Case Studies:
Maternal mental health: Medications, therapies and Outcomes

Teresa Baker MD
Professor and Regional Chair
Department of Obstetrics & Gynecology
Texas Tech University Health Sciences Center
Amarillo, TX
Co-Director of InfantRisk Center

1

Objectives: Maternal mental health: Medications, therapies and Outcomes

1. To review treatment of postpartum depression/anxiety along with the transfer/safety of medications in breastfeeding dyad
2. To review treatment of bipolar 1 and 2 disorder along with the transfer/safety of medications in breastfeeding dyad
3. To review treatment of attention deficit/hyperactivity disorder along with the transfer/safety of medications in breastfeeding dyad
4. To review treatment of postpartum psychoses and the transfer/safety of medications in breastfeeding dyad
5. To review treatment of insomnia and the transfer/safety of medications in breastfeeding dyad

2

	Total		Hispanic		Non-H				
					AI/AN		Asian		Bl
Condition	Number of pregnancy-related deaths	%	Number of pregnancy-related deaths	%	Number of pregnancy-related deaths	%	Number of pregnancy-related deaths	%	Number pregnan relate deaths
Mental health conditions[c]	224	22.7	34	24.1	2	-	1	3.1	21
Hemorrhage[d]	135	13.7	30	21.3	2	-	10	31.3	33
Cardiac and coronary conditions[e]	126	12.8	15	10.6	1	-	7	21.9	48
Infection	91	9.2	15	10.6	1	-	0	0.0	23
Embolism-thrombotic	86	8.7	9	6.4	0	-	2	6.3	36
Cardiomyopathy	84	8.5	5	3.6	0	-	2	6.3	42
Hypertensive disorders of pregnancy	64	6.5	7	5.0	0	-	1	3.1	30
Amniotic fluid embolism	37	3.8	6	4.3	1	-	7	21.9	10
Injury[f]	35	3.6	5	3.6	1	-	1	3.1	15
Cerebrovascular accident	25	2.5	2	1.4	0	-	0	0.0	10
Cancer	19	1.9	3	2.1	0	-	1	3.1	7
Metabolic/endocrine conditions	12	1.2	2	1.4	0	-	0	0.0	6
Pulmonary conditions	12	1.2	1	0.7	0	-	0	0.0	4

3

Table 3. Distribution of Pregnancy-Related Deaths by Timing of Death in Relation to Pregnancy, Data From Maternal Mortality Review Committees in 36 U.S. States, 2017–2019[a,b]

	Number of pregnancy-related deaths	%
During pregnancy	216	21.6
Day of delivery	132	13.2
1–6 days postpartum	120	12.0
7–42 days postpartum	233	23.3
43–365 days postpartum	301	30.0

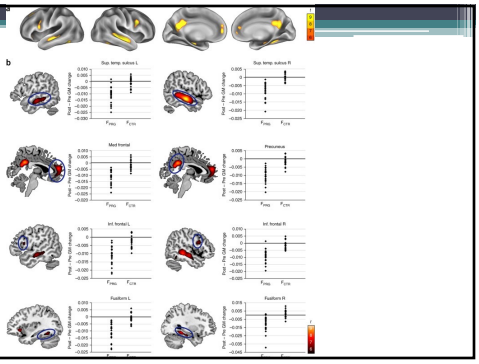
•1. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention. Maternal mortality. 2019. Available at: https://www.cdc.gov/reproductivehealth/maternal-mortality/index.html Accessed June12, 2020

4

Who is most at risk for mental health changes?

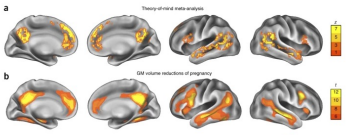
- Changes in hormone levels (Estrogen/Progesterone/Thyroid)
- History of Depression/Anxiety (1/10 women are depressed at some point in time; Highest rate in 25-44 yo)
- Emotional factors (unplanned pregnancy, sick baby, sick mother)
- Social stresses (Support, family, $)
- Fatigue

5



6

Figure 4: Similarity between theory-of-mind network and GM volume changes of pregnancy.



(**a**) The theory-of-mind network as extracted from the meta-analysis by Schurz *et al.*[22]. Statistical map of permutation-based *z*-values of the pooled meta-analysis was provided by Schurz *et al.*[22] and displayed using Caret software. (**b**) Reductions in GM volume ($P < 0.05$, FWE-corrected) in the group of women who were pregnant between sessions in the current study.

Hoekzema E, Barba-Müller E, Pozzobon C, Picado M, Lucco F, García-García D, Soliva JC, Tobeña A, Desco M, Crone EA, Ballesteros A, Carmona S, Vilarroya O. Pregnancy leads to long-lasting changes in human brain structure. Nat Neurosci. 2017 Feb;20(2):287-296.

7

Postpartum Depression

- 24 yo G1P1 s/p SVD presents 6 weeks postpartum. She is tearful and states she is struggling with nursing and feels very isolated. She has a history of depression and was previously treated with Sertraline. She and her partner are doing "ok" but states it is very stressful.

