Thrombin generation in women with preeclampsia

A. Rosenkranz1, M. Hiden1, B. Leschnik1, E.-C. Weiss2, D. Schlembach2, U. Lang2, S. Gallistl1, W. Muntean1

1Klinische Abteilung für Allgemeine Pädiatrie, Universitätsklinik für Kinder- und Jugendheilkunde, 2Klinische Abteilung für Geburtshilfe, Universitätsklinik für Frauenheilkunde und Geburtshilfe, Graz

Patients, material, methods

Collection of blood samples

In this study we compared 17 preeclamptic women with 80 healthy pregnant women during third-trimester pregnancy, who were recruited during a regular maternity clinic check-up at the Department of Obstetrics and Gynecology, Medical University of Graz. After their consent to participate in this study, blood was collected into plastic tubes containing sodium citrate (0.1 mol/l end concentration) using S-Monovette® tubes from Sarstedt (Nürnberg, Germany) and immediately afterwards, plasma was separated by centrifugation at 2800g for 10 min at room temperature and stored at –70°C.

Reagents and devices, statistics

Thrombin generation was measured by means of calibrated automated thrombography in platelet poor plasma using PPP-reagent with a content of 5 pmol/l tissue factor and 4 µmol/l phospholipids purchased from Thrombinoscope BV (Maastricht, The Netherlands) and the fluorogenic substrate Z-Gly-Gly-Arg-amino-methyl-coumarin purchased from Bachem (Bubendorf, Switzerland) for 60 minutes. Assays were performed by means of Fluoroskan Ascent plate reader (Thermo Labsystem, Helsinki, Finland) and Thrombinoscope® software (Thrombinoscope BV, Maastricht, The Netherlands) as described by the manufacturer.

In addition, TAT and F1+2 were measured in the plasma using commercially available ELISA assay systems (Enzygnost TAT® and Enzygnost F1+2®, Dade Behring, Marburg, Germany).

For comparison of parameters the Mann-Whitney U test was performed. All statistical analyses were performed with SPSS® software (SPSS Inc., Chicago, Illinois, USA) and P-values less than 0.05 were considered as significant.

Results

The ETP was significantly higher in preeclamptic women when compared to controls (Fig. 1). The time until the thrombin peak was reached (TTP) was significantly prolonged in preeclamptic women (Fig. 1), while no significant difference was found for the thrombin peak (p = 0.157) or lag time (p = 0.446). F1+2 and TAT were significantly higher in preeclamptic women when compared to controls (p = 0.0001).

Discussion

The coagulation system is known to be activated in pregnancy. This was confirmed in a previous study, showing that endogenous thrombin potential and prothrombin activation markers do increase with duration of normal uncomplicated pregnancy (10). In the present study, we investigated all parameters of continuous thrombin generation in preeclamptic women and significant higher levels of ETP and prolonged TTP were observed, while no significant differences were found for lag time and peak height. These data show that preeclamptic women have the potential to generate significantly higher amounts of thrombin and that the time until the thrombin concentration approaches zero is significantly elongated in comparison to women with uncomplicated pregnancies. In addition, F1+2 and TAT were significantly higher in preeclamptic women representing in-vivo an increased activity of the coagulation system, which is in accordance with previous studies on coagulation in preeclamptic pregnancies (5–8).
**Conclusion**

ETP values are higher in preeclamptic women when compared to normal controls. Our results suggest that it might be worthwhile to investigate, whether an increased ETP in early pregnancy is predictive for the development of future preeclampsia.

**References**


**Correspondence to:**

Wolfgang Muntean, M.D.
Department of Pediatrics, Medical University of Graz
Auenbruggerplatz 30, 8036 Graz, Austria
Tel. +43/316/3 85 26 09
Fax +43/316/3 85 26 19
E-mail: wolfgang.muntean@meduni-graz.at