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The usefulness of celite-activated thromboelastography for evaluation of fibrinolysis

Purpose: Although thromboelastography is useful for measuring both coagulability and fibrinolysis, it takes about two hours to measure all parameters including fibrinolytic rate. The present study aimed to investigate the usefulness of celite-activated thromboelastography (TEGc) to evaluate fibrinolytic status in non-cardiac surgery.

Methods: Whole blood samples were obtained from 30 patients for non-cardiac surgery, and used for measurements of both native TEG (TEGn) and TEGc. The final concentration of 1% (w/v) celite was used for TEGc.

Results: Time for measurement of the fibrinolytic rate (FR) of TEGc in patients (56.7 ± 4.0 min) was less than half that of FR of TEGn (123.3 ± 15.6 min) ($P < 0.05$), suggesting a more rapid assessment of fibrinolytic status. A linear relationship was observed between FR values of TEGc and those of TEGn ($r = 0.93$, $P < 0.0001$), suggesting the usefulness of the fibrinolytic parameter of TEGc.

Conclusion: TEGc is a useful technique for a more rapid assessment of fibrinolytic status.

Objectif : Bien que la thromboélastographie soit utile pour mesurer la coagulabilité et la fibrinolyse, il faut environ deux heures pour mesurer tous les paramètres, y compris la vitesse fibrinolytique. L'étude actuelle avait pour but d'examiner l'utilité de la thromboélastographie activée par les diatomées (TEGd) pour évaluer l'état fibrinolytique lors d'une chirurgie non cardiaque.

Méthode : Des échantillons de sang total ont été prélevés chez 30 patients devant subir une chirurgie non cardiaque et utilisés pour les mesure de TEG non dénaturée (TEGn) et de TEGd. La concentration finale de 1% (p/v) de diatomées a été utilisée pour la TEGd.

Résultats : Le temps de mesure de la vitesse fibrinolytique (VF) de la TEGd chez les patients ($56,7 \pm 4,0$ min) représentait moins de la moitié du temps de la VF de la TEGn ($123,3 \pm 15,6$ min) ($P < 0,05$), ce qui indique une évaluation plus rapide de l'état fibrinolytique. Une relation linéaire a été observée entre les valeurs de VF de la TEGd et celles de la TEGn[®] ($r = 0.93$, $P < 0.0001$), suggérant ainsi l'utilité du paramètre fibrinolytique de la TEGd.

Conclusion : La TEGd est une technique utile pour obtenir plus rapidement l'évaluation de l'état fibrinolytique.

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Accepted for publication July 29, 1998.

IN cardiac surgery, thromboelastography (TEG) is a valid method of assessing fibrinolysis as well as coagulability.¹⁻³ However, it takes at least two hours to assess fibrinolysis by means of conventional TEG techniques. 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 a TEG activator to yield more rapid assessment of haemostasis.^{4,5} The present study aimed to investigate the usefulness of the celite-activated TEG (TEGc) technique to evaluate fibrinolysis in non-cardiac surgery.

Methods

After ethics committee approval and informed consent, 30 adult patients, scheduled for minor surgery were studied. Patients were excluded from the study if they had any abnormality of blood coagulability and/or had taken medications such as anticoagulants preoperatively. With the exception of small amounts of midazolam ($0.05 \text{ mg} \cdot \text{kg}^{-1}$), no other sedative/hypnotic premedication was given.

In the operating room, blood was collected from a peripheral vein via an 18-gauge needle using the two-

syringe technique. The first sample ($\sim 10 \text{ ml}$) was discarded to avoid tissue contamination of blood, and the second was used for TEG measurements. In the native TEG (TEGn) group ($n = 30$), $360 \mu\text{l}$ whole blood were pipetted into a prewarmed cuvette (37°C) of the computerized thromboelastograph (Thromboelastogram C-

A. Native TEG (TEGn)

B. Celite-activated TEG (TEGc)

FIGURE 1 Schematic diagrams of normal thromboelastography (TEG) tracings. Figures 1A and 1B represent native TEG (TEGn) and celite-activated TEG (TEGc) tracings, respectively. R; reaction time (time from sample placement in the cuvette until TEG tracing amplitude reaches 1 mm), K; clot formation time (time from R to the point where the amplitude of the tracing reaches 20 mm), MA; maximum amplitude (greatest amplitude on the TEG trace), LY60 (or LY30); amplitude of the tracing 60 (or 30) min after MA is achieved, and T_{LY60} (or T_{LY30}); time from sample placement in the cuvette until reaching LY60 or LY30.

