

Review

Epilepsy and recommendations for breastfeeding

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ABSTRACT

Purpose: The objective of this paper is to provide a synopsis of benefits and potential harmful effects of exposure to antiepileptic drugs (AEDs) via breastmilk, and present recommendations for breastfeeding in women with epilepsy.

Methods: The article is based on a discretionary selection of English language articles retrieved by a literature search in the PubMed database, the LactMed database, and the authors' clinical experience.

Results: Breastfeeding is associated with benefits for the infant, including nutrition, protection against infectious and immunological disease, and promotion of development and psychological attachment. Exposure to AEDs via breastmilk could potentially produce side effects or negatively affect development. Most studies on AED transfer through breastmilk report infant serum levels well below the limit of an expected pharmacological effect. Some drugs have the potential to reach significant serum levels in breastfed infants, such as barbiturates, benzodiazepines, lamotrigine, and ethosuximide. Thus, breastfed infants should be monitored for side effects. Still, adverse symptoms are rarely reported in breastfed infants of mothers taking AEDs, and prospective studies have failed to demonstrate any negative developmental effects in children that have been exposed to AEDs via breastmilk. The nursing infant's degree of drug exposure can be minimized by breastfeeding when drug concentrations in the milk are low, reducing maternal AED dosage to prepregnancy levels, and administering mixed nutrition.

Conclusion: Most AEDs are considered safe or moderately safe during breastfeeding. Mothers with epilepsy should be encouraged to breastfeed, provided careful monitoring of the infant.

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1. Introduction

The safety of breastfeeding while taking antiepileptic drugs (AEDs) is a major concern for pregnant women with epilepsy and their doctors. Exposure to AEDs in the womb is associated with an increased risk of congenital malformations [1–4], growth restriction [3,5], and neurodevelopmental delay in the child [6–10]. Proposed teratogenic mechanisms of action include folic acid antagonism, induction of apoptosis, oxidative stress, and receptor-mediated effects on brain cell proliferation, migration, differentiation, and synaptogenesis [11,12]. The central nervous system (CNS) is more vulnerable towards teratogenic agents than other organs, due to length of time over which developmental processes proceed, also including the postnatal period [13]. The formation of the blood–brain barrier is not completed until well after birth,

leaving the brain relatively unprotected against toxic substances during this period [13]. Thus, prolonged exposure to maternal AEDs via breastmilk could theoretically pose an additional risk to the infant who has already been exposed during pregnancy.

Conversely, the beneficial effects of breastfeeding for both mother and child are widely documented and acknowledged. Breastfeeding is an essential biological function of humans and the normative standard of infant feeding [14]. Restricting a mother's natural inclination to breastfeed must therefore be justified by evidence that any harmful effect is likely to outweigh the advantages. Counselling women with epilepsy with regard to breastfeeding is a challenging task since they have to choose between an artificial food source or exposing their infant to a CNS acting drug.

Due to limited data on AEDs' safety during lactation, mothers with epilepsy have often received conflicting breastfeeding advice from their neurologist, paediatrician or gynaecologist.

In 2009, the American Academy of Neurology (AAN) updated their practice parameter for the management of women with epilepsy during pregnancy, but did not give any specific recommendations concerning breastfeeding [15].

Abbreviations: AED, antiepileptic drug; CNS, central nervous system.

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The aim of this paper is to provide an updated synopsis of AEDs and their safety during the lactation period, as well as to present practical recommendations for women with epilepsy who are motivated to breastfeed.

2. Methods

The recommendations are based on a discretionary selection of articles retrieved by literature search in the PubMed database performed on September 15, 2014. English language articles only were included. The search terms 'breastfeeding', 'breastmilk', and 'lactation' were linked to the terms 'antiepileptic drugs' and 'epilepsy', as well as search terms of the individual antiepileptic drugs. Information from the online LactMed database was also included. The authors' scientific and clinical experience of work with women with epilepsy has influenced the evaluation and recommendations.

3. Benefits of breastfeeding in the general population

Human milk and its bioactive components are ideally adapted to the needs of the nursing child, and is the ultimate nutrient source for infants [16]. Human milk enhances growth and development, as well as long-term child and adult health. Breastfeeding reduces the risk of infectious diseases in infancy, such as lower respiratory tract and gastrointestinal infections [14]. Other benefits include a lower risk of sudden infant death syndrome [17], allergic disease [18,19], and possibly inflammatory bowel disease [20]. Breastfeeding also protects against childhood leukaemia [21], reduces the risk of obesity, and type 1 and 2 diabetes [22–24].

The association between breastmilk and neurocognitive abilities in infants remains controversial. Many studies have investigated this relationship, but the reported findings have been conflicting [25]. On average, breastfed children score several points higher on tests of cognitive function compared to those who solely received formula milk [26]. However, maternal factors such as socioeconomic status, education, and intelligence represent major confounders for the association between breastfeeding and cognitive child development [14].

