Prenatal and Peripartum Care for the Patient on Opiate Replacement

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Disclosure

• None
Objectives

1. Understand opioid use disorder during pregnancy and dispel misconceptions
2. Learn how opioid use disorder is managed during pregnancy and after delivery
3. Have confidence in counseling patients with opioid use while pregnant
Dramatic Increases in Maternal Opioid Use and Neonatal Abstinence Syndrome

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

Average length or cost of hospital stay:
- With NAS: 16.9 days, $66,700
- Without NAS: 2.1 days, $3,500

NAS and maternal opioid use on the rise.
Misconception #1
Addiction is a character flaw or moral failing

“It’s time to change how we view addiction...Not as a moral failing but as a chronic illness that must be treated with skill, urgency, and compassion. The way we address this crisis is a test for America.”

Vivek Murthy, MD
US Surgeon General

McCarthy M. US must address addiction as an illness, not as a moral failing, Surgeon General says. BMJ. 2016 Nov 22;355:i6265.
Misconception #1
Addiction is a character flaw or moral failing

1998 physician survey
Illicit drug use during pregnancy
• 52% favor child abuse for purpose of removing child from maternal custody
• Favor incarceration
  • Pediatricians 23%
  • Family 34%
  • OB 27%

Misconception #1

Addiction is a character flaw or moral failing

2013 physician survey
Beliefs about nature of addiction

<table>
<thead>
<tr>
<th>PCP’s Response</th>
<th>Moral Model</th>
<th>Psych Model</th>
<th>Disease model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>34%</td>
<td>2%</td>
<td>3%</td>
</tr>
<tr>
<td>A little</td>
<td>29%</td>
<td>14%</td>
<td>9%</td>
</tr>
<tr>
<td>Somewhat</td>
<td>30%</td>
<td>51%</td>
<td>39%</td>
</tr>
<tr>
<td>A lot</td>
<td>7%</td>
<td>33%</td>
<td>51%</td>
</tr>
</tbody>
</table>

Favor disease model
- Psychiatrists
- Female doctors
- Doctors with Asian heritage
- Northeastern US
- Age 45-53
- Less religious

“In a perfect world...drug use would be recognized as a medical issue, and legal entanglements would not flow from positive toxicology results. Societal resources would be committed to strengthening family bonds and to the well-being of each family member.”

Examining Bias

Options for screening
• Selective testing
• Universal testing
• Selective screening
• Universal screening

ACOG, AAP, AMA, CDC
• Universal Screening
• Questionnaires: 4P’s or CRAFT

Screening for substance use

4 P’s

Parents: Did any of your parents have a problem with alcohol or other drug use?

Partner: Does your partner have a problem with alcohol or drug use?

Past: In the past, have you had difficulties in your life because of alcohol or other drugs, including prescription medications?

Present: In the past month have you drunk any alcohol or used other drugs?

Scoring: Any “yes” should trigger further questions.
Screening for substance use

CRAFFT—Substance Abuse Screen for Adolescents and Young Adults

C Have you ever ridden in a CAR driven by someone (including yourself) who was high or had been using alcohol or drugs?

R Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?

A Do you ever use alcohol or drugs while you are by yourself or ALONE?

F Do you ever FORGET things you did while using alcohol or drugs?

F Do your FAMILY or friends ever tell you that you should cut down on your drinking or drug use?

T Have you ever gotten in TROUBLE while you were using alcohol or drugs?

Scoring: Two or more positive items indicate the need for further assessment.
Misconception #3

“Heroin will make my baby messed up”

Opioids and neurocognitive development and birth defects

Neurodevelopmental effects

Animal models note changes in dendritic length, synaptic plasticity, neuronal proliferation, cholinergic function, increase in apoptosis in dopaminergic cell structures in the hippocampus

• **Human studies**
  - Delay in cognitive function
  - Lower verbal, reading, arithmetic ability
  - Increased ADHD
  - Decreased brain volume


