



Breastfeeding and Illicit Drug use in Pregnancy

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Objectives


- Describe the incidence of drug use during pregnancy
- Describe the basic physiology of breast milk development
- Identify drugs of abuse and their breastfeeding recommendations



Statistics

- NIDA Pregnancy & Drug Use
 - 5.5% of 4 million women used illicit drugs during pregnancy
 - 757,000 women drank alcohol
 - 820,000 smoked cigarettes
 - 221,000 used illegal drugs


NIDA Infacts: Pregnancy and Drug Use Trends, 2005



Ethnic Considerations Illegal Substance Use


- 113,000 white women
- 75,000 African American
- 28,000 Hispanic
- 588,000 white women drank alcohol
- 105,000 African American women drank alcohol
- 54,000 Hispanic women drank alcohol


NIDA Infacts: Pregnancy and Drug Use Trends, 2005



Incidence

- All cultures
- All ethnicity
- All socioeconomic backgrounds
- Also use nicotine and alcohol





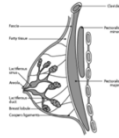
Physiology of Breast Milk Development

- Mammary Gland
 - Effective organ
 - Milk production
 - Glandular, fatty and fibrous tissue
 - Modified sweat glands
 - Tubalveolar glands
 - Part of the skin

Daisy, J. (2010)

Internal Breast Anatomy

- Lobes & Lobules
 - 15-25 lobes that radiate around the nipple
 - Each lobe – 20-40 lobules
 - A smaller milk duct that – 10-100 supporting alveoli



Internal Breast Anatomy

- Glandular tissue
 - 15-25 lobes that radiate around the nipple
 - Each lobe – 20-40 lobules
 - A smaller milk duct that – 10-100 supporting alveoli
- Connective tissue
- Blood vessels
- Nerves

Alveolar Unit

- Perfused with capillaries and lymphatics
- Capillaries
 - Primary source of nutrients
 - Fats
 - Hormones
 - Drugs taken by mother

Hale, T., (2004)

Pregnancy

- 1st Trimester
 - Ductal system proliferates and branches – estrogen
 - Lobular system proliferates - progesterone
- 2nd & 3rd Trimesters
 - Further lobular growth
 - Prolactin stimulates production of colostrum

Pregnancy

- 3rd Trimester
 - Cells of the alveoli differentiate into secretory cells
 - Capable of producing and releasing milk
 - Breast enlarges – increased secretory cells & distension of alveoli with colostrum
- Birth
 - Alveolar epithelial cells increase
 - Increase production of milk

Blackburn, S. (2007)

Drug Transfer into Human Milk

- Early stages of lactation
 - Alveoli or lactocytes are small
 - Intracellular spaces are large
 - Substances can easily transfer into milk
 - Drugs
 - Lymphocytes
 - Immunoglobulins
 - Proteins

Hale, T., 2004

Drug Transfer into Human Milk

- Transition from colostrum to mature milk
 - Changes in the milk
 - Rapid growth of the lactocyte
 - Closing the large gap
 - Tightening the junctions between the cells
 - Result: less transfer of drugs and other maternal proteins into the milk
 - Process starts 36 hrs after delivery and completed by 5 days

Hale, T., 2004

Factors Associated with Drug Transfer

- Molecular weight
- pKa – acidity constant
 - Drugs that are more basic become ionized at the pH of milk (7.0)
 - Become trapped in the milk
- Protein binding - Casein
- Maternal plasma concentration

Hale, T., 2004; Anderson, P, 1991

Factors Associated with Drug Transfer

- Lipid Solubility
 - Breast milk is 5-15% fat which is much lower than fat in plasma
 - Remain in the lipid fraction of milk
- Bioavailability
 - Amount of drug enters circulation (transluminally)
 - Drugs with poor oral bioavailability eliminates their absorption

Hale, T., 2004

Diffusion

- Passive or facilitative diffusion
- Free drug on each side of the membrane
- Transfer from a area of high to low concentration
- Drug levels sometimes reach equilibrium between the milk and maternal plasma (M/P ratio = 1)

