Thromboelastographic Changes in Healthy Parturients and Postpartum Women

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Thromboelastography (TEG) using disposable plastic cups and pins was performed with native whole blood (native group) in 17 nonpregnant volunteers, 134 healthy term pregnant women (>36 wk gestation), and 69 postpartum women. Thromboelastography was also performed with celite-activated whole blood (celite group) in 15 nonpregnant female volunteers, 38 healthy term pregnant women, and 34 postpartum women. The thromboelastographic parameters *r* and K were significantly decreased in pregnant and postpartum women compared with nonpregnant women in both groups ($P < 0.05$). The maximum amplitude MA, elastic shear modulus, and α angles were significantly increased in pregnant and postpartum women compared with nonpregnant women in both groups ($P < 0.05$). The TEG coagulation index was significantly greater in pregnant and postpartum women compared with nonpregnant women in both groups. In this study, TEG showed that pregnancy is a hypercoagulable state and that postpartum women remain hypercoagulable through the first 24 h postdelivery. The use of celite in TEG accelerated the speed of TEG analysis.

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Thromboelastography (TEG) provides an effective and convenient means of monitoring whole blood coagulation. It evaluates the elastic properties of whole blood and provides a global assessment of hemostatic function. It is recommended and commonly used in assessing hemostasis during liver transplantation and cardiac bypass surgery (1,2). Its use in obstetrics has also been described (3–6).

As TEG has gained popularity, certain modifications in its performance have been introduced. Metal cups and pins have routinely been used to perform TEG. However, metal surfaces may become rough after repeated use and may result in the activation of coagulation during TEG and, hence, affect its measurements. Alternatively, disposable plastic cups and pins are now available for use in TEG and are being used by many centers. As an adjunct to native whole blood, celite, which accelerates the coagulation of whole blood by activating coagulation factors and platelets, has been used as an activator for TEG in nonpregnant patients to yield quicker results and to allow for a more rapid assessment of hemostasis (7,8).

Incorporating the aforementioned measures, the purpose of this study, which used disposable plastic cups and pins, was to determine values for TEG variables for native and celite-activated whole blood in healthy parturients. Blood coagulability in the immediate postpartum period was also assessed using TEG.

Methods

After institutional approval, informed consent to collect blood samples for TEG analysis was obtained from 307 healthy nonpregnant, pregnant, and postpartum women. Women with a history of coagulation disorders, preeclampsia, hemorrhage, or women receiving magnesium sulphate, or aspirin, or heparin therapy were excluded from the study. TEG was performed on Thromboelastograph® computerized version (Haemoscope Corp., Skokie, IL) using disposable plastic cups and pins. Native whole blood (native group) was used for TEG in 17 nonpregnant female volunteers, 134 healthy term pregnant women (>36 wk gestation) presenting for elective cesarean delivery, and 69 women presenting for postpartum tubal ligation 12–24 h postdelivery. Celite-activated whole blood (celite group) was used for TEG in 15 nonpregnant female volunteers, 38 healthy term pregnant women (>36 wk) presenting for cesarean delivery, and 34 women presenting for postpartum tubal

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Table 1. Hematological Data

	Nonpregnant Native (n = 17) Celite (n = 15)	Pregnant (n = 134) (n = 38)	Postpartum (n = 69) (n = 34)
Platelet count ($10^3/mm^3$)			
Native	274 ± 60	222 ± 59*	215 ± 48*
Celite	295 ± 46	218 ± 42*	207 ± 71*
Hematocrit (%)			
Native	38.4 ± 1.5	35.8 ± 3.4*	32.9 ± 4.6*†
Celite	37.9 ± 1.7	34.9 ± 2.7*	33.9 ± 2.7*

Data are expressed as mean ± SD.
Native = native whole blood, Celite = celite-activated whole blood.
* $P < 0.05$ versus nonpregnant, † $P < 0.05$ versus pregnant.

