Treatment of Substance Use Disorders in the Perinatal Patient

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Disclosure Statement:
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Funding:
• Massachusetts Department of Mental Health via MCPAP for Moms

Other:
• Consultant, GLG Consulting
• Consultant Pennside Partners
• Uncompensated Co-investigator, Sage Therapeutics
Overview
“I was good for 51 yrs”

Ms C is a 52 yo woman, divorced 1.5 yrs ago, who was admitted to the medical hospital for treatment of pancreatitis

• Treated for alcohol withdrawal at the beginning of admission
• Alcohol use escalated after divorce
• Lost her job as a dental hygienist and nearly losing her home
• Declined referral for treatment
Sex based differences

- SUD are more common in men than women
  - The gap is closing
  - May be age related
Sex based differences

• Different course/natural history
  – Telescoping – accelerated progression from initiation of use to onset of dependence and initiation of tx – seen with ETOH, opioids, cannabis
  – Interpersonal factors modulate progression (partners and children)
Sex based differences

• Biological
  – Menstrual cycle, pregnancy, aging and menopause
  – Ovarian sex steroids impact effects of cocaine, amphetamines, cannabis
  – Sex-based ETOH thresholds

• Psychiatric comorbidity
  – Mood disorders
  – Eating Disorders
  – PTSD
Women can benefit from gender specific treatment

• Childcare, prenatal care, integrated HIV care
• Women only treatment associated with lower rates of relapse and improved outcomes in some studies
• A minority of programs offer women-targeted treatment
What makes pregnancy different?
“I just can’t get it together”

- Christy is a 32 yo F who presented to Labor and Delivery reporting she had abdominal pain and was “around 7 months pregnant”
  - One prenatal visit - “smelled of alcohol”
  - Outreach calls from midwife found patient to have slurred speech
  - DV, unstable housing, loss of custody, poor access to food and health care
  - Drinking daily
  - Accepted referral for substance tx though did not show for appt
Drug Use in the past month, Females 15-44

NSDUH 2012
Substance Abuse during pregnancy – opportunities and challenges

• Pregnancy is a motivator for cessation

• Persistence of substance abuse during pregnancy may represent a particularly refractory and high risk subpopulation

• Higher levels of use prior to pregnancy correlate with continued use during pregnancy

• Most women return to pre-pregnancy rates of smoking and alcohol abuse within 6-12 months postpartum

Detection of Substance Use in Pregnancy – Red Flags

- Late presentation to prenatal care
- Acute intoxication
- Requests for controlled substances
- Positive toxicologic screen in mother or baby
- IUGR detected during antepartum testing
- Withdrawal suspected in the neonate
Detection - Screening

- **4 P’s** – Validated for screening in pregnancy and postpartum
- **CRAFFT** – validated for use in adolescents
Detection - Toxicologic Screening

• Maternal screening
  – Prenatal and at the time of delivery
    • Universal toxicologic screen not recommended
    • Role of negative tests

• Neonatal screening
  – Serum/Urine reflect recent use
  – Hair/Meconium reflects use since 2\textsuperscript{nd} trimester
  – Cord blood

• Consent
Substance use in pregnancy presents barriers to treatment engagement

- Stigma and shame
- Refractory illness
- Providers’ own emotional reactions
- Concerns about DCF reporting
- Legal implications
- Access to treatment
- Time elapsed before recognition of pregnancy
Risk of untreated symptoms

Risk of treatment
Opioid Use in Pregnancy

• Opioids are not likely directly teratogenic\textsuperscript{1,2}
• Opioid dependence during pregnancy is associated with:
  – Intrauterine growth restriction
  – Intrauterine fetal demise and stillbirth
  – Preterm labor
  – Placental abruption
  – Postpartum hemorrhage
  – Reduced cognitive function in exposed children
• Risks related to peaks/troughs and intermittent w/d
• Lifestyle factors associated with use/relapse

Rates of Opioid Use in Pregnancy are increasing

Between 2000 and 2009, opioid use among women who gave birth increased in the United States from 1.19 to 5.63 per 1,000 hospital births per year.

Patrick JAMA (2012)
Medication treatment for OUD in Pregnancy

• No FDA approved treatment
• Mainstays of treatment include medication:
  – Methadone
  – Buprenorphine (single or combination)
• Withdrawal MAY present a risk to the fetus\(^1\)\(^-\)\(^5\)
  – Risk of stillbirth, IUFD, preterm labor, meconium
• High risk of relapse after discontinuation of opioids\(^6\)
• Neonatal Abstinence Syndrome

Benefits of medication in pregnancy

Maternal Benefits

• 70% reduction in overdose related deaths
• Decrease in risk of HIV, HBV, HCV
• Increased engagement in prenatal care and recovery treatment

Fetal Benefits

• Reduces fluctuations in maternal opioid levels; reducing fetal stress
• Decrease in intrauterine fetal demise
• Decrease in intrauterine growth restriction
• Decrease in preterm delivery
Methadone – Pharmacodynamic Considerations During Pregnancy

- Administered through a federally licensed facility
- Breakthrough withdrawal symptoms may appear in the third trimester
- Doses typically 80-120 mg
  - may need to increase in 3rd trimester
- Split dosing should be considered
  - From daily to twice a day

