



Celite-Activated Thrombelastography in Children

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Study Objective: To quantify global coagulation and establish normal ranges for the celite-activated thrombelastograph^R (TEG) in healthy pediatric patients.

Design: Prospective observational study.

Setting: Operating suite of a university-based hospital.

Patients: 110 healthy pediatric patients in four age groups and 25 healthy adult patients.

Interventions: Blood sampling for the celite-activated TEG was carried out after anesthetic induction.

Measurements: TEG indices: R time (reflecting time to fibrin formation), K time and alpha angle (fibrinogen-platelet interaction), maximum amplitude (reflecting maximal clot strength, platelet and fibrinogen function), TEG index (mathematical incorporation of the prior four measurements), and percent fibrinolysis at 30 minutes, were all recorded.

Main Results: Statistically significant differences between <12-month group in angle (compared to 25–48 month group) and % fibrinolysis (compared to all other pediatric groups). Significant differences in angle between two pediatric groups and adult group, and in the TEG index between three pediatric groups and adult group (all differences $p < 0.05$).

Conclusions: These data identify changes of small magnitude in three celite-TEG parameters in healthy children compared to adults, without implication of abnormal coagulation between groups. Changes do not seem to be consistently related to age and will be useful for clinicians using the TEG to monitor (ab) normal coagulation in pediatric patients. © 2001 by Elsevier Science Inc.

Keywords: Celite; children; Thrombelastograph^R.

Introduction

The thrombelastograph^R (TEG) is used as a functional measure of whole blood coagulation in pediatric cardiac surgical¹ and liver transplant patients,² and is a useful monitor in patients with major trauma and with coagulation deficits. To date, only one study has evaluated functional maturity of the coagulation system

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Thrombelastograph^R disposables were supplied by Haemoscope Corp., Skokie, IL

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in healthy surgical patients <2 years of age.³ Current use of celite-activated blood for TEG interpretation has superseded the native blood samples as used in Miller *et al.*'s³ study. Our aim was to assess global coagulation and establish normal ranges for the celite-activated TEG in healthy pediatric surgical patients, and to incorporate TEG data of children older than two years.

Materials and Methods

After University of Texas Medical School at Houston institutional approval and informed parental consent, healthy children presenting for superficial or minor surgery were enrolled in the study. Children with known bleeding abnormalities or receiving drugs, including non-steroidal antiinflammatory drugs (NSAIDs), which may have impaired coagulation were excluded from the study. After inhalational induction, 1 mL of blood was withdrawn after intravenous (IV) catheter placement with the first 1 mL being discarded either by passive drainage or with a two-syringe technique. If excessive force was required to withdraw blood from small veins or through small catheters, the sample was excluded from the study.

The 1-mL sample was immediately added to a 1% celite tube (Haemoscope Corp., Skokie, IL), inverted, allowed to incubate for two minutes, and then 0.36 mL was withdrawn for analysis in a standard manner. The TEG (Haemoscope Corp., Skokie, IL) underwent daily quality control testing for the duration of the study, and samples were analyzed by the same two individuals. TEG measurements included: 1) the R time (time to initial fibrin formation [mm]), 2) K time [mm], and 3) alpha angle [degrees] (both reflecting fibrinogen-platelet interaction), 4) maximum amplitude (MA—assessment of qualitative platelet function, with a smaller contribution from fibrinogen-[mm]), 5) index (dimensionless incorporation of the 4 preceding variables), and 6) percent fibrinolysis at 30 minutes. Standard parameters are indicated in *Figure 1*.

Patients were divided into four groups: ≤12 months, 13 to 24 months, 25 to 48 months, and 49 months to 9 years, and were compared with each other and an adult group of healthy patients presenting for surgery without coagulation abnormalities.

With native blood, variations in TEG parameters of ±25% were found among the pediatric groups.³ For this study, power analysis to detect similar differences with an alpha of 0.05 and a beta of 0.1 predicted a minimum sample size of 22 to 24 in each group for the various parameters. Groups were compared with analysis of variance and subsequent two-sided *t*-test if significance was found. Significance was assumed with a *p*-value < 0.05.

Results

One hundred ten children were enrolled: ≤12 months (25 children), 13–24 months (33 children), 25–48 months (24 children), and 49 months–9 years (29 children). The mean age of the adult group (25) was 45.5 ± 8.7 years.

