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Original Article

Comparison of Two Techniques of Measuring Activated Clotting Time During Cardiac Surgery

Waqas Alam, Syed Aqeel Hussain, Muhammad Ali, Muhammad Adnan Akram, Muhammad Umar Farooq, Rehan Masroor, Hafsa Khalil, Ayesha Sana

Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD)/National University of Medical Sciences (NUMS) Rawalpindi, Pakistan

ABSTRACT

Objective: To compare two techniques of activated clotting time (ACT) measurement by two different devices to evaluate the correlation and agreement between these techniques at different points of time during cardiac surgery.

Study Design: Comparative Cross-sectional Study.

Study settings: Cardiac Anesthesia Department, Armed Forces Institute of Cardiology and National Institute of Heart Diseases, Rawalpindi Pakistan, from Feb 2022 to Apr 2022.

Methodology: Hundred patients undergoing CABG surgery on pump were included by non-probability consecutive sampling technique. Two devices operating on different techniques of measurement were used to measure ACT at four different points of time during surgery. Same sample was used to measure ACT from both devices. Data was collected and analysed by SPSS V.20.0. Pearson's chi square test and paired sample t-test were applied to measure the significance. Linear regression analysis was done to find correlation and Bland Altman plot was used for checking agreement between ACT values from both devices. *p*-value less than 0.05 was considered significant.

Results: Out of 100, male patients were 79 and female patients were 21. Their mean age was 54.18±11.91 years and mean weight was 79.06±18.49 kg. Moderate positive correlation was found with Pearson r value of 0.55. There was poor agreement between the ACTs measured by two devices. On average Hem R measures ACT 63.54±50.83 seconds higher than Hem JSP. Average mean and median values for Hem R group are 400.03±59.39 sec and 397.75sec respectively and for Hem JSP group are 336.49±44.63 sec and 340.5 sec respectively.

Conclusion: There is moderate positive correlation but poor agreement between the values of ACT measured by Hem R and Hem JSP due to different techniques of measurement so these should not be used interchangeably.

Keywords: Activated clotting time, CABG, Cardiac surgery, Hemochron, Heparin.

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INTRODUCTION

It is an estimation that around the globe more than 2 million cardiac surgeries are being performed every year.[1] Systemic anticoagulation has prime importance in the safe conduct of these surgeries both on-pump and off-pump. Inadequate anticoagulation can result in thrombo-embolism with fatal consequences. So far unfractionated heparin is the most trusted anticoagulant and protamine is used to reverse its effects. There is no consensus on the dosage of heparin. 300 IU/kg to 500 IU/kg heparin is being administered in different institutions.[2] Activated Clotting Time (ACT), a whole blood test, is used to monitor the level of anticoagulation and it is in practice since 1970.[3] It is measured in seconds and its normal range is from 70 to 120 seconds. This test is simple, inexpensive and easy to perform for which no specialized laboratory persons are required.[4] In this test a catalyst activates the intrinsic pathway when blood is exposed to it and time is measured in seconds till blood clots. ACT is a bedside test used not only in cardiac surgery theatres but also in, extracorporeal units, cardiac catheterization labs and intensive care units.[5]

Most ACT devices are cartridge-based and use activators like kaolin, celite, silica, or mixtures. The discrepancies of results exist among these devices due to differences in technology. Several studies have shown that significant variability exists among measured values and these devices cannot be used interchangeably.[6] It is recommended that devices should be validated against each other before shifting from one device to another in clinical practice.[7] The same device should be used throughout the procedure to avoid over or under correction of ACT by protamine.[8]

In our institution Hemochron® Response (Hem R) has been used to measure ACT. Recently Hemochron® Jr Signature Plus (Hem JSP) has been introduced which requires a very small amount of blood and takes less time to measure ACT compared to Hem R. Both devices have different techniques for mea-

Correspondence: Dr Waqas Alam, Department of Cardiac Anaesthesia, Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi, Pakistan

suring ACT. Hem R uses Celite in a glass tube while Hem JSP calculates ACT by detecting movement of blood in a cuvette. Aim of this study is to compare these two techniques by parallel measurement of ACT from same sample to evaluate correlation and agreement between these techniques.

METHODOLOGY

This Comparative Cross-sectional Study was conducted at Cardiac Anesthesia Department, Armed Forces Institute of Cardiology and National Institute of Heart Diseases, Rawalpindi Pakistan, from February 2022 to April 2022.

Sample Size: Calculated sample size was 34 as mentioned in reference article by taking 95% CI and 5% margin of error, but we included 100 patients[9].

Inclusion Criteria: Adult patients undergoing CABG surgery on-pump were included in the study.