Breastfeeding is nevertheless an important aspect of the psychological mother–child relationship and promotes attachment security. Mothers who breastfeed demonstrate more sensitive parenting behaviour in early infancy [27]. Breastfeeding is also associated with positive effects on maternal health and well-being, including prolonged lactational amenorrhea, a reduced risk of postpartum depression, type 2 diabetes mellitus, and breast and ovarian cancer, as well as beneficial economic aspects [25,28].

4. Breastfeeding practice in women with epilepsy

Many factors influence a mother's decision to breastfeed. It is a common misconception that drugs taken by the mother are retained in the breastmilk [29]. Amongst women taking AEDs, some believe that the drug exposure for the child is higher during breastfeeding than pregnancy. Many are concerned that breastmilk will produce an unnecessary prolonged drug exposure for the infant, and regard formula milk as a safer alternative. Sleep-deprivation and missed medication during the postpartum period increase the risk of seizures [30]. Thus, some mothers fear that seizures might affect the safety of breastfeeding, or that breastfeeding could affect the risk of seizures.

Socioeconomic factors such as maternal education, income, employment, and social class affect both the initiation rate and duration of breastfeeding [28,31]. Women with epilepsy are at increased risk of having adverse outcome for such factors [5,32], probably affecting their ability or motivation to breastfeed. Indeed,

Meador et al. [33] showed that breastfeeding mothers with epilepsy had higher IQ compared to those not breastfeeding. Emotional status and self-esteem may represent determinants for a mother's capacity to breastfeed. Women with epilepsy are especially vulnerable during pregnancy and in the post-partum period, with higher rates of depression and anxiety [32,34,35]. Hence, personal support and advice from family and health care workers can be essential for a mother in coping with the emotional and practical challenges of breastfeeding [30].

The child's developmental status may affect the practical aspects of breastfeeding, as AEDs during pregnancy are associated with delayed motor and social skills in the child during the lactation period [36]. In infants with inadequate developmental resources, i.e. reduced suckling or latching abilities, failure to succeed with breastfeeding can occur even if the mothers are motivated to do so.

Rates of breastfeeding vary between and within countries [28]. In the US, the initiation rate is 79%, with only 41% exclusively breastfeeding at 3 months [37]. The NEAD study group reported that overall 42% of women with epilepsy were breastfeeding at 3 months [33]. In Scandinavia, where the initiation rates of breastfeeding are around 90%, women with epilepsy have higher breastfeeding rates, as shown using data from the Norwegian Mother and Child Cohort Study (Fig. 1). In this study, women using either AED polytherapy or lamotrigine monotherapy had substantially lower breastfeeding rates compared to both non-epileptic controls as well as women taking other AED monotherapy. This indicates that the mothers and their physicians had safety concerns regarding specific drug groups.

5. Pharmacokinetic considerations

To affect the nursing infant, any drug used by the mother has to transfer through the breastmilk and reach the child's systemic

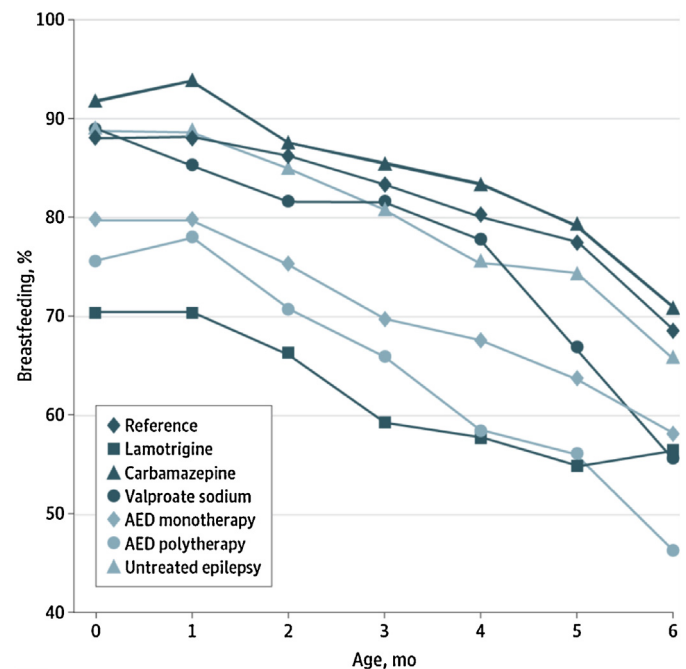


Fig. 1. Exclusive or mixed breastfeeding at ages 0–6 months. Frequency of breastfeeding in epilepsy groups and the reference group at 0 to 6 months after delivery. AED indicates antiepileptic drug.

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