Objectives

- Identify the scope and prevalence of opioid use in pregnancy and the postpartum period
- Identify fetal and maternal risks associated with opioid use in pregnancy
- Review screening and testing for opioid use in pregnancy
- Discuss treatment options and review recommended pregnancy surveillance for those with opioid use disorder

Introduction

- What are Opioids?
  - Natural or synthetic chemicals that interact with mu receptors on nerve cells, gastrointestinal tract, spinal cord, and brain.
  - Powerful effect on brain—positive and negative reduction of feeling of pain
  - Can lead to addiction
  - Tolerance—escalate the dose to achieve same desired effect
  - Dependence—withdrawal symptoms in the absence of the drug

Types

- Codeine (only available in generic form)
- Oxycodone (Oxycontin)
- Aspirin and oxycodone (Percodan)
- Hydrocodone (Hydingia ER, Zohydro ER)
- Hydrocodone/acetaminophen (Vicodin)
- Hydromorphone (Dilaudid)
- Meperidine (Demerol)
- Methadone (Dolophine, Methadose)
Scope of Opioid Epidemic

• Fewer than 5% of world’s population live in US, but nearly 80% of world’s opioid are written for in US
  • more than enough to give every American adult their own bottle of pills
• 2012, 259 million prescriptions were written in the US
• 2015, 2 million people abuse opioids
  • 1,400,000 from prescription abuse
  • 600,000 from heroin
  • 80% started with prescription opioids

• 2015, 52,404 drug overdose deaths
  • 33,000 from Opioids
  • 12,000 deaths due to heroin
  • 80 people every day
  • Over 60% are from prescription Opioids
• Drug overdose is now the leading cause of accidental death in the US
  • 1999-2015, the deaths from Opioid prescriptions
  • Female deaths increased by 471%
  • Male deaths increased by 218%
  • Estimated cost of $78 Billion each year due to Opioid abuse

Scope of Opioid Epidemic

We are part of the problem

- Emphasis on post operative pain control
- National campaign to improve patients experience with pain
- Concurrently, marketing efforts by pharmaceutical industry to reassure medical community that patients would not become addicted

Peripartum Opioid Use

- 1:300 opiate naive women will become addicted after receiving opiates after cesarean

Opioid use during pregnancy

- US Medicaid
- US Commercial
- Canada
- Norway
- Scotland
- Norway
- Scotland

Percentage

Anesthesiology. 2014 May;120(5):1216-24
Obstet Gynecol. 2014 May;123(5):997-1002
Eur J Clin Pharmacol. 2011 Sep;67(9):953-60
Drug Saf. 2010 Jul 1;33(7):593-604
Maternal and Fetal risks

- Lack of prenatal care
- Risk of infectious disease
  - HIV, Hep C, STI's
- Criminal activity and arrests
- Maternal trauma
- Loss of child custody
- Depression
- Under nutrition
- Prematurity
- Growth restriction
- Abortion
- Stillbirth
- Congenital anomalies
- Neonatal Abstinence Syndrome/Neonatal Opioid Withdrawal Syndrome (NAS/NOWS)

Endogenous opioids are regulators of development
Exogenous opioids may impact development
Animal studies: May be toxic to the developing CNS

Teratogenicity

<table>
<thead>
<tr>
<th>Condition</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spina bifida</td>
<td>1.8 (1.1–3.0)</td>
</tr>
<tr>
<td>HLHS</td>
<td>2.5 (1.3–4.3)</td>
</tr>
<tr>
<td>Pulmonary stenosis</td>
<td>2.0 (1.3–3.1)</td>
</tr>
<tr>
<td>Gastrochisis</td>
<td>1.9 (1.2–3.1)</td>
</tr>
<tr>
<td>Teratology of Fallot</td>
<td>2.1 (1.2–3.5)</td>
</tr>
<tr>
<td>Perimembranous VSD</td>
<td>1.8 (1.2–3.0)</td>
</tr>
<tr>
<td>ASD/VSD</td>
<td>2.3 (1.2–4.1)</td>
</tr>
<tr>
<td>Cleft palate</td>
<td>2.9 (1.3–6.4)</td>
</tr>
</tbody>
</table>

Pregnancy Outcome

<table>
<thead>
<tr>
<th>Condition</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal growth restriction</td>
<td>2.7 (2.4–2.9)</td>
</tr>
<tr>
<td>Abortion</td>
<td>4.4 (3.2–5.9)</td>
</tr>
<tr>
<td>Premature birth</td>
<td>3.1 (1.5–6.2)</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>1.5 (1.1–1.8)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>4.3 (1.3–13.1)</td>
</tr>
<tr>
<td>Died during hospitalization</td>
<td>4.6 (1.6–13.1)</td>
</tr>
</tbody>
</table>

Screening for Opioid Use in Pregnancy

- American College of Obstetricians and Gynecologists (ACOG, 2015 and 2017)
- Screening should be:
  - "part of comprehensive obstetric care"
  - "done at first prenatal visit in partnership with the pregnant woman"
  - "applied equally to all people, regardless of age, sex, race, ethnicity, or socioeconomic status"
  - "rely on validated screening tools, such as questionnaires, including 4P, NIDA quick screen and CRAFFT (for women 26 years and younger)."

