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Clinical Investigations

Assessment of Changes in Coagulation in Parturients with Preeclampsia Using Thromboelastography

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Abstract

Background: Preeclampsia is associated with a risk of abnormal hemostasis that occurs most commonly secondary to thrombocytopenia. Thromboelastography measures whole blood coagulation and has been used to manage coagulation defects in obstetric patients. The authors conducted this investigation in a large number of preeclamptic women to assess changes in coagulation using thromboelastography.

Cited Here...: Thromboelastography and platelet counts were performed in 52 healthy pregnant women, 140 mild preeclamptic women, and 114 severe preeclamptic women in

active labor using disposable plastic cups and pins and native whole blood. In preeclamptic patients with a platelet count <100,000/mm^3, conventional coagulation tests were also performed. Epidural analgesia was provided in some women when they requested pain relief.

Cited Here...: Fifteen percent of all preeclamptic women (38 of 254) and 2% (1 of 52) of healthy pregnant women had a platelet count <100,000/mm^3. The incidence of thrombocytopenia <100,000/mm^3 was 3% (4 of 140) and 30% (34 of 114) in mild preeclamptic patients and severe preeclamptic patients, respectively. Severe preeclamptic patients with a platelet count <100,000/mm (^{3}) were significantly hypocoagulable when compared to the other study groups. Ten severe preeclamptic women with a platelet count <100,000/mm^3 had a maximum amplitude <54 mm (the lower limit of maximum amplitude in healthy pregnant women enrolled in this investigation). None of the mild preeclamptic women had a maximum amplitude <54 mm. Five severe preeclamptic women with a platelet count <100,000/mm^3 had an abnormal coagulation profile, whereas all four mild preeclamptic women with a platelet count <100,000/mm^3 had a normal coagulation profile.

Conclusion: This study shows that severe preeclamptic women with a platelet count <100,000/mm^3 are hypocoagulable when compared to healthy pregnant women and other preeclamptic women.

PREECLAMPSIA is associated with a risk of abnormal hemostasis that occurs most commonly because of thrombocytopenia, [1,2] and rarely because of mild disseminated intravascular coagulation. [3,4] The risk of abnormal hemostasis increases with the severity of preeclampsia. [1] The platelet count is routinely used as a primary test to evaluate the coagulation status in preeclamptic parturients. [5] It has been shown that when the platelet count is less than 100,000/mm^3, other hemostatic abnormalities, such as prolonged prothrombin time (PT) and partial thromboplastin time (PTT), and reduced fibrinogen concentration may also be present. [6] As a result, PT, PTT, and fibrinogen levels have been recommended to evaluate hemostasis when preeclampsia is complicated by a platelet count <100,000/mm^3. [6]

Thromboelastography is commonly used to assess coagulation during cardiopulmonary bypass surgery and liver transplantation. [7,8] It measures whole blood coagulation and provides information about the adequacy of platelet function and all other clotting factors in a short time. [9,10] Recently, many investigators have used thromboelastography to manage coagulation defects in obstetric patients. [11-13] Furthermore, a study in preeclamptic women showed that the maximum amplitude (MA) from thromboelastography has a better correlation with a low platelet count than bleeding time has with low platelet count. [14]

We conducted this investigation in a large number of preeclamptic women to assess changes in coagulation using thromboelastography in relation to conventional tests of hemostasis.

