OPIOID USE DISORDER IN PREGNANT PATIENTS

Tuesday, January 7th 2020 Damali Campbell Oparaji MD Assistant Professor Rutgers, New Jersey Medical School Department of Obstetrics, Gynecology and Reproductive Health Board Certified in Addiction Medicine

Disclosures

- No financial disclosures
- I am a member of the NJ Maternal Mortality Case Review Team- we review the death of all women within 1 year of a pregnancy regardless of how and when that pregnancy ended who reside in NJ.



- Review the unique factors to consider in dealing with SUD in pregnancy
- Review recommended treatments for OUD in pregnancy
- Recognition of postpartum vulnerabilities for women with OUD

The scope of the problem

- Growing numbers of women use nicotine, alcohol and illicit substances and since 1990's rising use of nonmedical use of prescription opioids
- A 2013 national survey on drug use and health summarizes that substance use is common in women of childbearing age.
- Approximately:
 - $_{\odot}$ 55% drink alcoholic beverages,
 - 23% smoke cigarettes
 - And 10% use illicit drugs or prescription drugs without a prescription

45 % of pregnancies are unplanned

 All providers, including those who treat women with substance use disorder need to be asking :

One Key Question

- Do you want to be pregnant in the Next 1 year ?
- Yes
- No
- Possibly

ACOG, AAP, AMA, ASAM and CDC

- Recommend Universal Screening for substance use in annual well visits and at least at first pregnancy visit (consider once a trimester)
 - first visit regardless of race, country of origin, socioeconomic, insurance status, zip code, gestational age at presentation
 - The best way to make this non judgmental is to make it a part of your habit and routine.
 - In the past year how often have you taken a medicine for pain relief: Tylenol with codeine, Percocet, morphine, dilaudid, heroin? If yes, was this prescribed? By whom? When?
 - Annual basis for well women care

5% of Women in Pregnancy use Illicit Substances

- Marijuana- currently 11 states and District of Columbia have legalized recreational Marijuana and an additional 22 states have legalized marijuana for medical use
- Heroin
- Cocaine
- Stimulants
- Misuse of prescription Percocet, oxycodone, Vicodin

Best Practice:

Screen Everyone at the First Prenatal Visit

<u>4 P's</u>

- Did either of your **parents** have a problem with alcohol or other drug use ?
- Does your partner have a problems with drug or alcohol use ?
- In the past have you had difficulties in your life because of alcohol or other drugs, including prescription medications?
- In the **past month** have you drunk any alcohol or used any other drugs ?
- **<u>CRAFFT</u>** (26 years or younger)-2 or more positive items indicate need for further assessment.
- Have you ever ridden in a CAR driven by someone who was high or using drugs or alcohol ?
- Do you ever use alcohol or drugs to RELAX, feel better about yourself or fit in ?
- Do you ever use alcohol or drugs whole you are by yourself or ALONE ?
- Do you ever **FORGET** things you did while using alcohol or drugs ?
- Do your **FAMILY** or friends ever tell you that you should cut down on your drinking or drug use ?
- Have you ever gotten in TROUBLE while you were using alcohol or drugs ?

Definition of Opiate Use Disorder

Opioid Use disorder (OUD) is characterized by:

- Tolerance, Craving, Inability to control Use, Continue use despite Adverse Consequences
- DSM-5 Criteria- recurring symptoms in a 12 month period:
 - failed efforts to stop or cut down, craving, increasing use over time, increasing time spent drug seeking/drug using, failure to meet obligations because of use, use despite social/interpersonal problems, decrease in other activities because of use, use despite physical risk, tolerance, use despite knowledge of problems cause by opiate use, withdrawal in absence of use
 - Severity of OUD- Mild (2-3), moderate (4-5), severe (6 or more)

What is unique about pregnancy?

- Patient typically has extra motivation to achieve and maintain sobriety for unborn child.
- Physiologic changes in pregnancy may present challenges for patient and/or treatment challenges for providers.
- Pharmacokinetics unique to pregnancy

Assessment of the Pregnant Patient with SUD

- Prior pregnancy history
- Prior treatment received: positive or negative experience
- History of other illicit Drugs, alcohol, Marijuana, nicotine, prescription and OTC meds
- Medical history
- Feelings about current pregnancy
- FOB involvement and family support
- Additional labs: metabolic panel, screening for Hepatitis B and C, syphilis, testing for tuberculosis

Comprehensive Treatment for Opioid Use Disorder in Pregnancy

- All treatments should be a part of Comprehensive Treatment including:
- Medication
- Addiction Counseling
- Family therapy,
- nutritional education,
- other medical and psychosocial services as indicated for pregnant women with opioid use disorder.

Medication Treatment Options for Opioid Use

- No medicine-Abstinence (not recommended particularly for those with SUD)
 - Abstinence only programs and short term treatment programs are associated with high relapse rates
- Methadone
- Buprenorphine
- Naltrexone

What is happening here?