4P's and NIDA Quick Screen
Peripartum Opioid Use

Bateman et al.
- What is the risk that women exposed to opioids after CD go on to become persistent opioid users?
- Over 80,000 opioid-naive women dispensed opioids following CD
- Trajectory models used to define distinct patterns of opioid use for 1 year following CD


Bateman et al.

Risk Factors
- Younger age
- Smoking
- Cocaine abuse

Pain Conditions:
- Back pain
- Fibromyalgia
- Headache
- Benzodiazepine use

Pain in pregnancy
- Common in pregnancy
  - Low back pain
  - Pelvic girdle pain
  - Hip and knee pain
  - Leg cramps
  - Carpal tunnel
- Acute and Chronic conditions unrelated to pregnancy
- Postpartum pain

Strategies to minimize opioid use in pregnancy
- Vaginal delivery
  - If Opioids REALLY needed
  - If so limit duration to 3 days or less
- Maximize Non-opioid treatment options
  - Pharmacologic:
    - NSAIDS, acetaminophen, adjuvant pain medicines
  - Non pharmacologic:
    - Exercise, PT, behavioral therapy, etc
- Shared decision making model
Strategies to minimize opioid use in pregnancy-Cesarean Delivery

- Popcorn theory of opioid prescribing

Post Discharge Opioid Use After Cesarean

- % Women did not use all prescribed opioids
- median of 10 unused tablets of 5 mg oxycodone
- Majority of unused opioids are stored in unlocked locations, risking potential nonmedical use and diversion
- A small subset use all opioids prescribed
- Homogenous or “one-size-fits-all” opioid prescribing risks underprescribing to an important subset of the population.

Postpartum pain management

- Contributes to opioid epidemic
- Opioid exposure as a precipitant for persistent use
- Excessive prescribing leading to leftover medication
  - Over 50% of opioids used more than medically were obtained from a friend or family member

All Things Considered
National Public Radio  January 23, 2017
Patterns of Opioid Prescription and Use after Cesarean

- Survey at 6 academic medical centers in the U.S. from 9/2014 to 1/2016.
  - MGH
  - BWH
  - Michigan
  - Columbia
  - Wake Forest
  - Stanford

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>25th–75th Percentile</th>
<th>10th–90th Percentile</th>
<th>Range</th>
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<tbody>
<tr>
<td>Tablets dispensed</td>
<td>40</td>
<td>38–48</td>
<td>24–61</td>
<td>5–68</td>
</tr>
<tr>
<td>Tablets consumed</td>
<td>20</td>
<td>5–36</td>
<td>5–36</td>
<td>5–36</td>
</tr>
<tr>
<td>Tablets unused</td>
<td>21</td>
<td>1–35</td>
<td>0–15</td>
<td>3–26</td>
</tr>
</tbody>
</table>

Bateman B, Obstet Gynecol 2017;130:29–35

Opioid Use Disorder in Pregnancy

- Ethical Considerations
- Prenatal Care
- Medical Assisted Therapy (MAT)

Ethical Considerations

- Key principles
  - Respect of autonomy—Nothing without disclosure and permission
  - Justice—policies, approaches, benefits and burdens are equally shared
  - Truth—honest in disclosing plans and consequences
  - Beneficence—screening/testing should be directed toward improving health and outcomes: treatment not punishment

Normative opioid consumption after cesarean

<table>
<thead>
<tr>
<th>Number of pills</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dispensed</td>
<td>40 (30-60)</td>
</tr>
<tr>
<td>Consumed</td>
<td>20 (8-35)</td>
</tr>
<tr>
<td>Leftover</td>
<td>15 (6-26)</td>
</tr>
</tbody>
</table>

95% had not disposed of leftover at time of the interview

Obstet Gynecol 2017;130(1):29-35
Ethical Considerations

• Disease and illness should not be treated as a moral failing
  – Care, not prosecution, will result in best and healthiest outcomes for women with OUD in pregnancy
• If consequence/purpose is separation of child from mother
  – What evidence that this benefits the mother?
  – What evidence that this benefits the child?

ACOG: “Ob/Gyn’s have an ethical responsibility…to discourage separation of parents from children solely based on substance use disorder either suspected or confirmed.”

