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ASSESSMENT OF ANTICOAGULATION USING ACTIVATED CLOTTING TIME (ACT) IN PATIENTS RECEIVING ENOXAPARIN AND HEPARIN DURING PERCUTANEOUS CORONARY INTERVENTION (PCI).

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ABSTRACT

Introduction: The standard of therapy for some patients with coronary artery disease, particularly those who arrive with acute coronary syndrome, is percutaneous coronary intervention (PCI) (ACS). To avoid thrombotic problems during PCI, the American College of Cardiology (ACC) and the European Society of Cardiology (ESC) advise using anticoagulation in addition to dual antiplatelet treatment (DAPT). **Objective:** to assess how enoxaparin affects the active clotting time (ACT) and how UFH reacts to enoxaparin. **Material and methods:** The intervention cardiology department at Hayatabad Hospital Complex in Peshawar did this cross-sectional descriptive research from June 1 to April 30, 2022. By using a non-probability sequential sampling strategy, patients were included. After a thorough history, examination, and informed permission, all patients 18 years old having PCI were included in the research. Individuals with known blood dyscrasias or thrombophilia, as well as those who had received anticoagulation within the previous 12 hours or just prior, were excluded from the trial. **Results:** Among the patients who received heparin, ACT increased from 104.76±27.31 seconds to 448.34±169.11 (t-statistic=13.750, 95% CI: 293.9540 to 393.2060, p: <0.01) whereas among patients who received enoxaparin, this number increased from 99.58±27.68 seconds to 334.37±166.45 seconds (t statistic=6.817, 95% CI: 165.4597 to 304.1203, p:<0.01). The post-anticoagulation ACT was significantly higher in the heparin group compared to enoxaparin group i.e. 448.34±169.11 and 334.37±166.45 seconds respectively (t statistic=2.700, 95% CI: 29.7639 to 198.1661, p:<0.01). **Conclusion:** After taking i.v. enoxaparin and heparin, the ACT is extended in patients for around 15 minutes, and this prolongation may help track the anticoagulant action of the medication. Moreover, in this situation, ACT levels and ENOX clotting times are correlated. A bigger experiment will be necessary to determine the association between ACT level and clinical effectiveness utilising intravenous enoxaparin.

Keywords: ACT (activated clotting time), enoxaparin, heparin, percutaneous coronary intervention (PCI).

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INTRODUCTION

The standard of therapy for some patients with coronary artery disease, particularly those who arrive with acute coronary syndrome, is percutaneous coronary intervention (PCI) (ACS). To avoid thrombotic problems during PCI, the American College of Cardiology (ACC) and the European Society of Cardiology (ESC) advise using anticoagulation in addition to dual antiplatelet treatment (DAPT).[1, 2] Traditionally, anticoagulation is achieved with UFH (intravenous unfractionated heparin) but the anticoagulant effect of UFH needs to be monitored repeatedly with activated clotting time (ACT) during the procedure (ACC Class I recommendation).[1, 3] This monitoring is recommended due to the fact that UFH has a short half-life (1 hour) and the effect of UFH is not only unpredictable but it also has a narrow therapeutic window which can lead to heparin-induced thrombocytopenia and major bleeding events.[4] On the contrary, intravenous enoxaparin use has a more reliable and sustained anticoagulant effect and is given a Class IIA recommendation for use by the ACC during PCI.[5, 6] But some studies had previously shown occasional cases of catheter thrombosis with enoxaparin because it had a weaker anticoagulant response as compared to UFH.[7, 8] Recent studies refute these results and claim that enoxaparin is both safe and effective as an anticoagulant during PCI.[9] Anti-factor Xa level needs to be measured during therapy with enoxaparin to monitor its anticoagulant effect.[1, 10] Anti-factor Xa levels are not only costly but are also widely not available in our setup in the great majority of cardiac catheterization centers. ACT has been recommended to monitor the anticoagulant effect of UFH during PCI but studies have shown that enoxaparin also has a significant effect on the ACT during PCI.[11] The ACT response with UFH follows a linear dose-response model whereas with enoxaparin, there is no linear dose-response which results in less increase in ACT with enoxaparin compared to UFH. Some authors have suggested an ACT of 175 and 200 seconds for PCI with and without planned use of Glycoprotein IIb/IIIa inhibitors but these claims need to be further investigated and evaluated.[11, 12.] Nevertheless, the use of enoxaparin offers obvious advantages over UFH in that its effect is more reliable and has potentially less bleeding complications compared to UFH, especially in patients undergoing trans-femoral PCI. This study's objective was to assess enoxaparin's impact

on the ACT & whether ACT can be used to measure its response during PCI in our setup. In addition, our secondary objective was to compare the ACT response of UFH with enoxaparin.