Exclusion Criteria: Patients with coagulation disorders, Off pump CABG surgeries, valve cases, and those patients who did not stop anticoagulation and antiplatelet medication before surgery were excluded.

After institutional ethical review board (IERB# 9/2/R&D/2022/168) approval and consent from patients, 100 cardiac patients undergoing Coronary Artery Bypass Grafting (CABG) surgery were included in the study by non-probability Consecutive Sampling technique. Four ACT samples were drawn from the arterial line at set points during CABG surgery. After induction of anesthesia and central venous line insertion in operation theatre a baseline sample of ACT was drawn. Then the second sample was taken three minutes after administration of 300IU/kg of unfractionated heparin. Third sample half-hour after heparin administration and the last sample ten minutes after protamine administration. Each sample was used to measure ACT from both HEM R and HEM JSP devices. However, ACT value from HEM R was used for any intervention such as additional heparin or protamine administration to achieve target ACT.

Demographic data of patients, heparin dose and ACT values were recorded on a form prepared for data collection. Anonymity of patients was maintained by special identification numbers placed on the forms. All the data was analyzed by SPSS v 20.0. Categorical variables were presented as frequencies (percent) while continuous variables were presented as mean±SD. Pearson's chi square test and paired sample t-test were applied to measure the significance. Linear regression analysis was done to find correlation and Bland Altman plot was used for checking agreement. *p*-value less than 0.05 was considered significant.

RESULTS

Total 100 adult patients undergoing on pump CABG surgery were included in the study. Male patients were 79% and female patients were 21%. Their mean age was 54.18±11.91 years and mean weight was 79.06±18.49 kg. Mean dose of heparin administered was 25720±5844.93 units. Comparison of mean ACT values measured by two devices at different time intervals is shown in Table-I. There is significant difference in mean ACT values by both devices except at baseline values.

Table-I: Mean ACT Values Measured by two Devices

Time	HEM R(sec)	HEM JSP(sec)	*p*-value
Baseline	125.34+36.37	120.92+19.13	0.173
3 min after Heparin	662.27+161.78	564.64+114.95	<0.001
30 min after Heparin	656.62+169.31	520.11+128.24	<0.001
10 min after Protamine	155.89+59.86	140.29+42.68	<0.001

Linear regression analysis showed a moderate positive correlation between Hem R and Hem JSP ACT values. Pearson r value was 0.55. Figure-1 shows overall correlation between ACT values from both the devices.

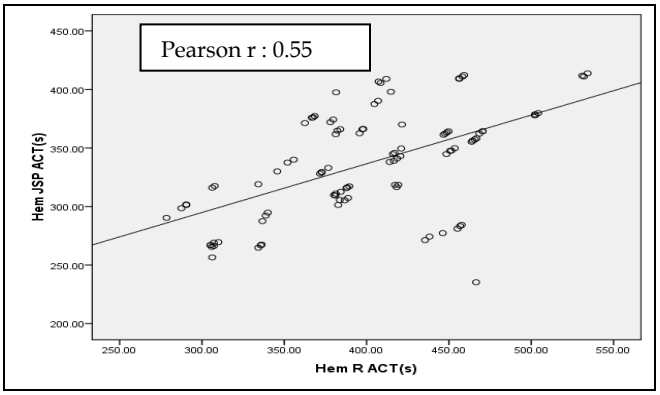

Figure-1: Linear corelation between HEM R and HEM JSP

Figure-2 shows Bland Altman plot showing overall difference between values from Hem R and Hem JSP, plotted against the mean ACT values of both devices. This graphical representation shows poor agreement between the ACTs measured by two devices. Mean difference is 63.54±50.83 seconds which depicts that across the totals of paired measurements, on average Hem R measures ACT 63.54±50.83 seconds higher than Hem JSP.

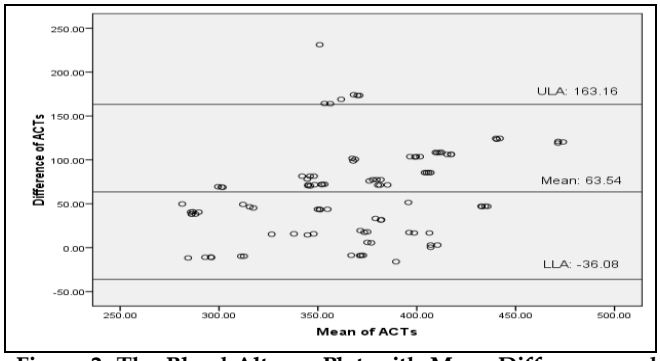

Figure-2: The Bland-Altman Plot with Mean Difference and Upper and Lower Limits of Agreement