- 25 year old G 1P0 presented for prenatal care@ 25 weeks of pregnancy
- History of IV heroin use
- Had partner who was sober
- Both patient and partner working
- stable in recovery for approximately 3 years on Methadone 70 mg

Patient and Partner concerned because over the past month patient has increased cravings and has began to use illicit drugs in the evening To combat cravings and prevent withdrawal symptoms

Methadone

- Full opiate agonist, 24 hour half life
- Dispensed on a daily basis from a registered opiate treatment program
- Maternal methadone dosages are managed by addiction treatment specialists and are generally titrated based on patients symptoms to avoid withdrawal
- Methadone can be initiated in the hospital for pregnant women in opiate withdrawal (No need to be addiction specialist or x waivered), max dose allowed 30 mg day, next day follow up must be arranged for continuation at discharge. Federal regulation www.gpo.gov/fdsys/pkg/CFR-2016-title21-vol9/xml/CFR-2016-title21-vol9-sec1306-07.xml)

Methadone during pregnancy

- Methadone dosage may need to adjusted (increased or split dosage to twice daily) to accommodate:
 - the increasing maternal blood volume, second and third trimester and
 - Rapid metabolism of methadone that develops during pregnancy, especially in third trimester.
 - Not all women will require dosage alterations, so that dose adjustments should be made on a clinical basis
 - Incidence and duration of NAS does not differ based on the maternal dosage of methadone treatment, so there is no need to minimize dose of methadone.

Inadequate dosage may lead to withdrawal, fetal stress, craving and relapse.

Pharmacokinetics

- Induction of the cytochrome P450 enzyme system by the hormones of pregnancy
- Methadone and buprenorphine are both CYP450 substrates whose metabolism is accelerated by pregnancy.

End goal of therapy must be individualized for the patient to prevent withdrawal.

Methadone versus Buprenorphine

Methadone

- Decades of research supporting methadone's high rate of maternal recovery
- Safety of induction with no risk of precipitating withdrawal
- Access only thru licensed federal programs
- Many drug interactions, may require dosage adjustment in pregnancy

Buprenorphine

- More widely available making, access easier
- Risk of precipitated withdrawal if patient not in withdrawal
- More rapid stabilization on a therapeutic dose
- Less drug interactions, usually no dose adjustment required in pregnancy





Maternal Opioid Treatment: Human Experimental Research (MOTHER)—approach, issues and lessons learned

Hendrée E. Jones^{1,2}, Gabriele Fischer³, Sarah H. Heil⁴, Karol Kaltenbach⁵, Peter R. Martin⁶, Mara G. Coyle⁷, Peter Selby⁸, Susan M. Stine⁹, Kevin E. O'Grady¹⁰ & Amelia M. Arria¹¹

Departments of Psychiatry and Behavioral Sciences and Obstetrics and Gynecology, Johns Hopkins University School of Medicine, Baltimore, MD, USA,¹ and RTI International, Research Triangle Park, NC, USA,² Department of Psychiatry and Psychotherapy, Medical University Vienna, Vienna, Austria,³ Departments of Psychiatry and Psychology, University of Vermont, Burlington, VT, USA,⁴ Departments of Pediatrics and Psychiatry and Human Behavior, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, USA,⁵ Department of Psychiatry, Vanderbilt University, Nashville, TN, USA,⁶ Department of Pediatrics, The Warren Alpert Medical School of Brown University, Providence, RI, USA,⁷ Department of Family and Community Medicine, Department of Psychiatry, and Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada,⁸ Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, USA,⁹ Department of Psychology, University of Maryland, College Park, College Park, MD, USA,¹¹

Buprenorphine

- Partial agonist, partial antagonist, acts at the same mu receptor as heroin and methadone, its function as a partial agonist makes overdose less likely than with methadone
- Needs to be initiated when patient is in mild to moderate w/d to prevent precipitated w/d
- Available as a mono product and combined with naloxone (opioid antagonist)
- Fewer drug interactions than methadone
- Is the only opioid against approved for the treatment of OUD in outpatient setting which eliminates the need for daily dispensing
- Infants exposed in utero have milder NAS

Buprenorphine

- Disadvantages
- Induction requires patient to be in mild to moderate withdrawal, if not precipitated withdrawal can occur
- Rare hepatic dysfunction
- Abuse/ Diversion potential- higher with mono product
- Limited knowledge of long term effects in exposed infants/children
- Inappropriate for patients that require intensive supervision and more structure

Case

- 27 year opioid dependence attributed to pain pills prescribed after a MVA.
- Patient for last 6 months reports trying to wean on buprenorphine 8 mg but since finding out about pregnancy she has been dividing film into pieces to last 2-3 days.
- Patient referred for continued treatment.
- Checked PMP, but there was no buprenorphine prescription on file.

• What's going on? How do we proceed ?