8

How to differentiate "Baby Blues" from Postnatal Depression

- Typical for Baby Blues
  - Within 2-3 days of birth
  - Feel anxious/depressed/angry
  - Cry for no clear reason
  - Have trouble sleeping, eating, and making choices
  - Question whether they can handle caring for the baby
  - Usually getting better within 1-2 weeks

9

Edinburgh Postnatal Depression Scale

1. I have been able to laugh and see the funny side of things.
   1. As much as I always could
   2. Not quite so much now
   3. Definitely not so much now
   4. Not at all
2. I have looked forward with enjoyment to things.
   1. As much as I ever did
   2. Rather less than I used to
   3. Definitely less than I used to
   4. Hardly at all
3. I have blamed myself unnecessarily when things went wrong.
   1. Yes, most of the time
   2. Yes, some of the time
   3. Not very often
   4. No, never
4. I have been anxious or worried for no good reason
   1. No, not at all
   2. Hardly ever
   3. Yes, sometimes
   4. Yes, very often
5. I have felt scare or panicky for no very good reason.
   1. Yes, quite a lot
   2. Yes, sometimes
   3. No, not much
   4. No, not at all
6. Things have been getting on top of me.
   1. Yes, most of the time I haven't been able to cope at all
   2. Yes, sometimes I haven't been coping as well as usual
   3. No, most of the time I have coped quite well
   4. No, I have been coping as well as ever
7. I have been so unhappy that I have had difficulty sleeping.
   1. Yes, most of the time
   2. Yes, sometimes
   3. Not very often
   4. No, not at all
8. I have felt sad or miserable
   1. Yes, most of the time
   2. Yes, quite often
   3. Not very often
   4. No, not at all
9. I have been so unhappy that I have been crying.
   1. Yes, most of the time
   2. Yes quite often
   3. Only occasionally
   4. No, never
10. The thought of harming myself has occurred to me.
    1. Yes, quite often
    2. Sometimes
    3. Hardly ever
    4. Never

Add numbers next to answers

(and/or) Positive response to question 10

Score of 8 and above needs to be assessed by health care provider

10

SIGECAPS

A difference in mood for more that (2) weeks affecting (4) or more of the following

Sleep
Interest
Guilt
Energy
Concentration
Appetite
Psychomotor Activity
Suicide

11

Options for Treatment

- Antidepressant medication
- Talk Therapy
- Exercise
- Sunlight
- Peer support

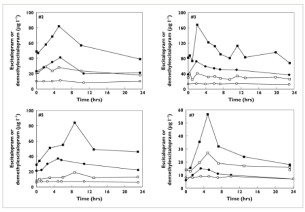
12

SSRIs in Breastmilk

Drug Name	Relative Infant Dose (%)
Amitriptyline (Elavil)	1.9% - 2.8
Bupropion (Wellbutrin)	0.2% - 2
Citalopram (Celexa)	3.56% - 5.37
Desipramine (Norpramin)	0.3% - 0.9
Doxepin (Sinequan)	1.2% - 3
Escitalopram	5.2% - 7.9
Fluoxetine (Prozac)	1.6% - 14.6
Paroxetine (Paxil)	1.2% - 2.8
Sertraline (Zoloft)	0.4% - 2.2
Vortioxetine (Trintellix)	1.84%
Venlafaxine (Effexor)	6.8% - 8.1

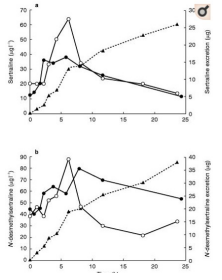
13

Transfer of Citalopram into Breast Milk



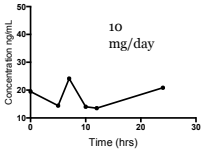
14

Transfer of Sertraline into Human Breast Milk



15

Transfer of Vortioxetine (Trintellix) into Breast Milk



Manuscript in preparation
Unpublished Data

28 year old mother with 1 month-old exclusively breastfed infant. Being treated for depression and anxiety with 10 mg/day Vortioxetine.

Parameter (units)	Trintellix
AUC$_{0-\infty}$ (ng.hr/mL)	414.3
C_{ss} (ng/mL)	17.3
C_{max} (ng/mL)	24
T_{max} (hr)	7
Infant Dose (mg/kg/day)	0.002
RID (%)	1.84

16

Neonatal abstinence syndrome

Klinger G, Merlob P, Sirota L. Serotonin reuptake inhibitor induced neonatal abstinence syndrome. *Isr J Psychiatry Relat Sci.* 2008;45(2):107-113.

