

Lithium and Lactation

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Medication use by the nursing mothers is a controversial topic, with the potential for infants to be exposed via breastmilk. This ethical dilemma has led to health professionals, authorities, and parents considering infant formula to be a reasonable alternative to mitigate risk. As a consequence, there is a lack of evidence about the safety and efficacy of many medications during lactation, including lithium¹. Decisions to use lithium during the perinatal period are challenging because information about the efficacy and safety for the mother-child dyad come from observational studies of lactation outcomes, which have important limitations and biases^{2,3}.

Breastfeeding is an important public health issue because it promotes health, prevents disease, and contributes to reducing health inequalities in mothers and nursing infants. Breastfeeding is also a great benefit to the environment and society⁴. Human milk is uniquely tailored to meet the nutritional needs of human infants, including premature and ill newborns. It has the appropriate balance of nutrients provided in easily digestible and bioavailable forms. Optimal infant and young child feeding practices include exclusive breastfeeding for the first 6 months of life, if possible, followed by combining breastmilk with adequate, safe, and appropriate complementary foods until the infant is at least 1–2 years old⁵.

According to the US National Centers for Disease Control and Prevention, there are few contraindications to breastfeeding. These include maternal infection with HIV, human T-cell lymphotropic virus type 1 or 2, active untreated tuberculosis, or herpes simplex lesions on the breast. Additionally, maternal use of illicit street drugs (i.e., phencyclidine or cocaine), chemotherapeutic agents (drugs interfering with cell replication), and radioactive isotope therapies should contraindicate breastfeeding. Concerning the infants themselves, those with galactosemia should not be breastfed⁶. However, a 2012 clinical report by the American Academy of Pediatrics⁷ indicated that most medications and immunizations are safe to use during lactation.

A common reason for never starting or for interrupting breastfeeding is medication use by the nursing mother. Any pharmacologic therapeutic decision during lactation should be guided by the best available evidence and the importance of benefit for each patient. Factors influencing the decision to breastfeed converge around the advantages and risks of breastfeeding for the mother and infant, the socio-demographic and clinical features of the mother, personal experience and family tradition, the presence of a support system (whether professional or partner, family, social), and personal choice. The optimal time to explore women's preferences for breastfeeding and to educate the family about treatment options during breastfeeding is before they conceive or early in pregnancy⁸. Options include exclusive breastfeeding,

breastfeeding supplemented with formula, or exclusive formula feeding.

Bipolar disorder is a chronic mental illness that affects about 350 million people worldwide, equating to 3% of the world population. It affects men and women in comparable rates, often starting before age 25 years, without cultural or ethnic variation^{9,10}. There seems to be a higher risk for women to suffer bipolar II (hypomania), rapid cycling, and mixed episodes compared with men. Lithium use for the treatment of bipolar disorder has been reported since late 1940s¹¹ and was approved in 1970 by the US Food and Drug Administration (FDA) for the treatment of acute mania and in 1974 for the long-term maintenance of bipolar disorder. It is also prescribed as adjunctive treatment in major depressive disorder and for preventing suicidal behavior in patients with affective disorders¹²⁻¹³.

Women with bipolar disorder are at high risk of symptom relapse during the perinatal period¹⁴. Although its use during the first trimester has been associated to a dose-dependent increase risk of congenital malformations¹⁵, it has proven to be an effective preventive treatment during perinatal period¹⁶. In relation to treatment at others stages of life, some peculiarities must be considered for the management of lithium treatment during the perinatal period. For example, physiological renal changes during pregnancy¹⁷ may alter the pharmacokinetics of lithium, and its serum concentrations will decline throughout pregnancy. This necessitates preferably weekly monitoring in the third trimester with dose adjustment to maintain therapeutic levels¹⁸. Lithium also has a complete placental passage and equilibrates between the maternal and fetal circulation across a wide range of maternal concentrations (0.2–2.6 mEq/L)¹⁹. It has been shown that neonatal serum lithium concentrations >0.64 mEq/L may be associated with an increased rate of neonatal complications such as lethargy, cyanosis, hypothermia, hypotonia, hypothyroidism, hypoglycemia, polyuria, respiratory problems, and poor drinking ability¹⁹⁻²⁰. Postpartum, serum lithium concentrations in the mother gradually return to their preconception levels, and this presents a risk for lithium intoxication if women have had their dose increased during pregnancy. Lithium serum concentration should be measured twice weekly for the first 2 weeks after delivery and monthly thereafter for the next 3–6 months¹⁸.

Lithium is a cation that transfers easily into breast milk. The recommendations for its use during breastfeeding vary due to the high variability of its diffusion into breastmilk, the secondary risk of lithium toxicity in the newborn, and the risk of relapse associated with sleep deprivation during the period of exclusive maternal breastfeeding²¹. There are limited data about the long-term effects



of lithium exposure via breastmilk, but it does seem that the risk of serious adverse events in the nursing infants is relatively low⁷. Two recent systematic reviews concerning clinical lactation and lithium showed that exposure of the nursing infant to lithium is less during breastfeeding than during pregnancy. However, there was also a high degree of heterogeneity between the studies, including exposure durations, the presence of polypharmacy, lithium sampling times, type of breastfeeding, and age of infants^{2,3}. Nevertheless, it is certainly plausible that nursing infants would be vulnerable to the same side effects as adults, including changes in thyroid and renal functions. In turn, this necessitates regular clinical and blood monitoring (e.g., serum lithium, thyroid stimulating hormone, blood urea nitrogen, and creatinine) immediately postpartum and at regular intervals while breastfeeding²².

Given the many benefits of breastfeeding, some women who may also benefit from lithium in the postpartum period are likely to consider breastfeeding. The professionals involved in this consultation must be adequately trained about the pharmacology of lactation⁸. Women should then have an individualized breastfeeding plan drafted in collaboration with perinatal psychiatrists, obstetricians, pediatricians, midwives, nurses, and family physicians. Research in international collaborative networks would be interesting to increase current evidence to support women in achieving their breastfeeding goals.

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