

Management of Pregnancy

Opioid Addiction Treatment

Perinatal Opioid Addiction

- Pharmacotherapy and co-ordination of care are essential elements in the comprehensive care of pregnant patients with opioid addiction.
- Comprehensive MMT with adequate prenatal care can reduce the incidence of obstetrical and fetal complications, in utero growth retardation, and neonatal morbidity and mortality¹.

1. Finnegan, LP Treatment issues for opioid-dependent women during the perinatal period. J Psychoactive Drugs. 1991 Apr-Jun;23(2):191-201. Review.

Standard of Care

- Methadone, Category C drug
 - FDA Approval
- National Institutes of Health (NIH) Consensus Panel in 1998 recommended methadone as standard of care in pregnant women with opioid addiction
- Substance Abuse Mental Health Services Administration (SAMHSA) is not aware of evidence that an unborn baby has been harmed from the mother's use of methadone
- Buprenorphine, Category C drug
 - Not FDA approved
 - May be use to treat pregnant women in the US

Methadone Dosage

- Pharmacology of methadone in pregnancy has been evaluated thoroughly
- Widely distributed in the body after ingestion, extensive nonspecific tissue binding, reservoirs releasing unchanged methadone back into the blood, contributing to long duration of action.¹
- Lower blood methadone levels due to increased fluid volume, large tissue reservoir for methadone and altered opioid metabolism in both the placenta and fetus.²

1. Dole and Kreek, Methadone plasma level: sustained by a reservoir of drug in tissue. Proc Natl Acad Sci U S A. 1973 Jan;70(1):10. 1973; 2. Weaver, et al, Perinatal Addiction. In Graham, et al Principles of Addiction Medicine. 3ed, 2003 pp. 1231-1246.

Methadone Dosage

- Methadone dosages for pregnant women should be determined individually to achieve an effective therapeutic level.¹
- Consensus panel knows of no compelling evidence supporting reduced maternal methadone dosages to avoid neonatal abstinence syndrome (NAS).¹
- Higher dosages have been associated with increased weight gain, decreased illegal drug use, improved adherence with prenatal care, increased birth weight and head circumference, prolonged gestation and improved growth of infants born to women in OMT.²

1. Treatment Improvement Protocol (TIP) #43 Chapter 13; 2. De Petrillo and Rice, Methadone dosing and pregnancy: Impact on program compliance, *International Journal of Addictions* 30(2):207-217, 1995, Hagopian et al. Neonatal outcome following methadone exposure in utero, *Journal of Maternal-Fetal Medicine* 5(6):348-354, 1996.

Induction and Stabilization

- Criteria
 - Methadone before pregnancy
 - Pregnancy, not previously on methadone
- ## Induction
- Outpatient setting
 - Inpatient hospitalization, ideal to evaluate prenatal health status, document physiological dependence, initiate methadone, available resources

Induction and Stabilization

- Widely accepted protocol
 - Initial dose 10 to 20 mg, patient's history
 - Have pt return for follow up end of day, adjust dose 5 to 10 mg based upon therapeutic response
 - Twice daily observation until stable
 - Serial follow up until delivery, documentation of prenatal care
 - Concurrent counseling

Split Dosing

- Widely accepted for pregnant patients
- Altered pharmacokinetics during 3rd trimester often require dose increases and often a split dose to “flatten the curve” and improve maternal and fetal stability.
- Unstable patients, qualifying for take-home medications, not advised

Withdrawal from Methadone

- Medically supervised withdrawal (MSW), dose tapering during pregnancy is not recommended
- Considered after thorough assessment
 - Relapse
 - Social support

Withdrawal from Methadone

- Appropriate for MSW ¹:
 - Lives where methadone maintenance is unavailable
 - Have been stable in MAT and request MSW before delivery
 - Refuses to be maintained on methadone
 - Plan to undergo MSW through a structured treatment program ²
 - patient has been so disruptive to the treatment setting that the treatment of other patients is jeopardized, necessitating the removal of the patient from the program, absolute last resort

1. TIP #43 Chapter 13; 2. Archie, C. Methadone in the management of narcotic addiction in pregnancy [editorial]. Current Opinion in Obstetrics and Gynecology 10(6):435-440, 1998; Kaltenbach, K, et. al Opioid dependence during pregnancy. Effects and management. Obstetrics and Gynecology Clinics of North America 25(1):139-151, 1998.

