

SYNOPSIS OF THE TRIAL

Aims of the Trial: To assess in the fetus where one intrauterine fetal transfusion has been performed for anaemia due to red cell alloimmunisation, whether fetal middle cerebral artery (MCA) peak systolic velocity (PSV) can be safely used to determine the timing of second and subsequent fetal blood transfusions, without increasing the risk of adverse fetal and neonatal health outcomes.

Primary Trial Hypothesis: is that the use of fetal MCA PSV measurements in the fetus who has undergone one blood transfusion for fetal anaemia secondary to red cell alloimmunisation will reduce the number of invasive procedures required for fetal blood transfusion without increasing the risk of adverse outcomes for the infant related to alloimmunisation.

Background: Red cell alloimmunisation is estimated to affect 0.1 to 0.6% of all live births. Treatment of the resultant fetal anaemia with intrauterine fetal blood transfusion has been associated with survival rates in excess of 90%. However, intrauterine fetal blood sampling and transfusion is an invasive procedure, with recognised complications, which may result in the need for early birth, and rarely mortality. More recently, reports have emerged utilising Doppler ultrasound to measure the fetal middle cerebral artery (MCA) peak systolic velocity (PSV) to determine the presence of fetal anaemia.

Systematic review of the literature has indicated a lack of information from randomised controlled trials comparing this technique with standard measures based on prediction in the rate of fall in the fetal haemoglobin. Cohort studies reporting the use of fetal MCA PSV in this setting yield conflicting results. Clearly, high quality trials are a priority to assess the role of MCA-PSV in determining the timing of second and subsequent fetal intrauterine blood transfusions, and the impact this has on fetal and neonatal morbidity, when compared with estimating the fall in haemoglobin using a standard nomogram.

Research Plan: Study Design: Multicentred randomised, controlled trial.

Inclusion Criteria: Women with fetal anaemia secondary to red cell alloimmunisation (due to any antibody alone or in combination) as indicated by the need to have performed a single intrauterine fetal blood transfusion.

Treatment Schedules: Women randomised to Timing of Transfusion by MCA-PSV will have weekly ultrasound determination of the fetal MCA PSV, with a serial upward trend with values greater than 1.5 MoM being considered indicative of the need for subsequent fetal transfusion.

Women randomised to Timing of Transfusion by Predicting the Fall in Fetal Haemoglobin will have subsequent fetal blood transfusions timed according to accepted criteria, based on an estimated fall in haematocrit of 1% per day.

Outcomes: The primary study outcome is a composite of **adverse outcomes for the infant related to alloimmunisation**. The secondary study outcomes include the number of procedures & related complications; adverse outcomes for the woman and her infant; maternal quality of life and well-being; and costs of health care.

Sample Size: For women eligible for this trial, the best estimate of the incidence of the primary outcome is 46.75%. To reduce this by 30% to 32.73% (alpha 0.05; power 90%), we will need to recruit 564 women to this trial.