Ingestion of Drug by Infant

- Concentration of drug in milk
- The frequency of breastfeeding
- Volume of milk consumed
- Drug absorption
- Metabolism
- Typically, baby gets <2% of mother's dose

Powers & Slusser, 1997)

Maternal Drug Use & Breastfeeding

- Marijuana, cocaine, heroin, amphetamines, alcohol use should not breastfeed
- Pump & Dump
 - Alcohol – 24 hrs
 - Marijuana – 48 hrs
 - Cocaine – 72 hours
- Not Useful

Wilton, J. (1992); Anderson, 1991

Maternal Drug Use & Breastfeeding

- AAP Committee on Drugs 2001
 - Cocaine – intoxication
 - Amphetamines – irritability/ poor sleep patterns
 - Heroin – tremors/restlessness
 - Marijuana – transfer found in human milk (Perez et al, 1982)
 - Alcohol – 1 gm daily inhibits milk ejection

Maternal Drug Use & Breastfeeding

- Academy of Breastfeeding Medicine
 - Abstain from use for 90 days before delivery
 - Enrolled in substance abuse treatment program



Academy of Breastfeeding Medicine, 2009

Maternal Drug Use & Breastfeeding

- Negative drug screen at delivery
- Consistent prenatal care
- No other contraindications for breastfeeding



Academy of Breastfeeding Medicine, 2009

Breastfeeding & Alcohol

- Standard drink = 13.7 gm (0.6 oz) pure
- This amount is found in:



- 12 oz beer
- 8 oz malt liquor
- 5 oz wine
- 1.5 oz shot (Gin, Rum, Vodka, Whiskey)
- 20 oz of beer or 6.5 oz wine – 0.5% - 3.3% transferred to baby

Breastfeeding & Methadone

- AAP Committee on Drugs
- 1994
- None if maternal dose \leq 20 mg/day
- Case Reports – minimal transmission of into breast milk regardless of mother's methadone dose (Geraghty, et al, 1997)

Foremilk VS Hindmilk

- Methadone is deposited in fat
- Foremilk
 - Less fat
- Hindmilk
 - More fat
- Amount found in milk
 - Fat content varies
 - Peak levels occur 4 hrs after oral dose

McCarthy & Posey, 2000

Milk/Plasma Ratio for Methadone 1997-1999

- Range from 0.05 - 1.89
- Wide range
- Average ratio – 0.6 over a 24 hr period
- Less variation and milk-plasma ratio's higher when mother splits does into two 12 hour intervals
- Maximum amount in milk 5.7mg/l
- Average amount secreted in milk – 2.2%

Geraghty, et al, 1997

Breastfeeding & Methadone

- Study by Begg et al, (2001)
 - Blood & milk samples
 - 2.8% of mother's methadone dose gets to infant through breast milk
- Study by McCarthy & Posey, (2000)
 - Maternal dose & milk samples
 - Range maternal dose – 25 to 180 mg/day
 - Levels of methadone in milk – 27 to 260 ng/ml (mean 95ng/ml)

Study by McCarthy & Posey

- 27 ng = .000027 mg
- 260 ng = .00026 mg
- 95 ng = .000095 mg
- Baby consumes 475 ml/day at average of 95 ng/ml baby would get 0.05 mg of methadone/day.



Other Studies from 1974 to 1997

- Report a range of 10 to 570 ng/ml – baby getting 0.01 to 0.27 mg/day
- Kreek, M., et al, (1974). Analysis of methadone and other drugs in maternal and neonatal body fluids. Use in evaluation of symptoms in a neonate of mother maintained on methadone. American Journal of Drug & Alcohol Abuse, 1, 409-419.
- Blinick, G., et al, (1975). Methadone assays in pregnant women and progeny. American Journal of Obstetrics & Gynecology, 121, 617-621.
- Wojnar-Horton, R., et al., (1997). Methadone distribution and excretion into breast milk of clients in a methadone maintenance program. British Journal of Clinical Pharmacology 44, 543-547.
- Geraghty, B., et al., (1997). Methadone levels in breast milk. Journal of Human Lactation 13, 227-230.

