MANAGEMENT OF PERINATAL PRESCRIPTION OPIOID USE

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LEARNING OBJECTIVES

- To review the prevalence of prescription opioid use during pregnancy
- To review an approach to the comprehensive management of prescription opioid addiction in the perinatal period
- To discuss benefits and risks of pharmacotherapy options for opioid use disorders during pregnancy
- To gain an understanding of neonatal abstinence syndrome (NAS) and recommendations for management

SUBSTANCE USE DISORDER

- New **DSM V** definition
- Encompasses substance abuse and substance dependence
- Single disorder on a continuum from mild to severe depending on number of symptoms
- Mild: 2-3 symptoms
- Moderate: 4-5 symptoms
- Severe: 6+ symptoms

DSM V CRITERIA

1. Taking the substance in **larger amounts or for longer** than intended
2. Wanting to **cut down** or stop using the substance but not able to
3. **Spending a lot of time** getting, using, or recovering from use of substance
4. **Cravings** and urges to use the substance
5. Not managing to do what you should at work, home or school, because of substance use
6. Continuing to use, even when it causes **problems in relationships**
7. Giving up important **social, occupational or recreational activities** because of substance use
8. Using substances again and again, even when it puts the you in danger
9. **Continuing to use**, even when the you know you have a physical or psychological problem that could have been caused or made worse by the substance
10. Development of **tolerance**: needing more of the substance to get the effect
11. Development of **withdrawal** symptoms, relieved by taking more of the substance

CASE SCENARIO

Cathy is a 32 yo old G2P1, married, with 1 year old son

Asking for advice about use of Percocet – started after first pregnancy for "back pain"

Initially prescribed by MD, then started obtaining medication from other sources

"Can I stop using Percocet? Is it safe for my baby?"

Prevalence of prescription opioid use during pregnancy

PREVALENCE OF OPIOID USE: GENERAL POPULATION

- Prescription opioids are becoming primary drugs of misuse – over heroin and other street drugs
- Treatment for prescription opioids is fastest growing segment of admissions to publicly funded treatment programs
- Admissions to funded addiction services also doubled for narcotics abuse: 10.6% in 2005/6 to 18.6% in 2010/11

PREVALENCE DURING PREGNANCY

- Perinatal Canadian data related to prescription opioid use is limited
- **2010 U.S. National Survey on Drug Use and Health**: 4-5% of pregnant women reported illicit drug use in past 30 days, 0.1% heroin use and 1-2 % non-medical use of prescription opioids
- **2009 Canadian Maternity Experiences Survey**: ~7% of women reported street drug use in 3 months prior to pregnancy, reduced to 1% once pregnancy recognized

ONTARIO – NEONATAL ABSTINENCE SYNDROME (NAS) DATA

Year	Number of infants with NAS diagnosis	Average length of stay (days)	Beds per day utilized across province for NAS
2003-2004	171	11.9	5.6
2004-2005	199	13.9	7.6
2005-2006	265	13	9.5
2006-2007	249	15.4	10.5
2007-2008	358	14.5	14.2
2008-2009	380	14.6	15.2
2009-2010	482	15	20
2010-2011	**654**	**13.1**	**23.4**

Ref: Canadian Institute for Health Information (CIHI)

ONTARIO NAS: Summary

- Reported incidence of NAS in Ontario has increased from 1.3 cases in 2004 to 3.2 cases per 1,000 births in 2009.
- ~3 % of neonatal beds occupied by infants diagnosed with NAS
- Average length of stay (LOS) for these neonates is 13 days versus 1.4 days for a term newborn
- Range of LOS highly variable, >42 days in some hospitals
- Some centers with interest/need/expertise can have 10-20% of newborns in special care nursery with diagnosis of NAS

Provincial Council for Maternal and Child Health

POLYSUBSTANCE USE

- Polysubstance use is commonly reported among pregnant women with prescription opioid dependence
  - regular **alcohol and cigarette smoking** is common
  - comorbid use of licit and illicit drugs is highly prevalent: **benzodiazepines, marijuana and cocaine** most commonly reported

Ref: Sander & Hays 2005. Ordean et al. 2013.

