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To Study The Correlation Between Activated Clotting Time And Hypothermia In Pediatric Patients Undergoing Cardiopulmonary Bypass

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ABSTRACT

Background: Cardiopulmonary bypass is a form of extracorporeal circulation whose function is to temporarily give circulatory and respiratory support along with temperature management to facilitate surgery on the heart and great vessels. Depending on the duration and extent of artificial surface exposure, anticoagulation is necessary in order to avoid the formation of thrombus in the cardiopulmonary bypass circuit. The fundamental principle underlying the use of hypothermia with CPB is decreasing temperature to reduce metabolic activity. The ACT is commonly used to assess the therapeutic effects of anticoagulant medications prior to the initiation of CPB.

Aim: This study aims to study the correlation between activated clotting time and hypothermia in pediatric patients undergoing cardiopulmonary bypass.

Materials And Method: It is a prospective study of 50 pediatric patients ,who underwent cardiac surgery using cardiopulmonary bypass at tertiary cardiac care center. Pediatric patients aged between 0 to 10 years were included in this study. Adult patients undergoing cardiopulmonary bypass, emergency surgeries and heparin resistance patients are excluded from this study. Heparin dosage, CPB duration, aortic cross clamp time, added priming solution, Activated clotting time and temperature of baseline , initiation of cardiopulmonary bypass, during cardiopulmonary bypass , termination of cardiopulmonary bypass and protamine infusion were taken.

Results: Fifty paediatric patients underwent first time cardiopulmonary bypass were investigated. In which the baseline mean ACT was 150.24±26.617 secs at mean temperature of 36.466±0.3068ºC. After initiation of cpb, the mean ACT increased as 753.12±29.979 secs at mean temperature of 32.308±0.9940ºC this was due to the addition of 300- 400 USP units/kg heparin sodium injection (5000 I.U/ml), injected in the central venous line of a patient five minutes before the initiation of CPB . During CPB the mean ACT further increased as 937.18±39.301secs at mean temperature of 23.002±3.6488ºC this prolongation was due to the decreased temperature. Here the P<0.005 which proved significant. The mean ACT decreased as 665.78±38.054 secs at termination of cpb with mean temperature of 35.164±0.3789ºC, this decrease is due to rewarming.

CONCLUSION: In this study we observed that the activated clotting time correlate well with hemodilution and hypothermia. The activated clotting time increases with decrease in temperature and decreases with increase in temperature. Decrease in temperature make the clotting factors less functional and increases the activated clotting time. Increase in temperature increases metabolic activity thus increases the function of clotting factors resulting in decreased activated clotting time.

Keywords: *Activated clotting time, Hypothermia, cardiopulmonary bypass, Temperature, Anticoagulation*

1. INTRODUCTION

During cardiac surgery, several processes create an environment conducive to clot formation. Cardiopulmonary bypass (CPB) exposes blood to a large artificial surface, which creates a pro-coagulant state leading to thrombin generation. In neonates and infants, this balance is more difficult to achieve because of inherent developmental characteristics of the coagulation and haemostatic system. [3]The technical challenge of preventing thrombosis within the extracorporeal circuit (ECC) was overcome with the use of heparin.[4,5] and its effective antidote, protamine.[6,7] which allowed for safe anticoagulation to be established and subsequently reversed at the end of surgery. The adequacy of heparin anticoagulation during CPB commonly is monitored using the activated clotting time (ACT).[8] The ACT is considered to be the gold standard for monitoring anticoagulation during CPB.[9] The target ACT values maintained during CPB are usually between 400 and 480 seconds.[8] Measurement of ACT involves the use of a contact activator, such as celite, kaolin, or glass beads, which activates the intrinsic and common pathways of the clotting cascade when exposed to fresh, whole blood by mimicking the negatively charged foreign surfaces of the CPB circuit.

Prolongation of the ACT in the heparinized patient is directly proportional to the concentration of heparin in the blood. [11] However, it has been reported that the ACT may be influenced by variables other than heparin concentration.[12] Hemodilution, coagulation factor depletion and hypothermia have been shown to prolong the ACT. Other phenomena may also vary the ACT during CPB. Hypothermia induces reversible platelet membrane dysfunction, partially inhibits platelet aggregation. Decreasing blood temperature most probably reduces the activity rate of coagulant enzymic systems. Anticoagulant substances also may be released during hypothermia.