Study by Jansson, et al, 2008

- 8 Breastfeeding mothers
- Methadone doses between 50 – 105 mg/day
- Measured breast milk methadone levels on day of life 1,2,3,4,14 & 30
- Collected foremilk at the feeding before mother's methadone dose (peak)
- Hindmilk – 3 hrs after dose (trough)

Study by Jansson, et al, 2008

- Results:
 - Examined milk days 1-4, 14 & 30
 - Average amount of methadone in breast milk ingested by infant was small across sampling periods and was < 0.2 mg/day at day 30 despite maternal methadone dose.

Jansson, L., et al, 2008.

Study by Jansson, et al, 2008

- Concentration of methadone in milk was 21 to 462 ng/ml
- Mean plasma: milk ratio was between 0.36 and 0.49
- Levels in infant plasma – 2.2 to 8.1 ng/ml
- No differences between maternal methadone doses and infant plasma methadone concentrations

Milk: Plasma Ratio

- Typically used
- Calculations at non-steady states can provide false results
- Water soluble drugs & drugs with high molecular weight are more sluggish when passing into and out of the milk than drugs that are more lipid soluble or have lower molecular weight

Milk/Plasma Ratio

- M/P ratio is dependent on the time of sampling with respect to dose
- Ratio calculated after single dose can vary after multiple doses
- Better to measure the concentration of the drug in the milk

Anderson, 1991

Breastfeeding to Control NAS

- Retrospective study – New Zealand
 - Reviewed 121 infant records
 - Mother's on methadone maintenance
 - Infants treated for NAS & breastfed went home 8 days earlier than formula fed babies
 - Conclusion: Reduced duration of treatment & length of hospital stay

Malpas, et al, 1997

Breastfeeding to Control NAS

- Malpas & Darlow, 1999
 - Case Report – 2 infants
 - NAS after abrupt discontinuation of breastfeeding
 - Mother's methadone dose – 70-130 mg/day



Breastfeeding to Control NAS

- 16 infants
- Maternal methadone maintenance 30-100 mg/day
- Exclusively breastfed
 - Did not require treatment
 - Discharged 8-29 days earlier than infants treated with oral morphine or methadone

Ballard, 2002 article & Presentation at Academy of Breastfeeding Medicine Annual Meeting, November, 2001, Washington, DC.

Breastfeeding to Control NAS

- Retrospective Review (1998-2004)
 - 190 drug dependent women
 - 85 breastfed; 105 bottle fed
 - Average maternal methadone dose – NS differences: 69 (\pm 31 mg) in breastfed group; 80 (\pm 41mg) in bottle fed group
 - Finnegan score over 9 days

Breastfeeding to Control NAS

- Results
 - Breast fed group
 - Withdrawal occurred later in breast milk group (10 vs 3 days)
 - Less pharmacologic treatment (53% vs 79%)
 - Morphine dose lower to treat NAS
 - 6 in breast fed group vs 18 in formula fed group also required phenobarbital in addition to morphine
- Conclusion

Summary

- Breastfeeding can occur
- Evidence to support
- M/P Ratio's are small
- Infant gets between 0.01-0.27 mg/day
- May decrease severity of NAS
- May require less treatment
- Should not be the only treatment



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Testing Sites

- USDTL
- http://www.usdtl.com/breast_milk.html
 - Our Breast Milk test is available in 5-, 7-, 9- and 12-drug panels with a buprenorphine add-on assay to any profile.
 - **Drug Panels**
 - 5-drug panel: amphetamines, cannabinoids, cocaine, opiates, phencyclidine (PCP)
 - 7-drug panel: 5-drugs plus methadone and barbiturates
 - 9-drug panel: 7-drugs plus benzodiazepines and propoxyphene
 - 12-drug panel: 9-drugs plus meperidine, tramadol and oxycodone

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