Factor V Leiden mutation and pregnancy

Haemostasis during pregnancy in non-carriers and carriers of factor V Leiden mutation, with special emphasis on placenta-mediated and venous thromboembolic complications and on blood coagulation and fibrinolysis markers for prediction of complications.

Factor V Leiden (FVL) mutation elevates the risk of venous thromboembolism (VTE) in general. During pregnancy, the haemostatic balance is changed in the direction of hypercoagulability, resulting in an increased incidence of VTE. 42 women were followed longitudinally during pregnancy and the puerperium. Classic and modified activated protein C (APC) ratios decreased during pregnancy. However, the modified ratio was above the lower limit for non-carriers, and can be used to detect the FVL mutation during pregnancy. Increased levels of prothrombin fragment 1+2 (F1+2), soluble fibrin (SF) and D-dimer indicated activation of blood coagulation. Fibrinogen, Factor VIII and plasminogen activator inhibitor type 1 and type 2 levels increased. Free protein S and tissue plasminogen activator activity decreased. Protein C levels remained unchanged. Sonoclot analyses indicated hypercoagulability during pregnancy. The same reference Sonoclot curve can be used throughout pregnancy. 5 986 women were genotyped for the FVL mutation; the prevalence of FVL carriership was 8.1%. 500 carriers and 1 058 controls were followed longitudinally and haemostatic markers were analysed. There were no differences regarding placenta-mediated complications or gestational age at delivery. The incidences of neonatal asphyxia, eclampsia, intrauterine fetal death, intrapartum death and unexplained late miscarriage were low. The incidence of blood loss exceeding 1000 ml at delivery was lower in FVL carriers. There were three VTEs among FVL carriers and none among controls. No difference in superficial thrombophlebitis was found. Genotyping for the FVL mutation in healthy pregnant women without heredity for VTE is doubtful, nor can genotyping be justified in women with obstetric complications. F1+2 and D-dimer increased during pregnancy and levels were higher than eight weeks postpartum. Alterations in SF were minor or absent. Levels of F1+2 and SF in carriers and non-carriers were the same during pregnancy. Carriers had higher levels of D-dimer than non-carriers during both pregnancy and the puerperium. The levels of all markers were in the same ranges in women with and without complications, and were unaffected by zygosity or additional thrombophilia. F1+2, SF or D-dimer cannot serve as predictors of placenta-mediated complications or VTE in FVL carriers.

Keywords
Activated protein C, D-dimer, Factor V Leiden, fibrinolysis, haemostasis, obstetric complications, platelet function, pregnancy, prothrombin fragment 1+2, soluble fibrin, Sonoclot, thrombosis

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Akademisk avhandling

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av Ulla Kjellberg

Avhandlingen baseras på följande arbeten:

1. **APC Resistance and other Haemostatic Variables during Pregnancy and Puerperium**
   Ulla Kjellberg, Nils-Erik Andersson, Steffen Rosen, Lilian Tengborn, Margareta Hellgren
   Thromb Haemost 1999; 81: 527-31

II. **Sonoclot signature during normal pregnancy**
   Ulla Kjellberg, Margareta Hellgren.
   Intensive Care Med 2000; 26: 206-11

III. **Factor V Leiden allelic variant and pregnancy – a prospective study**
   Ulla Kjellberg, Marianne van Rooijen, Katarina Bremme, Margareta Hellgren
   Submitted

IV. **Can increased blood coagulation and fibrinolysis markers predict placenta-mediated complications or thrombembolism in carriers of Factor V Leiden allelic variant?**
   Ulla Kjellberg, Marianne van Rooijen, Katarina Bremme, Margareta Hellgren
   Submitted

Fakultetsopponent:
Professor Per Morten Sandset
Fakultetsdivisjon Ullevål universitetssykehus
Det medisinske fakultet
Universitetet i Oslo

Handledare:
Docent Margareta Hellgren
Institutionen för kliniska vetenskaper
Sahlgrenska akademin
Göteborgs universitet

UNIVERSITY OF GOTHENBURG