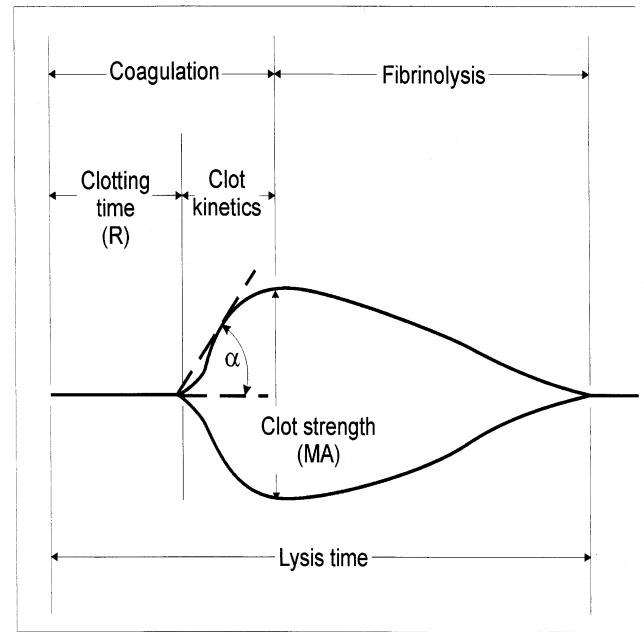


Figure 1. Standard TEG trace and measured parameters. MA = maximum amplitude (mm). Fibrinolysis measured as: 100% - MA (30 min)/MA (maximum). K time = time from end of R time to 20 mm separation of trace (not shown on graph to ensure clarity of existing parameters). Index = mathematical incorporation of R time, K time, angle and MA (not shown).

There were no differences in type of surgery among pediatric groups, with the commonest procedures being myringotomy (31%), tonsillectomy ± adenoidectomy (21%), strabismus surgery (16%), urological (circumcision and hypospadias repair—15%), minor surgical, orthopedic, or plastic surgical procedures (17%). As anticipated in healthy children, only 13 patients had preoperative hematocrit, prothrombin time, partial thromboplastin time, or platelet count performed: these limited data precluded statistical analysis among groups, and all values were within the normal range.

TEG data are presented in *Table 1*. There were no significant differences in R and K times or MA. Statistically significant differences were present in the *angle* between the <12-month group and the 25–48 month group, and between the <12-month and 12–24 month groups compared to the adult group (*p* < 0.05). The *index* was greater in the <12-month, 13–24 month, and 48 month–9-year groups compared to the adult and 25–48-month groups (*p* < 0.05). *Percent fibrinolysis* was greater in the <12-month group compared to all other groups (*p* < 0.05). However, all differences found were of small magnitude with no clinical implication of abnormal coagulation.

Discussion

Use of the TEG in the pediatric population has been described in cardiac surgery¹ and liver transplantation²

Table 1. Celite-activated Thrombelastographic (TEG) values (means \pm SD)

	I. ≤ 12 months	II. 13–24 months	III. 25–48 months	IV. 49 months–9 years	V. Adult
R (mm)	10.1 \pm 3.1	9.8 \pm 3.3	10.5 \pm 3.0	9.6 \pm 2.5	11.1 \pm 3.0
K (mm)	2.4 \pm 0.5	2.5 \pm 0.6	2.7 \pm 0.7	2.8 \pm 0.6	2.7 \pm 0.6
Angle (degrees)	74.2 \pm 3.5* [†]	73.2 \pm 3.1 [†]	71.2 \pm 4.2	72.9 \pm 4.2	70.7 \pm 3.9
MA (mm)	70.2 \pm 6.1	70.2 \pm 4.7	68.4 \pm 5.2	70.5 \pm 3.3	70.2 \pm 3.7
Index	2.7 \pm 1.6 [‡]	2.6 \pm 1.5 [‡]	1.9 \pm 1.5	2.7 \pm 1.3 [‡]	1.8 \pm 1.7
Fibrinolysis (%)	3.4 \pm 2.9 [§]	2.1 \pm 1.3	2.1 \pm 1.4	2.0 \pm 1.1	1.8 \pm 1.12

R = time to fibrin formation, K = time from end of R to 20 mm separation of trace, MA = maximum amplitude, Index = mathematical incorporation of R time, K time, angle, and MA.

*p < 0.05 vs group III and V.

[†]p < 0.05 vs group V.

[‡]p < 0.05 vs group V.

[§]p < 0.01 vs all other groups.

and TEG abnormalities described in children with cancer⁴ and malnutrition.⁵ Only three studies to date have investigated TEG parameters in normal children: an early study using citrated blood,⁶ a comprehensive investigation in children less than 2 years of age using native blood³ and a study using cord blood in neonates.⁷ Podolsak *et al.*,⁶ found no statistically significant differences in children aged 2 through 14 compared to adults, and Miller *et al.*,³ confirmed functional integrity of the hemostatic system in children aged less than 2 years, with the nonsignificant tendency toward hypercoagulability in children less than 6 months of age compared to adults. In an inhomogeneous neonatal population, Suzuki⁷ found shorter R and K times and increased MA in samples taken from the umbilical vein after cord clamping, compared to adults. All these studies used native blood without celite activation.