Methods

After Institutional Review Board approval, informed consent to collect blood samples for thromboelastographic analysis was obtained from 52 healthy pregnant women in active labor and 254 laboring preeclamptic women at Parkland Hospital in Dallas from January 1995-June 1996. Mild preeclampsia was defined as a systolic blood pressure >140 mmHg, a diastolic blood pressure >90 mmHg, and proteinuria >1 g/l (2 + using dipstick measurements). Severe preeclampsia was diagnosed by one or more of the following criteria: a systolic blood pressure >160 mmHg, a diastolic blood pressure >110 mmHg, and proteinuria of 3+ to 4+ g/l using dipstick measurements. Obstetric treatment of preeclamptic women included magnesium sulphate for seizure prophylaxis and intermittent intravenous hydralazine to lower diastolic blood pressure that had reached 110 mmHg or greater. Healthy pregnant women were initially studied to determine baseline values of thromboelastography parameters in healthy pregnant women. Laboratory tests that were performed both in healthy pregnant and in preeclamptic women included a hematocrit level and a platelet count using a Coulter counter, which is very accurate even at low platelet counts. Thromboelastography was performed on Thromboelastograph, computerized version (Haemoscope Corp., Skokie, IL), using disposable plastic cups and pins and native whole blood, after admission to the delivery suite or before epidural placement for labor pain relief. Blood was collected from a peripheral vein via an 18-gauge needle using a two-syringe technique. The first sample was discarded to avoid tissue contamination of blood, whereas the second sample was used for thromboelastographic measurements and other laboratory tests. Three hundred sixty microliters of whole blood was pipetted into a disposable plastic cup within 4 min of blood sampling, and then placed in a prewarmed (37 [degree sign]C) thromboelastograph.

Thromboelastographic parameters included reaction time (r), clot formation time (K), MA, clot formation rate ([small alpha, Greek] angle), and a thromboelastographic coagulation index (CI). [10] A thromboelastographic CI is derived from a linear Equation thatcombines all the thromboelastographic parameters (native whole blood: CI = -(0.1227)r + (0.0092)K + (0.1655)MA - (0.041)[small alpha, Greek] -5.0220; normal range for nonpregnant women = +2 to -2). A coagulation profile, including PT, activated PTT (aPTT), and fibrinogen concentration, was also performed in all preeclamptic women with a platelet count <100,000/mm^3.

Epidural analgesia was provided when women requested pain relief. In preeclamptic women with a platelet count <100,000/mm^3, thromboelastographic parameters from healthy pregnant women were used as a reference for epidural placement. Epidural placement was performed in the sitting position via a midline approach at interspace L2-L3 or L3-L4 using a 17-gauge Tuohy needle and a 20-gauge multiorifice catheter and loss of resistance to air to

identify the epidural space. The local anesthetic used for labor analgesia was boluses of bupivacaine, 0.25%, followed by an infusion of bupivacaine, 0.125%. All women were observed for neurologic complications in the postdelivery period.

All data are expressed as mean +/- SD (range), n(%). Data were analyzed using SAS statistical software (SAS Institute, Cary, NC). Analysis of parametric data was performed by one-way analysis of variance, and results were assessed by Bonferroni post hoc test. Pearson correlation was performed between thromboelastographic parameters and laboratory tests. All tests were two-sided and a P value <or= to 0.05 was considered significant.

Results

In this study, thromboelastography was performed in 306 women. Of these 306 women, 52 were healthy pregnant women, 140 were mild preeclamptic, and 114 were severe preeclamptic. Demographic characteristics with regards to age, weight, height, and gestational age were similar in all four groups (Table 1). Hematocrit values were significantly reduced in the postdelivery period in all groups. Platelet counts were similar in healthy pregnant women, mild preeclamptic women, and severe preeclamptic women with a platelet count <or= to 100,000/mm^3 (Table 1). Results of the coagulation profile in preeclamptic women with a platelet count <100,000/mm^3 (n = 38) were as follows: PT = 11.7 +/- 2.1 (range, 10-18 s); PTT = 31.6 +/- 5.7 (range, 20-51 s); fibrinogen = 349 +/- 135 mg/dl (range, 93-587 mg/dl).

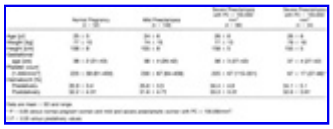

Table 1

There was no significant difference in thromboelastography parameters r, K, [small alpha, Greek] angle, and thromboelastography CI between healthy pregnant women, mild preeclamptic women and severe preeclamptic women with a platelet count >or= to 100,000/mm^3 (Table 2; Figure 1). However, in mild preeclamptic women, MA was significantly hypercoagulable compared to healthy pregnant and all severe preeclamptic women (Table 2). All thromboelastography parameters were significantly hypocoagulable in severe preeclamptic women with a platelet count <100,000/mm (^{3}) when compared to normal pregnant women, mild preeclamptic women, and severe preeclamptic women with a platelet count >or= to 100,000/mm^3 (Table 2; Figure 1).