2. MATERIALS AND METHODS

This investigation was designed as a prospective study of 50 pediatric patients ,who underwent cardiac surgery using cardiopulmonary bypass at tertiary cardiac care center. Pediatric patients aged between 0 to 10 years were included in this study. Adult patients undergoing cardiopulmonary bypass, emergency surgeries and heparin resistance patients are excluded from this study. Decadron, mannitol, ringer lactate are used to prime the cardiopulmonary circuit. Patients requiring the addition of blood or additional heparin during cardiopulmonary bypass were also excluded from this study. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all participants.

Anesthetic techniques were standardized for all patients. All surgeries were performed through a midline sternotomy. Heparin 400 IU/kg was administered intravenously prior to cardiopulmonary bypass to achieve activated clotting time above 480 seconds. Extracorporeal circulation was performed using a Sorin inspire adult membrane oxygenator, Sarns 8000 perfusion pump and a Spictra AF arterial line filter. Non-pulsatile perfusion was maintained at a flow rate of 2.2–2.4 L/m2 /min. The bypass circuit was primed using 1 L Plasmalyte A solution, 3 mg/kg 10% mannitol and 10,000 IU heparin. Moderate haemodilution with crystalloid prime and moderate systemic hypothermia were used. After aortic cross clamping, myocardial protection was achieved with intermittent antegrade cold blood cardioplegia administered through the aortic root or coronary ostium till the cardiac arrest occurred.

Patients body surface area; aortic cross clamp time were taken .Activated clotting time and temperature were analysed at the following times;

- Base line
- Before initiation of cardiopulmonary bypass
- Initiation of cardiopulmonary bypass
- During cardiopulmonary bypass
- After protamine infusion.
-

3. RESULTS

Baseline mean activated clotting time was 150.24±26.617secs and baseline mean temperature was 36.466±0.3068ºC. Before initiation of cardiopulmonary bypass, the mean activated clotting time was 654.04±32.186 secs and mean temperature was 34.852±0.5853ºC. At the time of initiation of cardiopulmonary bypass, the mean activated clotting time was 753.12±29.979 secs and the mean temperature was 29.979ºC. During cardiopulmonary bypass the mean activated clotting time was 937.18±39.301 and the mean temperature was23.002±3.6488ºC. At the time of rewarming mean activated clotting time was 823.88±39.359 and the mean temperature was 29.110±1.7239ºC. During termination of cardiopulmonary bypass the mean activated clotting time was665.78±38.054 secs and the mean temperature was 35.164±0.3789ºC.After protamine infusion the mean activated clotting time was152.72±25.507 and the mean temperature was36.408±0.2473ºC[shown in table1.1]. The p value obtained by comparing initiation of cardiopulmonary bypass and during cardiopulmonary bypass is significant[$p \leq 0.05$]. Thus increase in temperature decreases ACT value and decrease temperature increases ACT value.

Table 1.1 ACT and temperature during various duration of cardiopulmonary bypass

VARIABLE	ACT [MEAN±SD]	TEMPERATURE [MEAN±SD]
BASELINE	150.24±26.617	34.466±0.3068
BEFORE INITIATION OF CPB	654.04±32.186	34.852±0.5853
INITIATION OF CPB	753.12±29.979	32.308±0.9940
DURING CPB	937.18±39.301	23.002±3.6488
REWARMING	823.88±39.359	29.110±1.7239
TERMINATION ON CPB	665.78±38.054	35.164±0.3789
AFTER PROTAMINE INFUSION	152.72±.25.507	36.408±0.2473

