Neonatal Benzodiazepines Exposure during Breastfeeding

Lauren E. Kelly, MSc[1,3,2], Shirley Poon, BSc[1], Parvaz Madadi, PhD[4,5], and Gideon Koren, MD[2,4,5]

Objective To assess central nervous system depression and other adverse effects in infants exposed to benzodiazepines through breast milk.

Study design A prospectively recruited, retrospectively assessed cohort study of mothers who contacted the Motherisk program regarding the safety of benzodiazepines and were invited to participate in a follow-up program regarding the effects of these medications on their infants during lactation.

Results A total of 124 consenting women participated. Adverse outcomes, specifically sedation, was identified in only 1.6% (2 of 124) of infants and was not associated with benzodiazepine dose, number of hours breastfed, or any demographic trait. Mothers reporting adverse outcomes in themselves (26% [32 of 124]) were more likely to be taking concomitantly a greater number of central nervous system depressants.

Conclusions This study supports the continued recommendation to initiate breastfeeding while taking benzodiazepines postpartum. *(J Pediatr 2012;161:448-51)*.

Although encouraging women to breastfeed is important, consideration must also be made in treating underlying maternal conditions during the postpartum period. Many women exhibit anxiety and insomnia in the postpartum period, leading them to take benzodiazepines while breastfeeding.[1-4] Adverse effects associated with the use of benzodiazepines include sedation, confusion, and withdrawal symptoms that vary in severity, from insomnia to seizures and psychosis.[5,6] On the other hand, untreated maternal anxiety-related illness may adversely affect the mother's ability to care for herself and her baby.[5] Currently, breastfeeding is not contraindicated in women using psychotropic medications such as benzodiazepines.[7,8] Benzodiazepines include medications such as alprazolam, bromazepam, clonazepam, diazepam, flurazepam, lorazepam, midazolam, nitrazepam, oxazepam, temazepam, and triazolam, as well as several other less common molecules.[9]

Several benzodiazepines are transferred into breast milk as well as across the placenta.[6] Passive diffusion and carrier-mediated transport through the organic cation transporter and the breast cancer resistance protein are thought to play a role in benzodiazepine transfer into breast milk.[10,11] However, detailed knowledge of benzodiazepine transfer into human milk is limited and its clinical consequences in infants have yet to be elucidated. Rubin et al estimated the incidence of neonatal adverse drug reactions resulting from benzodiazepine use during lactation.[12] Based on relatively small numbers, this study reported infant adverse event rates of 17% (1 of 6), 22% (2 of 9), and 50% (1 of 2) when exposed to alprazolam, diazepam, and clonazepam, respectively.[12] Adverse effects in these infants included lethargy, irritability, poor weight gain, and apnea. This study did not report any adverse drug reactions in infants exposed to oxazepam, lorazepam, or temazepam.[12] The small sample size and relatively limited benzodiazepine range need further exploration in order for informed decisions to be made regarding breastfeeding.

We examined the safety of infant exposure to benzodiazepines during lactation. We also determined the epidemiology of common benzodiazepines used in the breastfeeding population and the incidence of adverse drug reactions in mothers taking benzodiazepines. Finally, we compared these characteristics to other central nervous system (CNS) depressing drugs, mainly opioids, used by lactating mothers.

Methods

A self-referred population of mothers who called the Motherisk Program at the Hospital for Sick Children in Toronto, Ontario, between January 2010 and May 2011 for advice regarding the use of benzodiazepines during lactation were contacted for follow-up. Inclusion criteria consisted of women consenting to the follow-up procedure who were able to be reached, were fluent in English, and used benzodiazepines during breastfeeding. For the sake of confidentiality, calls from lactation consultants, family members, nurses, and physicians were excluded. Mothers taking concomitant CNS depressants were not excluded. The study protocol was approved by the institutional research ethics board.

We used the breastfeeding follow-up form to collect information from breastfeeding mothers regarding their medication use, frequency of breastfeeding, the

CNS Central nervous system

From the [1]Schulich School of Medicine and [2]Molecular Toxicology, University of Western Ontario; [3]Department of Clinical Pharmacology, London Health Sciences Centre, London, Ontario, Canada; [4]Department of Clinical Pharmacology, University of Toronto; and [5]Division of Clinical Pharmacology and Toxicology, Hospital for Sick Children, Toronto, Canada

Supported by the Ivey Chair in Molecular Toxicology at the University of Western Ontario. L.K. and P.M. are funded by the Canadian Pharmacogenomics Network for Drug Safety and the Canadian Institutes of Health Research. The authors declare no conflicts of interest.

 10.1016/j.jpeds.2012.03.003