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ORIGINAL ARTICLE

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Major obstetric haemorrhage: monitoring with thromboelastography, laboratory analyses or both?

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ABSTRACT
Background: Haemorrhage is a common cause of morbidity and mortality in the obstetric population. The aim of this study was to compare the use of thromboelastography and laboratory analyses to evaluate haemostasis during major obstetric haemorrhage. A secondary aim was to evaluate correlations between the results of thromboelastography, laboratory analyses and estimated blood loss.
Methods: Forty-five women with major obstetric haemorrhage and 49 women with blood loss <600 mL were included. The following thromboelastography analyses were performed: time to start of clotting (TEG-R), time to 20 mm of clot firmness (TEG-K), rate of clot growth (TEG-Angle), maximum amplitude of clot (TEG-MA) and lysis after 30 min (TEG-LY30). In addition, platelet count, activated partial thromboplastin time, prothrombin time, fibrinogen, antithrombin and D-dimer were measured.
Results: Thromboelastography variables reflecting clot stability and fibrinolysis were decreased in women with massive obstetric haemorrhage compared to women with normal bleeding, while clot initiation was accelerated. Laboratory analyses also showed impaired haemostasis with the most pronounced differences in platelet count, fibrinogen concentration and antithrombin activity. The strongest correlations existed between fibrinogen and TEG-MA and between estimated blood loss and TEG-MA, fibrinogen and antithrombin, respectively.
Conclusions: Impaired haemostasis, demonstrated by thromboelastography and laboratory analyses, was found after an estimated blood loss of 2000 mL. Thromboelastography provides faster results than standard laboratory testing which is advantageous in the setting of on-going obstetric haemorrhage. However, laboratory analyses found greater differences in coagulation variables, which correlated better with estimated blood loss.

Keywords: Thromboelastography; Platelet count; Activated partial thromboplastin time; Prothrombin time; Fibrinogen; Antithrombin; D-dimer; Postpartum haemorrhage

Introduction

Haemorrhage is still a common cause of morbidity and mortality in the obstetric population. The latest UK Confidential Enquiry into Maternal Deaths reported a decline in mortality from postpartum haemorrhage (PPH) but it is still the sixth most common direct cause of death.[1] Several reports have described substandard care and stated the need for guidelines for managing PPH.[2–4] Postpartum haemorrhage has been reported to be responsible for 73% of all severe morbidity during pregnancy and is the most common obstetric cause of intensive care admission.[5] Laboratory analyses are usually used for diagnosis of haemostatic disorders in cases of obstetric haemorrhage and serve as a basis for decision-making and follow-up treatment. As the results of these analyses are reported with variable delay, immediate knowledge of the haemostatic condition has previously been unavailable, making early specific treatment difficult.

Two viscoelastic methods, thromboelastography (TEG) and thromboelastometry (TEM), have now been re-evaluated and technically improved. These global point-of-care tests simultaneously measure coagulation and fibrinolysis in whole blood and can detect haemostatic derangement within 10–20 min.[6] In a recent prospective longitudinal study in healthy pregnant women, TEG demonstrated faster blood coagulation

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with increased strength of the fibrin clot and less fibrinolysis during the pregnancy compared to eight weeks postpartum.[7] These results are supported by other studies reporting changes in TEG/TEM variables during the puerperium.[8,9] Few studies have evaluated TEG/TEM in women with PPH[10] and the significance of these methods in connection with obstetric haemorrhage is unclear.[11–14]

The primary aim of this prospective observational study was to describe the results of coagulation testing using TEG and traditional laboratory analyses during major obstetric haemorrhage (MOH) and to compare the findings with results of parturients with normal postpartum blood loss. A secondary aim was to study whether the results of TEG or laboratory analyses correlated with estimated blood loss (EBL).

