

Breastfeeding and Medication



Breastfeeding and Hypertension (raised blood pressure)

Hypertension (raised blood pressure) is defined as sustained blood pressure above 140/90. Diet, obesity, heredity, race and stress all impact on blood pressure. High cholesterol, high salt content in the diet and saturated fat intake increase the long-term health risk.

Breastfeeding women may have had a previous event which presents a challenge to pregnancy and lactation e.g. stroke, heart attack, renal complications, SVT etc. In the past these might have produced barriers to childbirth but now seem to be so well controlled mothers are able to give birth and look after their own health.

There are several types of drugs used to treat hypertension some of which we have no data on with respect to use in breastfeeding mother, others should be avoided where possible.

For more details and references see *Breastfeeding and Medication* Jones W Routledge 2018

Treatment options for hypertension with evidence of compatibility with breastfeeding:

- Labetolol
- Enalapril
- Amlodipine or Felodipine

Diuretics

All diuretics should be avoided unless essential for health of the mother. By removing excess fluid from the body diuretics may reduce milk supply. This is more likely with furosemide than

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Bendroflumethiazide or bumetanide, but this category of drugs should be avoided during lactation to control blood pressure but only fluid retention where essential

Bendroflumethiazide – unknown effect from low dose 2.5mg daily

Indapamide

Furosemide – not likely to reduce supply due to intense diuresis

Bumetanide – low risk in established supply

Spirolactone; an aldosterone receptor antagonist used as a diuretic in various conditions associated with oedema, as well as in the treatment of hypertension. Its value is in sparing potassium loss. It is metabolised to canrenone which was found in the breastmilk of one mother taking 25mg four times a day by Phelps (1977). He suggested the amount absorbed by the baby would be 0.2% of the mother's daily dose. Spirolactone is 90% plasma protein bound and has a bioavailability of 90% (Martindale 2017) 70% (Hale 2017). The American Academy of Paediatrics considers it compatible with breastfeeding. The BNF states that although its metabolite is present in milk, the amount is probably too small to be harmful.

ACE inhibitors

This family of drugs are potentially teratogenic but can be used during lactation

Enalapril. This is the ACE with most evidence of safety during lactation. Redman et al. (1990) studied five women taking 20 mg enalapril, it was not detectable after 4 hours in four of the five women while the average peak level of enalaprilat (the metabolite of enalapril) was 1.7 µg per litre. No adverse events were reported in four babies exposed to maternal levels of 5–10 mg. Huttenen et al. (1989) studied three women after single doses of enalapril up to 10 mg. Enalaprilat levels were not detected and the concentration of ACE activity in milk was unchanged. Rush et al. (1989) deduced that the total amount of enalapril and its metabolite to which a baby would be exposed was 2 µg of enalaprilat while unlicensed use of enalapril from 1 month (BNFC) is 100 µg per kilogramme per day. Relative infant dose quoted as 0.2% (Hale 2017 online access).

BNF data recommend that the drug is avoided in the first few weeks after delivery due to the risk of profound neonatal hypotension; it can be used in older infants if essential but recommends that the infant's blood pressure is monitored.

Compatible with breastfeeding. Amount transferred into breastmilk is significantly less than can be given directly to a baby more than 1 month of age.

Captopril: Devlin and Fleiss' study (1981) of 12 women showed that the concentration of captopril in breastmilk was about 1% of maternal plasma, equivalent to 4.7 µg per litre in breastmilk of mothers taking 300 mg daily and no adverse effects were noted in the babies. Compatible with breastfeeding. Amount transferred into breastmilk is significantly less than can be given directly to a baby more than 1 month of age.

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Ramipril: No data are available on transfer into breastmilk. Ramipril has an active metabolite ramiprilat, which is approximately 56% plasma protein bound.

Lisinopril: There is no information on the transfer of lisinopril into breastmilk, although the oral bioavailability is only 29%. It is not significantly bound to plasma proteins.

Perindopril: There are no data available on the transfer of perindopril into breastmilk. It is metabolised to perindoprilat which is the active drug. Plasma protein binding is reported to be 10–20% and oral bioavailability is 65–75%.

Quinapril: rapidly converted to its active metabolite quinaprilat. Begg studied 6 women taking 20mg quinapril daily. Four hours after the dose no drug was recovered from milk. No Quinaprilat was detected at any time. The authors therefor suggested that quinapril is safe in breastfeeding.

