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Does Initiation of Protamine Necessitate Discontinuing Pump Sucker?

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ABSTRACT

Background: Protamine is essential in cardiac surgery to reverse heparin effect. Despite the benefit of returning the shed blood back to patient through arterial line by using suction during and after using protamine, this practice has been unpredictably associated with the observation of clot in the cardiopulmonary bypass (CPB) circuit.

Objectives: This study aimed to evaluate the effect of protamine test dose on the activated clotting time value, which influence the timing of discontinuation of pump sucker.

Patients and methods: A prospective study that was conduct on 86 cardiac surgery cases in Menoufia University Hospitals. Effect of protamine test dose (PTD) on activated clotting time (ACT) was assessed to determine the proper timing for cessation of pump sucker.

Results: There was male predominance (60.5%) in the study group with a mean age of 49.57 years. Coronary artery bypass grafting (CABG) was the most frequent procedure in 38 cases (44.2%) followed by mitral valve replacement (MVR) in 16 cases (18.6%). There was a significant drop in the ACT after PTD, which was confirmed by comparing last ACT during CPB to that after PTD, which showed statistically significant difference.

Conclusion: The proper timing for cessation of field sucker is before initiation of protamine transfusion, so adequate hemostasis of surgical field should be obtained before ordering protamine transfusion.

Keywords: Protamine, Protamine test dose, Pump sucker, Cardiopulmonary bypass.

INTRODUCTION

Protamine, which was discovered in the 1870s in salmon sperm, a century later it was approved to be essential in cardiac, vascular surgeries and radiological interventions to neutralize heparin's anticlotting effects by forming a stable, inactive ion pair with heparin [(1, 2)].

Protamine overdosage has a paradox anticoagulant effect; caused by effects on platelets, inhibition of PIb-vWF interaction, reduction of thrombin generation, activation of factor V and VII, and factor VIII clotting effect [(3)]. Heparin-protamine interaction can be associated with a substantial decrease in patients' systemic blood pressure, increased pulmonary artery pressure, and an overall decrease in systemic vascular resistance. These secondary responses to protamine administration ultimately result in decreased cardiac output, which puts the patient at risk of postcardiotomy decompensation. Therefore, a protamine test dose (PTD) is routinely administered to examine a patient's hemodynamic response to protamine before full heparin reversal in patients who have undergone cardiopulmonary bypass (CPB) [(4)].

There was no standardization to cease the recovery of mediastinal shed blood into the bypass circuit during and after PTD administration because it was believed that such a small dose would not significantly affect patient' activated clotting times (ACTs). Therefore, suction devices draining directly into the CPB circuit have been routinely used during and after PTD and have been discontinued only when the remainder of the protamine dose is administered [(5, 6)].

This has the benefit of blood conservation as shed blood is returned back through the CPB arterial line, as well as working under the assumption that the team can recommence CPB urgently if necessary. However, on occasion this practice has been unpredictably associated with the observation of clot in the CPB circuit, thus rendering the circuit unusable. Therefore, the aim of this study was to investigate the PTD and the impact on patient ACT levels and, ultimately, answering the query about timing of discontinuing the use of pump sucker [(6)].

PATIENTS AND METHODS

This prospective study was performed in the Cardiothoracic Surgery Department-Menoufia University Hospital between November 2024 and May 2025. It was conducted on 86 adult patients who underwent on-pump cardiac surgery after being approved by The Local Ethics Committee of the Faculty of Medicine, Menoufia University.

All patients undergoing cardiac surgery using heart lung machine were included. There were no exclusion criteria. All the patients were subjected to the routine preparation and monitoring in the operating room. Heparin was given to each case at the proper time according to the procedure after calculation of the suitable dose for each patient weight. ACT was measured as baseline, after heparin administration, before initiating CPB, during CPB and after administration of protamine test dose and full dose. The data of the enrolled patients were collected, which included the procedure done,

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baseline ACT, ACT before and during CPB, ACT after administration of PTD and after protamine full dose.