GIL KLINGER AND PAUL MERLOB 111

Table 3. *Protocol for observation of newborns exposed in utero to selective serotonin reuptake inhibitors*

Side effects	Clinical signs	Observe
I General	• Increase in prematurity rate • Increase in SGA*** rate • Increase in NICU** admissions	• Routine observation as required by degree of prematurity • Routine observation as required for SGA infants
II Cardiovascular	• Labile blood pressure • Tachycardia • ECG changes (prolonged QT, atrial and ventricular premature beats)	• Monitor blood pressure • Continuous ECG monitor • ECG
III Hematologic	• Anemia, Thrombocytopenia, Neutropenia • Increased hemorrhages	• Complete blood count • Physical examination
IV Metabolic	• Hypoglycemia • Abnormal liver tests • Hyponatremia, Hypokalemia	• Monitor glucose (first hours after birth) • Blood chemistry (3rd day of life)
V NAS*	• CNS signs • Gastrointestinal signs • Autonomic system signs • Respiratory signs	• Finnegan score (6, 36)

* NAS — neonatal abstinence syndrome, ** NICU — neonatal intensive care unit, *** SGA — small for gestational age

17

Talk Therapy

- Structured psychotherapy
- Cognitive Behavioral Therapy

18

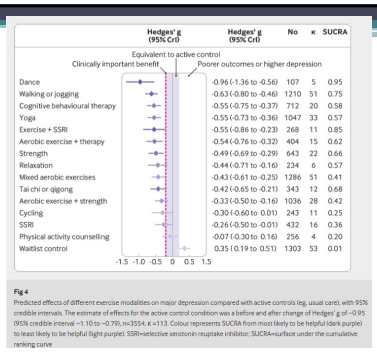


Fig 4
Predicted effects of different exercise modalities on major depression compared with active controls (eg, usual care), with 95% credible intervals. The estimate of effects for the active control condition was a before and after change of Hedges' g of −0·95 (95% credible interval −1·10 to −0·79), n=3554, K =113. Colour represents SUCRA from most likely to be helpful (dark purple) to least likely to be helpful (light purple). SSRI=selective serotonin reuptake inhibitor; SUCRA=surface under the cumulative ranking curve

Noetel M, Sanders T, Gallardo-Gómez D, Taylor P, Del Pozo Cruz B, van den Hoek D, Smith JJ, Mahoney J, Spathis J, Moresi M, Pagano R, Pagano L, Vasconcellos R, Arnott H, Varley B, Parker P, Biddle S, Lonsdale C. Effect of exercise for depression: systematic review and network meta-analysis of randomised controlled trials. BMJ. 2024 Feb 14;384:e075847. doi: 10.1136/bmj-2023-075847. Erratum in: BMJ. 2024 May 28;385:q1024. doi: 10.1136/bmj.q1024. PMID: 38355154; PMCID: PMC10870815.

19

What is at risk if Postnatal Depression is left untreated?

- **For mothers**
  Untreated postpartum depression can last for months or longer, sometimes becoming a chronic depressive disorder. Even when treated, postpartum depression increases a woman's risk of future episodes of major depression.
- **For fathers**
  Postpartum depression can have a ripple effect, causing emotional strain for everyone close to a new baby. When a new mother is depressed, the risk of depression in the baby's father may also increase. And new dads are already at increased risk of depression, whether or not their partner is affected.
- **For children**
  Children of mothers who have untreated postpartum depression are more likely to have emotional and behavioral problems, such as sleeping and eating difficulties, excessive crying, and attention-deficit/hyperactivity disorder (ADHD). Delays in language development are more common as well.

20

Preexisting Depression/Anxiety

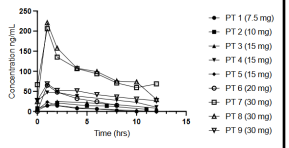
- 34 yo G3P3 presents at 24 weeks for prenatal care. Has had depression and anxiety for a few years and is stable on Lexapro 20mg qd with Buspirone as needed.
- She wants to discuss plan for postpartum management

21

Alleviating anxiety while breastfeeding: evaluating buspirone transfer into human milk

Participant No	Dose (mg BID)	Maternal weight adjusted dose mg/kg/12 hrs	AUC $_{12}$ ng*hr/mL	Infant Daily dose (mg/kg/12 hrs)	Relative infant dose
1	7.5	0.11	71	0.0004	0.42%
2	10	0.17	148.6	0.0009	0.55%
3	15	0.23	178.7	0.0011	0.49%
4	15	0.19	386.3	0.0024	1.26%
5	15	0.27	91.33	0.0005	0.21%
6	20	0.26	266.3	0.0016	0.64%
7	30	0.34	1172	0.0073	2.17%
8	30	0.46	1212	0.0075	1.66%
9	30	0.30	508.5	0.0031	1.06%

Individual patient pharmacokinetic data



Buspirone active metabolite (1-PP) concentration over a 12-h dosing period in human milk.

- Buspirone was not quantifiable in any of the samples, however its active metabolite 1-PP levels were determined
- Drug concentrations were dose proportional with inter-participant variability.
- Baseline values supported the presumption of steady-state conditions

Krutsch K, et al. *Arch Womens Ment Health*. 2024 Aug;27(4):619-623.

22

Bipolar Disorder

- 36 yo presents for postpartum care. She has a h/o bipolar depression and states she is struggling. She states she cries most days and finds very little joy in mothering. She isn't sleeping well and she is trying to nurse but she is going back to work next week and isn't sure she can continue like this.

