Breastfeeding an older baby whilst experiencing Hyperemesis

The information on this sheet is based upon my professional experience as a pharmacist with a specialised interest in the safety of drugs in breastmilk, supported by evidence from expert sources. However, I cannot take responsibility for the prescription of medication which remains with the healthcare professionals involved. I am happy to discuss the evidence by email wendy@breastfeeding-and-medication.co.uk

Many more women are now breastfeeding their babies for longer and may still be feeding when they fall pregnant. For those who suffer from hyperemesis this is a tough time. Sadly, some healthcare professionals do not understand that there is benefit to a child from being breastfed to the age of two years and beyond (WHO) alongside a normal weaning diet. Being asked to abruptly wean your older child in order to take medication is not an easy option and is not necessary. Sometimes sitting quietly to breastfeed whilst you fight the feeling of nausea is essential.

In this fact sheet I have provided links to detailed information on the medication which can help prescribers to reach an evidence based decision on the safety of the drug to the breastfeeding baby which is not available in standard reference texts like the British National Formulary (BNF). The linked pdf files contain information sourced from LACTMED July 2020

Promethazine (Avomine) : When used for hyperemesis in mother may possibly cause some drowsiness in the nursling but anecdotally appears to happen rarely . See https://www.ncbi.nlm.nih.gov/books/NBK501081/

Promethazine has been associated with sudden infant death when administered **directly to infants** (Kahn and Blum 1979, 1982; Kahn et al. 1985; Stanton 1983; Pollard and Rylance 1994; Starke et al. 2005). Kahn prospectively studied 52 victims of sudden infant death syndrome (SIDS), 32 near miss and 175 controls. He found 23% of SIDS infants, 22% of the near-miss infants, but only 2% of controls were taking a phenothiazine medication. They

suggested that these drugs can cause central and obstructive apnoea as well as reduced arousal. The European Commission reported that it was likely that the risk of apnoea is associated with all sedative drugs.

Promethazine is widely used to reduce nausea particularly associated with travel sickness as well as symptomatic relief of urticaria and as an over-the-counter (OTC) hypnotic for short-term use. No data are available on transfer into breastmilk but it is believed that it does pass into breastmilk. It is licenced for use in children over 2 years."

1. Kahn A, Blum D, Possible role of phenothiazines in sudden infant death, The Lancet, 1979;ii:364–5.
2. Kahn A, Blum D, Phenothiazines and sudden infant death syndrome, Pediatrics, 1982;70:75–8.
3. Kahn A, Hasaerts D, Blum D, Phenothiazine-induced sleep apneas in normal infants, Pediatrics, 1985;75:844–7.
4. Pollard AJ, Rylance G, Inappropriate prescribing of promethazine in infants, Arch Dis Child, 1994;70:357.
5. Stanton AN, Sudden infant death syndrome and phenothiazines, Pediatrics, 1983;71:986–7.
6. Starke PR, Weaver J, Chowdhury BA, Boxed warning added to promethazine labeling for pediatric use, N Engl J Med, 2005;352:2653.

Cyclizine (Valoid) : May possibly cause some drowsiness in the nursling but anecdotally appears to happen rarely . See https://www.ncbi.nlm.nih.gov/books/NBK501749/

Cyclizine is an anti-emetic used to treat nausea and vomiting including motion sickness, post-operative nausea and vomiting, after radiotherapy, in drug-induced situations, as well as for nausea in pregnancy. There are no reports of levels entering breastmilk (BNF) or data on which to base conclusions. There is an unlicenced dose for children aged over 6 years.

