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Three cases of lithium exposure and exclusive breastfeeding

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Abstract

The aim of this study was to provide data to aid decision making regarding lithium use during lactation. Three women treated with lithium for bipolar disorder during pregnancy and lactation and their four infants provided lithium levels at 1 month postpartum. Infant levels ranged from 10% to 17% of maternal levels. Two infants experienced early feeding problems which were overcome with breastfeeding education and support. Women taking lithium can be supported to breastfeed, and their infants should be followed closely until breastfeeding is well established.

Keywords

Lithium; Breast milk; Lactation; Bipolar disorder

Background

Breastfeeding confers a well-documented range of health benefits for mothers and also for infant health, growth, immunity, and development (American Academy of Pediatrics Section on Breastfeeding 2005; Agency for Healthcare Research and Quality 2007). However, data to guide the use of psychotropic medication during lactation are sparse. For example, although lithium has been the mainstay of treatment for bipolar disorder for decades, few data have been published. Results from five case reports and one case series published between 1969 and 1976 estimate that fully breastfed infants receive 11% to 42% of the mother's weight-adjusted lithium dose from breast milk (Drug and Lactation Database (LactMed) 2011). Moretti et al.'s (2003) series from 11 mothers and 2 infants estimated that infants receive 0% to 30% of the maternal weight-adjusted dose (Moretti et al. 2003). Viguera et al.'s case series (2007) reported infant serum levels of 0.05 to 0.30 meq/L and a range of infant to maternal serum concentrations of 11% to 56% (Viguera et al. 2007).

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In addition to the adverse neonatal outcomes from fetal exposure to lithium (Kozma 2005), adverse effects have been reported in four newborns exposed to lithium during both pregnancy and lactation. A 5-day-old infant had cyanosis and ECG changes; the mother was taking a diuretic which may have decreased infant lithium elimination and increased serum levels (Tunnessen and Hertz 1972). Another case of lithium toxicity was also attributed to dehydration (Skausig and Schou 1977), and two cases of increased TSH in early infancy were reported (Viguera et al. 2007; Drug and Lactation Database (LactMed) 2011). Published data provide limited support for breastfeeding among mothers taking lithium and suggest that infants be closely monitored, particularly if they were exposed during fetal life. The aim of this report is to provide additional data to aid decision making regarding lithium use during lactation.

Methods

Three women enrolled in an observational study, Antimanic Use during Pregnancy (R01 MH 075921), were treated with lithium for bipolar disorder during pregnancy and lactation. Women and infants had serum lithium levels drawn at 1 month postpartum, and one dyad also had samples at 6.5 months. Infants were examined by a pediatrician or family nurse practitioner at each visit (Table 1).

Lithium level analysis

Blood samples were obtained via venipuncture into 5-ml BD Vacutainer serum tubes without additives. Our sampling containers did not contain lithium heparin to avoid falsely elevated lithium levels (Tanaka et al. 2008). Serum samples were immediately frozen and shipped with dry ice overnight to MEDTOX Scientific, Inc. (St. Paul, MN). Both mother and infant serum samples were analyzed for lithium using the technique of inductively coupled plasma-mass spectrometry (quality control CVs of 4.0% to 7.0% at target levels of 0.025 and 1.800 meq/L with a lower limit of 0.01 meq/L).

Results

Patient 1 developed postpartum psychosis following her first delivery. She was hospitalized and treated successfully with lithium. Depressive symptoms recurred when she tapered her lithium. Throughout the second pregnancy, she received lithium 900 mg daily; her thyroid function tests were normal, and lithium levels ranged from 0.2 to 0.55 meq/L (Table 2). She remained euthymic throughout her pregnancy, with scores on the 17-item Hamilton Rating Scales≤2 and Mania Rating Scale00 throughout her pregnancy. She delivered her healthy son whom she breastfed. He had 4.2% weight loss on day 2 and 5.9% on day 7. On day 15, his weight gain was 77 g in 8 days (<10 g/day; the goal is a minimum of 15–30 g/day weight gain after the weight nadir), and he was less than birth weight (goal: back to birth weight by 10 days). The mother's milk supply was low, and she was encouraged to freely breastfeed and offer expressed milk or formula. At day 21, he had gained 20 g/day from almost exclusive breast milk feedings. The mother continued to breastfeed past 1 year. At 2 months of age, her son had mild hypotonia; he received early intervention care for gross and fine motor delay through the first year.