23

TABLE 2. Diagnostic Criteria for Major Forms of Bipolar Disorder

Bipolar I disorder
Essential diagnostic features:
a. At least 1 lifetime manic episode
b. The manic episode was not due to effects of medication, substances, or medical illness
Diagnostic note: an episode of depression is not required to make a diagnosis of bipolar I disorder

Bipolar II disorder
Essential diagnostic features:
a. At least 1 lifetime hypomanic episode
b. At least 1 lifetime major depressive episode
c. Neither the hypomanic nor the depressive episode(s) was due to effects of medication, substances, or medical illness

Cyclothymic disorder (cyclothymia)
Essential diagnostic features:
a. Numerous hypomanic and depressive symptoms for ≥2 y
b. Diagnostic criteria for hypomanic episodes and for major depressive episodes not met
c. No symptom-free period lasting ≥8 wk during the 2-y period

Other specified bipolar and related disorders
Examples include:
- Major depressive episodes + short episodes of hypomanic symptoms (2-3 d) that do not meet duration criteria for hypomanic episodes
- Major depressive episodes + episodes of hypomanic symptoms that do not meet symptomatic criteria for hypomanic episodes
- Hypomanic episodes with no previous major depressive episodes
- Short-duration cyclothymia, with symptoms persisting for <2 y

Substance/medication-induced bipolar and related disorders
Clues to the diagnosis:
- Mood disturbance (mania, hypomania, depression) develop during or soon after exposure to (or withdrawal from) the implicated substance/medication
- The implicated substance/medication is capable of producing the mood disturbance
- Mood disturbance abates soon after exposure to the implicated substance/medication ends
- Reemergence of mood disturbance during rechallenge with the same substance/medication or a pharmacologically related alternative implicates the exposure as being causal, absent other factors

Bipolar and related disorders due to another medical condition
Clues to the diagnosis:
- Mania, hypomania, or depression develops in the context of existing or newly diagnosed medical illness
- The medical illness is capable of causing the mood disturbance

Data from American Psychiatric Association.[1]

24

Olanzapine and Quetiapine

Parameter	Olanzapine	Quetiapine
Breast milk drug concentration, ng/mL		
11 P.M.	7.6 (4.8–12.3)*	0.9 (0.5–1.1)†
4 A.M.	12.7 (9.5–17.2)	10.7 (8.3–14.5)†
8 A.M.	10.0 (9.2–17.2)	3.7 (3.3–7.7)†
AUC_{24h}, ng.h/mL	212.4 (193.3–334.2)	102.3 (78.5–145.5)
AUC_{hf}, ng.h/mL	137.7 (119.9–233.1)‡	40.1 (34.3–70.1)‡
Infant exposure to AUC_{24h}, %	63.5 (59.0–67.9)	45.2 (38.2–50.8)
Absolute infant dose, µg/kg per day	1.29 (1.12–2.19)	0.38 (0.32–0.66)
Relative infant dose, %	0.74 (0.64–1.25)	0.02 (0.01–0.03)

Data are presented as median (25th–75th quartile).
*$P < 0.001$ when compared with 4 A.M. and 8 A.M.
†$P < 0.001$ when compared with every other time point within group.
‡$P < 0.001$ when compared with AUC_{24h}.

Aydin B, Nayir T, Sahin S, Yildiz A. Olanzapine and quetiapine use during breastfeeding: excretion into breast milk and safe breastfeeding strategy. J Clin Psychopharmacol. 2015 Apr;35(2):206-8. doi: 10.1097/JCP.0000000000000291. PMID: 25679127.

25

Olanzapine

TABLE 1. Maternal and Perinatal Characteristics of Infants Exposed to Olanzapine During Breastfeeding Versus Nonexposed Infant Control Groups

Characteristic	Olanzapine, breastfed (n = 22)	Olanzapine, non-breastfed (n = 13)	Acetaminophen, breastfed (n = 31)	p value
Mean maternal age (years) (SD)	31.3 (5.6)	30.7 (5.3)	31.9 (4.4)	NS
Mean number of pregnancies (SD)	2.7 (2.0)	2.3 (2.2)	2.0 (1.4)	NS
Mean number of deliveries (SD)	2.7 (2.0)	2.3 (2.2)	2.0 (1.3)	NS
Pregnancy duration (weeks) (SD)	38.7 (1.9)	37.6 (3.1)	39.6 (1.3)	0.001*
Cesarean delivery/pregnancy	5	8	7	NS
Tobacco smoking during pregnancy	1	0	2	NS
Mean daily olanzapine dose (mg) (SD)	6.25 (4.10)	5.68 (2.25)	NR	NS
Olanzapine use during pregnancy (%)	18 (82%)	12 (86%)	0 (0%)	NS
Additional drug use during lactation (%)	6 (27%)	10 (67%)	0 (0%)	<0.001
Birth weight (g) (SD)	3,295 (974)	3,133 (652)	3,253 (581)	NS
Male gender (%)	8 (36%)	7 (47%)	21 (42%)	NS

*Comparison of olanzapine-exposed non-breastfed to acetaminophen group.
NR, not relevant; NS, not significant.

