NATIONAL CURRICULUM IN REPRODUCTIVE PSYCHIATRY

Substance Use Disorders

Perinatal Methamphetamine Use Disorder (MUD)

Self-Study

Contributor

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Learning Objectives

1. Describe the epidemiology of perinatal methamphetamine use, including changes in use over time
2. Discuss the risks of methamphetamine use during pregnancy and lactation
3. Describe treatment options for perinatal methamphetamine use disorder
4. Explain the relationship between perinatal methamphetamine use disorder and other substance, psychiatric, and medical comorbidities

Introduction and history

- Methamphetamine is a more potent compound than its parent drug, amphetamine.
- Also known as: Meth, speed, ice, crystal, black beauties, biker's coffee
- World War II
  - Given to soldiers for fatigue and appetite suppression
- 1950-1960s
  - Amphetamines widely prescribed for depression and obesity.
- 1970's
  - Abuse potential recognized.
  - Reclassified to a more restricted schedule which limited medical use
- 2005
  - Combat Meth Act restricted public access to pseudoephedrine
  - Rates of meth use began to decrease
- 2005-present
  - Manufacturers began using P2P (phentyl-2-propanone) methods (schedule II)
  - Meth is now more pure, potent and cheaper
    - Price decreased 61% between 2007 to 2010 from $270 to $105 per gram
    - Purity increased from 39% to 83% in this same time period

Epidemiology

- 2nd most commonly used illicit substance worldwide
- Methamphetamine is the 3rd most commonly used substance in some Western and Midwestern states (behind alcohol and tobacco)

- 2009 RAND Corporation estimated the burden of disease in US associated with methamphetamine use to be $23.4 billion
- 2012 National Survey of Drug use and Health:
    - 4.7% of US adults have used methamphetamines in their lifetime
    - 0.4% of US adults have used in last year
    - 0.2% of US adults used in past month
    - 7.2% of pregnant women ages 12-44 reported ever using stimulants including methamphetamines
- Estimates appear to be growing.
    - According to World Drug Report (2013) "The market for amphetamines appears to be expanding in terms of locations of manufacture and trafficking routes, as well as in terms of demand."
- Treatment admissions of pregnant women in federally-funded treatment programs rose from 8% in 1994 to 24% in 2006
- TEDS (Treatment Episode Data Set) 2012
    - Data set for patients seeking inpatient admission for substance use disorders at federally-funded treatment programs
    - 6.6% were admitted for primary methamphetamine use disorder
    - 47% admissions for methamphetamine use disorder were female
- Infant Environment and Lifestyle study (2006)
    - 5.2% of women in highest use areas (Western and Midwestern states) reported use methamphetamine during pregnancy

Pharmacology

- Methamphetamine is psychostimulant
    - Exists in 2 stereoisomers (L and D)
    - D form is a more powerful psychostimulant (3-5x the CNS activity v. L form)
    - Both can release dopamine and cause stereotypy and psychosis at high doses
- May be sold as pure D form or racemic mixture
- May be powder or crystal in form which is smoked.
    - Crystal is a highly potent D form and similar in potency to IV
    - Crystal has increased risk for dependence
- Lipophilic molecule
- Mechanism of action:
    - Stimulates the release and partially blocks the reuptake of newly synthesized catechol amines in the CNS
    - Inhibits MAO further enabling buildup of monoamines in the synapse
- Longer half-life (12h v. 1h) than cocaine
- Metabolized in liver with multiple metabolites and excreted by kidney
    - 70% is excreted in using within 24h.
    - With repeated doses, it can accumulate in urine.
- Routes of administration
    - Can be smoked (most common), snorted, injected or ingested orally or anally
    - Smoking and IV use
        - Near-immediate euphoric effect that lasts several minutes
        - Bioavailability: 90%
    - Nasal and oral use

        - 15-20 minutes to reach peak euphoric state
        - Bioavailability: 67%

Physical effects of intoxication/withdrawal

- Low-moderate doses (5-30mg)
    - euphoria, arousal, reduced fatigue, tachycardia, pupil dilation, peripheral hyperthermia, reduced appetite, behavioral disinhibition, short-term improvement in cognitive domains, anxiety
- High doses (>30mg)
    - Psychotic symptoms, agitation
    - Frequent, high doses over the long-term cause neurotoxicity.
        - Irreversible damage of serotonin and norepinephrine nerve terminals and neuron cell bodies
- Long term: addiction, anxiety, confusion, insomnia, memory loss, weight loss, dental problems, depression, violent behaviors, psychotic symptoms (paranoia, VH, delusions). May last for months or years after use and recur over time.
- Withdrawal
    - Depressive symptoms are hallmark.
        - Anhedonia, hypersomnia, irritability, anxiety, intense cravings.
        - Severity appears to be related to frequency of use.
        - Symptoms usually resolves spontaneously and within 14 days.
        - Protracted withdrawal may take several weeks and obstacle to sustained recovery.

