

The Thrombophilia in Pregnancy Prophylaxis Study (TIPPS)

Objective:

We seek to determine the safety and efficacy of Low Molecular Weight Heparin (LMWH) in preventing pregnancy complications (venous thromboembolic events (VTE), pre-eclampsia, intrauterine growth restriction (IUGR), abruptio placentae, miscarriage and stillbirth) in thrombophilic women.

Background:

Thrombophilias are common disorders (usually detected by laboratory testing) that result in a predisposition to develop venous thromboembolic events (deep vein thrombosis and pulmonary embolism). Recent evidence indicates that pregnant women with thrombophilia are not only at increased risk of VTE, but also increased risk of pre-eclampsia, IUGR, abruptio placentae, miscarriage and stillbirth. Placental vascular thrombosis and abnormal placentation have been postulated to cause pre-eclampsia, IUGR, abruptio placentae, miscarriage and stillbirth. Therefore it is biologically plausible that anti-thrombotic prophylaxis of thrombophilic women will reduce the incidence of these complications of pregnancy by preventing placental vessels thrombosis and/or abnormal placentation. In support of this, small non-randomised studies suggest LMWHs are of benefit in preventing these pregnancy complications. However, prolonged LMWH use throughout pregnancy would be expensive and may cause complications including heparin-induced thrombocytopenia, osteoporotic fractures and bleeding. We propose to undertake an efficacy study to determine whether LMWH will safely reduce these complications of pregnancy in high-risk thrombophilic women.

Design:

A multicenter double blind randomized placebo control trial. Study participants: Thrombophilic women < 16 weeks gestation with: 1) a history of previous pre-eclampsia, IUGR, abruptio placentae, miscarriage or stillbirth; or 2) a symptomatic first degree relative with thrombophilia. Intervention: Subcutaneous injections of dalteparin or saline placebo throughout pregnancy. Main Outcome Measures: 1) VTE, 2) Pre-eclampsia, 3) IUGR, 4) Abruptio placentae 5) Miscarriage, 6) Stillbirth, 7) Pre-term delivery, and 8) Safety outcomes (bleeding, heparin induced thrombocytopenia, reductions in bone mineral density and fractures).

Importance of study:

The morbidity and mortality associated with pre-eclampsia, IUGR, abruptio placentae, miscarriage, stillbirth and venous thromboembolism in pregnancy represents a significant disease burden for women. Pulmonary embolism remains the most common cause of maternal mortality. Pre-eclampsia frequently leads to maternal morbidity, causes one third of maternal deaths and is a frequent cause of fetal and neonatal morbidity and mortality. Miscarriage and stillbirth are devastating events for pregnant women and their families. IUGR often results in long-term effects in the developing child including developmental delay, poor school performance and as adults they are significantly less likely to attain higher academic and professional achievement. The burden of these complications of pregnancy is increased in thrombophilic women. The clinical, emotional and economic

importance of complications of pregnancy in this high risk prevalent subgroup, dictate that potential effective interventions, such as LMWH, must be examined in properly conducted randomised controlled trials.

Sites: 10 sites currently participating.
Looking for 20 additional sites in Canada, US or UK. We are looking for sites that can enroll *at least* 10 subjects per year.

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