ACTIVATED CLOTTING TIME (ACT): ITS DIAGNOSTIC VALUE IN MONITORING LOW DOSE HEPARIN THERAPY

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ABSTRACT

Objective: To study diagnostic value of Activated Clotting Time (ACT) in monitoring of low dose Heparin therapy.

Material and Methods: One hundred cases were included in this study. Among them 50 healthy normal subjects (group I) were taken as control, while 50 were taken among patients of myocardial Infarction (group II) receiving continuous heparin therapy. For both groups of patients the laboratory test ACT and APTT were performed.

Results: Sensitivity of ACT in low dose heparin therapy was 64.28% and specificity was 62.5%. Sensitivity of APTT was 90% and specificity was 100%.

Conclusion: ACT cannot be substituted for APTT though it can be used as a bedside test to monitor heparin therapy. It is a useful indicator where over heparinization or under heparinization is suspected and APTT results are awaited.

Key Words: ACT, APTT, Heparin, MI

INTRODUCTION

Blood circulation is a physiological process that is maintained by haemostasis[1]. Haemostatic system is a complex mosaic of activating or inhibitory feed back or feed forward pathways, integrating its five major components blood vessels, blood platelets, coagulation factors, coagulation inhibitors and fibrinolysis)[2]. In pathological processes, blood coagulates inside the vessel and forms a thrombus. Thrombosis is a serious disorder. It can cause fatal pulmonary embolism and often leads to post thrombotic syndromes with symptoms ranging from discolouration to ulceration[3]. Four types of anticoagulant therapy are in use i.e. anticoagulants (like heparin), vit. K antagonists, thrombolytics agents (that are Streptokinase, Urokinase etc.) and surgical removal of thrombi or emboli. Heparin is drug of choice in rapid anticoagulation. When given intravascular it is effective in the prevention of venous thrombosis, pulmonary embolism, mural thrombosis (after myocardial infarction), in patients with unstable angina and in acute myocardial infarction.

The anticoagulant effect of heparin is monitored by ACT and APTT. This anticoagulant effect of heparin is mediated largely through antithrombin III[4].

APTT is readily available in most laboratories and because it is a part of an ongoing quality control program, APTT is the preferred test for monitoring heparin therapy.

Contrary to the old recommendations the latest concept about the use of APTT in monitoring UFH (unfractioned heparin) as indicated in various studies are that, though the APTT is the standard laboratory test used to estimate the degree of heparin anticoagulation but unfortunately, it does not correlate reliably with heparin concentrations, since factors such as reagent sensitivity, temperature, collection methods, and haemodilution may influence assay variability. Inaccurate assessment by a single device or tremendous APTT variation among several instruments could complicate monitoring and result in inappropriate dosage adjustments. In addition, similar values obtained from different instruments may not reflect the same level of

anticoagulation[5]. Also the normal APTT range vary from a short 18 28 seconds to a longer 35 55 seconds. Heparin therapeutic ranges, with the most popular commercial reagents, show a more dramatic spread and may be as short and tight as 34 50 seconds to a more prolonged and sensitive range of 80 130 seconds[6]. It is also stated that commonly accepted therapeutic range of APTT ratio (APTT of the patient divided by the APTT of the control) prolongation is 1.5 3.0 x baseline. Recent studies have found that the APTT varies depending on the reagent and may not adequately reflect an accurate anticoagulant response[7]. College of American Pathologists recommends that to cope with this practical problem patient's baseline APTT is recommended to determine the therapeutic range[8].

All these factors and the disadvantage of the time period of three to four hours that lapses between the sample taking and the result of APTT obtained from the lab necessitates a test that is done on the bedside, gives immediate results depicting the actual heparinization status of the patients blood. ACT is a bed side test done on whole blood in a ACT TIMER(machine) that gives result in less than five minutes.