Medically Supervised Withdrawal

- Not recommended for pregnant women
- Associated with higher relapse rates (59-90%) and poorer pregnancy outcomes (ref1)
- More recent studies show no clear association between medically supervised withdrawal and fetal death and preterm delivery. (ref2)

- Ref1- Saika, Schiff D, etal. Caring for pregnant women with Opioid Use disorder in the USA: expanding and improving treatment. Curr Obstet Gynecol Rep 2016;5:257-63
- Ref2-LutyJ,Nikolaou V, Bearn J. Is opiate detoxification unsafe in pregnancy ? J Subst Abuse Treat 2003;24:363-7

Naltrexone

Nonselective opioid receptor antagonist- blocks euphoric effects of opioids

- Administered orally (poor adherence) or by injection
- Injection More effective than placebo
- Limited information regarding use in pregnancy, unknown fetal effects
- Continuation of use during pregnancy requires in depth counseling
 - Limited safety data vs risk of relapse if treatment discontinued

Care of the pregnant Women with OUD

- Prenatal Care
- Intrapartum Care
- Postpartum Care

Intrapartum Care

- Collaboration between Specialties
 - OB, anesthesia, pain management, psychiatry, addiction medicine specialists
- Collaboration between disciplines
 - Physicians and residents, nurses, social worker
 - Family support or doula care

Postpartum Care

- Many physiologic symptoms can mimic or be confounding: exhaustion, achy and emotional states experienced after delivery
- Time of increased vulnerabilities for these women
- Continue MAT- dosage reduction not needed routinely
 - Consider particularly if dose changed during pregnancy and based on symptoms, close follow up
- Role of skin to skin and rooming in: lessen the risk of NAS
- Breastfeeding benefits if there is not illicit drug use reduce SIDS and NAS
- Counseling about polysubstance use , even OTC and increased risk for Overdose postpartum
- Another opportunity to discuss about Contraceptive choices if patient undecided

Naloxone

- Short acting opioid antagonist
- Can rapidly reverse life threatening opioid overdose
- Can and should be used in pregnant women who overdose
- Can be administered SUBQ, IV, intranasal
- Naloxone kits can and should be prescribed and if possible teach family members how to use before discharge from hospital

Healthy Beginnings Clinic at UH in Newark, NJ

- Focused on effort to increase access to women with SUD
- Providers Ob/ Gyn with additional training in Addiction medicine, we provide obstetrical and gynecological care for patients with SUD
- Also prescribe for patients who are appropriate for buprenorphine treatment
- Coordinate with SUD centers so that patients can keep their current SUD treatment providers
- Also offer tobacco cessation treatment meds and individual and/or group counseling

Info regarding state Prescription Drug Monitoring Program

- Newjersey.pmpaware.net
- Currently via interconnect you can see prescribing in several other states as well- including NY, PA, MD, Connecticut, Delaware, DC, Maine, Minnesota, Massachusetts, NH, NC, Ohio, SC,RI, VA, WV, Vermont

As a member of the NJ Maternal Mortality Case Review Team

- More and More cases are being seen where opioid overdose, alcohol and polysubstance use are involved in the cause of death
- Usually seen beyond 42 days of traditional pregnancy related time period

HEALTH RISK BEHAVIORS ASSOCIATED WITH MATERNAL MORTALITY, NEW JERSEY, 2009-2013

Of the total maternal deaths during this time period more than 10% of these women had a drug and tobacco use history.

Pregnancy related-death of a woman while pregnant or within 1year, from a cause related to or aggravated by her pregnancy, not accidental

Pregnancy associated-death of a woman while pregnant or within 1 year, due to a cause unrelated to pregnancy

Undetermined-consensus not reached by case review team

	Total	Pregnancy Related	Pregnancy Associated	Undetermined
Alcohol	13 (5.8%)	2	9	2
Drugs	35 (15.6%)	4	29	2
Tobacco	41 (17.8%)	9	29	2
STI	9 (4.0 %)	3	6	0

Take Away Points

- Universal Screening for Substance Use in Women is Essential
- Methadone and Buprenorphine are both reasonable options for treatment of OUD in pregnancy.
- Women on MAT have better recovery rates than women who attempt to abstain from opioids. Counseling is needed in addition to medicine to deal with comprehensive recovery.
- Breastfeeding can mitigate NAS in babies when women are stable in recovery and reduce risk of SIDS.
- Offering contraception allows these women to further there recovery efforts and minimize unwanted pregnancy.
- If we are thinking about prevention, increased focus on these women postpartum may help in reducing pregnancy associated deaths related to OUD.

References

- ACOG committee opinion # 711, August 2017
- The ASAM Principles of Addiction Medicine, sixth edition, 2019
- www.gpo/fdsys/pkg/CFR-2016-title21-vol9/xml/CFR-2016-title21-vol9sec1306-07.xml
- MOTHERS study
 - <u>www.ncbi.nlm.nih.gov/pmc/articles/PMC4497510</u>