ligation 12–24 h postdelivery. 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, and the second sample was used for TEG measurements and other laboratory tests. In the native group, 0.36 mL of whole blood was pipetted into a disposable plastic cup within 4 min of blood sampling and then placed in a prewarmed (37°C) TEG. In the celite group, 1.0 mL of whole blood was immediately placed in a vial containing 90 μL of celite particles in normal saline (1% celite concentration), and after being mixed by inversion of the vial 8–10 times, 0.36 mL of celite-activated whole blood was pipetted into a disposable plastic cup and then placed in a prewarmed TEG. The TEG was allowed to run until LY60 (reduction in maximum amplitude of the TEG tracing after 60 min) could be determined. TEG variables included r (reaction time), K (clot formation time), rK (r + K, or coagulation time), MA (maximum amplitude), α angle (clot formation rate), G (elastic shear modulus in dyn/cm^2 = 5000 · MA/100-MA) (9), LY60, and a TEG coagulation index (CI) (10,11). A TEG CI is derived from a linear equation that combines all the TEG variables (native whole blood CI = $-[0.1227]r + [0.0092]K + [0.1655]MA - [0.041]\alpha - 5.0220$, celite-activated whole blood CI = $-[0.3258]r - [0.1886]K + [0.1224]MA + [0.0759]\alpha - 7.7922$, normal range for nonpregnant women = +2 to −2). Other laboratory tests that were performed in all women included a hematocrit and a platelet count. A coagulation profile such as prothrombin time (PT), activated partial thromboplastin time (aPTT), D-dimer (cross-linked fibrin degradation products), and fibrinogen concentration were also performed in 30 pregnant women in the native group to determine their correlation with TEG variables.

All data are expressed as mean ± SD (range) and n (%). Demographic and hematological data between groups were analyzed by one-way analysis of variance, and results were assessed by using the Newman-Keuls *post hoc* test. TEG data were analyzed by using the Kruskal-Wallis test and followed by Tukey multiple comparisons. Spearman's correlation was performed between TEG variables and laboratory tests. All tests were two-sided, and a P value ≤0.05 was considered significant.

Results

Demographic characteristics with regard to age and height were similar in nonpregnant, pregnant, and postpartum women in both the native and celite groups. However, the weight of pregnant and postpartum women was significantly higher when compared with nonpregnant women in both groups (native: nonpregnant 64 ± 5 kg vs pregnant 73 ± 11 kg vs postpartum 71 ± 16 kg, $P < 0.05$; celite: nonpregnant 63 ± 5 kg vs pregnant 74 ± 10 kg vs postpartum 71 ± 12 kg, $P < 0.05$). The hematocrit and platelet counts were significantly lower in pregnant and postpartum women when compared with nonpregnant women in both groups (Table 1).

Values for r and K were significantly decreased in pregnant and postpartum women when compared with nonpregnant women in both groups (Table 2). The value for α angle was significantly increased in postpartum women when compared with pregnant women in the native group (Table 2). The values for MA, α angle, and G were significantly increased in pregnant and postpartum women when compared with nonpregnant women in both groups (Table 2). The TEG CI was significantly greater in pregnant and postpartum women (native +4.3 to −0.6, celite +5.1 to +2.7 and native +3.9 to −0.5, celite +5.7 to +2.2, respectively) when compared with nonpregnant women (native +2 to −2, celite +1.5 to −1.2) in both groups (Figure 1). The value for LY60 in both groups was similar in nonpregnant, pregnant, and postpartum women (Table 2).