Current use of celite-activated blood samples for TEG analysis have supplanted native blood because the accelerated TEG parameters allow for rapid clinical evaluation and support more robust statistical analysis with narrower data ranges. Use of celite-activated samples also has been validated in adults undergoing cardiac surgery,⁸ in parturients⁹ and in other surgical patients.¹⁰

Our data demonstrated statistically significant differences in the angle, index, and percent fibrinolysis among some of the pediatric groups and the adult group. These changes were not consistent for any particular age group, although the nonsignificant trend toward an increased angle and index in the < 12 month group suggests increased global coagulation. This finding supports Miller *et al.*'s³ findings of a nonsignificant trend toward increased coagulation in a neonatal group compared to children up to two years of age. As both our study and Miller *et al.*'s were adequately powered, it is unlikely that further patient enrollment would have encouraged statistical significance in age-related changes.

As with any clinical investigation, statistically significant findings may not imply clinical significance. The narrow standard deviation of our celite-data facilitated statistical analysis, especially with the angle, and all of the data followed a normal distribution. This finding suggests that small changes in TEG parameters may not signify major

clinical hypercoagulability, as has been previously demonstrated in children with cancer.⁴

Potential mechanical factors, which may have influenced results, were avoided with meticulous technique to ameliorate thromboplastin-mediated activation of coagulation with traumatic aspiration of blood samples. Since our patients were undergoing minor surgical procedures, invasive catheters, which would have facilitated phlebotomy, were not placed.

This investigation of celite-activated TEG parameters in healthy children supports similar findings with native blood. In the absence of available celite-TEG normal ranges for children, our data are useful to clinicians using the TEG in pediatric patients, enabling management of TEG abnormalities based on known pediatric parameters, rather than extrapolation from marginally different adult data.

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References

- Martin P, Horkay F, Rajah SM, Walker DR: Monitoring of coagulation status using thrombelastography during pediatric open-heart surgery. *Int J Clin Monitor Comput* 1991;8:183–7.
- Kang Y, Borland LM, Picone J, Martin LK: Intraoperative coagulation changes in children undergoing liver transplantation. *Anesthesiology* 1989;71:44–7.
- Miller BE, Bailey JM, Mancuso TJ, et al.: Functional maturity of the coagulation system in children: an evaluation using thrombelastography. *Anesth Analg* 1997;84:745–8.
- Hathaway WE, Hays T: Hypercoagulability in childhood cancer. *J Ped Surg* 1975;10:893–9.
- Jain K, Singh SD, Mukerjee DP: Observations on thromboelastographic patterns and coagulation changes in malnutrition (Marasmus and kwashiorkor). *Indian Pediatr* 1979;16:1115–9.
- Podolsak B, Mingers A-M, Oller J: Thrombocyte functions, thrombelastograms and fibrinogen of healthy children in different age groups. *Eur J Pediatr* 1977;127:27–39.

7. Suzuki S: Blood coagulation and fibrinolysis of the newborn viewed as perinatal factors. *J Perinat Med* 1977;6:274–83.
 8. Shore-Lesserson L, Manspeizer HE, DePerio M, Francis S, Vela-Cantos F, Ergin MA: Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. *Anesth Analg* 1999;88:312–9.
 9. Sharma SK, Philip J, Wiley J: Thromboelastographic changes in healthy parturients and postpartum women. *Anesth Analg* 1997; 85:94–8.
 10. Pivalizza EG, Pivalizza PJ, Weavind LM: Perioperative thromboelastography and sonoclot analysis in morbidly obese patients. *Can J Anaesth* 1997;44:942–5.
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Functional Maturity of the Coagulation System in Children: an Evaluation Using Thrombelastography

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There are quantitative deficiencies in the coagulation system for at least the first 6 months of life. Clinical experience, however, does not indicate an increased risk of excessive bleeding during surgical procedures. Thrombelastography, a test providing a functional evaluation of coagulation, was used to assess the hemostatic system of pediatric patients under 2 years of age. Thrombelastographic data were obtained from 237 healthy pediatric patients less than 2 years of age undergoing elective noncardiac surgery. Five groups were distinguished: under 30 days, 1–3 mo, 3–6 mo, 6–12 mo, and 12–24 mo. Thrombelastography revealed no defects in coagulation when these groups were compared to each other or to adults, indicating a functionally intact hemostatic process, even in neonates. Indeed, children less than 12 mo of age were found to initiate and develop clot faster than adults, with the coagulation process slowing to adult rates after 1 yr of age. In addition to defining functional integrity, our data represents a set of pediatric control thrombelastographic values that have not been previously reported and that may become important in understanding coagulation changes that accompany disease states and surgery in pediatric patients.

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