Molecular action of new therapies for Obstetric Cholestasis in the placenta

Lay Summary

This project will study how specific drugs can protect the unborn baby from complications of obstetric cholestasis (OC). This disease affects about 1 in 200 pregnancies in the UK per year and can cause preterm birth, lack of oxygen and stillbirth. In preliminary experiments we have shown that raised bile acid levels seen in OC are associated with damage to the placenta and that bile acids may cause reduced oxygen delivery to the baby via the placenta. The drug ursodeoxycholic acid (UDCA) reverses most of these abnormalities. This project will discover how this happens. We are also studying three other drugs, heparin, rifampicin and nor-UDCA, because some women do not respond to UDCA so we need safe alternative therapies to protect the unborn baby.

Our preliminary results show heparin protects the placenta from bile acid-induced damage. If this is confirmed we can evaluate it as a treatment to protect the unborn baby in OC in the near future as it is known to be a safe drug in pregnancy. Rifampicin is occasionally used with some benefit as a second-line treatment for OC and needs to be studied further. Nor-UDCA is more effective than UDCA at reversing cholestasis in animal models and is now being used in clinical trials in non-pregnant patients. If it is more effective it can be considered as a treatment in pregnancy. However it will be important to ensure it is safe for the unborn baby and to evaluate whether it can cross the placenta.

The aim of all the experiments proposed in this project is to establish whether new drugs improve the symptoms of OC and whether they are likely to protect against the complications that can cause babies to be very unwell and in some cases cause stillbirth.