A. Difference against mean for FR data

B. Regression relationship

FIGURE 2 Relationship between $FR_{(30)}$ values of TEGc and $FR_{(60)}$ values of TEGn obtained from 30 patients. A and B represent Bland & Altman analysis⁷ and regression analysis, respectively. Regression line for the relation between them is: $Y [FR_{(30)} \text{ of TEGc}] = 1.43X [FR_{(60)} \text{ of TEGn}] - 0.18$; $r = 0.93$ ($n = 30$, $P < 0.0001$). $FR_{(60)}$ or $FR_{(30)}$; fibrinolytic rate (MA-LY60 (or LY30))/MA00 (LY60 or LY30); amplitude 60 or 30 min after MA), TEGn; native TEG, TEGc; celite-activated TEG.

3000™, Haemoscope, Glenview, IL, USA). In the celite-activated TEG (TEGc) group ($n = 30$), 1.0 ml of the remaining blood was immediately placed in a vial containing 90 μ l of celite particles in normal saline (1.0% celite concentration), and then mixed by repeatedly inverting the vial, 360 μ l of this whole blood were pipetted into another prewarmed cuvette. Both samples were placed in the cuvettes within one minute of sampling, and mineral oil was spread over the blood surface to prevent evaporation of blood. Thromboelastography records the activity of whole blood coagulation, including cellular and humoral elements such as interactions of red blood cells, platelets, coagulation factors, and calcium.⁶ The TEG was allowed to run until reaching LY60 [mm, amplitude of the TEG tracing 60 min after maximum amplitude (MA)] in the TEGn group, and until reaching LY30 (amplitude 30 min after MA) in the TEGc group, respectively (Figure 1). For the TEGc measurements, LY30 was used instead of LY60 to assess fibrinolytic status more rapidly. The TEG variables included: R (reaction time, mm), K (clot formation time, mm), MA (mm), $FR_{(60)}$ or $FR_{(30)}$ [fibrinolytic rate, %; (MA-LY60 (or LY30))/MA00], and T_{LY60} or T_{LY30} (time from starting TEG measurements to reaching LY60 or LY30) (Figure 1).

All data are expressed in scatter diagrams or as means $\pm$ SD. The usefulness of the FR through the use of TEGc was assessed both by analysis of the variance of regression coefficients with TEGn and by Bland & Altman analysis.⁷ Comparisons for all other data were analyzed with paired, two-tailed *t* test. In all comparisons, $P < 0.05$ was considered significant.

Results

The TEG parameters obtained using TEGn and TEGc techniques are shown in the Table. Both R and K values of TEGc were shorter than those of TEGn by ~50% and ~53% respectively ($P < 0.05$). The MA of TEGc was larger than that of TEGn by ~19% ($P < 0.05$) and the $FR_{(30)}$ of TEGc ($9.1\% \pm 3.3\%$) was higher than $FR_{(60)}$ of TEGn ($6.5\% \pm 2.2\%$) by ~40% even when LY30 was used for the TEGc measurement

(Figure 2A): the ranges of this parameter were 4.7% to 18.3% and 2.9% to 11.4%, respectively. The $T_{LY(30)}$ of TEGc (56.7 ± 4.0 min) was less than half of $T_{LY(60)}$ of TEGn (123.3 ± 15.6 min) ($P < 0.05$) (Table). There was a linear relationship ($r = 0.93$, $n = 30$, $P < 0.0001$) between $FR_{(30)}$ values of TEGc and $FR_{(60)}$ values of TEGn as shown in Figure 2.