Park 2012
Methadone – Fetal considerations

- Decreased heart rate and heart rate variability
  - Greater at peak than trough
- Slower breathing movements on BPP
- Decreased fetal movements on BPP
Buprenorphine causes shorter duration and less severe NAS
Buprenorphine is an office based treatment

- Buprenorphine is a high affinity partial agonist at the mu opioid receptor

- Buprenorphine has lower OD risk, fewer drug interactions, office based administration, less risk of sedation than methadone

- Use buprenorphine alone (not combined with naloxone) (Brand name: Subutex)
  - theoretical risk of inducing maternal/fetal withdrawal
  - animal data re teratogenicity

Jones 2010, Blandthorn 2011, Park 2012
Buprenorphine is Effective in Pregnancy

- Similar to methadone in reduction of illicit drug use/relapse risk
- No apparent difference between buprenorphine and methadone for:
  - Maternal weight gain
  - Cesarean section
  - Abnormal presentation
  - Use of analgesia
  - Positive drug screen
  - Medical complications at delivery

- Implications for peripartum pain management

Jones 2012
Buprenorphine – Fetal effects

- In analyses of MOTHER participants buprenorphine exposed fetuses had
  - Less motor suppression
  - Lower incidence of non reactive Non Stress Tests
  - Clinical significance of these findings not clear
Naloxone should be prescribed to all opioid users

• Opioid overdose is a leading cause of death in the US
  – Suicide and OD leading causes of maternal mortality
• Fetal effects have been reported
• *Risk of maternal death outweighs fetal risks in the case of overdose*
Naltrexone

• Limited human data
• Animal data suggests not teratogenic
• Induction onto naltrexone in pregnancy is not recommended
• For those already using extended release naltrexone/implantable naltrexone, maybe reasonable to continue during pregnancy

Saia 2016
How do I choose?

• Methadone and Buprenorphine are both effective options
• In a patient stable on treatment, no need to switch
• In a patient new to treatment or who wishes to switch consider:
  • Patient preference
  • Access
  • Need for structured treatment
  • Methadone ->buprenorphine is difficult and not recommended
Neonatal Abstinence Syndrome

SIGNS
• Neurologic excitability
  – Tremor, seizure, inc muscle tone, yawning, sneezing, irritability
• GI dysfunction
  – Feeding diff, vomiting, diarrhea, poor wt gain
• Autonomic signs
  – Diaphoresis, fever/temp instability

IDENTIFICATION OF RISK
• Maternal history
• Onset depends on which agent/confounding agents
  – Not dose dependent
• Tox screens
• Validated scales
  – All are subjective
• Unclear long term consequences
Rates of Neonatal Abstinence Syndrome have increased

The incidence of NAS increased from 1.20 per 1,000 hospital births per year in 2000 to 3.39 per 1,000 hospital births per year in 2009.
New England has the second highest rate of Neonatal Abstinence Syndrome

Neonatal Abstinence Syndrome is Costly

- Newborns with NAS were more likely to have
  - low birthweight
  - respiratory complications
- Mean hospital charges for discharges with NAS increased from $39,400 in 2000 to $53,400
  - Average LOS 16 days
  - $720 million in 2009

Wiles 2014; Patrick 2012
Treatment of NAS

• NON Pharmacologic treatment is first line
  – Breastfeeding – low levels of opioids in BM
  – Rooming in, low stim enviro, swaddling, sucking
• Morphine
• Methadone
• Buprenorphine
• Adjunctive Medications
  – Phenobarbital, clonidine
Maternal Dose and NAS Severity

• No correlation between maternal opioid maintenance therapy dose and the duration or severity of NAS

• Women should be encouraged to report any symptoms of withdrawal through her pregnancy without fear a dose increase will affect her baby’s hospital stay or need for NAS treatment

• Tobacco and SSRI use may worsen NAS

Cleary et al. 2010; Iseman et al. 2010;
Mothers on MAT should be encouraged to consider breastfeeding

- Amount of methadone in breastmilk is low
  - 1-6% of weight adjusted maternal dose
- Amount of buprenorphine in breastmilk is low
  - 1-20% of maternal weight adjusted dose present in breastmilk
  - Poor oral bioavailability further limits exposure
- Can observe for neonatal sedation
- Enhance maternal infant bonding and Reinforce maternal role
- Improve NAS outcomes

Alcohol Abuse during Pregnancy is common and carries known risk

• Epidemiology
  – 12.2% of pregnant women reported alcohol use during the prior month
  – NO safe amount defined
  – New AAP statement on FASD Oct 2015
  – DSM5: Neurobehavioral DO assoc w Prenatal Alcohol Exposure (ND-PAE)

• Fetal effects
  – Spontaneous AB, PTL, stillbirth, IUGR
  – Ethnic variation, polymorphisms change risk for fetal effects

• Neonatal effects
  – 1st tri use – 12x risk of FASD
  – Intoxication and Withdrawal
  – SIDS

• Childhood effects
  – Learning DO, ADHD, executive dysfunction, anxiety DO, mood DO, SUD
Neurobehavioral DO associated with prenatal Alcohol Exposure (FASD)
Figure 1. T-ACE and TWEAK for problematic alcohol use

**T-ACE**

**T** How many drinks does it take to make you feel high? (Tolerance)

**A** Have people annoyed you by criticizing your drinking?

**C** Have you felt you ought to cut down on your drinking?

**E** Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover? (Eye-opener)

Scoring: **T**: 2 points if > 3 drinks; **A, C, E**: 1 point for each yes answer

A total of 2 or more points indicates patient is likely to have an alcohol problem.