TABLE 2. Adverse Long-Term Outcomes in Olanzapine-Exposed Versus Nonexposed Infants

Characteristic	Olanzapine, breastfed (n = 22)	Olanzapine, non-breastfed (n = 13)	Acetaminophen breastfed (n = 31)	p value
Any adverse outcomes (%)*	3 (14%)	1 (7%)	4 (8%)	NS
Feeding problems	0	0	1	NS
Speech delay	1	0	0	NS
Motor developmental delay	1	0	0	NS
Failure to gain weight	2	0	3	NS
Small head circumference	0	1	0	NS

Gilad O, Merlob P, Stahl B, Klinger G. Outcome of infants exposed to olanzapine during breastfeeding. Breastfeed Med. 2011 Apr;6(2):55-8. doi: 10.1089/bfm.2010.0027. Epub 2010 Oct 29. PMID: 21034242

26

Lithium

TABLE 1. Lithium Concentration in Maternal and Infant Serum and Breast Milk and Infant Renal and Thyroid Function in 10 Nursing Infant-Mother Pairs

Infant-Mother Pair	Infant Age at Sampling (week)	Maternal Dose of Lithium Carbonate (mg/day)	Maternal Serum Lithium Concentration (meq/liter)	Breast Milk Lithium Concentration (meq/liter)	Infant Serum Lithium Concentration (meq/liter)	Infant Serum Urea Nitrogen (mg/dl)[a]	Infant Serum Creatinine (mg/dl)[b]	Infant Serum Thyroid-Stimulating Hormone (µU/ml)[c]
A	9	600	0.45	0.30	0.10	1.00	0.3	2.30
A	13	600	0.70	0.25	0.20	6.00	0.3	1.50
B	21	600	0.70	—	0.22	6.00	0.3	0.88
B	52	600	0.80	0.30	0.10	6.00	0.2	1.25
C	1	625	0.80	—	0.30	6.00	0.3	—
C	8	625	0.70	—	0.30	5.00	0.3	1.87
C	16	725	0.70	—	0.20	8.00	0.4	1.75
C	24	725	0.80	0.44	0.10	8.00	0.4	1.35
C	30	725	0.60	—	—	—	—	—
C	55	750	0.70	0.46	—	19.00	0.6	1.32
D	32	700	0.80	0.36	0.09	—	—	—
E	12	900	1.00	0.25	0.20	3.00	0.3	2.80
E	52	900	1.00	0.23	0.10	3.00	0.2	1.30
F	7	900	0.41	0.25	0.23	7.00	0.3	7.31
G	2	900	0.80	—	0.10	9.00	0.2	2.89
G	5	900	0.80	0.55	0.13	5.00	0.2	2.62
G	12	900	0.92	0.40	0.10	5.00	0.2	2.50
G	52	900	0.92	—	0.10	7.00	0.2	1.34
H	32	900	—	—	0.19	23.00	0.3	2.58
H	8	900	1.21	—	0.14	7.00	0.3	1.73
I	6	1200	1.16	0.48	0.19	4.00	0.3	1.40
I	25	1200	1.05	—	0.05	6.00	0.3	1.75
J	4	1200	0.55	0.37	0.10	5.00	0.2	1.67
J	9	1200	0.55	—	0.10	5.00	0.2	1.60
J	14	1200	0.67	0.40	0.18	6.00	0.3	1.23
J	25	1200	0.85	—	0.14	5.00	0.3	1.07

[a] Normal blood urea nitrogen range for newborn to 2-year-old children: 5–15 mg/dl (5).
[b] Normal creatinine range—1–30-day-old infants: 0.2–1.0 mg/dl; 1-month to 1-year-old infants: 0.2–0.6 mg/dl (5).
[c] Normal thyroid-stimulating hormone range—1–30-day-old infants: 0.52–16.08 µU/ml; 1-month to 5-year-old children: 0.55–7.18 µU/ml (5).

Viguera AC, Newport DJ, Ritchie J, Stowe Z, Whitfield T, Mogielnicki J, Baldessarini RJ, Zurick A, Cohen LS. Lithium in breast milk and nursing infants: clinical implications. Am J Psychiatry. 2007 Feb;164(2):342-5. doi: 10.1176/ajp.2007.164.2.342. PMID: 17267800.

27

Monitoring Lithium in Breast Milk: An Individualized Approach for Breast-Feeding Mothers

Moretti, Myla E.[*]; Koren, Gideon[*]; Verjee, Zulfikarali[†]; Ito, Shinya[*]

Author Information

Therapeutic Drug Monitoring 25(3):p 364-366, June 2003.