Beta blockers

Beta blocker of choice in a mother during breastfeeding based on evidence of benefit and safety for the baby is **Metoprolol, propranolol** or **labetolol**

In many maternity units the use of beta blockers triggers the hypoglycaemia policy involving blood sugar testing. The amount of labetolol, propranolol and metoprolol passing into breastmilk is low and these drugs are less likely to lower blood sugars than atenolol (which has low plasma protein binding and passes more extensively into milk). The risk to the baby stems from the fact that babies born to mothers with pre-eclampsia may be born (or induced) early or may have experienced intra-uterine growth retardation. The efficacy of the baby's feeding and milk transfer should be assessed as well as blood sugars. If necessary, the mother may need to hand express and syringe/cup/spoon feed colostrum to her infant.

Atenolol; diffuses into breastmilk in concentrations similar to or higher than those in maternal blood demonstrated by m/p ratios of 1.5–6.8. Despite this, the authors calculated the infant would only be exposed to 0.13 mg per day following a maternal dose of 50 mg per day (Liedholm 1983). Cyanosis and bradycardia in a 5-day-old term infant associated with maternal intake of 50 mg atenolol twice daily in breastmilk has been reported. The infant recovered when breastfeeding was interrupted (Schimmel et al. 1989). Other authors have reported no adverse effects in 15 infants aged 3 days to 2 weeks exposed to 50–100 mg atenolol (Bhamra et al. 1983; White et al. 1984; Kulas et al. 1984). It is not licensed for use in children under the age of 12 years. Relative infant dose quoted as 6.6% (Hale 2017 online access).

Atenolol has low plasma protein binding and therefore passes more freely into breastmilk. Caution is particularly advised in neonates because of the renal excretion of this drug.

Labetolol; Michael's study of 25 patients (1979) taking between 330 and 800 mg labetolol daily showed a m/p ratio less than 1, although one patient taking 1200 mg daily produced milk samples where the concentration in milk exceeded that in maternal plasma. Lunell et al.'s study (1985) produced similar results. However, no baby in these studies exhibited any adverse drug reactions. Mirpuri et al. (2008) reported that a 26-week premature baby exhibited bradycardia and

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premature beats when tube fed expressed breastmilk from its mother who was receiving 300 mg labetalol twice daily. Its condition returned to normal when formula milk was substituted. McGuinness identified that a mother's intake of labetalol had triggered symptoms of Raynaud's syndrome due to restriction of blood flow to the extremities. This should be borne in mind with any mum reporting painful breastfeeding when on beta blockers.

Metoprolol; Studies have shown that metoprolol also produces m/p ratios in excess of 1 (Sandström and Regårdh 1980; Liedholm et al. 1981). However, the absolute level of drug transferring to the baby is small and studies have failed to detect metoprolol at significant levels in infant plasma (Kuklas et al. 1984). Although the drug is well-absorbed, it undergoes extensive first-pass metabolism. No adverse events have been reported in babies exposed to metoprolol via breastmilk (Ho et al. 1999; Lindeberg et al. 1984)

Bisoprolol: Only one study of the use of bisoprolol appears in the literature. Khurana studied a mother who was initiated on it 6 days after birth for a cardiac condition. She expressed samples of milk on day 11 and 18 after birth. Drug levels in milk were undetectable but the baby did not receive any breastmilk, so data is incomplete. See <https://breastfeeding-and-medication.co.uk/fact-sheet/bisoprolol-and-breastfeeding>

Propranolol: 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.

In adults it may be used to lower blood pressure, to relieve symptoms of hyperthyroidism, to prevent migraines or to prevent panic attacks. See <https://breastfeeding-and-medication.co.uk/thoughts/propranolol-and-breastfeeding>

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.

Angiotensin II receptor antagonists

This group of drugs is given to patients who are unable to tolerate ACE inhibitors to treat hypertension and heart failure. As with ACE inhibitors, this group of drugs is contra-indicated in pregnancy. There are few data on transfer into breastmilk and the use of ACE inhibitors is recommended. This class of drug might be expected to produce low levels in breastmilk because of the high protein binding and low bioavailability but no data exist to support this assumption.