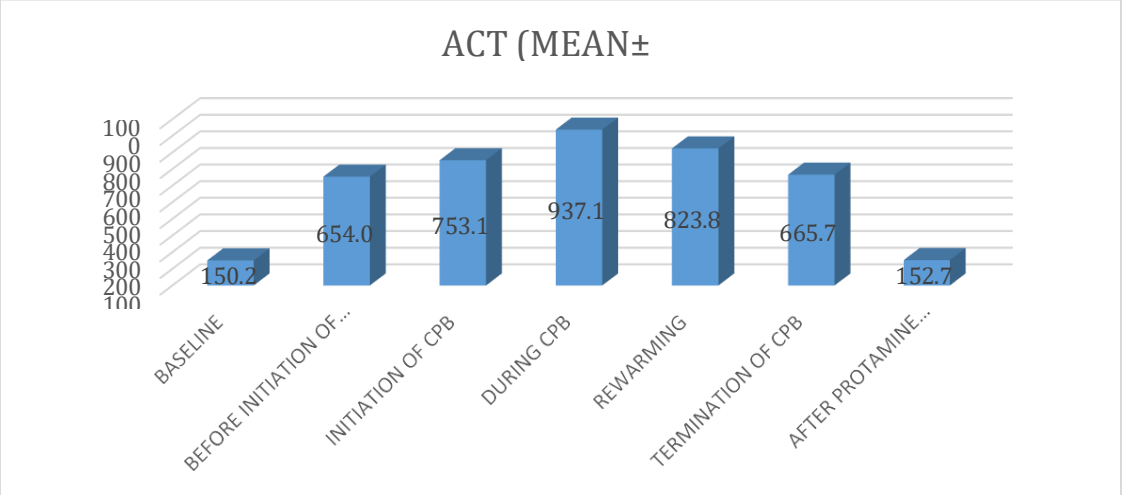

FIGURE 1.1 : Activated clotting time during various duration of cardiopulmonary bypass

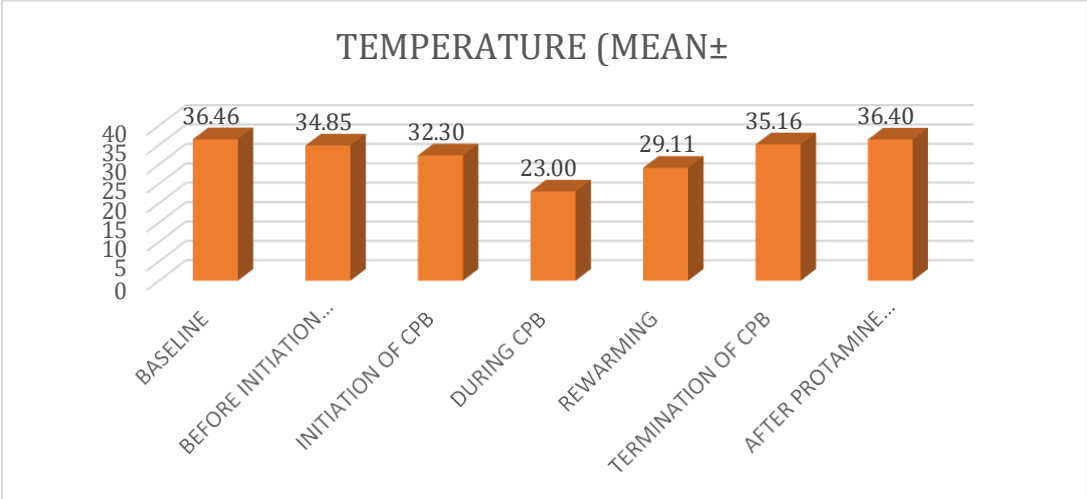

FIGURE 1.2: Temperature during various durations of cardiopulmonary bypass

4. STATISTICAL ANALYSIS

The pair 1 shows comparision between baseline and initiation of cardiopulmonary bypass ACT and temperature values which is not significant. The pair 2 shows comparision between initiation of cardiopulmonary bypass and during cardiopulmonary bypass ACT and temperature values which is significant [$p \leq 0.05$] [Shown in figure 1.1&1.2]. The pair 3 shows the comparison between during cardiopulmonary bypass and termination of cardiopulmonary bypass ACT and temperature values which is not significant. The frequency, mean standard deviation, percentage, chi square test was used to analyse the data by SPSS version 20. The p value less than 0.05 were considered to be significant. This study was approved by the institutional ethics committee.

5. DISCUSSION

The management of cardiopulmonary bypass for pediatric cardiac surgery is more challenging than that in adults due to the smaller size, immaturity, and complexity of the anatomy in children. Despite major improvements in cardiopulmonary bypass, there remain many subjects of debate .We have been using Activated Clotting Time (ACT) test to evaluate anticoagulation of heparin During CPB. Exposure of blood to artificial surfaces during cardiopulmonary bypass (CPB) activates the blood platelets, and coagulation system, results in excessive thrombus formation. The systematic administration of heparin prior to the induction of CPB and the neutralization of heparin by protamine sulfate at the end of CPB are essential for performing cardiac surgery.