Abstract

Lithium is a drug of choice for the management of bipolar disorder, a disease frequently affecting women in their childbearing years. Unfortunately, this drug has typically been contraindicated in nursing women. Data in humans are limited with respect to the use of this drug in lactating women, and early reports suggest high excretion into milk. The purpose of this report was to verify the excretion of lithium into human milk and to assess infant safety after breast-feeding. The authors found wide interpatient variability in lithium dose offered to the infant through breast milk (from 0% to 30% of maternal weight-adjusted dose), indicating that therapeutic drug monitoring of lithium in milk and/or in infant's blood, coupled with close monitoring of adverse effects, is a rational approach. Since therapeutic drug monitoring of lithium is routine, physicians caring for these women and infants should be encouraged to individualize their recommendations.

28

Attention Deficit Hyperactivity Disorder

- 25 yo Go presents with history of ADHD and has been stable on Adderall since college. She is wondering about management during pregnancy and breastfeeding.

29

Adderall (Dextroamphetamine)

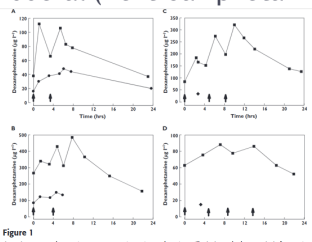


Figure 1
(A–D) Dexamphetamine concentration–time plots in milk (■) and plasma (●) for patients A to D. Doses were taken orally at the times shown by the arrows as follows: patient A, 10 mg and then 5 mg; patient B, 20 mg and then 25 mg; patient C, 3 × 5 mg; and patient D, 4 × 5 mg. Measured concentrations of dexamphetamine in infant plasma are shown by the (◆) symbol in C and D

30

Mother–infant pair	Milk C_{max} (μg l^{-1})	Milk C_{av} (μg l^{-1})	Plasma C_{single} or C_{ss} (μg l^{-1})	M/P*	Maternal dose (μg kg^{-1} day^{-1})	Absolute infant dose (μg kg^{-1} day^{-1})	Relative infant dose (%)
A	112	66	34	1.9	259	10	3.9
B	486	313	131	2.4	643	47	7.3
C	325	206	41	4.2	224	31	13.8
D	86	73	14	5.3	274	11	4.0
Median (IQR)	219 (99–406)	140 (70–260)	38 (24–86)	3.3 (2.2–4.8)	267 (242–459)	21 (11–39)	5.7 (4–10.6)

Ilett KF, Hackett LP, Kristensen JH, Kohan R. Transfer of dexamphetamine into breast milk during treatment for attention deficit hyperactivity disorder. Br J Clin Pharmacol. 2007 Mar;63(3):371-5. doi: 10.1111/j.1365-2125.2006.02767.x. Epub 2006 Sep 12. PMID: 17380592; PMCID: PMC2000726.

31

Methylphenidate

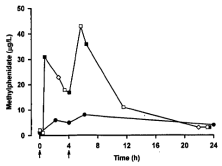


Figure 1. Methylphenidate concentration–time plots for plasma (filled circles) and milk (squares; open squares show fore-milk, closed squares show hind-milk, and the open diamonds are an equal mix of fore- and hind-milk). Methylphenidate 40 mg was taken at each arrow.

Hackett LP, Kristensen JH, Hale TW, Paterson R, Ilett KF. Methylphenidate and breast-feeding. Ann Pharmacother. 2006 Oct;40(10):1890-1. doi: 10.1345/aph.1H159. Epub 2006 Aug 29. PMID: 16940409.

32

Caffeine

Disposition of dietary caffeine in milk, saliva, and plasma of lactating women

C M Berlin Jr, H M Denson, C H Daniel, R M Ward

PMID: 6691042

Abstract

Caffeine is present in many dietary substances; its appearance from these sources in human milk has not previously been studied in detail. Fifteen lactating women ingested a known amount of a caffeinated beverage (36 to 335 mg). Simultaneous milk and saliva samples were collected at intervals for the subsequent 12 hours and assayed for caffeine content. Eleven of 15 mothers excreted measurable caffeine in milk. Caffeine was detected by 15 minutes in saliva and milk; peak levels in milk (2.09 to 7.17 micrograms/mL) and saliva (1.24 to 9.22 micrograms/mL) were achieved within 1 hour. Elimination half-lives were 1.3 to 13.5 hours (mean 4.0 +/- 3.7 [SD] hours) for saliva and 1.5 to 14.5 hours (mean 6.1 +/- 4.4 [SD] hours) for milk. Assuming each infant would ingest 90 mL of milk every three hours for 24 hours after maternal ingestion of caffeine, it is possible to estimate potential exposure of the nursing infant to caffeine. The amount of caffeine available for infant absorption ranged from 0.01 to 1.64 mg or 0.06% to 1.5% of the maternal dose. Caffeine was not present in the infants' urine collected for five hours after the first nursing period. The maternal ingestion of a single cup of caffeinated beverage does not appear to present significant doses of caffeine to the nursing infant.

33

Postpartum Psychosis

- 28 yo G1P1 s/p SVD 1 week ago presents with her husband who notes she hasn't showered or slept in 3 days and she is hearing voices that aren't real.

