Breastfeeding and Medication

Raised cholesterol and breastfeeding

1. If a breastfeeding mother has raised cholesterol (not familial) encourage diet and lifestyle changes and monitor at intervals
2. If the breastfeeding mother has familial hypercholesteraemia it is likely that the baby has been born with high cholesterol and it is assumed that even reducing the level in maternal milk will still exceed that in standard infant formula together with added protective cardio-vascular properties of breastmilk (Holmsen)
3. Standard Infant formula contains no cholesterol (Lawrence) but also lacks the cardio protective properties of breastmilk (Tschiderer)
4. Breastfeeding has many factors to protect the mother and baby from future cardiovascular disease

NB This data has been taken from expert sources but there is currently an absence of data and research studies on the effect of statins on breastfed babies.

This document provides an overview of research and is not intended as a recommendation. Treatment of raised cholesterol in breastfeeding should be made after informed discussion between parents and their professionals whilst protecting breastfeeding.

Cholesterol

Cholesterol is necessary for the development of brain tissue, myelination of nerves, and is the basis for many enzymes. Breastfed infants have higher plasma cholesterol levels than those fed standard artificial formulas as these products contain no cholesterol at all. The higher cholesterol levels in breastmilk protects babies against the consequences of hypercholesterolemia in adult life (Lawrence 2016).

Breastfeeding and Cardio-vascular disease (CVD)

Research shows that being breastfed leads to better outcomes with respect to coronary artery disease in later life (UNICEF). Cessation of breastfeeding may have consequences for the mother and baby and a recommendation to stop should not be undertaken without examining the literature for benefit and risk to the baby of the medication.

Nguyen (2019) reported that ever breastfeeding was associated with lower risk of CVD hospitalization and mortality compared with never breastfeeding, and breastfeeding ≤12 months/child was significantly associated with lower risk of CVD hospitalization. WHO (2021) and UNICEF recommend: early initiation of breastfeeding within 1 hour of birth; exclusive breastfeeding for the first 6 months of life; and. introduction of nutritionally adequate and safe complementary (solid) foods at 6 months together with continued breastfeeding up to 2 years of age or beyond.

Schwartz (2009) studied 139,681 women who had breastfed for more than 12 months across their lactations and showed a 10-15% reduction in hypertension, diabetes, hyperlipidaemia, and cardiovascular disease than those who had not breastfed.

Hui (2019) looked at an association between breastfeeding in the first three months of life with lipid profile and adiposity at around 17.5 years in a population in Hong Kong. The team found that exclusive breastfeeding, (but not mixed feeding) at 0 to 3 months, compared with formula feeding was associated with lower total cholesterol and low-density lipoprotein (LDL) cholesterol but not with high-density lipoprotein cholesterol (HDL). LDL is sometimes referred to as “bad” cholesterol because it collects in the walls of blood vessels. HDL is seen as “good” cholesterol, because it absorbs cholesterol and carries it back to the liver. The liver then flushes it from the body. High levels of HDL cholesterol can lower the risk for heart disease and stroke

Singhal (2004) studied 926 preterm babies and determines evidence for the long-term benefits of breastmilk feeding on the risk of atherosclerosis.

Owen (2002) conducted a cross-sectional study of 1,532 adolescents in 10 British towns and determined that breastfeeding is associated with increased mean serum total cholesterol and low-density lipoprotein cholesterol in infancy but with lower levels in adult life providing long-term benefits for cardiovascular health.

These studies should not be taken as the advantages of breastfeeding but rather the risk of deleterious health outcomes for babies exclusively fed with infant formula (Renfrew 2012).

Raised cholesterol

Cholesterol is a fatty substance which is made in the liver. It is also found in foods. The Mediterranean diet is generally recommended to decrease cholesterol obtained through consumption of foods.