METHODOLOGY

From June 1, 2021, to April 30, 2022, a cross-sectional descriptive research was undertaken at the intervention cardiology department of the Hayatabad Medical Complex in Peshawar. By using a non-probability sequential sampling strategy, patients were included. After a thorough history, examination, and informed permission, all patients 18 years old having PCI were included in the research. The Patients who got anticoagulation in the previous 12 hours or just before and those with known blood dyscrasias or thrombophilia were excluded from the study. ACT was measured for all patients undergoing PCI immediately prior to and at 15 minutes after receiving anticoagulation with either IV UFH or IV Enoxaparin. The dose of UFH used for PCI was 75-100 IU/kg whereas enoxaparin was given at a dose of 1mg/kg. Afterwards, patients were divided into the UFH group and the Enoxaparin group. On an already created proforma, all data was gathered. Categorical variables were reported as frequencies/percentages and continuous variables as meanSD. The ACT between the UFH group and the Enoxaparin group was compared before and at 15 minutes after administration of either UFH or Enoxaparin, respectively, using a two sample t test. P values below 0.05 were considered significant. The statistical analysis and data input were carried out using SPSS version 20.0.

RESULTS:

71 cases in all, with a mean age of 5711. The research covered 52 years, of which 48 were men and 23 were women. Of these, 47 patients received heparin whereas 24 patients received enoxaparin during PCI. The presentation of 19 patients was ACS whereas 52 patients underwent elective PCI. In this study, 50 patients had a history of hypertension, 25 had history of diabetes mellitus, 19 patients had a history of dyslipidemia and only 2 patients were current smokers and 6 were ex-smokers. Moreover, 12 individuals had a lower LVEF compared to 59 patients with a preserved left ventricular ejection fraction (LVEF). Table 1 lists all baseline characteristics.

Among the patients who received heparin, ACT increased from 104.76±27.31 seconds to 448.34±169.11 (t-statistic=13.750, 95% CI: 293.9540 to 393.2060, p: <0.01) whereas among patients who received enoxaparin, this number increased from 99.58±27.68 seconds to 334.37±166.45 seconds (t statistic=6.817, 95% CI: 165.4597 to 304.1203, p:<0.01). The post-anticoagulation ACT was significantly higher in the heparin group compared to enoxaparin group i.e. 448.34±169.11 and 334.37±166.45 seconds respectively (t statistic=2.700, 95% CI: 29.7639 to 198.1661, p:<0.01). Table 2.

Table 1: Baseline Characteristics

Characteristic	Frequency
Gender	
Male	48(67.6%)
Female	23(32.4%)
Presentation	
ACS	19(26.76%)
Elective	52(73.24%)
Co morbidities	
Hypertension	50(70.42%)
Diabetes Mellitus	25(35.21%)
Dyslipidemia	19 (26.76%)
Smoking status	
Current Smoker	2(2.81%)
Ex-smoker	6(8.45%)
Never smoker	63(88.73%)
LVEF	
Preserved	59(83.09%)
Reduced	12(16.91%)

Table 2: Comparison of ACT between two groups

Characteristic	Mean ± SD	t statistic (95% CI)	P value
Pre Heparin ACT (seconds) n=47	104.76±27.31	13.750 (95% CI: 293.9540 to 393.2060)	<0.01
Post Heparin ACT (seconds) n=47	448.34±169.11		
Pre Enoxaparin ACT (seconds) n=24	99.58±27.68	6.817 (95% CI: 165.4597 to 304.1203)	<0.01
Post Enoxaparin ACT(seconds) n=24	334.37±166.45		
Post Heparin ACT (seconds) n=47	448.34±169.11	2.700 (95% CI: 29.7639 to 198.1661)	<0.01
Post Enoxaparin ACT (seconds) n=24	334.37±166.45		

DISCUSSION

Several revisions have been piloted to examine the safe keeping & efficacy profiles of enoxaparin with unfractionated heparin (UFH) using various criteria. and it has been established that enoxaparin is effective with better clinical long-term outcomes and is safe to use in the management of patients with ACS who undergo PCI without posing a major bleeding risk.[9.] Therefore, the need for utilizing and evaluating methods for monitoring the effects of enoxaparin need to be established and studied. The results of our study, which tracked how enoxaparin affected the ACT (activated clotting time), were statistically significant. Similarly, ACT measurement was also used as a tool of comparing the effects of UFH and enoxaparin.