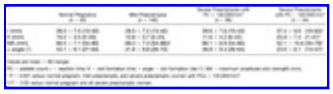

Table 2

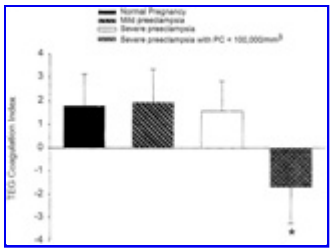

Figure 1

Fifteen percent of all preeclamptic women (38 of 254) and 2% (1 of 52) of healthy pregnant women had a platelet count <100,000/mm^3. The incidence of thrombocytopenia <100,000/mm^3 was 3% (4 of 140) and 30% (34 of 114) in mild preeclamptic women and severe preeclamptic women, respectively (Table 3). Of the 114 severe preeclamptic women, 10 women with a platelet count <100,000/mm^3 had an MA <54 mm, which was the lower limit of MA in healthy pregnant women enrolled in this investigation (Table 3 and Table 4). None of the mild preeclamptic women had an MA <54 mm. Five severe preeclamptic women with a platelet count <100,000/mm^3 had an abnormal coagulation profile, whereas all four mild preeclamptic women with a platelet count <100,000/mm^3 had a normal coagulation profile (Table 3 and Table 4).

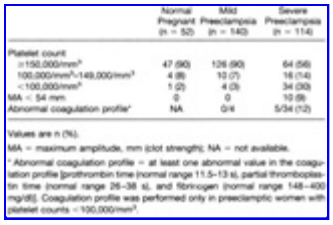

Table 3

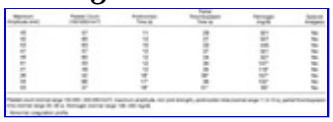

Table 4

Correlation coefficients between the platelet count and thromboelastography parameters are shown in Table 5. Reaction time (r) had a weak correlation with the platelet count (r = -0.13; P = 0.05). Correlation of the platelet count with MA and thromboelastography CI was stronger in women with a low platelet count. The correlation coefficient of a platelet count <150,000/mm^3 with MA was r = 0.61 (P <0.01) and with thromboelastography Ci was r = 0.55 (P = <0.001), and the correlation coefficient of a platelet count <100,000/mm^3 with MA was r = 0.61 (P <0.001) and with thromboelastography CI was r = 0.65 (P <0.001). The relationship between the platelet count and MA for severe preeclamptic women and for all women together is shown in Figure 2 and Figure 3, respectively. This relation was linear for women with platelet counts <100,000/mm^3 (Figure 2).

Table 5

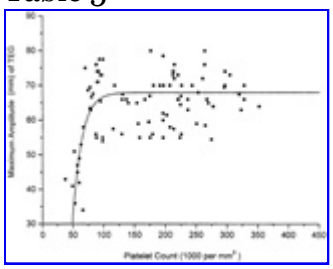

Figure 2

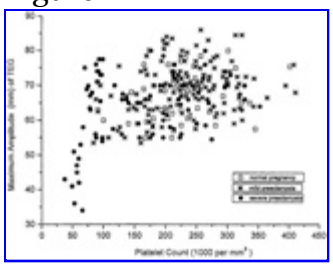

Figure 3

One hundred eighty-three women, including 35 healthy pregnant women, 85 mild preeclamptic women, and 63 severe preeclamptic women, received epidural analgesia during labor. No patient after epidural analgesia had any neurologic complications in the postdelivery period.

Discussion

This study of coagulation using thromboelastography shows that mild preeclamptic women are hypercoagulable when compared to healthy pregnant women. However, as the severity of preeclampsia increases, blood coagulability decreases, and severe preeclamptic women with a platelet count <100,000/mm^3 are significantly hypocoagulable when compared to healthy pregnant women, mild preeclamptic women, and severe preeclamptic women with a platelet count >or= to 100,000/mm^3. There is a strong correlation between a low platelet count and MA from thromboelastography.