Patient 1 had a second baby 2 years later. During this pregnancy, she again remained euthymic and received lithium 900 mg daily with normal thyroid function. She delivered a healthy daughter without hypotonia whom she exclusively breastfed. Her daughter regained birth weight by 1 week of age and gained weight appropriately in follow-up.

Patient 2 had bipolar I disorder; in adolescence, she had mainly mixed episodes. With lithium therapy, she became euthymic. After she discontinued lithium, she had stable mood

for 2 years. In pregnancy, the mood episodes recurred; she cycled rapidly each month from hypomania to mixed and depressed episodes. At 23 weeks gestation, she began lithium 300 mg bid after confirmation of normal thyroid function. At 33 weeks gestation, the lithium dose was increased to 300 mg in the morning and 600 mg in the evening. Both her Hamilton Rating Scale and Mania Rating Scale scores remained low (≤3 and 0, respectively, throughout pregnancy). She delivered a healthy son whom she exclusively breastfed. On day 2, he had 5.2% weight loss. On day 3, his weight loss was 8.5%, and he appeared less vigorous and was breastfeeding for brief durations. The mother was told to breastfeed every 2–3 h for 20–30 min then to pump her milk and bottle feed her son the expressed breast milk until she felt he was waking on his own and sustaining his feedings. The following day, he had gained 75 g and was waking every 2 h for feedings. His mother continued to exclusively breastfeed until he was 4 months old.

Patient 3 had bipolar disorder type I and a prominent history of recurrent mania with lithium discontinuation. She had polyhydramnios and a near-term stillbirth in her first pregnancy and an 11-week miscarriage, both while taking lithium. For the index pregnancy, she began heparin to reverse the effects of factor V Leiden mutation (which increases the risk of venous thromboembolism) that was diagnosed following her miscarriage. She received lithium with close monitoring for polyhydramnios. She remained euthymic during her pregnancy (Hamilton Rating Scale ≤3 and Mania Rating Scale ≤1). Patient 3 delivered her healthy daughter whom she exclusively breastfed until 8 weeks postpartum when her lithium level was 2.0 meq/L. Her dose was held for 2 days, and then she resumed daily dosing with 600 mg. She provided previously collected frozen breast milk to her daughter and discarded her milk for 2 days until her serum lithium level declined to 0.7 meq/L. She continued to successfully breastfeed until 7 months.

Discussion/conclusions

Infant serum levels of lithium ranged from 10% to 17% of maternal serum levels. These data are consistent with Viguera et al.'s report (infant/maternal serum, 11–56%) (Viguera et al. 2007) but on the low end of their reported range. Two of four infants experienced early feeding problems. The first infant born to patient 1 had mild sustained hypotonia, which has been associated with antenatal lithium exposure and feeding difficulties. The infant of patient 1 was also exposed to bupropion antenatally, and a transient neonatal syndrome may have contributed to initial feeding difficulties. However, research on the association of antidepressants with neonatal syndrome has focused on serotonergic drugs rather than bupropion (Moses-Kolko et al. 2005). Patient 1's second baby and the infant of patient 3 were exposed to bupropion and citalopram, respectively, and neither had feeding problems. Importantly, these mothers were able to successfully breastfeed with lactation education and support.

The benefits of breastfeeding (Ip et al. 2007) are often underestimated in part because of the availability and perceived safety of infant formula. Focus groups conducted by the Ad Council in preparation for a national breastfeeding promotion campaign found that women were more likely to consider breastfeeding when told that infant formula increased risks of negative outcomes than if told that breast-feeding improved outcomes. More women taking lithium might choose to breastfeed if the risk–benefit discussion was presented similarly. According to the Surgeon General's Call to Action to Support Breastfeeding, the excess health risks associated with formula feeding instead of breastfeeding full-term infants include: 100% for ear infections, 47% for eczema, 178% for vomiting and diarrhea, 257% for hospitalization for lower respiratory tract diseases in the first year, 64% for type 2 diabetes mellitus, and 56% for sudden infant death syndrome (partial list) (U.S. Department of Health and Human Services 2011).