Ethical approval: This investigation received ethical clearance from The Research Ethics Committee, Faculty of Medicine, Menoufia University. All subjects provided written informed consents prior to their participation. The consent process included explicit information about data use and publication, with guarantees of privacy and confidentiality. The study conformed to the principles of the World Medical Association's Declaration of Helsinki.

Statistical Analysis

The statistical analysis of the data was performed using IBM SPSS software version 20.0 (Armonk, NY: IBM Corp, released 2011). Categorical data were summarized as numbers and percentages. For continuous data, normality was assessed using the **Kolmogorov-Smirnov** test. Quantitative data were presented as range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). For normally distributed quantitative variables **Paired t-test** was used to compare between two periods**.** The significance level for all statistical tests was set at 5%.

RESULTS

The included patients were predominantly males (60.5%) and age ranged between 22 to 78 years with a mean age of 49.57 years. Coronary artery bypass grafting (CABG) was the most frequent procedure in 38 cases (44.2%) followed by mitral valve replacement (MVR) in 16 cases (18.6%). Aortic valve replacement was done in 15 cases (17.4%) and double valve replacement (DVR) was done in 11 cases (12.8%). Combined procedure i.e. CABG and valve replacement was least frequent by only 6 cases (7%).

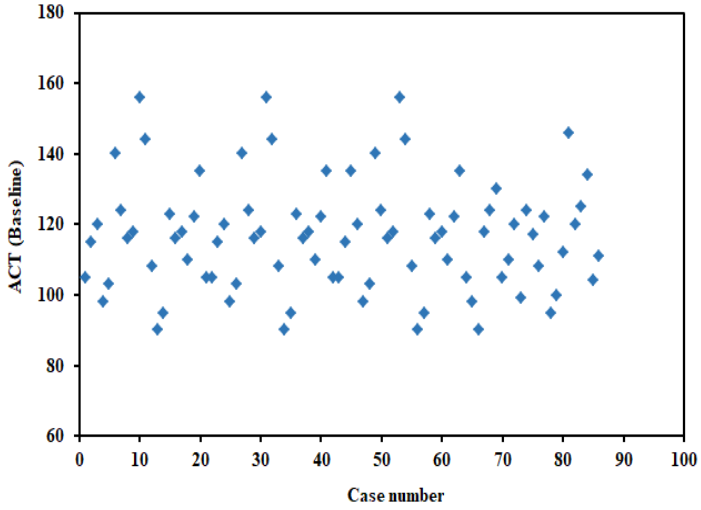

Figure (1): ACT baseline.

First ACT was measured as baseline, presented in scatterplot demonstrating the values as shown in figure (1). After heparin administration, ACT values measured were shown in figure (2).

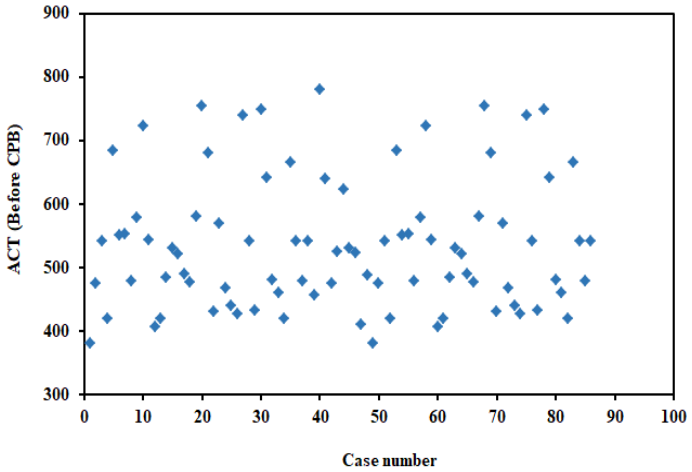

Figure (2): ACT before CPB.

The anticoagulation state was maintained throughout the bypass by monitoring the ACT and giving heparin accordingly. The last value of ACT during bypass (last CPB) ranged from 380.0 to 780.0 with a mean of 538.09. In comparison with the ACT after protamine test dose, which ranged from 175.0 to 469.0 with a mean of 273.2, there was statistically significant difference. This demonstrated the significant drop in the anticoagulation value regardless the amount of administered protamine, which varied from 5 to 25 % of calculated dose as shown in table (1).