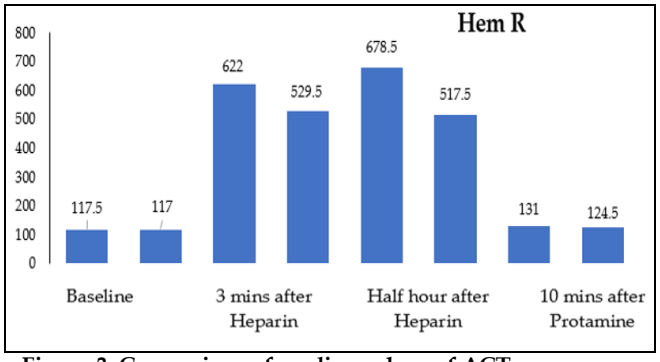

Figure-3: Comparison of median values of ACT

Similarly, linear regression analysis also showed that no agreement exist between two devices. *p*-value for regression coefficient was 0.001. In general ACT values measured by Hem R were higher than Hem JSP as shown by the mean values in Table-I and median values in Figure-III. At baseline median values from both devices are almost similar like mean values at baseline. Average mean and median values for Hem R group are 400.03±59.39 sec and 397.75sec respectively and for Hem JSP group are 336.49±44.63sec and 340.5sec respectively.

DISCUSSION

Devices used in this study measure ACT by different techniques. Hem R device uses 2.0 ml of whole blood in a glass tube containing celite to measure ACT. A precision aligned magnet is within test tube and a magnetic detector is present in machine. Tube slowly rotates in the machine and magnetic detector senses the magnet in tube. When clot starts to form, it displaces the magnet which is no longer sensed by the detector and coagulation time is displayed by the machine.[10] While Hem JSP device uses a disposable cuvette in which about 0.2 ml of blood is used. It has two channels, one for testing sample and other for excess blood. Blood in testing channel is moved forward and backward. Two LED detectors are aligned to measure ACT by detecting decrease in movement of blood due to clot formation.[11] Hem JSP not only uses small amount of blood but also gives result in lesser time than Hem R.

We found that ACTs measured by both techniques had moderate positive correlation with Pearson r value of 0.55. But there was poor agreement between these techniques. Matte *et al.* also found similar results with Pearson r of 0.6 to 0.4 and that there was significant difference between ACT values measured by these techniques.[12] They found that an ACT of 480 by celite tube correlates with ACT of 410-440 by cuvette device. Similarly, we found that celite tube device measures ACT 63.54±50.83 seconds higher than cuvette device. Thenappan *et al.* also found significant correlation with r of 0.84 and 8% to 20% disagreement between the values of two devices. They argued that these devices should not be used interchangeably.[13].

Lee *et al.* found good positive correlation with r of 0.956 and mean difference of 34.43 seconds between cartridge based and cuvette based devices.[14] Similarly, Svenmarker *et al.* compared the ACT using the HemoTec and Hemochron Jr. during CPB and found the correlation with r of 0.526 but a difference of 100 sec.[15] Dirkmann *et al.* compared four devices for measurement of ACT and found that devices with similar mechanism of measurement have good correlation and agreement but devices with different mechanisms of ACT measurement showed moderate correlation but poor agreement.[16]

Other studies also compared devices with different mechanisms for measurement of ACT and found significant difference between results. They concluded that results of devices with different mecha-nisms should not be used interchangeably.[17-19] These study agree with our findings that devices having different mechanisms of measurement show difference in results. These results should not be used interchangeably and same device should be used before and after heparin administration and till the correction of ACT by protamine.

Otherwise under or overdosing of heparin or protamine can occur. Another recent study showed similar results and concluded that the variability of different devices for measurement of ACT should be known and taken into account during clinical practice.[20]

LIMITATIONS OF STUDY

Limitation of our study was that ACT was measured only during CABG surgery with CPB. It should also be tested in surgeries without CPB and postoperatively in ICU.

CONCLUSION

There is moderate positive correlation but poor agreement between the values of ACT measured by Hem R and Hem JSP due to different techniques of measurement. The mean and median values have significant difference so these devices should not be used interchangeably for measurement of ACT.

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Conflict of interest: None

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

WA: Concept, Literature review, manuscript writing

SAH: Concept, Review of manuscript, critical review

MA: Data collection, Manuscript writing, data entry

MAA: Literature review, interpretation, study design

MUF: Data collection, data management, manuscript writing

RM: Data analysis, Manuscript review, intellectual contribution

HK: Data collection, data analysis, proof reading

AS: Article formatting, editing, referencing

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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