The ratio of the mean rK time between the celite and native groups in nonpregnant women was 1:2 (18.8: 42.4 mm), while in pregnant and postpartum women,

Table 2. Thromboelastographic Variables

	Nonpregnant Native (n = 17) Celite (n = 15)	Pregnant (n = 134) (n = 38)	Postpartum (n = 69) (n = 34)
r (mm)			
Native	30.8 ± 5.3 (24–43)	26.3 ± 6.7 (13—41)*	27.9 ± 4.7 (18–38)*
Celite	14.3 ± 2.4 (11–17)	7.2 ± 1.9 (4–11)*	6.3 ± 2 (4–10)*
K (mm)			
Native	11.6 ± 2.5 (9–17)	9.3 ± 3.2 (5–17)*	8.6 ± 2.1 (5–14)*
Celite	4.4 ± 1.2 (3–7)	2.5 ± 0.5 (1.5–3)*	2.3 ± 0.4 (2–3)*
MA (mm)			
Native	56.8 ± 5.1 (46–63)	66.4 ± 7.1 (54–80)*	67.7 ± 7.8 (52–80)*
Celite	61.5 ± 4.5 (55–68)	71.7 ± 4.5 (58–76)*	72.4 ± 2.8 (67–78)*
α angle (°)			
Native	33.4 ± 6.1 (24–42)	42.5 ± 9 (27–65)*	47.1 ± 8.1 (37–67)*†
Celite	64 ± 6.1 (54–74)	73.4 ± 4.2 (65–81)*	74.2 ± 5.3 (61–80)*
G force (1000 × dyn/cm^2)			
Native	6.7 ± 1.3	10.6 ± 3.8*	11.4 ± 3.9*
Celite	8.2 ± 1.6	13.0 ± 2.4*	13.3 ± 2.0*
LY60 (%)			
Native	4.8 ± 1.5 (2–7)	4.8 ± 2.5 (0.5–10)	5.1 ± 2 (2–10)
Celite	4.8 ± 2.4 (1–8)	4.4 ± 1.9 (1–9)	5 ± 1.5 (3–9)

Values are mean ± SD (range).
r = reaction time, K = clot formation time, α angle = clot formation rate, MA = maximum amplitude (clot strength), G = shear elastic modulus, LY60 = % reduction in MA at 60 min.
* $P < 0.05$ versus nonpregnant, † $P < 0.05$ versus pregnant.

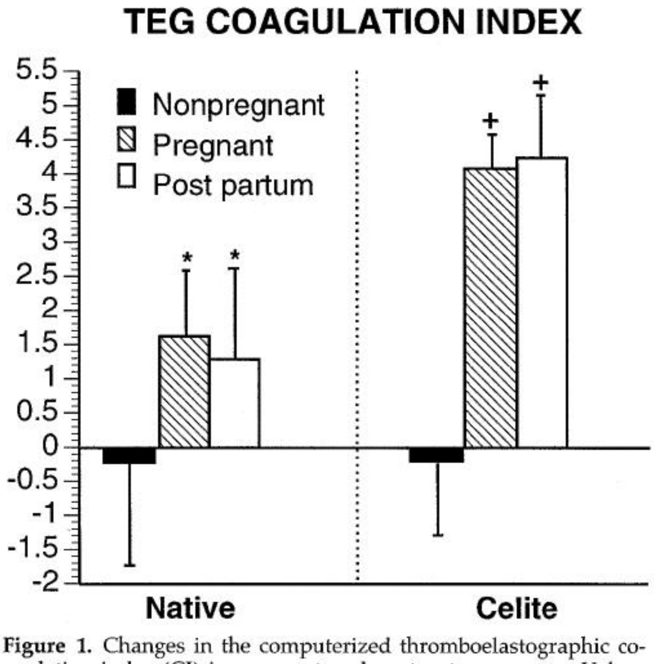

Figure 1. Changes in the computerized thromboelastographic coagulation index (CI) in pregnant and postpartum women. Values are expressed as mean ±SD. *$P < 0.05$ nonpregnant versus pregnant and postpartum women using native whole blood. +$P < 0.001$ nonpregnant versus pregnant and postpartum women using celite-activate whole blood.

the ratio was 1:4 (9.8:37 mm) and 1:4 (8.6:36 mm), respectively. The mean value of G force increased by 22% in nonpregnant, 23% in pregnant, and 17% in postpartum women when celite was used. Similarly, the mean value of α angle increased by 92%, 73%, and 58% in nonpregnant, pregnant, and postpartum women, respectively, when celite was used.