Co-morbidities

- Psychiatric disorders
    - Methamphetamine users are twice as likely to have a psychiatric condition compared to the general population
    - Lifetime
        - Mood disorders (33-51%)
        - Anxiety disorder (25-39%)
- Other substance use disorders
    - Current
        - 78% tobacco
        - 14% alcohol
        - 24% tested positive for other illicit substances
    - Lifetime
        - 57% have lifetime dependence on other substances
            - Alcohol 33%
            - Cocaine 27%
            - Cannabis 15%
            - Opioids 12%
- Medical conditions
    - HIV
    - Hepatitis C
- Social conditions
    - Associated with homelessness, crime, imprisonment and unemployment

Gender Differences in Methamphetamine Use Disorder (MUD)

- About 50% of methamphetamine users are female.
- Male and female users differ in several areas
  - Demographic differences
    - Female users are more likely to:
      - Be younger
      - Be unmarried
      - Have children under the age of 17 living with them
      - Live with partners who sold drugs or who had been incarcerated
  - Psychological Differences
    - Female users were more likely to:
      - Have received a mental health diagnosis
      - Have experienced abuse and neglect as children
  - Patterns of use
    - Female users are more likely to:
      - Became dependent more quickly (shorter lag between first use and presentation for treatment)
      - List benefits of methamphetamine
        - Doing more housework, caring for children, weight loss, not be depressed, help with self esteem
  - Legal Differences
    - Female users more likely to have been arrested for theft and prostitution in the past year
  - Pregnant women and women with small children in treatment
    - Multiple responsibilities at home
    - High levels of exhaustion and may believe that struggles can be overcome with meth use

Effects on pregnancy

- Comorbidities
  - More likely to use marijuana and alcohol during pregnancy
- Maternal complications
  - Higher rates of (after adjusting for confounding variables):
    - Gestational HTN (OR 1.8)
    - Preeclampsia (OR 2.7)
    - IUFD (OR 5.1)
    - Placental abruption (OR 5.5)
    - Preterm birth (OR 2.9)
- Effects on fetal growth
  - Low birth weight (LBW) and small-gestational-age (SGA) consistently demonstrated compared to controls
  - Prospective study with methamphetamine users
    - Rate of SGA was 3.5X higher after controlling for alcohol, tobacco and weight gain
- Data exist from case reports and retrospective studies, but prospective studies do not confirm cardiac, GI, limb and lip/palate abnormalities

Effects on neonate/children

- Effects on neonate
    - Higher rates of (after adjusting for confounding variables):
        - Neonatal death (OR 3.1)
        - Infant death (OR 2.5)
    - ? Withdrawal symptoms
        - Decreased arousal, feeding difficulties, sleep disruptions, abnormal muscle movements
            - Symptoms resolve spontaneously within a few weeks and only 4% require supportive medical intervention
- Effects on children:
    - Childhood behavioral abnormalities

Lactation

- Effects on milk supply
    - Inhibits prolactin release and may decrease milk supply
- Infant plasma concentration
    - 2.8-7.5x than maternal plasma concentration
- Effects on infant
    - Irritability, agitation and increased crying
- Recommendation
    - Women who are using methamphetamines should not breastfeed
    - Breastfeeding can be safely initiated in mother whose urine MA screen has turned negative for over 24 hours

Screening

- UDS only done with consent and women informed of positive results
- Meconium testing after parental consent and confirmed with gas chromatography because false positive is frequent
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Treatment

- Treatments available are mostly psychosocial
    - Contingency management
    - CBT with relapse prevention
    - 12 step programs
    - Trauma-focused interventions
    - Housing support
- No FDA approved medications for methamphetamine use disorder
    - No studies done on pregnant women
    - Recommendation to treat co-morbid psychiatric and substance use disorders

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