Thromboelastography measures whole blood coagulation and provides information about the adequacy of platelet function and other clotting factors, all in a short time. [9] Thromboelastographic parameters are interrelated and reflect activities of clotting factors, platelets, and fibrinogen, and their interaction, [15] whereas coagulation profiles monitor an isolated portion of the coagulation cascade and do not reflect the interaction among clotting factors, platelets, and fibrinogen. Therefore, thromboelastography provides a better assessment of whole blood coagulability than does routine coagulation profiles. [16] The principle and interpretation of thromboelastography is well described in the literature. [9,10] Individual thromboelastographic parameters from thromboelastography include r, which indicates clotting factor activity, and K, MA, and [small alpha, Greek] angle, which indicate platelet and fibrinogen activity. In addition, a computerized thromboelastographic CI

derived from r, K, MA, and [small alpha, Greek] angle can be used to reflect all activities of clotting factors, platelets, and fibrinogen. Because it combines all the parameters from a thromboelastograph, a CI reflects the overall coagulability of blood. [10] Normal values for CI in nonpregnant women for native whole blood, using disposable cups and pins, range from -2 to +2. Outside this range, a more positive value would reflect greater hypercoagulability, whereas a more negative value would reflect greater hypocoagulability.

As shown previously [17] and in this study, mild preeclamptic women were hypercoagulable when compared to healthy pregnant women, as reflected by an increase in MA. However, severe preeclamptic women with a platelet count <100,000/mm^3 were significantly hypocoagulable when compared to all other women, as shown by an increase in r and K and a reduction in [small alpha, Greek] angle and MA. It suggests that severe preeclamptic women begin to show significant hypocoagulability when the platelet count decreases to <100,000/mm^3. Leduc et al. [6] demonstrated that in severe preeclamptic women when the platelet count is less than 100,000/mm^3, other coagulation indices also become abnormal. They have therefore recommended PT, PTT, and fibrinogen levels in these instances to detect additional hemostasis abnormalities. [6]

After Ramanathan et al. [18] and Schindler et al. [19] demonstrated a prolonged bleeding time in severe preeclamptic women with platelet counts less than 100,000/mm^3, some anesthesiologists have long presumed a connection between a prolonged bleeding time (> 10 min) and the risk of epidural hematoma formation in patients with severe preeclampsia. Schindler et al. [19] recommended bleeding time in preeclamptic women with platelet counts <100,000/mm^3 before providing regional anesthesia. However, there is no evidence to suggest that a bleeding time >10 min is associated with an increased risk of epidural hematoma formation after epidural anesthesia in preeclamptic women. Furthermore, Channing-Rodgers and Levin, [20] in their review of 862 publications of bleeding time, indicated that bleeding time is not a sensitive indicator of platelet function and does not reliably predict the risk of hemorrhage. The recommendation by some authorities that epidural analgesia be withheld in women whose platelet count is <100,000/mm^3 has no supporting experimental data. Preeclamptic women with platelet counts much less than 100,000/mm^3 have received uncomplicated epidural anesthesia. [21-23] In our study, 183 women, including 27 preeclamptic women with a platelet count <100,000/mm^3, received epidural analgesia during labor. Neurologic complications did not develop in any of these women; however, given the limited number of patients, we cannot make any comments regarding the safety of epidural anesthesia in such patients or about the risk of epidural hematomas in patients with coagulopathies.

In conclusion, this study shows that severe preeclamptic women with platelet counts <100,000/mm^3 are significantly hypocoagulable when compared to healthy pregnant women, mild preeclamptic women, and severe preeclamptic women with platelet counts

>or= to 100,000/mm^3. The level of thrombocytopenia or thromboelastography parameters that would safely allow epidural anesthesia in preeclamptic women is not known. Finally, thromboelastography may be used to assess hemostasis in preeclamptic women.

