

## Lamotrigine Effects on Breastfed Infants

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**Abstract-** Lamotrigine is a safe anti-epileptic drug among pregnant and lactating women. Some concerns exist regarding the safety of lamotrigine during breastfeeding and related neonatal complications. In this brief review, this matter was evaluated and discussed. In this review study, the medical literature available in search databases such as Embase, Scopus, PubMed, and Medline and even also local medical search engines were evaluated. The results indicated that lamotrigine is a safe anti-epileptic drug for breastfeeding women with rare and usually mild adverse effects among neonates exposed to high milk concentration of this drug and its metabolites. However, close periodical monitoring for infants whose mothers are utilizing lamotrigine is recommended to decrease the probability of severe side effects among them.

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### Introduction

The optimal management of women with epilepsy during pregnancy and postpartum period involves attaining an ideal balance between reduction of fetal and neonatal exposure to the toxic influences both of antiepileptic drugs and of seizures (1). The serum concentration of anti-epileptic drugs may decreaseduring pregnancy leading to more frequency of seizures. It has been established that the elimination of some anti-epileptic drugs such as lamotrigine is enhanced during pregnancy (1,2). This matter would require special attention to achieve treatment goals for epilepsy during pregnancy.

This issue is also extended to postpartum period when the women are lactating their neonates (2,3). Lamotrigine is eliminated gradually in breast-fed infants, but while lamotrigine concentrations in the infant can rise to pharmacological levels, no clinically relevant adverse effects are reported to be caused by lactation (2). However, the breastfed infants would maintain the lamotrigine plasma concentrations of approximately 30% of the mother's plasma levels (4). These pharmacological aspects have resulted in some concerns about the safety of lamotrigine during breastfeeding and related neonatal complications. This

brief review study, this matter is evaluated and discussed.

### Materials and Methods

In this review study, the medical literature available in medical databases such as Embase, Scopus, Pubmed, and Medline and even also local medical search engines were evaluated and the results about the lamotrigine pharmacological properties during breastfeeding and the probable adverse effects in infants were obtained and compared to develop some clinical considerations about neonatal adverse effects of lamotrigine in breastfeeding children.

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As reported in previous studies extensive passage of lamotrigine into breast milk and a slow elimination in the newborn would result in such concentrations in the breastfed infant that are required for representation of pharmacological effects (5). Since the neonates have been in contact with even higher concentrations of lamotrigine during pregnancy, some adaptations may be seen in responsible for less toxic presentations among neonates. While a single case of toxicity has been reported in a neonate exposed to lamotrigine via breast

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milk, in most conditions, breastfeeding can be initiated and maintained given the incredible benefits of mothers' milk (6).

However, even further follow up periods more than breastfeeding course, has shown no developmental side effects among infants exposed to lamotrigine during infantile period (7). Serum concentrations of lamotrigine in breastfed children are usually higher than expected; in some cases reaching "therapeutic" ranges and these high concentrations may be explained by poor neonatal drug elimination because of inefficient glucuronidation (8).

While even therapeutic levels of lamotrigine in infants is not reported to be dangerous; monitoring of blood levels in breastfeeding infants and the possible require for personal counseling in women with epilepsy regarding breastfeeding are recommended by some authors (8). The mean milk/plasma ratio for lamotrigine among breastfed infants is nearly 40%, and there is a non significant trend for higher concentrations of Lamotrigine in breast milk four hours after the maternal dose (9). However, in such situation the only side effect has been shown to be mild thrombocytosis without clinical importance (9).

Severe apnea in a fully breastfed infant exposed to lamotrigine in breast milk was also reported that was recovered when the breastfeeding was terminated (10). This shows the importance of determining serum concentrations of lamotrigine by definite methods such as gas chromatography and densitometry to develop better decision for infants whose mothers are using lamotrigine during breastfeeding period (11). However, considerable amount of lamotrigine (2-5 mg/day) may be excreted in breast milk. Usually no adverse effects are observed in the infants (12,13).

However, as lamotrigine crosses the placenta and also excretes into the milk, a close monitoring of both mother and newborn is crucial (14).

Lamotrigine is a safe anti-epileptic drug for breastfeeding women with rare and usually mild adverse effects among neonates exposed to high milk concentration of this drug and its metabolites. However, close periodical monitoring of infants whose mothers are utilizing lamotrigine is recommended to decrease the probability of severe side effects among them. However, performing more studies especially with prospective cohort design may help better interpretation of lamotrigine effects among breastfeeding infants.

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