There was a significant correlation between the platelet count and K, MA, and α angle in pregnant women in the native group (coefficient/significance −0.31/<0.01, 0.24/<0.01, 0.33/<0.001, respectively). Furthermore, in the native group, the correlation between the platelet count and MA was stronger when the platelet count was <150,000/mm^3, n = 15 (r = 0.78, $P < 0.05$). A similar significant correlation between the platelet count and MA in pregnant women was also noted in the celite group (0.37/<0.05). Results of the coagulation profile for 30 pregnant women in the native group are as follows: (mean ± SD [range]) PT (s) = 11.1 ± 0.9 [9.4–12.4], aPTT (s) = 29.8 ± 3.1 [25.3–36.1], D-dimer (μg/mL) = 1.67 ± 0.84 [1–3], fibrinogen (mg/dL) = 416 ± 55 [340–527]. There was no correlation between TEG variables and results of the coagulation profile.

Discussion

TEG reflects the adequacy of whole blood coagulation within 30–40 minutes. The principle and interpretation of the TEG is well described in the literature (9,12). Individual TEG variables include r (reaction time), which indicates clotting factor activity; K (clotting time), MA (maximum amplitude), and α angle (clot formation rate), which indicate platelet and fibrinogen activity; and LY60 (reduction in maximum amplitude of the TEG tracing after 60 minutes), which measures fibrinolytic activity. In addition, the computerized TEG CI derived from *r*, K, MA, and α angle can be used to reflect all activities of clotting factors, platelets, and fibrinogen. Since it combines all the variables from a TEG a CI reflects the overall coagulability of blood (10,11). Normal values for CI in nonpregnant women for both native and celite-activated whole blood using disposable cups and pins range from -2 to $+2$ (10). Outside this range, a more positive value would reflect greater hypercoagulability, while a more negative value would reflect greater hypocoagulability. The elastic shear modulus (G) is related to MA and indicates clot strength in dyn/cm^2(9)

TEG is commonly used to assess hemostasis during liver transplantation and cardiac bypass surgery (1,2). It has also proven useful in diagnosing and treating coagulopathies in obstetrics. Landers et al. (3), during the management of severe coagulopathy in a pregnant patient, rapidly evaluated the patient's coagulation status and monitored the patient's response to goal-directed therapeutic interventions. Steer et al. (4) found TEG to be quick and cost effective in diagnosing and treating coagulation abnormalities in a patient with abruptio placentae and disseminated intravascular coagulation (4). To use TEG in pregnant women for such a purpose, reference values for TEG variables in healthy pregnant women need to be established. Steer (13) and Koh et al. (14) performed TEG in healthy pregnant women to determine values for TEG variables. However, in their investigations, their patient populations were very small, and they used metal cups and pins to perform TEG. The surfaces of metal cups and pins may become rough after repeated use and may result in the activation of coagulation during TEG, hence, affecting the results. Disposable plastic cups and pins are now available for use in TEG. In our study, using a sufficient patient population and disposable plastic cups and pins, we have determined values for TEG variables in normal pregnant women. In doing so, this investigation, like previous investigations (13,14), has shown that pregnancy is a hypercoagulable state, as reflected by shortened TEG values for *r* and K and increased TEG values for MA, G, α angle, and CI (Figure 2). These results support earlier findings that during pregnancy there is an increase in coagulation factors, a decrease in naturally occurring anticoagulants (15,16), and an increase in platelet reactivity (17). Furthermore, in our study, this hypercoagulability continued into the postpartum period for the first 24 hours. Further studies using TEG are warranted to assess whole blood coagulability beyond 24 hours postpartum to help determine the duration of hypercoagulability in postpartum women.

