The Management of Dyslipidaemia in Pregnancy

Introduction

There is a physiological increase in plasma concentrations of cholesterol and triglycerides during normal pregnancy (Hadden et al 2009, Vrijkotte et al 2012), as there is an increased delivery of nutrients to the feto-placental unit. Lipids are required for the rapid growth of the baby and placenta (Herrera et al 2002), and a healthy pregnancy.

The plasma lipid concentrations in healthy pregnant women and people do not reflect their usual lipid profile outside of pregnancy, and therefore plasma lipid concentrations are not routinely assessed. This temporary increase confers no additional risk to the pregnant individual or baby. In normal pregnancies, blood lipid levels remain elevated for at least one month following the birth of the baby, although triglyceride levels can fall more rapidly in individuals who breastfeed. Checking a lipid profile should be delayed for at least 2-3 months following delivery.

However individuals with high serum cholesterol levels before pregnancy, such as those with familial hypercholesterolaemia, may show a more dramatic deterioration of their lipid profile during pregnancy, compared to those with a normal lipid profile (Hadden et al 2009). Individuals with very high blood levels of triglycerides before pregnancy may develop severe hypertriglyceridaemia. These high levels of plasma triglycerides may be associated with an increased risk of acute pancreatitis. Whilst this is uncommon, it is a very serious complication resulting in severe central abdominal pain and may also be associated with skin manifestations, eruptive xanthoma, a maculopapular rash, that can be widely distributed and intensely itchy. In addition, there is an increased risk of adverse outcome in pregnant women and people with hypertriglyceridaemia including pre-eclampsia and fetal growth restriction (Vrijkotte et al 2012).

Pregnancy and familial hypercholesterolaemia

An otherwise healthy woman with familial hypercholesterolaemia (FH) should not be discouraged from becoming pregnant, or breastfeeding their baby. However all women with FH who are of childbearing age should be aware of the need for pre-pregnancy counselling prior to embarking on a pregnancy, and what they should do if they have an unplanned pregnancy; 45% pregnancies and 30% of births are unplanned in the UK. This information should be revisited at least annually (NICE CG 71).

Women or people with FH, contemplating becoming pregnant should be referred to/discussed with the lipid clinic for pre-pregnancy counselling. All women of childbearing age should be aware of drugs to stop in the event of an unplanned pregnancy.

Pre-pregnancy counselling

- Medication review and planning
    - Drugs to stop prior to conception– includes statins and ezetimibe
    - Planned drug regime during pregnancy (including the use of apheresis if indicated) – no lipid lowering therapy (if patient is particularly high risk e.g. secondary prevention and FH consider lipid clinic advice in regards to apheresis and bile acid sequestrants)
    - Additional vitamin supplementation (when bile sequestrants are used)
    - Breastfeeding / chest feeding
- An assessment of the risk of coronary artery disease
- An overall risk assessment of coming off standard lipid lowering treatment whilst attempting to conceive and completing a pregnancy (including the duration of breastfeeding)

Pregnant women with FH should be under the shared care of specialists: lipidologist (lipid clinic), cardiologist and maternal medicine obstetrician / obstetric physician and are best managed in a combined clinic with close links to the lipid clinic. **All individuals should have a baseline ECG.**

Pregnancy and lipid-lowering medication

For most women, lipid-lowering drug therapy should be stopped altogether during pregnancy

Many cholesterol-lowering medicines, such as **statins and ezetimibe** can cross the placenta and may potentially harm the unborn baby. Whilst this risk is small (Ofori et al 2007, Karalis et al 2016), these medications are contra-indicated during pregnancy and breastfeeding (Regitz-Zagrosek et al 2018).
PCSK-9 inhibitors (alirocumab and evolocumab) are not licenced for use during pregnancy, nor breastfeeding, and again should also be stopped before attempting to conceive.
Fibrates and omega-3 fatty acids may be considered for patients with hypertriglyceridaemia (see below).

Women are advised to stop their lipid-lowering medication for at least 1 month (Goldberg et al 2011), and preferably 3 months (Wierzbeicki et al 2008) before attempting to conceive.

Individuals who have severe forms of FH may require apheresis to reduce their plasma cholesterol levels during pregnancy.

Bile acid sequestrants are not absorbed systemically, do not cross the placenta and so are the only cholesterol-lowering medication that can be safely prescribed during pregnancy, and whilst breastfeeding / chest feeding (Balla et al 2020). They should only be prescribed under specialist supervision. Bile acid sequestrants can reduce the absorption of fat-soluble vitamins. **Vitamin D (800-1000 units once a day) should be prescribed to prevent deficiency. Higher doses may on occasion be needed (secondary care recommendation only on basis of low measured levels).**

Some women may accidentally conceive while still taking their statin or other medicines. Although the risk to the baby is believed to be small, women are strongly advised to stop their medication as soon as they are aware they are pregnant and contact their prescribing GP, specialist or other healthcare professional without delay.

Aspirin should be continued (75 - 150mg od) if previously prescribed.

Breastfeeding / Chest feeding

For most postnatal women and people, lipid-lowering drug therapy is stopped during breastfeeding/chest feeding. Treatment with resins can be continued (NICE CG 71)

Breastfeeding has health benefits both to the individual and baby. There are no clinical trials examining the safety of statins in breastfeeding and currently women are advised to avoid statins if breastfeeding. Dependent on the lipophilicity of the statin, milk: serum concentration ratios are reported to be from 0.5-2 (Balla et al 2020). The hydrophilic statins Rosuvastatin and Pravastatin may be associated with lower transfer into breast milk (Lecapetier E 2012, Lwin EMP 2018). Although standard advice is to avoid statins in breastfeeding, case-by-case advice for women with FH is recommended.

Bile acid sequestrants
Resins can be continued during breastfeeding (NICE CG 71).

Pregnancy and hypertriglyceridaemia
With respect to the treatment of severe hypertriglyceridaemia during pregnancy, whilst **omega-3 fatty acids** can be safely used (Barrett et al 2014), there are very limited data for other treatment modalities (Stone et al 2013). In very severe hypertriglyceridaemia (Familial Chylomicronaemia Syndrome), diabetes mellitus is often a co-morbidity, and improving diabetic control is a critical first step**. Fenofibrate** and a very low-fat diet combined with omega 3 fatty acids has been suggested for use in the second trimester (Jacobson et al 2015). Apheresis has also been successfully used in this condition (Schwartz et al 2016) although it is not easily available locally and may need referral to a specialist centre.

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