CANADIAN COHORT OF OPIOID-DEPENDENT PREGNANT WOMEN

- National cohort of 102 opioid-dependent pregnancies, receiving care at 3 integrated care programs in Vancouver (Sheway), Toronto (T-CUP) and Montreal (Herzl Family Practice)
- Demographics: 29.7 years, 64% white, 50% single, 61% on social assistance
- 50% on methadone prior to conception, other half initiated during pregnancy at 20.7 weeks gestational age

CANADIAN COHORT (2)

At first visit, pregnant women reported

- 46% heroin use, 27% prescription opioid use
- Geographical differences: prescription opioid use more common in Toronto (48%) , heroin use more frequent in Vancouver (80%) and Montreal (50%)
- Polysubstance use: 87% nicotine, 44% cocaine, 25% alcohol, marijuana, benzodiazepines

By delivery, significant reductions in heroin (16%) and prescription opioids (10%), cocaine (19%), marijuana (7%) and alcohol (5%) use

CHARACTERISTICS OF PREGNANT SUBSTANCE USING WOMEN

- Young age: 15-25 years
- Single, not partnered
- Lower education and income level
- Family history of mental health & addiction
- Concurrent psychiatric disorders: mood 45%) & anxiety disorders (20%)
- Childhood history of sexual abuse & trauma (35%)

REASONS FOR OPIOID USE

- Cope with problems/stress
- Cope with feelings of lack of self-worth or inadequacy
- Influenced by substance use of partners: frequently introduced to opioid use by male friend and then end up living with a male drug-using partner

Effects of perinatal opioid use

RISKS OF OPOID MISUSE DURING PREGNANCY

- Effects of opioids during pregnancy compounded by other confounding factors such as:
  - poor nutrition
  - concomitant substance use
  - inadequate prenatal care
  - chaotic lifestyle

EFFECTS ON FETUS

Negative consequences of opioid use due to repeated cycles of intoxication and withdrawal

Prescription opioid misuse associated with:

- Increased risk of spontaneous abortion
- Increased risk of prematurity and low birth weight leading to increased neonatal morbidity & mortality rates
- Increased risk of SIDS (sudden infant death syndrome)

EFFECTS ON MOTHER

- High-risk behaviours associated with illicit opioid use (eg. prostitution, theft, violence)
- Increased risk of sexually transmitted infections and other infectious disorders associated with injection drug use (eg. hepatitis C, HIV)
- Increased risk of physical and sexual abuse, legal charges and incarceration, and loss of child custody

LONG-TERM EFFECTS OF OPIOID EXPOSURE IN UTERO

- 14 studies (case control and case series) from 1966 to 2008, follow-up from 2 months up to 12 years
- ~800 opiate-exposed infants included in studies
- Variety of study designs to assess development and co-factors
- Studies needed to control for other substance use and environmental factors that can affect developmental outcomes (low socio-economic status, parenting skills) – not done uniformly

LONG-TERM EFFECTS: RESULTS (2)

- Conflicting evidence about effects of opioids on child development
- Overall, opioid-exposed newborns are <u>at risk</u> for poorer neurodevelopmental outcomes (physical and cognitive development)
- Based on findings, delays may be result of environmental deprivation & parental history of drug addiction rather than drug itself

FETAL EFFECTS

Alcohol: increased risk of spontaneous abortion; fetal alcohol spectrum disorder (fetal alcohol syndrome, alcohol-related neurodevelopmental disorder, alcohol-related birth defects)

Smoking: increased risk of spontaneous abortion, intrauterine growth restriction, placental abnormalities & prematurity;
possible increased risk of learning disabilities & behavioural problems

FETAL EFFECTS (2)

Marijuana*:* prematurity with regular use; neonatal neurobehavioral changes (tremors, sleep disturbances)

Cocaine*:* increased risk of spontaneous abortion, intrauterine growth restriction, obstetrical complications (placental problems, preterm labour, stillbirth), & cerebral hemorrhage in utero;

?association with birth defects (renal tract);

?association with language delay & behavior problems (conflicting results)

Identification of opioid use disorder

SCREENING FOR SUBSTANCE USE

- **No optimal screening tool for identifying substance use during pregnancy**
- Goal: To distinguish between women who have used a substance in pregnancy and those who have a substance use disorder during pregnancy
- Maternal interview using open-ended, non-judgmental questioning is more likely to result in disclosure about substance use
- Develop own comfort level & style when asking about substance use during pregnancy
- Ask about polydrug use (prescription & illicit drug use)