Methods

The Regional Ethical Review Board in Gothenburg, Sweden approved this study. Written informed consent was obtained from all participants. Women with MOH and women with blood loss <600 mL were included. Women with MOH were brought to the operating room, if not already there because of caesarean section, and blood sampling was performed after an EBL of ⩾2000 mL. The first sample was performed after admission to the operating room or when the decision to assess coagulation was made. Women were asked to participate in the study when stabilized after intervention: all agreed to participate. Women undergoing uncomplicated delivery with blood loss <600 mL were asked to participate before blood sampling. Bleeding at delivery and postpartum were determined by weighing surgical sponges and pads and by measuring collected blood. Patients were treated according to local guidelines. Depending on the amount of bleeding, treatment included crystalloids, colloids, blood and blood products, and tranexamic acid.

Venous blood sampling from women with MOH was performed as part of the intervention to stop the bleeding. Venous blood sampling from women after normal delivery without haemorrhage was performed within 2–6 h postpartum on the delivery ward. The sampling procedure was similar to that previously reported, using a butterfly device (Terumo Quick Fit, Tokyo, Japan) or a Venflon needle (BD Medical, Franklin Lakes, NJ, USA).[7] The first portion (9–10 mL) was discarded. The second sample was collected with a 2-mL syringe (Codan, Lensahn, Germany) for TEG analysis, followed by collection directly into tubes for activated partial thromboplastin time (APTT), international normalised ratio (INR), fibrinogen, antithrombin and D-dimer. Finally, blood was collected for platelet count.

The TEG® 5000 version 4.2 software (Haemoscope Corporation, Niles, IL, USA) was used for all TEG analyses. Kaolin served as an activator as previously described.[7] Kaolin reagent, cups and pins were supplied by the manufacturer. One millilitre of whole blood was gently mixed with kaolin and 360 μL of this preparation was pipetted into a TEG cup pre-warmed to 37°C. Analysis was performed within 4 min of blood sampling and read after 5–10 min when a result could be provided. Thereafter the TEG proceeded for 90 min. Trained nurses performed the analyses. The following TEG variables were assessed: R time (TEG-R), time to start of clotting; K (TEG-K), time to 20 mm clot firmness; Angle (TEG-Angle), clot growth rate; MA (TEG-MA), maximum clot amplitude. Finally, LY30 (TEG-LY30), lysis 30 min after MA, was determined. Blood for APTT, INR, fibrinogen, antithrombin and D-dimer analysis was collected in tubes containing 0.13 M citrate. EDTA tubes were used for determination of platelet count. The blood samples were handled within 30 min and centrifuged at 2000 *g* at room temperature for 20 min. Laboratory analysis data are shown in Appendix A.

Statistical analysis

The number of women to be included in each group was based on data from our previous studies of laboratory variables during different periods of pregnancy.[7,15] The current study was planned when power analysis was not mandatory so this was not performed. Results are presented as mean ± standard deviation (SD) and 95% confidence interval (CI) or median [range]. The t test (normally distributed continuous variables) was used for group comparisons. For sub analysis, the MOH group was further divided into MOH 2–3 L and MOH > 3 L. Correlations between EBL, TEG variables and haemostatic laboratory analyses were assessed by Pearson's correlation. In order to control for multiple analysis, only a correlation coefficient ⩾0.5 and/or a *P* value <0.01 was considered significant. If INR was <0.9, we used 0.8 in the calculations and if the D-dimer level exceeded 20 mg/L, we used 21 in the calculations. All descriptive and statistical analyses were performed in SPSS version 19 (IBM, NY, USA).

Results

Forty-five women with MOH and 49 women with blood loss <600 mL were included. Patient characteristics are shown in Table 1. Treatments at the time of blood sampling are shown in Table 2. Major obstetric haemorrhage was secondary to placental retention ($n = 17$), caesarean section ($n = 14$), uterine atony ($n = 6$), uterine rupture ($n = 2$), placenta praevia ($n = 2$), cervical or vaginal lacerations ($n = 2$), abruptio placentae ($n = 1$) and placenta accreta ($n = 1$).

Thromboelastography variables are shown in Table 3. Those reflecting clot stability and fibrinolysis were