Withdrawal from Methadone

- Protocol
 - Fetal monitoring
 - Second trimester preferred¹
 - Danger of miscarriage 1st trimester
 - Danger of premature delivery and fetal death
 - Consensus panel found no systemic studies on whether withdrawal should be initiated only during the second trimester.²
 - 1.0 to 2.5 mg/day for inpt; 2.5 10.0mg/wk outpt
 - Fetal movement monitoring, stress tests

1. Kaltenbach, K, et. al Opioid dependence during pregnancy. Effects and management. Obstetrics and Gynecology Clinics of North America 25(1):139-151, 1998; Ward, et al Methadone maintenance during pregnancy. In Ward, et al, Methadone Maintenance Treatment and Other Opioid Replacement Therapies., 419-440,1998; 2. TIP #43, Chapter 13

Breast-Feeding

- FDA Advisory 2006
 - Women are specifically told to decide on either methadone therapy or breast feeding, but not both
- TIP #43 Consensus Panel
 - Mothers maintained on methadone can breast-feed if they are not HIV positive, are not abusing substances and do not have a disease or infection in which breast-feeding is contraindicated.¹
 - Hepatitis C is not longer a contraindication for breast-feeding
 - Studies have found minimal transmission of methadone in breast milk regardless of maternal dose
 - No dose limits

1. Kaltenbach K, et al Methadone maintenance during pregnancy. In: State Methadone Treatment Guidelines (TIP) Series 1.1993, reprinted 2000, 2002.

Pregnancy – FDA Advisory

- New information for patients:
 - Women who might receive methadone are advised to tell the doctor if they are: **1) pregnant** or plan to become pregnant; methadone may harm an unborn fetus
 - or **2) breast-feeding**; methadone passes through breast milk and could harm an infant
 - Women are specifically told to decide on either methadone therapy or breast feeding, but not both

Neonatal Abstinence Syndrome (NAS)

- Hyperactivity of the central and autonomic nervous systems that is reflected in changes in the gastrointestinal tract and respiratory system
- Uncoordinated sucking reflex, difficulty feeding¹
- Withdrawal symptoms, variable, begin minutes to hours after birth to 2 wks, average within 72 hrs

1. Kaltenbach, K, et. al Opioid dependence during pregnancy. Effects and management. Obstetrics and Gynecology Clinics of North America 25(1):139-151, 1998

Neonatal Abstinence Syndrome (NAS)

- Factors influencing onset of NAS ¹
 - Mother's substance use pattern
 - Timing and dosage of methadone before delivery
 - Characteristics of labor
 - Type and amount of anesthesia or analgesia during labor
 - Infant maturity and nutrition
 - Metabolic rate of infant's liver
 - Presence of intrinsic in infants

Neonatal Abstinence Syndrome (NAS)

- Treatment of NAS¹
 - Methadone
 - Tincture of Opium
 - Paregoric
 - Morphine
- Neonatal opium solution² (0.4 mg/mL morphine-equivalent; starting dosage, 0.4 mg/kg/day orally in six to eight divided doses [timed with the feeding schedule])
 - Dosage is increased by 0.04 mg/kg/dose until control is achieved or a maximum of 2.0 mg/kg/day is reached.

Neonatal Abstinence Syndrome (NAS)

- Consensus panel knows of no compelling evidence supporting reduced maternal methadone dosages to avoid neonatal abstinence syndrome (NAS).¹

Developmental Sequelae

- In utero methadone exposure found infants through 2-year-olds function well within the normal developmental range ¹
- No significant developmental differences between children of mothers maintained on methadone and children of mothers still using heroin or using no opioids, when sociodemographic, biological and other health factors were considered ²
- Other data suggested that maternal drug use is not the most important factor in how opioid-exposed infants and children develop but that family characteristics and functioning play a significant role ³
- More research is needed

1. Kaltenbach K, Finnegan L, Developmental outcome in infants exposed in utero. A longitudinal study. *Pediatric Research* 20:57 1986; 2. Lifschitz, et al Factors affecting head growth and intellectual function in children of drug addicts. *Pediatrics* 75(2):269-274, 1985. 3. Johnson H, et al Path analysis of variables affecting 36-month outcome in a population of multi-risk children. *Infant Behavior and Development* 10:451-465, 1987.

Contingency Contracting

- Positive reinforcement for behavioral change
- Comparative study, enhanced treatment vs. unenhanced treatment, contingency management component ¹
 - 3 consecutive negative UDSs
 - Earn \$15/wk
 - Enhanced group, better neonatal outcomes; did not differ in percentage of positive UDSs
- Brief voucher incentives ²
 - Low value incentives, did not influence substance use
 - Greater value incentives, escalating reinforcement procedures, decreased substance use and increased full day outpatient treatment attendance

1. Carroll K, et. al Improving treatment outcome in methadone maintained pregnant women: Results from a randomized clinical trial. American Journal on Addictions. 4(1):56-59.1995. 2. Jones H, et al. The effectiveness of incentives in enhancing treatment attendance and drug abstinence in methadone maintained pregnant women. Drug and Alcohol Dependence. 67”297-306, 2001.

Buprenorphine during Pregnancy (Buprenorphine component)