34

Haloperidol

- RID 0.2%-12%
- Monitor for sedation or irritability, apnea, extrapyramidal symptoms

Ohkubo T, Shimoyama R, Sugawara K. Measurement of haloperidol in human breast milk by high-performance liquid chromatography. J Pharm Sci. 1992 Sep;81(9):947-9. doi: 10.1002/jps.2600810922. PMID: 1432646.

Stewart RB, Karas B, Springer PK. Haloperidol excretion in human milk. Am J Psychiatry. 1980 Jul;137(7):849-50. doi: 10.1176/ajp.137.7.849. PMID: 7386670.

35

Aripiprazole

- Antipsychotic
- Dopamine Receptor Partial Agonist
- 0.7%-6.44%

Naughton S, O'Hara K, Nelson J, Keightley P. Aripiprazole, brexpiprazole, and cariprazine can affect milk supply: Advice to breastfeeding mothers. Australas Psychiatry. 2023 Apr;31(2):201-204. doi: 10.1177/10398562231159510. Epub 2023 Feb 24. PMID: 36825499. Schlotterbeck P, Leube D, Kircher T, Hiemke C, Gründer G. Aripiprazole in human milk. Int J Neuropsychopharmacol. 2007 Jun;10(3):433. doi: 10.1017/S1461145707007602. PMID: 17291382.
Nordeng H, Gjerdalen G, Brede WR, Michelsen LS, Spigset O. Transfer of aripiprazole to breast milk: a case report. J Clin Psychopharmacol. 2014 Apr;34(2):272-5. doi: 10.1097/JCP.0000000000000079. PMID: 24525642.

36

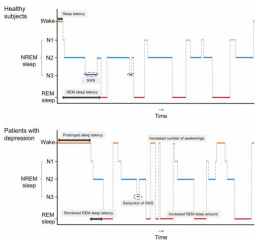
Risperidone

- RID 2.8% - 9.1%
- Risk for sedation or irritability; apnea; poor feeding

Ilett KF, Hackett LP, Kristensen JH, Vaddadi KS, Gardiner SJ, Begg EJ. Transfer of risperidone and 9-hydroxyrisperidone into human milk. Ann Pharmacother. 2004 Feb;38(2):273-6. doi: 10.1345/aph.1D326. Epub 2003 Dec 30. PMID: 14742766.

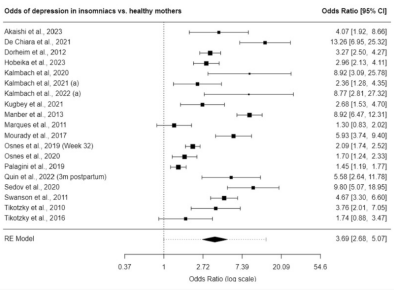
Uguz F. Adverse Events in a Breastfed Infant Exposed to Risperidone and Haloperidol. Breastfeed Med. 2019 Nov;14(9):683-684. doi: 10.1089/bfm.2019.0093. Epub 2019 May 28. PMID: 31135176.

37



Yasugaki S, Okamura H, Kaneko A, Hayashi Y. Bidirectional relationship between sleep and depression. Neurosci Res. 2025 Feb;211:57-64. doi: 10.1016/j.neures.2023.04.006. Epub 2023 Apr 26. PMID: 37116584.

38



39

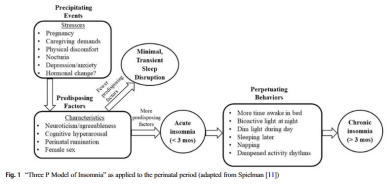


Fig. 1 "Three P Model of Insomnia" as applied to the perinatal period (adapted from Spielman [11])

40

Psychiatric Manifestations of Withdrawal Following Domperidone Used as a Galactagogue

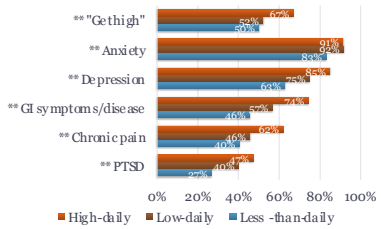
Elleana Majdinasab,[1] Sarah Haque,[1] Amy Stark,[2] Kaytlin Krutsch,[1] and Thomas W. Hale[3]

Abstract

Background: Domperidone is a dopamine-2 antagonist used off-label to increase breast milk production. Dosages commonly promoted for lactation are often far above those of studied on-label indications and might pose additional risks, especially upon discontinuation of the drug.
Patients: Three U.S. patients are presented who used domperidone for lactation and experienced varying degrees of psychiatric withdrawal symptoms lasting months during dosage tapering and after cessation.
Conclusion: Domperidone as a galactagogue may pose a significant psychiatric risk upon discontinuation. This presentation is commonly confused with, but clinically distinct from, postpartum depression. Lactating mothers who present with psychiatric symptoms should be explicitly probed about domperidone use, even in areas where domperidone is not authorized for use. Maternal hesitancy to disclose domperidone use may lead to suboptimal outcomes for the patient and delay management of withdrawal manifestations. The best course of treatment remains unknown, but a slow hyperbolic taper to gently discontinue domperidone may minimize withdrawal symptoms in these patients. Individuals exploring domperidone use should be informed of potential risks upon withdrawal, including psychiatric manifestations, requisite taper, and potential impacts of using unstudied high doses.