Cholesterol levels may be found to be raised at routine monitoring of a woman. Diet and lifestyle issues should be addressed before considering the initiation of cholesterol lowering medication to avoid unnecessary medication. Raised cholesterol is mainly caused by:

- eating fatty food,
- not exercising enough,

- being overweight,
- smoking and drinking alcohol

It is recommended that those with high cholesterol eat more:

- oily fish, like mackerel and salmon
- brown rice, bread, and pasta
- nuts and seeds
- fruits and vegetables

and eat less:

- meat pies, sausages, and fatty meat
- butter, lard, and ghee
- cream and hard cheese, like cheddar
- cakes and biscuits
- food that contains coconut oil or palm oil (NHS)

They should aim to exercise more (150 minutes (2.5 hours) a week. This might include walking until the heart starts beating faster (pushing a pram round a local park or carrying baby in a sling whilst you walk possibly with a group of other mothers), swimming or cycling. However, as a new mother it is acknowledged this can be difficult. Smoking cessation can improve the levels too (for more information https://www.breastfeedingnetwork.org.uk/smoking/)

When undertaking a review of cardiovascular risk, a calculator is used to determine the likelihood of cardiovascular disease occurring in the next 10 years. Risk calculators should not be used for people already identified as being at high risk, such as those with diabetes or familial hypercholesterolaemia (see below). The risk is calculated taking into account many other factors including height, weight, age, smoking status, alcohol consumption, blood pressure, family history, chronic medical conditions, cholesterol level etc (https://qrisk.org/three/). This permits discussion with a health professional on possible lifestyle changes or initiation of medication. (See https://www.nhs.uk/conditions/nhs-health-check/your-nhs-health-check-results-and-action-plan/ for further information.

Cholestyramine may be considered as first line if medication continues to be necessary due to its low oral bioavailability (0%) so that so it cannot transfer to breastmilk, nor to the infant's plasma via breastmilk.

Familial hypercholesterolaemia

Women with familial hypercholesterolaemia are currently advised to discontinue breastfeeding prior to beginning statin therapy after pregnancy. This is because we have little data from studies on the compatibility of statins with breastfeeding. There has always been a concern that we do not know what effect potentially lowering cholesterol in the breastfed baby has.

Familial hypercholesterolaemia (FH for short) is an inherited condition which can lead to extremely high cholesterol levels. It's passed down through families in the genes. Without treatment, FH can lead to heart disease at a very young age. But once it's been diagnosed, it can be treated with medicines and a healthy lifestyle (HEARTUK). As a result of their FH, the incidence of fatal or non-fatal myocardial infarction without treatment is about 50% by the age of 50 years in men and about 30% by the age of 60 years in women. (NHSEI)

The current recommendation is that statins should be discontinued three months before attempting to conceive, during pregnancy and lactation (Shala-Haskaj 2020). During this time the cholesterol level may become significantly raised even if the woman is eating a healthy, balanced diet and keeping active (NHS).

It is reported by Holmsen et al that the FELIC study showed that hypercholesterolaemia in a woman during pregnancy increased the risk of atherosclerosis in the child (Napoli 1999). They state that animal studies have shown that statin treatment in pregnant and lactating mice has a cardioprotective effect not only in the pregnant mouse but also in the offspring (Elahi 2008, 213)

Cholesterol levels are normally increased by 40% during pregnancy and lactation in healthy women (Lawrence 2016). The cholesterol in breast milk is synthesized in the mammary gland and its concentration in breast milk ranges from 27 mg/dL in colostrum to 16 mg/dL in mature breast milk (>30 days post-partum) (Lawrence 2016). Cholesterol is used in brain tissue development, myelination of nerves and as a base for many enzymes. The role of higher cholesterol in colostrum is unclear (Lawrence 2016) The amount of cholesterol in breast milk that would remain after the hypothetical reduction in cholesterol produced by statins taken by the mother, would still be much higher than that provided by standard artificial formulas (Holmsen 2017). Standard artificial formula does not vary in composition at all and lacks cholesterol itself although it contains other lipids. Lawrence comments that interest in lipids in human milk has increased after reports of advance development at 12 months (Lucas 1992), 8-10 years (Lucas 1994) and even at 18 years (Horwood 1998).

Use of statins during breastfeeding

Although there are no current studies on the use of statins in breastfeeding (Hale) in one study, breast milk from a woman with familial hypercholesterolaemia gene contained three times as much cholesterol as that of healthy control women (Tsang 1978). Holmsen et al hypothesise that if cholesterol levels are normalised by statin use, it is reasonable to assume that the lipid content of breast milk will also decrease to more normal levels but will still exceed those of standard infant formula which contains no cholesterol.

