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Evaluation of TEG® and RoTEM® inter-changeability in trauma patients

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ABSTRACT

Background: Massive haemorrhage is a leading cause of preventable deaths in trauma. Traumatic coagulopathy is frequently present early after trauma, and is associated with increased mortality. A number of recent trials suggest that viscoelastic haemostatic assays (VHA), such as thromboelastography and thromboelastometry, are useful tools in guiding transfusion. Treatment algorithms exist for the use of VHAs but are not validated in traumatic haemorrhage. In this study we examined the inter-changeability of two commonly used VHAs, TEG® and RoTEM®.

Methods: A total of 184 trauma patients over the age of 18, requiring full trauma team activation, were included at three different hospitals in three different countries (Copenhagen, Denmark, San Francisco, CA, USA and Oslo, Norway). Blood samples were drawn immediately upon arrival, and TEG® and RoTEM® analyzed simultaneously. Correlations were calculated using.

Spearman's rank correlation coefficient. Agreement was evaluated by Bland–Altman plots and calculation of limits of agreement.

Results: The mean ISS in the total population was 17, and the mortality was 16.5%. Mean base excess was −2.8 (SD: 4.2). The correlation coefficient for corresponding values for the two devices was 0.24 for the *R*-time vs CT in all centres combined. For the *K*-time vs CFT the correlation was 0.48, for the α-angle$_{TEG}$ vs α-angle$_{RoTEM}$ 0.44, and for MA vs MCF 0.76. Limits of agreement exceeded the preset clinically acceptable deviation of 10% for all variables in all centres except for MA/MCF in one centre (Copenhagen). Generally, correlation coefficients were lower and agreement poorer in the one centre (Oslo) where measurements were performed bedside by clinicians.

Conclusion: Inter-changeability between TEG® and RoTEM® is limited in the trauma setting. Agreement seems poorer when clinicians operate the devices. Development and validation of separate treatment algorithms for the two devices is required.

Introduction

Massive haemorrhage accounts for up to 40% of trauma-related deaths in patients reaching hospital, and is considered to be the leading cause of preventable deaths.[1,2] Traumatic coagulopathy is detectable in 25–34% of patients on admission, and is highly predictive of poor outcome.[3,4] A number of recent studies suggest that viscoelastic haemostatic assays (VHAs), such as thromboelastography and thromboelastometry, are useful tools in guiding transfusions and pharmacological coagulation support in trauma patients.[5–9]

The principle behind VHAs is based on the tendency of blood to increase its viscosity and elasticity through the process of coagulation. The clot that eventually forms subsequently dissolves during fibrinolysis. The clot changes over time are visualized as an

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evolving trace where the time to initiation of clot formation, the rate of clot formation and the maximum strength of the clot are among the most commonly utilized variables.[5]

VHA has advantages over conventional plasma based coagulations tests in some aspects. The overall coagulation picture expressed by VHA may be more clinically relevant than conventional assays, as it reflects the coagulation process in whole blood, rather than in fragments of the coagulation system.[5,10] In addition, VHAs may be performed bedside, as point-of-care (PoC) measurements, reducing the time delay associated with conventional laboratory assays.

Two frequently used VHA devices are TEG® and RoTEM®. Both are marketed as PoC devices that give reliable and comparable results when operated in near patient environment by clinicians. However, they differ markedly in terms of function and user interface, and it is not clear whether this affects their performance in a clinical setting.[11]

Only a few studies have previously compared the inter-changeability of TEG® and RoTEM®.[12–14] They conclude that the assays to a certain extent may be inter-changeable. However, these studies have exclusively been performed within cardiac surgery and liver transplantation procedures, and not in a trauma population. There are indications that the mechanisms behind coagulopathy in trauma differ significantly from coagulopathy in other massive bleeding scenarios.[15,16] This may have implications for VHA, and consequently the inter-changeability of TEG® and RoTEM®. To the best our knowledge, no comparison between the two methods has been performed in a trauma patient population.

The aim of the current study was to compare the results of the initial TEG® and RoTEM® analyses in a cohort of trauma patients, and to assess the inter-changeability of the two devices.

Methods

Study design and patient selection

We performed a multi-centre observational study in three major trauma centres; San Francisco General Hospital, CA, USA; Rigshospitalet, Copenhagen, Denmark; Oslo University Hospital, Ullevål, Norway.