• However….

Physician attitudes concerning legal coercion of pregnant alcohol and drug abusers
Abel et al. AOG 2002

• 95% indicate that pregnant women have a moral responsibility to act for the health of a pregnancy
• 58% indicate that pregnant women have a legal responsibility to act for the health of a pregnancy
• 61-75% favor mandatory [testing] for alcohol abuse
• 43-55% favor mandatory [testing] for illicit drugs
• 61% fear that prosecution deters patients seeking prenatal care
• 52% believe that drug abuse in pregnancy should be defined as child abuse and neglect (for the purposes of removing from custody)
• 23-34% supported incarceration for drug abuse in pregnancy

Prenatal Care considerations

• Agree on things that promote healthy outcomes for mothers and fetuses/neonates
  – This is generally not a dichotomy
  – Focus on provision of treatment for OUD
• Focus less on presence and prevalence of NAS
  – Which is an expected outcome for MAT, a treatment that promotes healthier outcomes in women with OUD

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Prenatal Care of OUD Patient

• Universal screening—using validated method
• Early ultrasound (8-12 weeks) if possible
• Detailed anatomic survey ultrasound at 20 weeks
• Fetal echocardiogram ultrasound at 22-24 weeks
• Serial growth ultrasounds every 4 weeks
• 9T assessments (cervical length only if indicated)
• Antepartum testing in the third trimester
• Medication Assisted Therapy (MAT) using Buprenorphine
• Delivery at 39 weeks EGA
• Behavioral health/counseling
Postpartum Considerations of OUD Patient

- Women on MAT should have it continued intrapartum and postpartum
- Epidural/spinal anesthesia is appropriate
- Patients on Methadone should NOT receive partial agonists (e.g., butorphanol, nalbuphine, pentazocine) due to precipitating withdrawal
- Post operative pain can be successfully treated with acetaminophen, NSAIDs, and FULL agonist (e.g., oxycodone) when needed
- OUD patients may have hypersensitivity to pain and poor tolerance
  - most commonly in the first 24 hours post c/S
  - may require up to 50% more drug

Common Misconceptions Surrounding Pregnancy and Medication-Assisted Therapy (MAT)

Common Misconception
- Medication-assisted therapy must be stopped in order to achieve pain control with opioids (e.g., after C/S)
  - FALSE
- Patients with a history of opioid use disorder cannot be treated postoperatively with opioids for pain
  - FALSE
- Patients on medication-assisted therapy cannot breastfeed
  - NOT

Reasoning
- Pain control can be achieved with full opioid agonists despite taking medication-assisted therapy
- When prescribed for pain control, there is no evidence to suggest increased risk of withdrawal
- Breastfeeding has been shown to improve neonatal outcomes

ACOG Committee Opinion 711:

- Gold Standard Treatment
  - Methadone
  - Buprenorphine

Medication Assisted Treatment (MAT)

- Decreased:
  - Opioid use
  - Opioid related overdose
  - Opioid related mortality
  - Criminal Activity
  - Infectious Disease transmission
- Increased:
  - Social functioning
  - Employment
  - Treatment retention

Buprenorphine vs Methadone

- 8 site RCT
- 175 Perinatal OUD
- Comprehensive addiction and obstetric care
- Primary Outcomes
  - NAS, NAS treatment, length hospital stay
- Secondary Outcomes
  - Other neonatal outcomes (Wt., PTB, GA, Apgar) Maternal outcomes (c/S, complications, UDS)

Buprenorphine vs Methadone

Perinatal OUD Treatment

- Opioid Use Disorder [Heroin and/or IV Opioid Use]
  - Buprenorphine or Methadone

- Opioid Use Disorder [Prescription Opioids]
  - Buprenorphine or Methadone

  - If considering taper
    - Not to mitigate neonatal withdrawal, but for patient preference
    - Individual assessment
    - Long tapers, intensive follow-up care

Perinatal OUD Treatment

- MORE RESEARCH IS NEEDED!!

- Can we taper? Who can taper? Optimal treatments?
  - Large, prospective studies, in depth maternal, fetal and newborn assessments

- Buprenorphine, Naltrexone
  - Pharmacokinetics, Pharmacodynamics

- Naltrexone
  - Large, prospective studies, in depth maternal, fetal and newborn assessments

In Summary..

- Perinatal Opioid Use Disorders are a major public health issue in US
- Evidence based guidance for prevention and management in pregnancy is lacking
- Universal Screening at the first prenatal visit is recommended
- Testing should be performed with informed consent
- Antepartum, Intrapartum and Postpartum pain is common and should be treated appropriately
- Medication Assisted Treatment reduces severity of neonatal withdrawal and decreases relapse
- MUCH WORK IS NEEDED

Questions?

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