Breastfeeding and Medication

Migraine prophylaxis and breastfeeding

Migraines are different from normal headaches and can be totally debilitating. Pain is often accompanied by nausea and vomiting as well as sensitivity to light and sound. Some people also experience auras and changes in vision. Migraines are said to affect up to 20% of women. Triggers vary but migraines can be associated with missing meals and not drinking enough watery fluids. The pain is often described as throbbing.

Preventive treatment may be appropriate if the mother suffers at least two attacks a month, an increasing frequency of headaches, suffers significant disability despite suitable treatment for migraine attacks or cannot take suitable treatment for migraine attacks.

- Beta-blockers e.g., propranolol are effective.
- Tricyclic antidepressants e.g., amitriptyline
- Topiramate
- Pizotifen
- Botox
- Riboflavin

all of which are safe in breastfeeding.

Propranolol:

Compatible with breastfeeding because of low levels transferred into breastmilk determined in studies.

Propranolol is almost completely absorbed from the gastrointestinal tract but undergoes first-pass metabolism. It is highly lipid soluble and is approximately 90% plasma protein bound. It has at least one active metabolite but the impact of this is unclear. The half-life of propranolol is 3 to 6 hours. It is used to treat children with hypertension initially at a dose of 1 mg per kilogram but can be increased to 2 to 4 mg per kilogramme per day in divided doses. It is also

used to prevent migraines in children under the age of 12 at dose of 20 mg two or three times daily. It crosses the blood–brain barrier and the placenta. It is present in breastmilk.
In adults it may be used to lower blood pressure, to relieve symptoms of hyperthyroidism, to prevent migraines or to prevent panic attacks.
In a study of three women (Smith 1983) it was calculated that the maximum dose likely to be ingested by a breastfed infant would be less than 0.1% of the maternal dose. A m/p ratio range of 0.33 to 1.65 was reported. Bauer estimated that the maximal dose of cumulative propranolol to which a breastfed infant would be exposed at a maternal dose of 40 mg four times daily would be 21 µg per 24 hours. This dose is considerably less than the therapeutic dose of propranolol for infants. No adverse effects have been reported in breastfed infants whose mothers were receiving propranolol. The relative infant dose is quoted as 0.3–0.5% (Hale 2017 online access)
The BNF recommends that the amount of most beta blockers in breastmilk is probably too small to be harmful although it is advisable to monitor the infant for possible symptoms of beta-blockade.

Amitriptyline.

Compatible during breastfeeding due to extensive plasma protein binding and first-pass metabolism

Amitriptyline undergoes extensive first-pass metabolism. It is extensively bound to plasma proteins. The levels measured in breastmilk are low, because of this.
Bader and Newman (1980) studied a mother who took amitriptyline 100 mg daily for 6 weeks post-partum. She had breastmilk levels of amitriptyline and its metabolite nortriptyline of 151 and 59 µg per litre, respectively. This was calculated to represent 1.8% of the maternal weight-adjusted dosage. There were no reports of adverse effects on the baby. Misri and Sivertz (1991) followed-up a group of 20 breastfed infants whose mothers were taking a TCA for up to 3 years and found no adverse effects on growth and development even at a dose of 150 mg daily. Brixen-Rasmussen et al. (1982) studied a 3-week-old breastfed who had undetectable serum amitriptyline (<5 µg per litre) and nortriptyline (<15 µg per litre) during maternal amitriptyline use of 75 mg daily. Theoretical infant dose through breastmilk is quoted as 2145 µg per kilogramme per day maternal dose with a relative infant dose quoted as 1.5% (Hale 2017 online access).
The BNF states that the amount in breastmilk is too small to be harmful.

Topirimate

Probably compatible with use during breastfeeding. Observe for sedation, poor feeding and diarrhoea

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well as its role in controlling epilepsy, topiramate is being increasingly used to prevent migraines at a dose titrated up to 50mg twice daily. At this dose at least a 50% reduction in migraine frequency was seen in a study by D'Amico (2006) with 6% becoming migraine free.
Initial reports suggest that maternal doses of topiramate up to 200 mg daily produce low levels in infant serum despite the fact that transfer into breastmilk reaches significant levels (Öhman *et al.* 2002). Topiramate is only 9–17% protein bound, and metabolism may be affected by other enzyme inducing drugs, including other antiepileptic agents. It has been linked to cleft lip with or without cleft palate following first trimester use (Margulis *et al.* 2012).

Öhman observed five babies at delivery and followed three of them through lactation. Two to three weeks after delivery two of the breastfed infants had detectable but unquantifiable levels of topiramate and one had an undetectable concentration; m/p ratios of around 0.86 were determined throughout the study period and no adverse events noted.

One infant whose mother was taking 100 mg of topiramate daily developed watery, slimy stools with up to ten bowel movements daily at 40 days of age (Westergren *et al.* 2014). Topiramate levels in breastmilk were of 5.5 mg per litre. Breastfeeding was discontinued two weeks later. Within 24 hours, the stool frequency declined to two to three times daily, which were more solid, and the colour and odour normalised. Topiramate was the reported to be the probable cause of the diarrhoea in the infant.

Gentile (2009) reported a single case study of a mother who took 300 mg topiramate daily throughout pregnancy and breastfed for 8 months. Neither adverse drug effects nor neurodevelopmental delay were noted by the baby's paediatrician.

The infant exposed to topiramate through breastmilk, should be monitored for drowsiness, diarrhoea and adequate weight gain particularly if the mother is receiving a multiple drug therapy regimen. It is used as an adjunctive treatment in children from 2 years of age at 2.5–4.5 mg per kilogramme twice daily. Relative infant dose quoted as 24.5% (Hale 2017 online access). This is above the upper level of the safe range of 10% and should be used with caution. BNF states that manufacturer advises avoid as it is present in milk

Pizotifen: Amount probably too small to be harmful (BNF) but no research studies located.

Theoretically safe but no studies to confirm

Botox:

Theoretically safe but no studies to confirm

There are no studies into the passage of Botox but in a baby exposed to botulinum toxin via his mother's milk one infant was safely breastfed and no botulinum toxin was detectable in the mother's milk or infant. Since the doses used medically are far lower than those that cause botulism, amounts ingested by the infant, if any, are expected to be small and not cause any adverse effects in breastfed infants

Riboflavin (information taken from Hale Medications and Mother's Milk)

High-dose riboflavin (400 mg per day) has been proposed for migraine prophylaxis, although the evidence regarding efficacy is controversial. [Condo 2009, MacLennan 2008] No studies have been published examining this dosage in breastfeeding women. However, no toxic dose of this vitamin has been established in humans. [Maizels 2004]

- Condo M, Posar A, Arbizzani A, Parmeggiani A. Riboflavin prophylaxis in pediatric and adolescent migraine. The journal of headache and pain. Oct 2009;10(5):361-365.

- MacLennan SC, Wade FM, Forrest KM, Ratanayake PD, Fagan E, Antony J. High-dose riboflavin for migraine prophylaxis in children: a double-blind, randomized, placebo-controlled trial. Journal of child neurology. Nov 2008;23(11):1300-1304.

- Maizels M, Blumenfeld A, Burchette R. A combination of riboflavin, magnesium, and feverfew for migraine prophylaxis: a randomized trial. Headache. Oct 2004;44(9):885-890HIGHLIGHT

One breastfeeding mother who communicated with InfantRisk stated that her baby had no apparent symptoms after she began taking 400 mg per day, and that the baby's urine never turned the characteristic bright yellow color associated with riboflavin. No untoward effects have been reported via milk at this time.