DRUG TOXICOLOGY TESTING

- Biochemical markers (urine, blood, hair, meconium) can provide objective data about substance use during perinatal period
- **Not** recommended for **universal screening**
- Should be performed only after comprehensive assessment, to confirm substances used and with informed consent
- Single positive test result cannot diagnose substance use disorder

HAIR AND MECONIUM TESTING

- **Meconium** testing: positive test result indicates maternal drug use during second and third trimesters of pregnancy
- **Hair** testing: neonatal hair grows during third trimester of pregnancy
- Positive result indicates that the mother was using drugs long after pregnancy was recognized and, therefore, probably was addicted
- Not for routine clinical use –high costs & false positive test results

URINE DRUG SCREENING

- Detects **recent** substance exposure
- Provides information about presence of a drug in the urine at a particular point in time (need to be familiar with window periods for drug use detection)
- Valuable for monitoring compliance & treatment progress, enhancing motivation & documenting drug use for child protection services
- Sample collection should be supervised to prevent tampering – **must** have **informed consent**
- An unexpected positive result should be reviewed with the patient and confirmatory testing should be obtained

COMBINED SELF-REPORT & URINE DRUG SCREENING

- Addition of urine drug testing to structured maternal interview can increase detection of problematic substance use in pregnancy
- Detection can facilitate early intervention, including treatment of maternal and neonatal withdrawal, counseling and referral for long-term outpatient treatment

Approach to comprehensive management of perinatal prescription opioid use disorders

BARRIERS TO TREATMENT

- **Personal factors**: related to woman's personal attitudes or social situation
  - Feelings of guilt and shame
  - Denial – failure to acknowledge problematic use
  - Fear of losing love, support or of being isolated
- **Interpersonal factors:** related to family or peer relationships and attitudes
  - Fear of losing children to partner or child welfare
  - Lack of family support (resistance to treatment)

BARRIERS TO TREATMENT (2)

- **Societal factors**: related to societal attitudes
  - Stigma of substance use during pregnancy
  - Social stigma: perceived attitude of service providers
- **System factors**: related to program organization or barriers
  - Lack of appropriate treatment services for pregnant women
  - Lack of flexible services – including child care

APPROACH TO CARE FOR OPIOID USE DISORDER IN PREGNANCY

- Engagement and retention in care
- Opioid withdrawal management
- Opioid agonist treatment (OAT) during pregnancy
  - Methadone: maintenance vs. detoxification
  - Buprenorphine
  - Sustained-release preparations eg. morphine
- Comprehensive care including antenatal care and social services

PREGNANCY: Window of opportunity

- Pregnancy represents a window of opportunity to make a change - time when women are ready to make a change!
- Do not always present in action stage –may be pre-contemplative or contemplative
- Health Care Providers should see women over longer period of time and build therapeutic relationships in order to effect long-term change

PREGNANCY: Stage of change

- Pregnant women are more likely to access long-term substance abuse treatment programs (eg. methadone maintenance or residential treatment programs) due to interest in stopping drug use for child's health and fear of child protection services
- Overall, substance abuse treatment use was higher for pregnant group during 6 month period after initial detoxification

Daley et al., Addictive Behaviors, 1998

PREGNANCY: Engagement

- Establishing rapport is the single most important aspect of the initial encounter
- Prior relationships with health care providers have often been negative → Help them re-connect with the health care & social systems and advocate on behalf of women with child protection authorities

Remember that the appearance of belligerence or anger may signify fear, pain or withdrawal

GENERAL PRINCIPLES

- Woman-centered, nonjudgmental care is crucial
- Reduce harm related to drug use – abstinence is not only goal [harm reduction]
- There is a high percentage of survivors of sexual abuse among women with PSUP - sensitive interviewing is required

Pharmacotherapy for prescription opioid use disorder during pregnancy

MANAGEMENT OF WITHDRAWAL

- Treatment is based on specific substance(s) used so enquire about polydrug use (very common)
- Medical detoxification (ie. under medical supervision) recommended for opiates, benzodiazepines and alcohol withdrawal during pregnancy
- Supportive care for marijuana and cocaine withdrawal during pregnancy