Table (1): Comparison between last CPB and after PTD according to activated clotting time value (ACT)

	Last CPB	After PTD	t	p
Activated clotting time value (second**)**				
Min. – Max.	380.0 – 780.0	175.0 – 469.0		
Mean ± SD.	538.09 ± 96.38	273.2 ± 72.68	22.241	<0.001
Median (IQR)	522.0 (478.0 – 578.0)	266.0 (200.0 – 321.0)		

IQR: **Inter quartile range**, SD: **Standard deviation, t: Paired t-test,** p: p value for comparing between **Last CPB** and **After PTD**, *: Statistically significant at $p \leq 0.05$

DISCUSSION

Giving a PTD to ensure that the patient does not become hemodynamically unstable after weaning from CPB is common practice in cardiac surgery. Despite recommendations in the American Society for Extracorporeal Technology Standards and Guidelines for Perfusion Practice that cardiotomy suction to be discontinued at the onset of protamine administration to avoid clotting within the CPB circuit, it is still common practice that cardiotomy suction remains active until at least a PTD is administered [5].

This study supports these guidelines and showed that this practice is dangerous because of the unpredictable

drop in ACT after a PTD. Our study concluded that there was no reliable way to predict how a patient's ACT will respond, regardless of the protamine dose given during the PTD. So the potential exists for even a small dose of protamine to result in a dramatic normalization of coagulation that makes the CPB circuit at risk for thrombosis if mediastinal shed blood continues to be recovered directly into the venous reservoir.

The results of our study are comparable to the study of **Jansa *et al.*** [6] who noted circuit disintegration in cases who continued to use suction devices during and after PTD for blood conservation. They conducted the study on 120 patients who had CPB for different cardiac procedures.

CABG was the commonest procedure in both studies followed by AVR which coincides with the common practice nowadays in different cardiac centers. MVR was more common in our study, which might be due to prevalence of rheumatic valve affection in our population.

We had a lower PTD percentage of 5 to 25 % of calculated whole protamine dose while in **Jansa *et al.*** [6] it was 1 to 67%. We recommend that instead of a verbal recognition that the "test dose is given," communication should entail the actual dosage administered in milligrams, along with the percentage of the expected full dose. This supports complete standardization along with improved communication among all members of the cardiac team.

De Simone *et al.* [1] had a similar study group showing male predominance but they have more valve interventions comparted to our study. In spite of the well-established predominance of coronary interventions that might be explained more cases of off-pump CABG in their center and these cases were not included in our study neither their study.

The study conducted by **De Simone *et al.*** [1] showed that 0.84:1 protamine to heparin ratio showed to be sufficient to reverse the effects of heparin after cardiopulmonary bypass. These data are important because usually protamine is administered in a 1:1 ratio and, furthermore, a supplement of protamine (25 mg, 50 mg, or even 100 mg) is given during unsatisfactory hemostasis. These behaviors lead to a substantial increase of protamine dose administered to many patients and subsequent protamine-induced paradox hemostasis deficit. They also showed that a lower dose of 0.56:1 was effective in some cases, which support the idea that even using lower doses of protamine can reverse the anticoagulation effect of heparin than predicted. That makes cessation of pump sucker before starting protamine a wise decision for safer practice.

Different studies were conducted to optimize the protamine dosing after CPB to decrease the abuse of protamine usage, which may lead to many hazardous side effects. **Miles *et al*.** [7] used a mathematical method for calculation of adequate dose to have improved Thromboelastography (TEG) r-time and reduced the dose administered relative to a fixed ratio. The results did not only support that of **De Simone *et al.*** [1] that a lower dose of protamine was sufficient, but also confirmed no differences in postoperative bleeding or blood transfusion requirements.

The previous data raised the concern to answer the question about the proper timing of cessation of pump suction, which we recommend to be before starting any protamine. Acceptable hemostatic situation should be confirmed before ordering protamine initiation by anesthesiologist.

CONCLUSION

The proper timing for cessation of field sucker is before initiation of protamine transfusion, so adequate hemostasis of surgical field should be obtained before ordering protamine transfusion.

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