

Pregnancy and Thrombophilia

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Thrombophilic risk factors are common and can be found in 5% to 20% of Caucasian populations. Pregnancy is an acquired hypercoagulable state and women harboring thrombophilia may present with clinical symptoms of vascular complications for the first time during gestation or at the postpartum period [1].

Thrombophilia and Fetal Loss

Recurrent fetal loss is common affecting 3-5% of women at the reproductive age. The risk for fetal loss is greater in homozygotes than in heterozygotes with factor V Leiden (FVL) and in female siblings of thrombophilic women with FVL. A recent meta-analysis demonstrated that FVL and the factor II G20210A mutations are associated with early and late recurrent fetal loss [2]. Differences in type of pregnancy loss (i.e., primary or secondary, isolated or recurrent, consecutive or nonconsecutive) and timing (i.e., first, second, or third trimester) may also influence the magnitude of these associations.

A recent study demonstrated that in women who had thrombophilia and previous one pregnancy loss after 10 weeks gestation, enoxaparin at a dose of 40 mg daily resulted in a significantly better live birth rate compared with low-dose aspirin on subsequent gestation (86% versus 29%, respectively) [3]. The differences were found in women who had FVL, Factor II G20210A and protein S deficiency.

LIVE-ENOX is a multicenter, prospective, randomized study recently conducted in Israel [4] comparing two doses of enoxaparin, 40mg/d and 40 mg/every 12 hours, starting at 5 to 10 weeks of gestation, throughout pregnancy, and for 6 weeks postpartum in women who had thrombophilia and pregnancy loss. In 180 women enrolled, live birth rate before the study was only 28%, but during the study, live birth rates were 84% for the 40 mg/d group and 78% for the 80 mg/d group. Late gestational complications (preeclampsia, placental abruption), were also decreased during enoxaparin treatment.

A recent Canadian study demonstrated the efficacy of dalteparin in prevention of late pregnancy complications recurrence in women without thrombophilia [5]. LMWH prophylaxis during pregnancy enables modulation of systemic hemostatic parameters through inhibition of Factor Xa and an increase in plasmatic total and free tissue factor pathway inhibitor (TFPI) levels and may also modulate TFPI levels at the placental level [6,7].

Current Perspectives

Ongoing prospective randomized studies will ultimately define the role of antithrombotics, including LMWH and aspirin, in the setting of thrombophilia and vascular gestational complications. As complete thrombophilia work-up is currently elaborate and costly, screening tests are highly warranted. One such potential screening assay of the Protein C pathway was found to be abnormal in the majority of women with recurrent fetal loss and could also identify women without thrombophilic defect [8].

A recent study in mice demonstrated that a feto-maternal cross-talk at the placental vascular bed may result in modulation of coagulation by trophoblast cells [9] and microparticles have been suggested to play a major role in placental and maternal hemostasis [10].

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