OPIOID WITHDRAWAL

- **Physical** symptoms consist of flu-like symptoms including nausea, vomiting, diarrhea, myalgias
- **Psychological** symptoms: anxiety, insomnia, dysphoria, strong drug cravings → high risk of relapse to opioid use
- **Pregnancy specific symptoms** secondary to opioid withdrawal: uterine irritability leading to increased risk of miscarriage, premature labour, fetal distress and even fetal demise
- Onset & duration of symptoms is related to opioid half-life

OPIOID WITHDRAWAL MGMT: SYMPTOM-BASED

- Offer symptomatic relief until symptoms resolve or until alternative treatment becomes effective
- Nausea, vomiting: diclectin, gravol
- Loose stools: loperamide (Imodium)
- Muscle aches: acetaminophen, ibuprofen (contraindicated during third trimester)
- If patient develop more severe symptoms such as uterine cramping, consider opioid substitution treatment (eg. methadone)

OPIOID WITHDRAWAL MGMT

- Risk of significant opioid withdrawal includes increased risk of spontaneous abortion, fetal distress, premature labour and even fetal demise [based on early heroin studies]
- Women need to consider risk-benefit analysis of opioid withdrawal vs. opioid agonist treatment (eg.methadone or buprenorphine maintenance therapy)

MANAGEMENT OF OPIOID USE DISORDER – Opioid Agonist Treatment

- Current standard of care for opioid use disorder in pregnancy is methadone maintenance treatment (MMT)
- Due to limited experience with use of buprenorphine during pregnancy, its use can be considered after discussion of benefits and risks of buprenorphine
- Structured opioid-prescribing (eg. use of other sustained-release opioid preparations) can be last option if no access to methadone or buprenorphine

WHAT IS METHADONE?

- Synthetic opioid that can act as a substitute for heroin or other prescription opioids
- Accumulates in tissues with repeated daily oral administration
- Once stabilized on a dose of methadone, subsequent doses should not cause sedation, analgesia, or euphoria

WHAT IS METHADONE? (2)

- Dispensed as a liquid: solution made by dissolving methadone in orange drink (to prevent injecting of medication)
- Well-absorbed from gastrointestinal tract into bloodstream
- Methadone is effective within 30 minutes of ingestion, peak effect at 2-4 hours after drink
- Long duration of action: 24-36 hours

METHADONE SIDE-EFFECTS

- Constipation*
- Sweating*
- Weight gain
- Decreased libido, fatigue*
- Decreased level of consciousness, respiratory depression with excessive doses

* increase during pregnancy

RATIONALE OF METHADONE MAINTENANCE TREATMENT (MMT)

- Relieves symptoms of opioid withdrawal and reduces cravings for opioids by blocking euphoric effects of self-administered illicit opioids (cross-tolerance) leading to reduced illicit drug use
- Allows normal function to perform mental & physical tasks without causing sedation or euphoria

RATIONALE OF METHADONE DURING PREGNANCY

Methadone associated with steady maternal blood levels

- Decreases complications due to opioid withdrawal eg. miscarriage, premature labour and fetal death
- Improves adherence to prenatal care
- Decreases maternal risk behaviours and risk of hepatitis C & HIV infection

Methadone-maintained pregnancies have improved maternal & neonatal outcomes

RISKS OF METHADONE EXPOSURE

- Methadone does not increase risk of birth defects
- Infants have lower birth weight – difference resolve within 1-2 years
- Increased incidence of strabismus (cross-eyed)
- Inconsistent results regarding effect on neurological & developmental effects
- Safe to breastfeed since only a negligible amount of methadone in breast milk

FUNDAMENTALS OF MMT

- Comprehensive treatment program
- Involves long-term prescribing of methadone, as well as, counselling and other psychosocial supports
- Patient signs treatment contract: expectations (substance use, behaviour)
- Methadone dispensed at limited pharmacies; no specific regulations for pharmacies

MMT PROGRAM ELEMENTS

- Only physicians with exemption can prescribe methadone – regulated by CPSO guidelines
- Frequency of physician visits: every week until stability (more frequent at start of treatment or if relapse occurs)
- Each visit includes review of dose & substance use, counselling, urine drug testing
- Number of visits to pharmacy depend on number of drinks & carries