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REFERENCES

1. Cunningham FG, Pritchard JA: Hematologic considerations of pregnancy-induced hypertension. Semin Perinatol 1978; 2:29-38

2. Kelton LG, Hunter DJS, Neame PB: A platelet function defect in preeclampsia. Obstet Gynecol 1985; 65:107-9

3. Burrows RF, Hunter DKS, Andrew M, Kelton JG: A prospective study investigating the mechanism of thrombocytopenia in preeclampsia. Obstet Gynecol 1987; 70:334-8

4. Roberts JM, May WJ: Consumptive coagulopathy in severe preeclampsia. eclampsia. Obstet Gynecol 1977; 48:163-6

5. Voulgaropoulos DS, Palmer CM: Coagulation studies in the pre-eclamptic parturient: A survey. J Clin Anesth 1993; 5:99-104

6. Leduc L, Wheeler JM, Kirshon B, Mitchell P, Cotton DB: Coagulation profile in severe preeclampsia. Obstet Gynecol 1992; 79:14-8

7. Tuman KJ, Spiess BD, Ivankovich AD: Use of thromboelastography in the management of Von Willebrand's disease during cardiopulmonary bypass. J Cardiovasc Thorac Anesth 1987; 1:321-4

8. Kang YG, Martin DJ, Marquez JM, Lewis JH, Bontempo FA, Shaw BW Jr, Starzl TE, Winter PM: Intraoperative changes in blood coagulation and thromboelastographic monitoring in liver transplantation. Anesth Analg 1985; 64:888-96

9. Chandler WL:. The thromboelastograph and the thromboelastograph technique. Semin Thromb Hemost 1995; 21:1-6

10. Sharma SK, Philip J, Wiley J: Thromboelastographic changes in healthy parturients and postpartum women. Anesth Analg 1997; 85:94-8

11. Landers DF, Newland M, Penney LL: Multiple uterine rupture and crushing injury of the fetal skull after blunt maternal trauma. J Reprod Med 1989; 34:988-93

12. Whitta RKS, Cox DJA, Mallett SV: Thrombelastography reveals two causes of haemorrhage in HELLP syndrome. Br J Anaesth 1995; 74:464-8

13. Sharma SK, Vera RL, Stegall WC, Whitten CW: Management of postpartum coagulopathy using thrombelastography. J Clin Anesth 1997; 9: 243-7

14. Orlikowski CEP, Rocke DA, Murray WB, Gouws E, Moodley J, Kenoyer DG, Byrne S: Thrombelastography changes in pre-eclampsia and eclampsia. Br J Anaesth 1996; 77:157-61

15. Howland WS, Schweizer O, Gould P: A comparison of intraoperative measurement of coagulation. Anesth Analg 1974; 53:657-63

16. Zuckerman L, Cohen E, Vagher JP, Woodward E, Caprini JA: Comparison of thrombelastography with common coagulation tests. Thromb Haemost 1981; 46:752-6

17. Perry KG, Martin JN: Abnormal hemostasis and coagulopathy in preeclampsia and eclampsia. Clin Obstet Gynecol 1992; 35:338-50

18. Ramanathan J, Sibai BM, Vu T, Chauhan D: Correlation between bleeding times and platelet counts in women with preeclampsia undergoing cesarean section. Anesthesiology 1989; 71:188-91

19. Schindler M, Gatt S, Isert P, Morgans D, Cheung A: Thrombocytopenia and platelet functional defects in pre-eclampsia: Implication for regional anesthesia. Anaesth Intensive Care 1990; 18:169-74

20. Channing-Rodgers RP, Levin J: A critical reappraisal of the bleeding time. Semin Thromb Hemost 1990; 16:1-30

21. Letsky EA: Haemostasis and epidural anaesthesia. Int J Obstet Anaesth 1991; 1:51-4

22. Bellin Y, Jahn J, Comerford M: Safe epidural analgesia in thirty parturients with platelet counts between 69,000 and 98,000 mm^{-3}. Anesth Analg 1997; 85:385-8

23. Ramus KT, Rottman RL, Kotelko DM, Wright WC, Stone JJ, Rosenblatt RM: Unrecognized thrombocytopenia and regional anesthesia in parturients: A retrospective review. Obstet Gynecol 1989; 73:943-6

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