The ACT measurement is a reliable, inexpensive and convenient method of monitoring that can be done at the bedside and is recommended for monitoring.[11, 13.] Anti-factor Xa levels need to be monitored during the use of enoxaparin in PCI.[1, 10.] The estimation of anti-factor Xa tiers, prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time (TT), & fibrinogen level, however, are plasma tests (done on plasma, not whole blood), and they provide information about plasma coagulation instead of the status of patients' haemorrhage or coagulation propensity.[13.] In contrast, ACT measurement give a wholesome idea about patients' coagulation status (done on patient whole blood rather than just plasma taking into account the importance of platelets and phospholipids in coagulation) which is clinically more important and decisive in management. This helps especially in situations where a patient is bleeding and immediate intervention is needed.[13.] These factors makes ACT an important method of monitoring which requires further exploration of its importance and its standardization is needed keeping in view specific hospital setup and methods of measurement. Likewise, in situations when the procedure is prolonged and repeated anticoagulation is required, the use of enoxaparin (and utilization of ACT for monitoring) in such scenarios is more acceptable due to its sustained action and repeat dosing of UFH is avoided considering its short half-life.[13.]

Since ACT values correlates with the future bleeding risk and it was found that ACT values of more than 400s poses increased

risk of bleeding.[16.] In our study the ACT values achieved in enoxaparin group were more close to the safe operating range i.e 334.37±166.45 compared with heparin 448.34±169.11. Having these results, a large sample size will further help in defining ACT optimal range achieved with enoxaparin considering bleeding risk at one extreme and effective anticoagulation at the other extreme.

The prevalence of myocardial infarction is rising, and both elective and primary PCI are becoming more necessary.[15.] Especially, there is a dramatic increase in our healthcare facilities owing to multiple factors like commencement of health insurance, awareness of cardiovascular diseases and treatment options in general low socioeconomic population and easily accessible interventional cardiology centers. Keeping this in view, more reliable options for anticoagulation would be of benefit especially those that need less monitoring and has a stable action over time like enoxaparin.[14.] Important challenging factors in our healthcare facilities are the limited availability of resources, the development phase of meeting the standard of care, patients' affordability and patients' burden. In such a scenario, an easily accessible and interpretable test like ACT holds quite an important place in monitoring and management considering all these factors.

Our study excluded certain groups of subjects from the study such as patients who had received anticoagulation immediately before or in the past 12-hour, patients with known blood dyscrasias or thrombophilias and these significant values were achieved. More studies to use ACT for monitoring and its standard values to be set and proper recommendations advised considering multiple factors mentioned above in exclusion criteria and others including the concurrent use of other antiplatelet agents and other medication, whether elective or primary PCI, the weight and age of the patient, clot burden, area of occlusion and additional risks of bleeding. Our study will have implications for the design of future trials and will open the door for further work in this important area of intervention cardiology.

LIMITATION:

The sample size was small, even though statistically significant results were obtained. A dual arm, double blinded Randomized Controlled Trial is warranted to establish the efficacy, safety and optimal range of ACT for monitoring enoxaparin.

CONCLUSION:

After taking i.v. enoxaparin and heparin, the ACT is extended in patients for around 15 minutes, and this prolongation may help track the anticoagulant action of the medication. Moreover, in this situation, ACT levels and ENOX clotting times are correlated. A bigger experiment will be necessary to determine the association between ACT level and clinical effectiveness utilising intravenous enoxaparin.

Ethics Approval: The ERC gave ethical review approval
Consent To Participate: written and verbal consent was taken from subjects and next of kin
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Authors' Contributions: All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

Conflict Of Interest: No competing interest declared.

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