PHARMACY DOSING

- Initially patients go to pharmacy daily for methadone "drink" then earn "carries" based on abstinence from substance use & social stability
- Drinks: observed dose at pharmacy to avoid drug diversion or overdose on methadone
- Carries: take-home doses of methadone granted for patients who have been on methadone for at least 3 months, are stable with minimal or no illicit drug use
- Number of carries increases over time; maximum: 6 carries to ensure patient still tolerates dose

METHADONE: Dose Adjustment during Pregnancy

- Methadone metabolism increases from first to third trimester of pregnancy
- Pregnant women who report opioid withdrawal symptoms will require either an increased methadone dose or decreased dosing interval (ie. split-dosing – twice daily dosing)
- Pregnant women should be offered split-dosing when single dose not lasting

METHADONE TAPERING

- Some women want to taper off methadone so their baby will not experience withdrawal
- Studies of methadone tapering during pregnancy documented no adverse pregnancy outcomes (potential association with miscarriage in first trimester)
- Address clinical stability before starting taper due to high risk of relapse reported in studies

METHADONE TAPERING (2)

- Consider for highly motivated women with short addiction history, socially stable with good supports, no psychiatric disorders
- Rate for taper: 10% of dose every 1-2 weeks
- Fast taper may lead to severe withdrawal, uterine cramping & premature labour
- Hold taper if any adverse outcomes reported eg. relapse to drug use, increased cravings, or obstetrical complications

METHADONE: BREASTFEEDING

- Breastfeeding promotes interaction and bonding between mother & her infant; provides passive immunity and protects against otitis media, obesity, allergy, asthma, sudden infant death syndrome
- Breastfeeding safe even at higher doses since amount of methadone detected in breast milk is very small (ranges 0.01-0.1mg/day)
- Ingested amount equals to <1% of maternal weight-adjusted dose – amount unlikely to have any significant effect

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BREASTFEEDING (2)

- Amount of methadone in breast milk is not sufficient to prevent neonatal withdrawal; therefore, breastfed infants may require additional opiate treatment for withdrawal
- Unknown effect of long-term exposure to small amounts of methadone on developing infant's brain
- Breastfeeding process may be more difficult experience for methadone-exposed infants
- Benefits of breastfeeding outweigh any risks → breastfeeding is a safe alternative

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ALTERNATIVE TREATMENT OPTIONS TO METHADONE

- Buprenorphine maintenance treatment
- Structured opioid therapy prescribing -use of other sustained-release opioid preparations , if methadone or buprenorphine not available

WHAT IS BUPRENORPHINE?

- Sublingual tablet, approved for use in Canada for non-pregnant population in 2007
- Based on pharmacological properties, partial mu-opioid agonist - relieves withdrawal symptoms & suppresses opioid cravings for 24 hours or more
- Numerous randomized controlled trials documented that buprenorphine produces opioid-like effects equivalent to methadone → reduces opioid use (ie. effective opioid substitution therapy)

WHAT IS BUPRENORPHINE?

- Rapid absorption when placed under tongue
- Peak effect in 1-4 hrs, long half-life 24-60 hrs
- Ceiling effect: no further effect above certain dose is reached → safer in overdose
- Buprenorphine showed little physical dependence & milder withdrawal with abrupt discontinuation of medication in contrast to methadone

RATIONALE FOR BUPRENORPHINE DURING PREGNANCY

- Due to ability to produce milder withdrawal symptoms in adults
- Early data demonstrated promising results that newborns exposed to buprenorphine had shorter & milder neonatal abstinence syndrome than with methadone

→ benefits infants & families

→ reduction in health care costs significant

RISKS OF BUPRENORPHINE EXPOSURE DURING PREGNANCY

Based on limited clinical experience with use of buprenorphine during pregnancy

- No associated birth defects
- Safety of buprenorphine use during lactation is unknown
- Long-term effects uncertain – little published data

NAS after Methadone vs. Buprenorphine Exposure

- MOTHER study: Double-blind, double-dummy randomized controlled trial
- 8 sites: USA, Canada, and Austria
- Buprenorphine compared to methadone use in 175 pregnant women with opioid dependence
- 16/89 (18%) women in MMT and 28/86 (33%) women in buprenorphine group discontinued treatment – in keeping with previous findings
- Percentage of neonates requiring treatment for withdrawal did not differ

Jones et al. NEJM 2010; 363(24): 2320-2331.