Botha et al ((Botha 2018) retrospectively reviewed 39 pregnancies from a cohort of 20 genotypically confirmed female patients with Homozygous familial hypercholesterolaemia (HoFH). Twenty-five pregnancies were exposed to lipid-lowering therapy, of which 18 were exposed to statin therapy, just prior to or during the pregnancy. The infants of HoFH patients are obligate HeFH and likely already affected by atherosclerotic lesions at birth. Twelve of the 20 patients chose to breastfeed (21 infants). “Most patients breastfed for three to six months”; three patients opted to breastfeed for nine months. However, only 6 patients (11 infants) continued breastfeeding despite restarting statin therapy after delivery, while three patients (four infants) chose not to breastfeed while on statin therapy. Botha concluded that for many females with HoFH, despite the high cardiovascular risk, pregnancy is not uncommon and that lipid lowering therapy, particularly statin therapy during pregnancy, appears to be safe for both mother and foetus. Infants had no developmental or school learning problems. Botha et al recommended “patients should discontinue all lipid lowering therapy a month prior to planned conception and reinstate lipid lowering therapy, statin plus ezetimibe, during the second trimester. This limits the possible teratogenic effect of statins during the first

trimester while providing the mother with optimal care during a time of increased cholesterol production. Women's perceptions and preferences regarding statin use in pregnancy should also be considered when giving advice in these situations. It is interesting that no recommendation is made on breastfeeding despite the health outcomes associated with infant feeding (UNICEF).

Pan (1988) studied 11 lactating women who were not breastfeeding but taking 20 mg of pravastatin orally twice daily for 2.5 days. Serum and milk samples were taken and analysed for pravastatin and its active metabolite after the fifth dose. Peak milk levels averaged 3.9 mcg/L for pravastatin and 2.1 mcg/L for its metabolite. He suggested that negligible levels were excreted into breast milk, but that benefits, and risks should be carefully considered. Using the peak levels above, a fully breastfed infant would receive a maximum of 900 ng/kg daily with this dosage or about 0.13% of the maternal weight-adjusted dosage (LactMed).

Lwin (2018) studied a mother with a 13-month child still being breastfed who was commenced on Rosuvastatin 20mg at bedtime. The peak milk concentration was 58.6 mcg/L occurred 17 hours after the dose. The authors calculated a daily infant dosage of 4.63 mcg/kg, which corresponded to a weight-adjusted 1.5% of the maternal dose. Breastfeeding was discontinued so no analysis of the baby's plasma levels, or outcome were available.

Schutte (2018) published a case report of a woman with familial hypercholesterolemia who was started on rosuvastatin 40 mg daily on day 33 postpartum. Levels of the drug were measured up to day 80. All concentrations of the drug were in the range of 21 to 22 mcg/L. Despite the fact that samples were provided for 80 days there is no mention of the effect on the baby.

Pharmacokinetics of lipid lowering drugs

	Oral bioavailability %	**Plasma protein binding %**	**Theoretical dose**	**Relative infant dose**
Simvastatin	<5%	>95		
Atorvastatin	12 to 30	>98		
Pravastatin	17	50	0.001mg/Kg/d	0.15%
Rosuvastatin	20	88	0.003 mg/Kg/d	0.5 - 1 %
Ezetimibe	35 to 60	92-100		

The pharmacokinetic data (high percentage of protein binding, extensive first pass metabolism and low oral bioavailability) make it highly unlikely that significant quantities of statins will pass into breast milk (Elactancia). Data taken from Lennernäs 2003, NCBI StatPerls, Krishna 2009, Elactancia, Hale)

However, lack of passage into breastmilk has not been proven in research. Standard Infant formula milk contains no cholesterol but does contain other lipids.

Statins are grouped into low, medium, and high intensity according to the percentage reduction in low-density lipoprotein cholesterol (NICE CG 181 2016):

- a 20% to 30% reduction is low intensity e.g., pravastatin
- a 31% to 40% reduction is medium intensity
- a reduction of more than 40% is high intensity e.g., simvastatin 80mg, atorvastatin >20mg, rosuvastatin > 10mg.

MHRA (2014): there is an increased risk of myopathy associated with high dose (80 mg) simvastatin.

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