The literature to date suggests that women taking lithium can be supported to breastfeed their infants. Ideally, a shared decision-making approach (Towle and Godolphin 1999) would be used. Employing this model requires the physician to develop a partnership with the mother, determine her preferences for infant feeding, respond to her concerns and evaluate the evidence in relation to her situation (including providing information regarding risks and benefits of formula and breastfeeding), negotiate a decision, and agree on a maternal and infant monitoring plan.

Newport et. al. suggested changes to maternal lithium dosing at term to reduce infant exposure at delivery (Newport et al. 2005). Viguera et. al. suggested laboratory monitoring of infants in the immediate postpartum period (lithium, TSH, BUN/creatinine by 6 weeks of age and every 8–12 weeks as clinically indicated) (Viguera et al. 2007). This regimen is more intense than we implemented. We stressed frequent clinical pediatric assessments and targeted laboratory testing as indicated.

Information on lithium exposure via breast milk for preterm or ill infants is not available and would be an important contribution to the literature. Based on our experience and this review, we recommend the following for the lithium-treated mother who is breastfeeding her full-term infant:

- Suspend maternal lithium dose 24–48 h before scheduled Cesarean delivery or onset of labor for spontaneous delivery (Newport et al. 2005).
- Reduce maternal lithium dose to preconception amount immediately after delivery (Newport et al. 2005).
- Educate mothers/parents to monitor their infant for changes, including signs of dehydration, lethargy, and feeding problems.
- With the infant's pediatric care professional, closely monitor infant weight for the first 2 weeks (pediatric visit within 1–2 days of hospital discharge and every few days until gaining weight appropriately) (15+g/day and back to birth weight by 10 days).
- Obtain maternal and infant serum lithium levels if clinical concerns arise.
- Review state newborn screening results to verify normal thyroid screen (available through each states' newborn screening program).
- Obtain thyroid function studies and other clinically indicated studies if the baby has sustained behavioral change, poor feeding, hypotonia, slow growth.
- Monitor development and refer to early intervention service if there is hypotonia or there are other subtle neurological findings.

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Table 1

Mother–infant information

Patient	Maternal age (years)	Gravity–parity	Race	Meds other than lithium during pregnancy	Birth weight (kg)	Gestational age (weeks)	Apgar scores 1/5 min
1	28	G2P1→2	White	Bupropion, 300 mg; levothyroxine, 50 μg; prenatal vitamins; calcium; fish oil	3.405	40	8/9
1[a]	30	G3P2→3	White	Bupropion, 300 mg; levothyroxine, 75 μg; prenatal vitamins; fish oil; iron; vitamin D	4.026	41	9/9
2	19	G1P0→1	White	None	4.045	38	9/9
3	28	G3P0→1	White	Escitalopram, 10 mg; synthroid, 25 μg; heparin docusate, 200 mg daily; polyethylene glycol; prenatal vitamins; fish oil; magnesium, 400 mg BID	3.501	38	Not known

[a]Mother had second child while in the study

Table 2

Serum lithium concentrations in breastfeeding mother–infant dyads

Patient	Days from delivery	Maternal lithium dose (mg/day)	Maternal serum lithium (meq/L)	Infant serum lithium (meq/L)	Ratio infant/maternal serum lithium
1	−30	900	0.48	–	–
	31	900	0.72	0.08	11%
	183	900	0.48	0.08	17%
1[a]	−14	900	0.60[b]	–	–
	43	900	0.73	0.11	15%
2	−5	900	0.40	–	–
	4	900	0.78	–	–
	39	900	0.81	0.08	10%
3[c]	−180	1,350	0.85	–	–
	14	1,350	0.12	–	–
	31	1,350	0.97	0.11	11%

[a] Mother had second child in the study

[b] Sample run at hospital lab not through study lab

[c] Patient took 1,500 mg every other day alternating with 1,200 mg every other day