NAS after Methadone vs. Buprenorphine Exposure (2)

- Neonates exposed to buprenorphine required 89% less morphine, spent 43% less time in hospital & 58% less time in hospital receiving medication for NAS
- Buprenorphine resulted in reduced severity of neonatal withdrawal or neonatal abstinence syndrome (NAS)

COMPONENTS OF BUPRENORPHINE MAINTENANCE

- No restrictions – all pharmacies may dispense & all physicians can prescribe buprenorphine, BUT
- Recommended completion of prescribing course, one-day clinical observation of an opioid-dependency practice and ongoing continuing medical education in opioid dependence treatment
- Urine drug testing at each visit, no specific schedule

BUPRENORPHINE USE DURING PREGNANCY

- Buprenorphine is currently available at pharmacy as buprenorphine-naloxone combination product (**Suboxone**) to deter intravenous misuse (injected naloxone leads to withdrawal)
- Naloxone: lack of safety data during pregnancy
- Pregnant women should use buprenorphine mono-product (**Subutex**)

BUPRENORPHINE DURING PREGNANCY (2)

- Subutex is not available at the pharmacy
- Buprenorphine (Subutex) provided at no cost from manufacturer for duration of pregnancy only – requires Health Canada Exceptional Access Program approval first before medication can be shipped
- Woman needs to be switched back to Suboxone in immediate postpartum period

BUPRENORPHINE: TAPERING DURING PREGNANCY

- No studies involving pregnant populations
- Consider benefits and risks of buprenorphine for opioid detoxification vs. buprenorphine maintenance during pregnancy
- Longer treatment duration with buprenorphine maintenance has been associated with increased rates of abstinence from opioid use

Ref: Kornor H, Waal H, Sandvik L. Drug Alcohol Review, 2007.

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BUPRENORPHINE USE DURING LACTATION

- Buprenorphine & its metabolite, norbupre-norphine, detected in breast milk at low levesl & similar to maternal plasma levels – present in breast milk 2 hrs after ingestion
- Since buprenorphine has poor oral bioavailability, neonates exposed to smaller proportion (eg. 1/5 – 1/10) of total amount of buprenorphine

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BUPRENORPHINE USE DURING LACTATION (2)

- Literature reports on 40-50 women who breastfed on buprenorphine maintenance
- Buprenorphine in breast milk does not suppress NAS nor has NAS been observed after breastfeeding discontinued
- Given limited literature, women need to consider risks and benefits of breastfeeding vs. buprenorphine exposure in breast milk

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BUPRENORPHINE: LONG-TERM EFFECTS

- No definitive evidence published
- Literature reported outcomes up to age 5
- 3 studies included ~20 infants
- Majority reached developmental milestones
- Transient motor abnormalities reported from age 3-9 months in largest study

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STRUCTURED OPIOID PRESCRIBING

According to Narcotic control regulations:

-prescribing short acting opioids for patients who are opioid addicted, except in unusual circumstances, does not meet accepted standard of practice

-methadone is the only opioid approved for long-term use (greater than 180 days) for treatment of opioid dependence in Canada

STRUCTURED OPIOID PRESCRIBING (2)

Based on regulations, use of sustained-release opioids (eg. morphine) may be considered for <180 days (ie. time-limited trial), if methadone or buprenorphine not available

COMPONENTS OF STRUCTURED OPIOID PRESCRIBING

- treatment agreement
- prescribe small doses & schedule frequent follow-up visits
- daily/weekly dispensing at pharmacy
- urine drug screening

Methadone vs. slow-release morphine maintenance

- No difference in birth paramters
- No difference was found in duration (number of days) of neonatal withdrawal
- Fewer benzodiazepines and additional opioids were consumed by morphine-maintained women
- Summary: women can be maintained with other opiates, as part of a comprehensive program, for duration of pregnancy

Ref: Addiction 1999

Comprehensive Care

COMPREHENSIVE CARE

- Rationale: to overcome barriers to care for pregnant substance using women and to improve coordination of previously fragmented services
- Several studies documented that addition of prenatal care to addiction treatment improves pregnancy outcomes and reduces drug use by delivery
- Programs also focused on psychosocial needs: housing & financial assistance, child protection (antenatal self-referral) and parenting support (public health home visit nurse, parenting classes, drop-in centers)

INTEGRATED CARE PROGRAM

- Comprehensive programs that combine pregnancy care with substance use treatment in one location - "one-stop shop" model
- Meta-analysis found that women in integrated programs had improved neonatal outcomes (higher birth weight, fewer birth complications) and maternal outcomes (fewer positive drug screening, more prenatal visits & fewer preterm births)

Milligan et al., Addiction Research and Theory, 2011.