Pyridoxine

Another name for Pyridoxine is vitamin B-6. The recommended daily allowance for non-pregnant women is 1.6 mg/day. Slightly more is needed during pregnancy and lactation and most prenatal vitamin supplements contain from 12-25 mg/day. Very high doses (600

mg/day) were reported to decrease production of breastmilk by inhibiting prolactin. [1, 2] However, this data has been refuted in two studies [3, 4]

It is not advisable to use in excess of 100 mg/day because of the risk of peripheral neuropathy. One study clearly indicates that pyridoxine readily transfers into breastmilk and that B-6 levels in milk correlate closely with maternal intake. [5]

1. Marcus RG. Suppression of lactation with high doses of pyridoxine. S Afr Med J 1975; 49(52):2155-2156.

2. Foukas MD. An antilactogenic effect of pyridoxine. J Obstet Gynaecol Br Commonw 1973; 80(8):718-720.

3. de Waal JM, Steyn AF, Harms JH, Slabber CF, Pannall PR. Failure of pyridoxine to suppress raised serum prolactin levels. S Afr Med J 1978; 53(8):293-294.

4. Canales ES, Soria J, Zarate A, Mason M, Molina M. The influence of pyridoxine on prolactin secretion and milk production in women. Br J Obstet Gynaecol 1976; 83(5):387-388.

5. Kang-Yoon SA, Kirksey A, Giacoia G, West K. Vitamin B-6 status of breast-fed neonates: influence of pyridoxine supplementation on mothers and neonates. Am J Clin Nutr 1992; 56(3):548-55

Prochlorperazine

Low levels of prochlorperazine are secreted into breastmilk and it can be used when breastfeeding. Side effects for the mother include drowsiness, restlessness and occasional extra pyramidal effects but babies seem to exhibit no adverse reactions. It is licensed to be given directly to babies weighing more than 10 kg. See https://www.ncbi.nlm.nih.gov/books/NBK501080/

Prochlorperazine is used to treat vertigo, labyrinthitis, migraine or drug-induced emesis if severe vomiting is a problem. Its oral bio-availability is low due to high first-pass metabolism but, like all phenothiazines, it has many metabolites, some active. It is not generally used in travel sickness prophylaxis. It is a member of the phenothiazine family to which children are particularly sensitive. Long-term use should be avoided in breastfeeding where possible, particularly with very young babies where there is a potential risk of apnoea. However, short-term acute use probably poses few risks as it is licenced for use in children over 10 kg.

Ondansetron

This is a powerful anti-sickness tablet used to treat people who have severe sickness when being treated with chemotherapy for cancer. Little research seems to exist (or have been published) on use during breastfeeding but anecdotally it is being used with no apparent adverse effects. See https://www.ncbi.nlm.nih.gov/books/NBK500798/

This drug is a 5-HT3 antagonist with antiemetic activity. It is used in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy. It is also used for the prevention and treatment of post-operative nausea and vomiting that have not responded to other antiemetic agents. Ondansetron may also be used for nausea in

pregnancy. It is licenced for use in children from two years of age. It is 60% orally bio-available and 70–75% plasma protein bound. The terminal half-life is three hours after oral doses. There are no studies on transfer into breastmilk although it has been found in animal studies (BNF).

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Domperidone

Domperidone (Motilium®) has widely been used to increase milk supply in the past. Concerns were raised by the MHRA in 2014 about use in patients with heart defects, there has been some reticence by doctors to prescribe it. There are no reports of problems in the amounts passing through breastmilk https://www.breastfeedingnetwork.org.uk/domperidone/.

See https://www.ncbi.nlm.nih.gov/books/NBK501371/

Domperidone acts at the chemoreceptor trigger zone. It is used for nausea and vomiting associated with chemotherapy. It stimulates gastric emptying. It causes fewer central effects such as sedation and dystonia (although there are still reports of these) because it does not cross the blood–brain barrier as metoclopramide does. Its dopamine antagonist activity stimulates prolactin release, which makes it useful as a galactagogue (see section on drugs to increase lactation, pages 285–288). Domperidone is metabolised by cytochrome P450 so care should be taken with potential interactions. It is more than 90% bound to plasma proteins and has a low bio-availability on an empty stomach (15%) when taking orally due to first-pass hepatic and intestinal metabolism. Mean serum levels of domperidone measured in babies through maternal use of 10 mg three times daily was only 1.2 ng per millilitre. The total amount of the drug that would be ingested by the infant (Da Silva et al. 2001) would be extremely small (about 180 ng per kilogramme daily, assuming a daily milk intake of 150 ml per kilogramme). Relative infant dose quoted as 0.01– 0.04% (Hale 2017 online access). Doses of more than 60 mg per day have been associated with sudden cardiac death, although reports have been predominantly in the elderly and in those receiving intravenous doses (FDA 2004; Joss et al. 1982; Giaccone et al. 1984; Weaving et al. 1984; Roussak et al. 1984; Osborne et al. 1985; manufacturer's information 2012). p.208 The BNF states that the amount secreted into breastmilk is probably too small to be harmful. Compatible with use during breastfeeding due to extensive plasma protein binding. See also information on use as a galactogogue.