Opioids and neurocognitive development and birth defects

Neurodevelopmental effects

- Israel Study, N=160 5-12 year olds
  - Children exposed to heroin in utero
  - Controls:
    - 2 groups of normally developing children
    - Children with fathers using heroin
    - Children born to families with socioeconomic depravation
  - Highest rates of inattention in socioeconomic depravation group
  - Highest rates of inattention, hyperactivity, aggression children born to opioid using parents raised by biologic parents
  - Adopted children preformed normally

Opioids and neurocognitive development and birth defects

Neurodevelopmental effects

• Nygaard et al, 2015
  – N=72 children with opioid and polysubstance exposure
  – Assessed at 1, 2, 3, 4.5, 8.5 years
  – Controlled for socioeconomic status
    • Based on parental education
  – Exposed group lower cognitive scores
  – Boys scored significantly lower than girls
  – Did not see cognition catch up over time

Opioids and neurocognitive development and birth defects

Neurodevelopmental effects

“Children of mothers with heroin dependency, if born without significant neurologic damage seem to have normal intellectual potential, as their IQ can be normal if the children are raised in an environment without low SES of neglect.” Orney et al, 2001

Opioids and neurocognitive development and birth defects

Birth defects

  – Prospective trial
  – Overall opioids with no significant cause of birth defects
  – Codeine and respiratory defects not statistically sig
  – Propoxyphene and club feet not statistically sig

• Michigan Medicate Data 1985 – 1992
  – 229,101 pregnancies, 332 had opioid exposure
  – No increase in congenital heart disease

Opioids and neurocognitive development and birth defects

Birth defects
• National Birth Defect Prevention Study 1997 – 2005
  • 17,499 mothers with cases of birth defects
  • 2.6% used opioid analgesic use 4-12 weeks
• Increased risk of:
  – All CHD OR 1.4 (95% CI 1.1-1.7)
  – Spina bifida OR 2.0 (95% CI 1.3-3.2)
  – Hydrocephaly OR 2.0 (95% CI 1.0-3.7)

Opioids and neurocognitive development and birth defects

Neurodevelopmental effects and birth defects
• Carefully consider control groups in these studies
• Environment plays a major role in development
• Women with substance use disorder have increased incidence of other risk factors
• Risk for birth defects remains unclear
Misconception #4

“Opioids cause maternal pregnancy complications”

Pregnancy complications

- Pre-eclampsia
- Premature labor
- Premature preterm rupture of membranes
- Placental insufficiency
- Placental abruption
- Intrauterine growth restriction
- Intrauterine fetal demise
- Low birth weight
- Small head circumference
- Neonatal withdrawal syndrome

Misconception #5
“All I need to do is detox from everything”

Opioid detoxification during pregnancy

Stewart et al, 2013
– N=95 pregnant women detoxed with methadone
  • 53% patients successfully completed detox
  • 32% left the study

Jones et al, 2017
– Reviewed 500 documented cases of opioid detox
– Opioid detoxification associated with:
  • Less time in treatment, fewer prenatal care visits, less likely to deliver at study hospital
– No fetal losses attributed to medically assisted withdrawal
– Relapse 17-96% (average 48%)

Misconception #5
“All I need to do is detox from everything”

Opioid detoxification during pregnancy

• Detoxification not recommended due to:
  – Decreased neonatal birth weight
  – Decreased prenatal care
  – Illicit drug relapse
  – Resumption of high risk behaviors (IVDU, prostitution, criminal activity)

Medication assisted treatment (MAT)

• Reported success rates 63-82%

Misconception #6

“Opioids will make my baby small”
Misconception #6
“Opioids will make my baby small”

### Opioid use and decreases in birth weight (grams)

<table>
<thead>
<tr>
<th></th>
<th>MJ</th>
<th>Cocaine</th>
<th>Opioids</th>
<th>Smoking +10/day</th>
<th>Heavy drinking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted</td>
<td>-250</td>
<td>-475</td>
<td>-462</td>
<td>-543</td>
<td>-438</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>-24</td>
<td>-142</td>
<td>-85</td>
<td>-158</td>
<td>-30</td>
</tr>
</tbody>
</table>

*Adjusted for social, psychosocial, behavioral, and biomedical factors
Schemph and Strobino, 2008

Misconception #6  
“Opioids will make my baby small”

