Case Report

Probable topiramate-induced diarrhea in a 2-month-old breast-fed child — A case report

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A B S T R A C T

An infant developed a severe condition of recurrent and persistent watery diarrhea at 40 days of age. The child had been partially breast-fed, and the mother used topiramate for epilepsy. Hospital examination excluded a viral or bacterial infection and failed to identify any other potential cause. After two weeks, topiramate exposure was suspected to be the cause, and breast-feeding was suspended. The diarrhea ceased within 2 days. Analysis of the breast milk showed a topiramate concentration of 15.7 μmol/L (5.3 μg/mL). There is little information on the use of topiramate in breast-feeding women. The potential effects on the children are not known. Topiramate passes into breast milk, and the concentration may equal the therapeutic plasma concentration. In this case, the infant may have ingested up to 40% of the mother’s weight-adjusted dose. Diarrhea is a well-known adverse reaction to topiramate and has the potential to cause serious electrolyte disturbances in neonates and infants. The condition improved rapidly after suspension of breast-feeding. Topiramate in breast milk may reach levels that cause adverse effects in infants. Based on the adverse reaction profile of topiramate and the milk concentration, the diarrhea was assessed as a probable adverse drug reaction in the infant.

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1. Introduction

Topiramate is one of the newer antiepileptic drugs and is also approved for migraine prophylaxis [1]. There is little information concerning topiramate use in breast-feeding women, but case reports indicate that it is transferred into human milk and that milk concentrations may equal those in maternal plasma [2–5]. We report a case of long-lasting diarrhea in a breast-fed infant exposed to topiramate.

2. Case report

A patient with epilepsy, aged 31, had been treated with topiramate 100 mg/day for several years. The treatment was continued unchanged throughout her pregnancy with good therapeutic effect. A healthy girl with a birth weight of 2735 g was born after an induced birth 2 days after term. The topiramate treatment was continued while breast-feeding. In order to reduce infant exposure to topiramate, two daily breast milk meals were replaced with formula meals a week after birth. The baby initially thrived and had a normal development. At 40 days of age and body weight of 4735 g, she became ill, with 8–10 watery, foamy stools a day. No other family member had diarrhea or gastrointestinal upset. Her weight gain rate eventually declined, and diagnoses such as infection or somatic cause of the diarrhea were excluded, but she still suffered from diarrhea. After 18 days of frequent, watery stools, the general practitioner suspected a causal relationship with topiramate, and breast-feeding was suspended. Within 2 days, the frequency was reduced to 2–3 stools a day, and the mother observed more solid feces, with smell and color returning to normal.

While breast-feeding was suspended, the mother used a breast pump and stored the milk in a freezer (−20 °C). She gave her consent to have the milk analyzed for topiramate, and the milk was sent for analysis after a storage time of 4.5 months. A sample was analyzed for topiramate by fluorescence polarization immunoassay based on the competitive binding principle (InnoFluor Topiramate Assay System, Seradyn, Indianapolis, IN, U.S.A.). The assay system was used on a TDx

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were 10 six mother/infant pairs, plasma levels of topiramate in the infants

topiramate in human plasma stored for a period of 1 month at

of 150 mg in one patient 12 days after delivery[5].

views of 

child, and the child’s ability to eliminate the compound. In five of six mother/infant pairs, plasma levels of topiramate in the infants were 10–20% of the maternal plasma levels and in one case could not be detected [2,3]. In the case reported here, a milk concentration of 5.3 μg/mL (15.7 μmol/L) and an estimated daily intake of 450 mL of mother’s milk in an infant weighing 4735 g would result in a daily dose of 0.5-mg/kg topiramate. Other case reports have described theoretical infant dosages of 0.1–0.7 mg/kg/day [3] and 0.6 mg/kg/day [5]. The mother’s body weight was 70 kg, and the relative infant dose was estimated at 0.35. The infant described here may have ingested a topiramate dose of 35% of the mother’s weight-adjusted dose.

Withdrawal of breast milk was associated with rapid clinical improvement of the child’s condition, supporting the theory of an adverse drug reaction. Diarrhea is a well-known and very common adverse reaction to topiramate [6], and the infant’s condition improved upon withdrawal of topiramate. The diarrhea was assessed as a probable adverse reaction to topiramate in the breast milk. Other case reports describing topiramate use in breast-feeding women do not describe side effects in the children. To our knowledge, this is the first report of probable topiramate-induced diarrhea in a breast-fed infant. Infant diarrhea increases the risk of electrolyte disturbances, and topiramate in the breast milk may be a hitherto unknown risk factor.

The case has been reported to the National Health Authorities in Norway, registered as number NO-NOMAADVRE-RELISS-2008-5232.

Conflict of interest

The authors have received no funding to write the manuscript and have no conflicts of interest.

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