with partner
- Women respond well to positive interactions with health care providers

[Map of Vermont showing methadone/buprenorphine treatment centers]
ACKNOWLEDGMENTS

We would like to thank the infants and families we have had the pleasure of caring for – we continue to learn from them daily.

Discussion

Contact the NCSACW for additional information:
1-866-493-2758
ncsacw@cffutures.org
www.ncsacw.samhsa.gov

Resources

3-Part Webinar Series
Medication Assisted Treatment for Families Affected by Substance Abuse Disorders
Medication Assisted Treatment During Pregnancy, Postnatal and Beyond
Opioed Use in Pregnancy: A Community’s Approach. The Children and Recovery Mothers (CHARM) Collaborative

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Please complete the evaluation.

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Check back soon!