Discussion

Celite-activated TEG (TEGc) technique reduced the time taken for measurements of TEG parameters and the fibrinolytic rate (FR) measured by the use of TEGc was as reliable as that measured using native TEG (TEGn) (Table, Figure 2). Celite consists of chemically inert particles (silica) that provide a contact surface to activate a coagulation factor XII and platelets and, hence, accelerate coagulation in a blood sample. In our study, R and K values of TEGc reduced by ~50% and ~53% respectively, compared with those of TEGn. The MA of TEGc increased by ~19% compared with that of TEGn; this increase could be due to the celite activity on the platelets. Turnage⁸ and McCarthy *et al.*⁴ have investigated the usefulness of TEGc in volunteers and in pregnant patients and also found that TEGc accelerated the TEG tracing and allowed for a more rapid assessment of coagulation.

No other detailed study has been reported on fibrinolytic status by the use of TEGc. For a more rapid assessment of fibrinolytic status, we used LY30 instead of LY60 for the measurement of FR. We found a sufficient linear correlation between $FR_{(30)}$ of TEGc and $FR_{(60)}$ of TEGn ($r = 0.93$, Figure 2) and succeeded in shortening the time for assessment of fibrinolytic status to within one hour (Table). Therefore, this technique would be useful for surgical patients who have possible fibrinolytic abnormalities such as those undergoing liver transplantation^{9,10} or cardiac surgery with cardiopulmonary bypass.^{1,2} The $FR_{(30)}$ of TEGc ($9.1\% \pm 3.3\%$) was higher than $FR_{(60)}$ of TEGn ($6.5\% \pm 2.2\%$) by ~40% even when LY30 was used for the TEGc measurement instead of LY60; this increase might be due to the indirectly accelerated action of

TABLE TEG parameters obtained from TEGn and TEGc techniques. Data are mean $\pm$ SD (with normal ranges). R; reaction time, K; clot formation time, MA; maximum amplitude, $FR_{(60)}$ or $FR_{(30)}$; fibrinolytic rate (MA-LY60 (or LY30))/MA.100 (LY60 or LY30; amplitude 60 or 30 min after MA), T_{LY60} or T_{LY30} ; time from starting TEG measurements until LY60 or LY30, TEGn; native TEG, TEGc; celite-activated TEG. * denotes difference from values of TEGn by paired *t* test.

Technique	R (mm)	K (mm)	MA (mm)	$FR_{(60)}$ or $FR_{(30)}$ (%)	$T_{LY(60)}$ or $T_{LY(30)}$ (min)
TEGn ($n = 30$)	24.8 $\pm$ 3.4 (19 - 28)	9.2 $\pm$ 2.1 (8 - 13)	54.3 $\pm$ 7.2 (48 - 60)	6.5 $\pm$ 2.2 (< 10)	123.3 $\pm$ 15.6
TEGc ($n = 30$)	12.4 $\pm$ 1.6* (10 - 14)	4.3 $\pm$ 1.1* (3 - 6)	64.6 $\pm$ 7.5* (59 - 68)	9.1 $\pm$ 3.3* (4.7 - 18.3)	56.7 $\pm$ 4.0* (2.9 - 11.4)

celite on fibrinolytic cascade. We presume, therefore, that the normal range of $FR_{(30)}$ of TEGc is less than ~15% (Figure 2).

For more rapid assessment of coagulation for TEG, Turnage⁸ and McCarthy and colleagues⁴ tried to use the other specific activators of coagulation system platelet factor 3 and recombinant human tissue factor thromboplastin, respectively. They found that these agents might be useful activators of TEG coagulation analysis to shorten and reduce the variability of onset time and permit the earlier assessment of clot strength and integrity. However, the effect of these agents on fibrinolytic status has not been investigated, and further studies are needed to clarify the reliability of TEG fibrinolytic analysis through the use of these agents.

In conclusion, celite-activated TEG is a useful technique for a more rapid assessment of haemostasis including fibrinolytic status.

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