In San Francisco General Hospital and Rigshospitalet, the samples were transported to a laboratory facility and analyzed by laboratory-trained personnel. In Oslo University Hospital the tests were run as PoC measurements by a group of trained clinicians.

Patients more than 18 years old and who required full trauma team activation were eligible. Patients were excluded if the time from injury to admission was more than 2 h, if they had received more than 2000 ml of fluids pre-hospitally, if they were pregnant, had known liver failure or bleeding disorders, or were on anticoagulant medications other than acetyl salicylic acid. Data describing demographics, injury severity, admission physiology and outcome were retrieved from the institutional trauma registries. Ethics approval was obtained in accordance with local regulations for each centre.

Sampling and VHA methodology

In accordance with previously published studies, we chose the TEG® 5000 Hemostasis Analyzer System (Haemonetics Corp., MA, USA) with kaolin as an activator, and RoTEM® (Tem International GmbH, Munich, Germany) with tissue factor as the activating agent (ExTEM®). Blood was collected from patients upon arrival in the trauma room in a citrated tube, by puncture of the femoral or radial artery. For TEG®, 1000 μl of blood was pipetted and blended in the kaolin containing test tube. After 1 min 340 μl was extracted with a manually operated pipette, and deposited in the designated plastic cup with 20 μl of $CaCl_2$. The cup was then elevated into test position, and the measurements initiated within 20 s.

For RoTEM®, the automated pipette was used to extract 20 μl of $CaCl_2$ (StarTEM® reagent). An air cushion was applied in the tip before extraction of 20 μl of the ExTEM® reagent, and finally mixing with 300 μl of blood in the cup and measurement initiated within 30 s. The TEG® and RoTEM® assays were run simultaneously in all three centres, and with the temperature set at 37.0 °C.

We compared four widely used variables from the VHA trace: the reaction time from initiation of the assay to the first detectable coagulation, denoted *R*-time for TEG® and clotting time (CT) for RoTEM®; the time from start of coagulation to clot amplitude of 20 mm, called the *K*-time in TEG® and clot formation time (CFT) in RoTEM®; the angle by which the clot strength increases, called the α-angle for both devices; lastly, the maximum amplitude (MA) for TEG®, which corresponds to the maximum clot firmness (MCF) for the RoTEM® device.

Statistical analysis

Data are presented as mean and standard deviation (SD) or number (%) unless stated otherwise. For comparison of baseline data between the three centres, one-way ANOVA was used for continuous variables, and Chi Square-test for categorical variables. Injury severity score (ISS) was regarded as a continuous variable.

Correlation between TEG® and RoTEM® measurements was calculated using Spearman non-parametric correlation. For evaluation of agreement between TEG® and ROTEM® measurements, we applied Bland–Altman difference-mean plot, i.e. a plot of the methods differences of measurements (D) against the corresponding average (A), and estimation of corresponding limits of agreement (LoA), calculated as ± 1.96 SD from the mean difference of measurements.[17]

As TEG® and ROTEM® are technically different measurements of the same concept, a significant linear relationship in the Bland–Altman plot was expected. A log transformation is often recommended[17] but was unsuccessful in compensating for this relationship in our data. Instead, a generalized version of LoA using linear regression, as suggested in a revised version of the Bland–Altman methodology,[18] was used. In the Bland–Altman plots where there was a significant non-zero linear association between D and A, the linear relationship $D = aA + b$ was estimated using univariate linear regression, the estimated linear association extracted from each of the actual differences D, and subsequently calculating the SD and corresponding LoA on these transformed data $D^* = D - (aA + b)$.

A predefined set of clinically acceptable LoA was established based on clinical experience and previous publications.[12] These limits were based on the assumption that $a \pm 10\%$ deviation in corresponding variables is acceptable for mean values. Clinically acceptable LoA by these conditions were ±20.8 s for *R*/CT, ±10.9 s for *K*/CFT, 6.7° for the α-angle and 6.2 mm for the MA/MCF.

A p-value <0.05 was considered statistically significant. All calculations were made using SPSS 19.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 184 patients were included in the study. Patient characteristics are shown in Table 1. No statistically significant differences between centres were found except for ISS, which was significantly higher in the San Francisco population compared to both Oslo and Copenhagen ($p = 0.031$).

Scatter plots of the corresponding TEG® and RoTEM® values for the four predefined variables are shown in Fig. 1, and corresponding