Cardiopulmonary bypass in pediatric cardiac surgery is generally performed with hypothermia, flow reduction and hemodilution. Deep hypothermia with circulatory arrest, justified by reduced duration of CPB in small infants. In this study we observe the effect of temperature and hemodilution on activated clotting time. How these factors alter the value of ACT. It will help in better management of anticoagulation during and after CPB.

In this study 50 consecutive pediatric patients who underwent cardiopulmonary bypass had taken and we correlated activated clotting time and hypothermia in those patients by monitoring activated clotting time, cross clamp time, bypass duration and amount of priming solution added during cardiopulmonary bypass.

This study includes congenital heart disease patients of 0 to 10years. Anticoagulant was established with a dose of 300- 400 USP units/kg heparin sodium injection (5000 I.U/ml) administered five minutes before the initiation of CPB to achieve ACT value of >480 seconds.

The changes in ACT value were according to different factors. Pre CPB ACT value is 150.24±26.617 seconds when heparin was given to the patient before going on CPB, then CPB initiated, the ACT value increased to 753.12±29.979 seconds. The temperature was cooled down from 36.4±0.30 ˚C to 32.3±0.99 ˚C.

After aorta cross clamped patient was cooled down to 23±3˚C, we measured an increase in ACT value to 937.18±39.301 seconds. This decrease in temperature caused an increase in ACT value. Before termination of CPB rewarming was started, temperature increased to 35±1˚C and the ACT value decreased to 665.78±38.054 seconds. In the end, after termination of bypass protamine was given and value of ACT was decreased to 152.72±25.507 seconds.

This large decrease is due to efficient working of enzymes at optimum temperature and other factors like urination. The results of paired sample T-TEST were highly significant as the P value of each comparison is extremely small then zero. The pair 1 shows that Baseline relation with Initiation of CPB. Before CPB was initiated, the averaged pre-CPB ACT was 150.24±26.6617 seconds. After 5 minutes of initiation of CPB, Averaged ACT value increased as753.12±29.979 seconds. This prolongation was due to prime volume present in CPB circuit and the temperature was decreased from 36.4±0.30 ˚C to 32.3±0.99˚C.When CPB was initiated, it caused the dilution of clotting factors.

The pair 2 shows that initiation CPB relation with during cpb Before initiation of CPB heparin was used to raise the ACT value >480 seconds. When CPB started we study the change in this value due to hemodilution. It caused change in the averaged value of ACT from 753.12±29.979seconds to 937±39 seconds, which explained the effect of prime volume present in the circuit. Perfusionist can control the change in ACT value if he reduces the volume of prime. Further that the dilution of clotting factors also causes prolongation of ACT . After the above prolongation, patient is cooled down to 23±3.6˚C which help to decrease the O2 requirements and metabolic rate. Which was proved significant as $p<0.005$

The pair 3 shows that during cpb relation with termination of cpb. Before termination of CPB, rewarming was started and a change in ACT value was seen. The averaged ACT value change from937.18±39.301seconds to 665±38seconds. This decrease is due to optimum temperature. Before termination of CPB, an average 35±1˚C temperature was achieved. The averaged ACT value was decreased at rewarmed temperature. This decrease in temperature caused an increase in ACT value.

After termination, protamine was given, and ACT return back to baseline. The activated clotting time value of blood has inverse relationship with temperature.As the temperature decreases activated clotting time value increases and decreases when the temperature increases. so, it will help to understand changes that occur in hemostasis during cardiopulmonary bypass and better management of anticoagulation during cardiopulmonary bypass. The ACT is also prolonged by

hypothermia, hemodilution, platelet dysfunction, and low coagulation factor levels.

6. CONCLUSION

This study concluded that the activated clotting time of blood is directly related with hypothermia. As the temperature decreases, the activated clotting time of blood increases; as the temperature increases, the activated clotting time of blood decreases.

So, it will help us to understand hemostatic changes occur during cardiopulmonary bypass. We can reduce heparin dose in trauma patients who are already at bleeding risk. This helps better management of coagulation during cooling and rewarming phase of Cardiopulmonary bypass.

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