**TWEAK**

**T** Tolerance

**W** Have friends or relatives complained about your drinking? (Worried)

**E** Eye-opener

**A** Has a friend or family member ever told you about things you said or did while you were drinking that you could not remember? (Amnesia or black-out)

**K** Cut-down

Scoring: **T**: 2 points if > 3 drinks; **W, E, A, K**: 1 point for each yes answer

A total of score of 3 or more points indicates patient is at-risk drinking
Alcohol Withdrawal in pregnancy is managed with benzodiazepine taper

• Medically supervised withdrawal
  – Appropriate setting
  – Risk of withdrawal during pregnancy not well defined
  – Risk during labor and neonatal withdrawal
  – No RCTs to guide choice of medication
    • lorazepam or chlordiazepoxide

Gopalan 2015; Devido 2015, Gopalan 2014
Brief Interventions can impact alcohol use in pregnancy

- Pregnant women are generally motivated to change
- Physician relaying information
- Motivational interviewing
- Goal setting and evaluation of triggers
- Education re potential harms
Alcohol may impact lactation

- Alcohol can decrease breastmilk volume and milk ejection reflex
- Alcohol equilibrates across membranes within 30-60 minutes – high exposure risk
- Infant effects on growth, motor and feeding/sleeping behavior
- Varying recommendations regarding “safe” amount to consume

Giglia 2006
Cannabis is the most commonly used illicit substance in pregnancy

- 48-60% of users continue during pregnancy
- Rates of use increase with low SES
- No consistent data regarding structural teratogenesis
- No described neonatal intoxication or withdrawal syndrome
But it’s natural...

- THC in marijuana ↑ 25x since 1970s
- No compelling evidence that cannabis treats any condition
- Legalization and Medicalization make marijuana more accessible
- Not recommended in women of childbearing age or in nursing mothers.
Cannabinoids are lipophilic

- Readily cross BBB, placenta and into breastmilk
- Half life: 20-36 h to 4-5 d (chronic users)
  - 5 half lives for complete excretion
- Fetal plasma levels can be 10% maternal levels
- Higher concentration in fetal tissue with chronic use (animal)
- Deposits in maternal fat

Cannabis use can impact pregnancy through many mechanisms

• Implantation

• Growth Restriction
  – Dose response – greater effect with continued use
  – Birthweight and head circumference

• Neural Development (CB1 receptors in fetal brain, 60% fat)

• THC decreases fetal folic acid uptake (risk of SpAb, NTD, LBW)
ACOG urges preconception and pregnant women to stop marijuana

- Fetus has endocannabinoid receptors
- Cannabinoid use may disrupt brain development (animal studies)
- Intrauterine growth restriction and Low birth weight
- Increased risk of stillbirth (limited evidence)
- Developmental risks: visual processing, attention, behavior, inc risk for MJ use
- Risks associated with smoking

Cannabis use in lactation can result in significant exposure to the baby

• Lactation
  – Readily passes into breast milk
    • Regular consumption- 8x higher conc in BM!
  – May inhibit milk supply (inhibit GRH, prolactin, TSH)

• Women should be advised to abstain

Marroun et al (2009) JAACAP; Jacques
Journal of Perinatology (2014)
Cocaine

• Primary effects are due to vasoconstriction
  – Spontaneous abortion
  – Placental abruption
  – Placental insufficiency
• Increased risk for LBW, SGA, PTB
• Intoxication can mimic preeclampsia
• Not likely a structural teratogen
• Lasting effects on child growth and neurodevelopment

Cressman et al JOGC 2014; Cain et al Clin OG 2013
Stimulants

• Need to distinguish therapeutic use vs abuse
• Abuse of amphetamines associated with risks associated with placental vasoconstriction
• Data suggest with therapeutic use both amp and mph:
  – Not likely teratogenic
  – Impact on fetal growth (?before week 28)
• During pregnancy - appetite suppression/low mat wt gain
• Lactation – Relatively low exposure
  – Methylphenidate: RID of <1%
  – Dextroamphetamine: RID 5.7%

Bolea- Alamanac et al Br Journ Pharmac 2013; Freeman AJP 2014
Summary

• Women with SUD biological and social differences, especially in pregnancy
• OUD is a growing problem with emerging treatments
• Buprenorphine and methadone are mainstays for OUD
• Alcohol Use requires screening and counseling in pregnancy
• Cannabis use is prevalent and not recommended during pregnancy
• Cocaine and stimulants carry significant risk when abused
Questions?

www.mcpapformoms.org

Call 855-Mom-MCPAP
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Thank you!