OBSTETRICAL ISSUES

- Multidisciplinary team approach recommended for antenatal & intrapartum care - obstetrics, addiction medicine, psychiatry, pediatrics, anaesthesia, and social work
- Delivery plan can be developed with patient prior to labour and delivery
- Appropriate management of intrapartum and postpartum pain should be discussed – appropriate management will not trigger a relapse to drug use

LABOUR & DELIVERY

- Methadone or buprenorphine should be continued at same dose during labour & delivery, not effective for acute pain management (ie. intrapartum analgesia)
- Additional analgesics required to treat acute pain of labour (eg. short-acting opiates)
- Opioid dependent women may require larger & more frequent doses of analgesics during intrapartum & especially during postpartum period

LABOUR & DELIVERY (2)

- Epidural is most common labour analgesia
- Post-operative analgesia should use combination of opioids, anti-inflammatories (e.g. ibuprofen) and acetaminophen
- No evidence that opiate use during labor & delivery worsened addiction
- Opioids safe & effective option for pain management

CHILD WELFARE LEGISLATION IN ONTARIO

- Amendments to Child & Family Services Act (2000)
- Not legally obligated to report until baby is born, but early reporting may allow for better risk assessment and discharge planning
- Patient should be informed about legal obligation to report concerns about child safety

CHILD WELFARE SELF-REFERRAL

- Wait until viable pregnancy
- Decision matrix with patient – wait until stable or do ASAP (depending if other kids in home)
- Patient calls with social worker present or worker on behalf of patient; patient may call alone and release signed to verify information reported
- Review ways that patient may be able to prevent relapse & retain custody
- Foster hope – patients often do very well

Neonatal abstinence syndrome (NAS)

NEONATAL ABSTINENCE SYNDROME - NAS

- Most significant risk of any regular, daily opioid use during pregnancy is neonatal abstinence syndrome characterized by:
  - Central nervous system hyperirritability (eg. Increased muscle tone, tremors)
  - Gastrointestinal dysfunction (eg. Poor feeding, regurgitation, loose stools)
  - Metabolic, vasomotor & respiratory disturbances (eg. recurrent sneezing & yawning)
- Onset of symptoms and signs depends on half-life of opioid used

NAS: Methadone vs. Buprenorphine

- Greater severity on 5 NAS signs including CNS hyperirritability (eg. hyperactive Moro reflex, disturbed and undisturbed tremors, excessive irritability) and failure to thrive
- Sneezing, nasal stuffiness and loose stools were often observed with buprenorphine.
- Significant difference in median time to treatment initiation of 36 hrs for methadone vs. 59 hours in buprenorphine-exposed infants

NAS – Complicated by smoking

- associated with increased likelihood of requiring treatment for NAS
- also predicted higher total dose of medication required to treat NAS but did not lead to higher NAS scores or longer treatment
- heavy smoking (defined as $\geq$ 20 cigarettes/day), was associated with higher cumulative Finnegan score, higher daily Finnegan score and longer hospital stay

NAS – Complicated by polydrug use

- Neonatal symptoms more severe with polydrug exposure especially combinations of opioids and benzodiazepines
- Wachman et al. demonstrated that maternal use of methadone and psychiatric medications (including SSRIs, benzodiazepines and others) increased average length of stay from 22.9 days to 26.7, 29.1 and 28.0 days respectively

Wachman et al. J Addict Med, 2011.