As an adjunct to native whole blood, celite, which accelerates the coagulation of whole blood, is now available for use as an activator in TEG. Celite consists of chemically inert particles (silica) that provide a contact surface to activate factor XII and platelets and, hence, accelerate coagulation in a blood sample. Celite-activated whole blood has been used in nonpregnant patients to accelerate the TEG tracing and allow for a more rapid assessment of coagulation (7,8). In our study, the use of celite-activated whole blood reduced the time for rK to develop by up to four-fold and increased the α angle by 73% in pregnant women. This reflects further acceleration of coagulation in blood from pregnant women. The use of celite-activated whole blood also increased the elastic shear modulus by 23% in pregnant women, which reflects the increased degree of platelet-fibrin interaction that occurs with celite activation of whole blood.

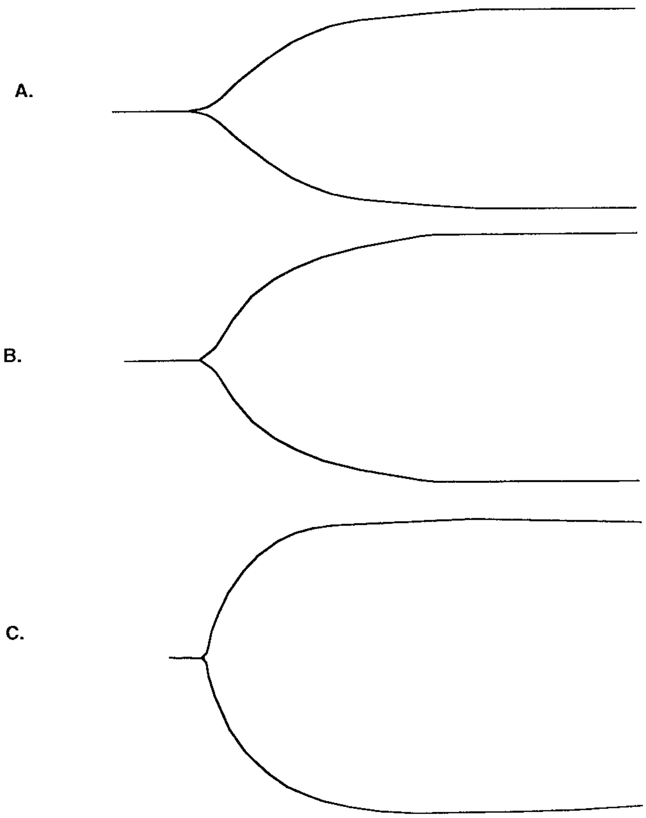

Figure 2. Examples of thromboelastograms (TEG) from nonpregnant and pregnant women. A, Nonpregnant woman, native whole blood TEG. B, Pregnant woman, native whole blood TEG: hypercoagulable (short *r* and K and increased α angle and MA). C, Pregnant woman, celite-activated TEG: acceleration of coagulation.

There was a weak but significant correlation between the platelet count and K, MA, and α angle in pregnant women using native whole blood. Furthermore, the correlation between the platelet count and MA was stronger when the platelet count was low. However, there was no correlation between TEG variables and the results of the coagulation profile. This lack of correlation can be explained by the fact that TEG variables are interrelated and reflect activities of clotting factors, platelets, fibrinogen, and their interaction (18), while coagulation profiles monitor an isolated portion of the coagulation cascade and do not reflect the interaction among clotting factors, platelets, and fibrinogen. Therefore, TEG provides a better assessment of whole blood coagulability than routine coagulation profile (19).

In conclusion, this study provides values for TEG variables for native and celite-activated whole blood for healthy parturients using disposable plastic cups and pins. This investigation, like previous investigations, shows that pregnancy is a hypercoaguable state. Furthermore, TEG also suggests that postpartum women remain hypercoagulable in the first 24 hours postdelivery. Finally, the use of celite to accelerate coagulation when performing TEG increases the speed of TEG assessment.

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