StAmP

A Proof of Principle, Double-Blind, Randomised, Placebo-Controlled, Multi Centre Trial of pravaStatin to Ameliorate Early Onset Pre-eclampsia.

Background

Pre-eclampsia is a serious condition of pregnancy, where the mother develops high blood pressure and high levels of protein in the urine (proteinuria). There are no effective drug treatments for pregnant women to reverse pre-eclampsia. Drugs can be given to help reduce blood pressure and prevent seizures. Doctors monitor the mother's blood pressure, blood tests and the baby's wellbeing and then recommend birth of the baby if you or your baby's health is threatened. However, if pre-eclampsia develops between 24-32 weeks and the baby is born prematurely, he or she will almost always need special care on a neonatal unit.

Recent scientific research has identified that changes in some specific blood chemicals (biomarkers) can lead to pre-eclampsia. Initial studies on samples of placenta and blood vessels, as well as animal experiments suggest that statins can reduce the level of these blood chemicals, and perhaps reduce or eliminate the effects and risks of pre-eclampsia. The StAmP study was the first step in determining if these same beneficial effects are seen in pregnant women.

What was the StAmP Trial?

The aim of the StAmP trial was to establish whether pravastatin will lead to a significant reduction of specific biomarkers implicated in the development and progression of pre-eclampsia in women with early-onset pre-eclampsia.The following questions were addressed:

1. Does pravastatin cause a greater inhibition of circulating adverse biomarkers in women with early-onset pre-eclampsia compared with placebo?

2. Are there any adverse or beneficial effects to the mother or the baby following gestational exposure to pravastatin?

3. If pravastatin appears to safely inhibit or reduce these biomarkers, how best can a substantive trial be undertaken to develop guidance for routine use of statins to prevent or ameliorate pre-eclampsia?

To be eligible for the StAmP Trial, the women must have been diagnosed with pre-eclampsia (according to the ISSHP criteria), have been over 16 years of age and between 24+0 weeks' and 31+6 weeks' pregnant with a single baby. Furthermore, the attending clinician must have considered that the pregnancy was capable of safely continuing for 48 hours or more. Women who were using, or couldn't use, statins, or who did not provide consent, were excluded.

Participants took either 40mg pravastatin or an identical placebo, once per day until their baby was born. Doctors could prescribe any drugs to manage the high blood pressure or other symptoms. The primary outcome measure was the decrease in the biomarkers, which would indicate the progression of pre-eclampsia was being slowed down. The aim was to recruit 64 women.

What impact will this study have?

The rationale for using statins to ameliorate pre-eclampsia is based on laboratory work that identified that statins suppress biomarkers that prevent blood vessel development in the placenta and are known to be elevated in pre-eclampsia. For this reason, StAmP is measuring maternal blood levels of these biomarkers. This trial is too small to look at changes in clinical outcome, such as differences in the length of pregnancy after randomisation, but this would be the next step.

The safety of statins in pregnancy is uncertain. Limited evidence on 550 women who inadvertently took statins in the first 12 weeks of pregnancy shows no higher level of fetal abnormality than in the general population. Early severe pre-eclampsia is a life-threatening condition for mother and offspring and although StAmP minimised the risks to the baby by only studying women after 24 weeks of pregnancy, away from the critical period when the baby's skeleton and organs develop and choosing pravastatin of all the statins, we feel the potential harm to the fetus of early severe pre-eclampsia is balanced by the benefits of potentially identifying an effective drug.

If our hypothesis is correct, and pravastatin is shown to safely reduce these specific biomarkers in women with pre-eclampsia, this trial will have informed a potential future study that could be designed to recruit enough women to show whether pravastatin can be used to prevent pre-eclampsia. Linked studies will measure pravastatin in the cord blood to identify whether this drug crosses the placenta in significant amounts.

EudraCT Number: 2009-012968-13

ISRCTN Number: 23410175

Funder: Medical Research Council

Grant Holder: Professor Asif Ahmed, Aston University

Sponsor: University College London

Chief Clinical Investigator: Dr David Williams

Trial Coordinating Centre: Birmingham Clinical Trials Unit, University of Birmingham