41

Reasons for cannabis use stratified by frequency group



Garner CD, Kendall-Tackett K, Young C, Baker T, Hale TW. Mode of Cannabis Use and Factors Related to Frequency of Cannabis Use Among Breastfeeding Mothers: Results from an Online Survey. Breastfeed Med. 2022 Mar;17(3):269-276. doi: 10.1089/bfm.2021.0151. Epub 2021 Dec 3. PMID: 34870449.

42

Medication Use in Lactation

MommyMeds for Mothers

InfantRisk Center for Health Care Providers

43

References for Maternal Mental Health

- Rampono J, Hackett LP, Kristensen JH, Kohan R, Page-Sharp M, Ilett KF. Transfer of escitalopram and its metabolie demethylescitalopram into breastmilk. Br J Clin Pharmacol 2006; 62(3):316-322
- Kristensen JH, Ilett KF, Dusci LJ, Hackett LP, Yapp P, Worjnar-Horton RE, Robers MJ, Paech M. Distribution and excretion of sertraline and N-desmethylsertraline in human milk. Br J Clin Pharmacol 1998; 45 (5): 453-457.
- Klinger G, Merlob P. Selective serotonin reuptake inhibitor induced neonatal abstinence syndrome. *Isr J Psychiatry Relat Sci.* 2008;45(2):107-113.
- Oberlander TF, Misri S, Fitzgerald CE, Kostaras X, Rurak D, Riggs W. Pharmacologic factors associated with transient neonatal symptoms following prenatal psychotropic medication exposure. *J Clin Psychiatry.* 2004;65(2):230-237. doi:10.4088/jcp.v65n0214
- Nulman I, Koren G, Rovet J, et al. Neurodevelopment of children following prenatal exposure to venlafaxine, selective serotonin reuptake inhibitors, or untreated maternal depression. *Am J Psychiatry.* 2012;169(11):1165-1174. doi:10.1176/appi.ajp.2012.11111721
- Casper RC, Fleisher BE, Lee-Ancajas JC, et al. Follow-up of children of depressed mothers exposed or not exposed to antidepressant drugs during pregnancy. *J Pediatr.* 2003;142(4):402-408. doi:10.1067/mpd.2003.139
- Lindahl V, Pearson JL, Colpe L. Prevalence of suicidality during pregnancy and the postpartum. Arch Womens Ment Health. 2005 Jun;8(2):77-87. doi: 10.1007/s00737-005-0080-1. Epub 2005 May 11. PMID: 15883651.
- Misri S, Abizadeh J, Sanders S, Swift E. Perinatal Generalized Anxiety Disorder: Assessment and Treatment. J Womens Health (Larchmt). 2015 Sep;24(9):762-70. doi: 10.1089/jwh.2014.5150. Epub 2015 Jun 30. PMID: 26125602; PMCID: PMC4589308.
- Murugappan MN, Westberg SM, Contag S, Melnik TE, Kumar A, Rajpurohit A, Thorsness K, Farley JF. Maternal ADHD and Perinatal Prescription Stimulant Use. J Atten Disord. 2022 Aug;26(10):1347-1356. doi: 10.1177/10870547211073472. Epub 2022 Jan 20. PMID: 35048729.
- Swanson LM, Kalmbach DA, Raglan GB, O'Brien LM. Perinatal Insomnia and Mental Health: a Review of Recent Literature. Curr Psychiatry Rep. 2020 Oct 26;22(12):73. doi: 10.1007/s11920-020-01198-5. PMID: 33104878; PMCID: PMC9109228.
- Palagini L, Cipriani E, Caruso V, Sharma V, Gemignani A, Bramante A, Miniati M, Riemann D. Insomnia During the Perinatal Period and its Association with Maternal and Infant Psychopathology: A Systematic Review and Meta-Analysis. Curr Psychiatry Rep. 2023 Nov;25(11):617-641. doi: 10.1007/s11920-023-01463-3. Epub 2023 Oct 11. PMID: 37819491.

44

References

ACOG Practice Bulletin: Clinical management guidelines for obstetrician-gynecologists number 92, April 2008 (replaces practice bulletin number 87, November 2007). Use of psychiatric medications during pregnancy and lactation. *Obstetrics and gynecology.* Apr 2008;111(4):1001-1020.

The American College of Obstetricians and Gynecologists Committee Opinion no. 630. Screening for perinatal depression. *Obstetrics and gynecology.* May 2015;125(5):1268-1271.

Postpartum Depression, Frequently Asked Questions: Labor, Delivery, and Postpartum Care. The American College of Obstetricians and Gynecologists Patient Education. 2013; http://www.acog.org/Patients/FAQs/Postpartum-Depression. Accessed August 16, 2016

Postpartum Depression, Washington D.C.: The American College of Obstetricians and Gynecologists, 2013.

45