Nørgaard et al, 2015  
• Danish retrospective study  
• N=564 compared to general population  
  • Low birth weight (LBW) <2,500 grams  
  • Small for gestational age (SGA) <2x SD  
  • Prevalence risk for opioid exposed (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>Opioid v. General population</th>
<th>Opioid + smoking v Gen pop + smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>LBW</td>
<td>4.3 (3.0-6.1)</td>
<td>2.7 (1.9-3.9)</td>
</tr>
<tr>
<td>SGA</td>
<td>2.7 (1.8-4.1)</td>
<td>1.5 (1.0-2.4)</td>
</tr>
</tbody>
</table>

Misconception #7

“Methadone or buprenorphine is trading one addiction for another”
Substance use disorder v
Physical dependence

• Opioid use disorder (DSM V)
  – Problematic pattern of use leading to clinically significant impairment or distress (in past 12 mo)
    1. Taken in larger amounts or longer duration
    2. Desire to cut back or unsuccessful efforts to cut back
    3. Great deal of time obtaining, using, or recovering
    4. Craving, strong desire, urge
    5. Recurrent use resulting in failure to fulfill obligations
    6. Continued use despite persistent or recurrent social or intrapersonal problems
Substance use disorder v
Physical dependence

• Opioid use disorder (DSM V)
  – Problematic pattern of use leading to clinically significant impairment or distress (in past 12 mo)
    7. Give up important social, occupational, recreational activities
    8. Recurrent use in physically hazardous situations
    9. Continued use despite knowing physical or psychological problems
    10. Tolerance*
    11. Withdrawal*
Substance use disorder v
Physical dependence

• Physical dependence
  – **Tolerance**: loss of effect after repeated use, leading to need for higher doses to achieve desired effect
  – **Withdrawal**: constellation of unpleasant symptoms that occur after abstinence to a substance
Medication Assisted Treatment

**Methadone**
- Full opioid agonist
- T1/2 = 36-48 hours
- Dosed at certified opioid treatment program

**Buprenorphine**
- Partial opioid agonist
- T1/2: 36 hours
- Physicians & PA and ARNP*
- Combination naloxone to prevent diversion
Misconception #8
“Buprenorphine is better than methadone”

Methadone

Pros:
• Daily observed dose
• Less risk for diversion
• Full opioid agonist
  – No precipitated withdrawal
• Ancillary services at methadone clinic
• Better retention

Cons:
• Daily observed dose
• QTc prolongation
• Medication interaction
• Prolonged induction
• More stigma
• Less available in rural area

Buprenorphine

Pros:
• Office based treatment
• Less stigma
• Less overdose risk
• Induction faster

Cons:
• Withdrawal to start
• Partial opioid agonist
  – Risk of precipitated withdrawal
• Higher diversion risk
• Ceiling effect for high equivalence doses
• Fewer prescribers
Misconception #9

“I don’t want my baby born addicted”
“I don’t want my baby to go through withdrawal”
Opioid Replacement in Pregnancy and NAS

Outcomes comparing methadone to buprenorphine

Figure 2. Mean Neonatal Morphine Dose, Length of Neonatal Hospital Stay, and Duration of Treatment for Neonatal Abstinence Syndrome.

Neonatal Abstinence Syndrome

• **Pearls:**
  - Explain ORT as a healthy treatment in pregnancy and treatment as NAS as part of it
  - Prepare and set expectations
  - Compare to glucose in neonates of GDM
  - Encourage mother to be mother
  - NAS improved with rooming in and skin to skin
  - NAS improved with breastfeeding
Misconception #10
“*I want to keep my dose low to decrease baby’s withdrawal*”

Dose of methadone not associated with severity of neonatal withdrawal

- Meta-analysis of 29 studies
- Less NAS with 20-40 mg
- No difference in risk when comparing the prospective studies or in studies with objective scoring tools

Misconception #11

“I’ll have to be on methadone the rest of my life”
“I’ll taper off after I deliver”

Discontinuation rates:

- Prenatal: 0-33%
- Postpartum: 26-64%
- 50% will be off methadone by 6 months

Encourage treatment as long as it is working

- At least 1 year

Misconception #14

“ORT is adequate for acute pain”
“You can’t have adequate pain relief on ORT”
“Prescribing opioids for pain will cause relapse”
Acute pain management while on buprenorphine or methadone