Candesartan: no studies in breastfeeding

Irbesartan; no studies in breastfeeding

Losartan; no studies in breastfeeding

Valsartan; no studies in breastfeeding

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Calcium channel blockers

Nifedipine: relaxes vascular smooth muscle and dilates coronary and peripheral arteries. It has activity in reducing blood pressure and in the treatment of Reynaud's syndrome. Nifedipine is almost completely absorbed from the GI tract but undergoes extensive first-pass metabolism. Side effects for the mother include flushing and headache, which may limit its usefulness. It is present in breastmilk but in levels too small to be harmful and there have been no reports of adverse effects in babies. See <https://breastfeeding-and-medication.co.uk/fact-sheet/february-is-raynaud-s-awareness-month-www-sruk-co-uk>

Amlodipine: A study of 31 postpartum women (Naito 2015) with pregnancy-induced hypertension received amlodipine 5 mg daily by mouth, with the dosage increased as needed to maintain blood pressure of 140/90 mm Hg or less (mean dosage for the group was 6 mg daily. Maternal blood and breastmilk samples were obtained after at least 6 days of therapy. The median milk concentration was 11.5 µg/L and no infant showed any adverse effects.

Felodipine: Small amounts of felodipine may get into breast milk, but it's not known if this is harmful to the baby (BNF)

Diltiazem: Diltiazem is used for its antiarrhythmic, anti-anginal and antihypertensive properties but rarely in women of childbearing age unless there are very specific indications from the medical history. It is rarely used simply to treat hypertension.

Alpha blockers

Avoid unless essential to mother's health. This class of drugs are generally only used in addition to other drugs with poorly controlled blood pressure. They are not normally used as first line or monotherapy

Doxazosin: Jensen published a paper on one mother breastfeeding a 6-month-old. She received 4 mg daily for 2 days. The maximum milk concentrations were 2.9 and 4.2 µg/L. This drug should only be used in extreme circumstances and with close monitoring of the infant, for drowsiness, poor feeding, low blood pressure.

Terazosin: no studies in breastfeeding

NICE Guidance NG 133 (June 2019)

www.nice.org.uk/guidance/ng133/chapter/Recommendations#antihypertensive-treatment-during-the-postnatal-period-including-during-breastfeeding

1.9 Antihypertensive treatment during the postnatal period, including during breastfeeding

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1.9.1 Advise women with hypertension who wish to breastfeed that their treatment can be adapted to accommodate breastfeeding, and that the need to take antihypertensive medication does not prevent them from breastfeeding. [2019]

1.9.2 Explain to women with hypertension who wish to breastfeed that:

- antihypertensive medicines can pass into breast milk
- most antihypertensive medicines taken while breastfeeding only lead to very low levels in breast milk, so the amounts taken in by babies are very small and would be unlikely to have any clinical effect
- most medicines are not tested in pregnant or breastfeeding women, so disclaimers in the manufacturer's information are not because of any specific safety concerns or evidence of harm.
- Make decisions on treatment together with the woman, based on her preferences. [2019]

1.9.3 As antihypertensive agents have the potential to transfer into breast milk:

- consider monitoring the blood pressure of babies, especially those born preterm, who have symptoms of low blood pressure for the first few weeks
- when discharged home, advise women to monitor their babies for drowsiness, lethargy, pallor, cold peripheries or poor feeding. [2019]

1.9.4 Offer **enalapril** [5] to treat hypertension in women during the postnatal period, with appropriate monitoring of maternal renal function and maternal serum potassium. [2019]

1.9.5 For women of black African or Caribbean family origin with hypertension during the postnatal period, consider antihypertensive treatment with: **nifedipine** [3] or amlodipine if the woman has previously used this to successfully control her blood pressure. [2019]

1.9.6 For women with hypertension in the postnatal period, if blood pressure is not controlled with a single medicine, consider a combination of **nifedipine** [3] (or **amlodipine**) and **enalapril** [5]. If this combination is not tolerated or is ineffective, consider either: adding atenolol or labetalol to the combination treatment or swapping 1 of the medicines already being used for atenolol or **labetalol**. [2019]

1.9.7 When treating women with antihypertensive medication during the postnatal period, use medicines that are taken once daily when possible. [2019]

1.9.8 Where possible, avoid using diuretics or angiotensin receptor blockers [5] to treat hypertension in women in the postnatal period who are breastfeeding or expressing milk. [2010, amended 2019]

1.9.9 Treat women with hypertension in the postnatal period who are not breastfeeding and who are not planning to breastfeed in line with the NICE guideline on hypertension in adults. [2019]

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