1. Da Silva OP, Knoppert DC, Angelini MM, Forret PA, Effect of domperidone on milk production in mothers of premature newborns: a randomized, double-blind, placebo-controlled trial, CMAJ 2001;164(1):17–21.

2. FDA Talk Paper: FDA Warns Against Women Using Unapproved Drug, Domperidone, to Increase Milk Production, FDA, 2004, www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm173886.htm.

3. Giaccone G, Bertetto O, Calciati A, Two sudden deaths during prophylactic antiemetic treatment with high doses of domperidone and methylprednisolone, The Lancet, 1984;ii:1336–7.

4. Joss RA, Goldhirsch A, Brunner KW, Galeazzi RL, Sudden death in cancer patient on high-dose domperidone, The Lancet, 1982;i:1019.

5. Osborne RJ, Slevin ML, Hunter RW, Hamer J, Cardiotoxicity of intravenous domperidone, The Lancet, 1985;2:385.

6. Roussak JB, Carey P, Parry H, Cardiac arrest after treatment with intravenous domperidone, BMJ, 1984;289:1579.

7. Weaving A, Bezwoda WR, Derman DP, Seizures after antiemetic treatment with high dose domperidone: report of four cases, BMJ, 1984;288:1728.

Metoclopramide

Metoclopramide has also been used to increase milk supply. It is associated with an increased risk of depression as well as other side effects if used long term. There are no reports of problems in the babies from the amount passing through breastmilk. https://www.breastfeedingnetwork.org.uk/domperidone/ See https://www.ncbi.nlm.nih.gov/books/NBK501352/

Metoclopramide is a dopamine antagonist and can cause extra-pyramidal side effects, in particular acute dystonia. This adverse effect is most commonly seen in children and young adults, especially females, so it is not a drug of choice in lactating mothers who generally fall into this age group. It may also precipitate hypotension and depression. Other side effects reported include headache, diarrhoea, dry mouth and change in appetite (Ingram et al. 2011). It stimulates prolactin secretion and has been used as a galactogogue but has now been superseded by domperidone because of the latter does not cross the blood–brain barrier (Ingram et al. 2012). The bio-availability of oral metoclopramide is about 75% but varies widely between patients due to its hepatic first-pass metabolism. Concentrations higher than those in maternal plasma may be reached in breastmilk, particularly in the early puerperium, although these decrease with increased maturity. Metoclopramide has pro-kinetic and anti-emetic properties and acts directly on the gastrointestinal tract without altering acid secretion. It may be used in combination with analgesics to treat migraine symptoms. In the UK its use is restricted for children below 20 years of age unless they have severe intractable vomiting of known cause, due to vomiting of radiotherapy or cytotoxics. p.209 It is more frequently used in the US where domperidone is not available. Relative infant dose is quoted as 4.7–14.3% (Hale 2017 online access). The BNF states that only a small amount is present in breastmilk but it should be avoided. Compatible with use during breastfeeding but avoid if possible due to risk of extra-pyramidal effects and link with depression. Use domperidone as an alternative.

1. Ingram J, Taylor H, Churchill C, Pike A, Greenwood R, Metoclopramide or domperidone for increasing maternal breastmilk output: a randomised controlled trial, Arch Dis Child Fetal Neonatal Ed, 2012;97(4):F241–5.