NEONATAL ABSTINENCE WORKING GROUP

- Convened by the Ontario Provincial Council for Maternal and Child Health (PCMCH)
- Goal: to address management of NAS resulting from use of opioids
- Outcome: developed recommendations during preconception, antenatal and postpartum stages based on research evidence and consensus

www.pcmch.on.ca

NEONATAL CARE

- Pregnant women should be educated about risk of neonatal withdrawal if participating in opiate substitution programs (methadone or buprenorphine) or using other opioids on a regular basis
- Observation for a minimum of 5 half-lives recommended to assess presence & severity of newborn withdrawal symptoms (eg. 5 days if on methadone maintenance treatment)

NEONATAL CARE (2)

- Objective scoring tool (such as the Modified Finnegan scoring tool) should be used to assess severity of withdrawal symptoms and to guide treatment in infants.
- Treatment may be indicated if severe symptoms develop

NAS MANAGEMENT

- Encourage parents to take active role in caring for newborns while in-hospital - provide support
- Non-pharmacological interventions should be utilized first
  - Swaddling to decrease arousals & prolong sleep
  - Cuddling, gentle handling, skin to skin contact and infant slings improve behavioural adaptation of infants with NAS
  - Reducing sensory stimulation in environment (eg. minimize overhead lighting, reduce noise)

NAS MANAGEMENT (2)

- Pharmacotherapy should be considered for treatment of NAS when supportive measures fail to adequately ameliorate signs of withdrawal
- Baby should be admitted to special care nursery or pediatric unit if pharmacologic treatment is indicated – to allow for cardiorespiratory monitoring
- Morphine is recommended first line agent

FUTURE DIRECTIONS

More research needed in certain areas:

- Long-term impact of opioid maintenance on children – unclear if outcomes secondary to drug effect or due to environmental factors; longer follow-up and larger sample sizes required to determine effect
- Long-term effects of tapering off opioid agonist treatment during pregnancy
- Safety of buprenorphine especially during lactation

CONCLUSIONS

- MMT remains standard of care & leads to higher retention in treatment
- Buprenorphine may be associated with less severe NAS but evidence too limited – consider after discussion of benefits and risks; many practical restrictions in access
- Urgent access to opioid agonist treatment recommended during pregnancy

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ADDICTION RESOURCES

- Motherisk: www.motherisk.org or 1-877-327-4636
- Best Start: Ontario's maternal, newborn and early child development resource centre www.beststart.org
- CPSO Methadone maintenance treatment guideline www.cpso.on.ca
- CAMH Buprenorphine maintenance guideline www.camh.ca

PREGNANCY SPECIFIC RESOURCES

- Toronto Centre for Substance Use in Pregnancy (T-CUP), St. Joseph's Health Centre (416) 530-6860 fax (416) 530-6160 for phone consultations
- SOGC guidelines on alcohol and other substance use during pregnancy www.sogc.org
- Pregnancy-related issues in management of addictions project (PRIMA): www.addictionpregnancy.ca
- CAN-ADAPTT www.can-adaptt.net (evidence-based smoking cessation guidelines)

Any questions?

REFERENCES

- Exposure to psychotropic medications and other substances during pregnancy and lactation: a handbook for health care providers. CAMH, 2007.
- Ordean A, Midmer D, Graves L, Payne S, Hunt G, and the PRIMA group. PRIMA (Pregnancy-Related Issues in the Management of Addictions): A Reference for Care Providers. Toronto (Canada): Department of Family and Community Medicine, University of Toronto, 2009.
- "Hospitals, Doctors and Pregnant Women with Substance Use Problems" in Highs and lows: Canadian perspectives on women and substance use. Nancy Poole and Lorraine Greaves, editors. CAMH, Toronto, 2007.
- "The Pregnant Woman and Problematic Substance Use" in Woman-Centered Care in Pregnancy and Childbirth. Sara G. Shields and Lucy M. Candib, editors. Radcliffe Publishing Ltd, UK, 2010.

REFERENCES (2)

- Methadone maintenance: A counsellor's guide to treatment. Garth Martin and David Marsh, editors. CAMH, Toronto, 2003.
- Methadone maintenance treatment: Client handbook. CAMH, 2008. Download online www.camh.net
- Handford C. Burpenorphine/naloxone for opioid dependence: Clinical practice guideline. CAMH, 2011.
- Fischer G et al. Comparison of methadone and slow-release morphine maintenance in pregnant addicts. Addiction 1999; 94(2): 231-239.