• Home dose not enough for acute severe pain
• Possible to have adequate pain control after delivery
  – Consider high affinity opioid mu receptor agonists
    • 2-4 times the normal dose
    • Hydromorphone PCA
    • Hydromorphone (Dilaudid) approx 3-6 mg q3h
  – Morphine (Duromorph) spinal (18hrs)
  – Utilize non-opioid medications like APAP & NSAIDs
  – Mildfulness, stress reduction
• No studies show that prescribing opioids for acute pain will cause relapse

Conclusions

• Opioid use disorder is a complex neurobiological, psychosocial disease
Conclusions

- Universally screen all pregnant women for substance use with 4Ps or CRAFT
Conclusions

• Opioid exposure in utero may be linked with neurocognitive deficits in children which may be overcome by environmental stability
Conclusions

- Lack of adequate control in studies and complicated confounders makes it difficult to ascertain if in utero exposure of opioids causes birth defects
Conclusions

• Opioid use during pregnancy is associated with poorer obstetrical outcomes
Conclusions

• Medication assisted treatment with methadone or buprenorphine is the standard of care for opioid use during pregnancy
Conclusions

• Methadone dose does not equate to severity of NAS
Conclusions

- NAS less incidence, severity, duration with buprenorphine compared with methadone
Conclusions

• Adequate pain control possible with on opioid replacement therapy
Work cited


• Hendrée E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stine, M.D., Ph.D., Mara G. Coyle, M.D., Amelia M. Arria, Ph.D., Kevin E. O'Grady, Ph.D., Peter Selby, M.B., B.S., Peter R. Martin, M.D., and Gabriele Fischer, M.D. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure N Engl J Med 2010; 363:2320-2331

end
Opioid Replacement in Pregnancy and NAS

NAS - methadone compared to buprenorphine

Side effects of MAT

• Feb 2017
  – N=49 Buprenorphine maintained pregnant women
    • Monitored 60 min peak and trough @ 24, 28, 32, 36 wk
    • Decrease in peak and trough fetal HR by 2-5 bpm
    • Decreased activity
    • Does not effect accelerations
“Diagnostic overshadowing refers to a well-described clinically and ethically problematic phenomenon in which clinicians ignore patients’ general health concerns because of that patient’s mental illness... such that legitimate general health problems are misattributed as originating from a patient’s mental illness.”

Artist Kumi Yamashita
Misconception #5
“All I need to do is detox from everything”

Opioid detoxification during pregnancy

Luty et al, 2003
– No clear evidence of safety for detoxification
– 101 pregnant women underwent 21 day detox
– One first trimester SAB, 1 premature delivery

Jones et al, 2008
– Methadone assisted withdrawal during pregnancy
  • Less time in treatment, fewer prenatal care visits, less likely to deliver at study hospital

Figure 4. Forest plot of comparison: I Flexible dose buprenorphine versus flexible dose methadone, outcome: I.1 Retention in treatment.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Buprenorphine</th>
<th>Methadone</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
</tr>
<tr>
<td>1.1.1 Double-blind flexible dose studies</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Johnson 2000</td>
<td>32</td>
<td>55</td>
<td>40</td>
</tr>
<tr>
<td>Mattick 2003</td>
<td>96</td>
<td>200</td>
<td>120</td>
</tr>
<tr>
<td>Petitjean 2001</td>
<td>15</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Strain 1994a</td>
<td>47</td>
<td>84</td>
<td>45</td>
</tr>
<tr>
<td>Strain 1994b</td>
<td>13</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>203</td>
<td>390</td>
<td>248</td>
</tr>
</tbody>
</table>

Total events: 697/694, 100.0%  
Risk Ratio M-H, Random, 95% CI: 0.83 [0.73, 0.95]  
Heterogeneity: Tau² = 0.03; Chi² = 22.79, df = 10 (P = 0.01); I² = 56%  
Test for overall effect: Z = 2.77 (P = 0.006)  
Test for subgroup differences: Chi² = 0.05, df = 1 (P = 0.82), I² = 0%