Many studies in which ACT has been used to monitor low dose heparin therapy show the confidence in the test. It supports the view that ACT gives uniform results. ACT can be introduced as a bedside test to monitor heparin therapy, as it is a useful indicator, when overheparinization or underheparinization is suspected and comprehensive laboratory results are awaited. 'ACT is a simple test of adequacy of anticoagulation that can be performed at the bedside

on whole blood in a reasonable time period and does not require a sophisticated piece of equipment or operator skill[9].

This study was conducted to study diagnostic value of Activated Clotting Time (ACT) in monitoring of low dose Heparin therapy.

MATERIAL AND METHODS

One hundred (100) subjects were included in this study. The subjects were selected from Post Graduate Medical Institute, Govt. Lady Reading Hospital, Peshawar. The selected subjects were divided into two groups. Group I comprising of normal healthy individual for Control and Group 11 comprising of Patients of MI receiving continuous heparin therapy.

Exclusion Criteria:

Subjects with bleeding disorders or liver diseases were excluded from the study.

Sample collection:

5 ml of blood was taken in a disposable syringe from the patients and the control for baseline values and was divided in the following way:

i. 3.6cc blood was transferred to tube containing 0.4cc of sodium citrate with the ratio of 1:9 for APTT.

Ii. 0.2 cc of blood was transferred to ACT cartridge.

Post-Heparin Collection for patients:

80u/kg bodyweight heparin was given by intravenous as a bolus dose followed by 5cc heparin (25,000 units) for continuous infusion in heparin pump (5cc heparin in 50cc normal saline). The first blood sample was taken 06 hours after the commencement of therapy, results recorded and dose was adjusted according to the table (Table: 1)10. Second blood sample was taken six hours after the dose adjustment.

RESULTS

In the present study, baseline ACT of the patients (group II) was 109.36 $\pm$ 11.52

THE STANDARD DOSE ADJUSTMENT

< 1.25 x Control	Rebolus with 80U/kg; increase the maintenance infusion by 4U/kg/hr.
1.2 1.5 x Control	Rebolus with 40U/kg; increase the infusion by 2U/kg/hr.
1.5 2.3 x Control	No change.
2.3 3.0 x Control	Decrease infusion rate by 2U/kg/hr
> 3.0 x Control	Stop infusion for 1 hour, then decrease infusion by 3U/kg/hr.

Table 1

POST-HEPARIN THERAPY INVESTIGATIONS IN PATIENTS (GROUP II) COMPARED WITH THE CONTROL

GROUP	ACT	ACT
II (n = 50)	143.88+12.98	69.36+7.12
I (Control) (n = 50)	110.04+12.53	34.54+1.52
p Value	p < 0.001	p < 0.001

Table 2

COMPARISON OF PRE AND POST HEPARIN INVESTIGATIONS IN PATIENTS

GROUP	ACT	ACT
PRE-HEPARIN	109.36+11.52	33.6 + 1.39
POST-HEPARIN	143.88+12.98	69.36+7.12
p Value	p < 0.001	p < 0.001

Table 3

and that of control subjects (group I) was 110.04 ± 12.53. Post-heparinized ACT of the patient was 143.88 ± 12.98. Compared with control(110.04 ± 12.53) there is a difference of 33.84. This difference is highly significant with a pvalue <0.001 (Table-2), This indicates the application of ACT in low dose heparin therapy. Comparing baseline result of the patients, the post-heparinized difference comes out to be 34.52. (Table-3)

APTT of the control subjects and baseline of the patients in the present study was well within normal limits. APTT of control subject was 34.54+1.52 while baseline of patients was 33.36+1.39. Postheparinized APTT in group II was 69.36+7.12. (Table: 2) The prolongation is 2 times in APTT compared with the control. This is highly significant (p < 0.001). Comparing baseline APTT of group II, the post-heparinized difference comes out to be 35.76. This gives a better result showing heparinization. (Table: 3).

In the present study sensitivity of ACT calculated in low dose heparin therapy was 64.28% and specificity was 62.5% and that of APTT was 90% and 100%. (Table: 4).

These results indicate that ACT is not the test of choice in monitoring low dose heparin therapy though it has advantages that it can be performed at the bedside (point of care test), results are rapidly obtained and that it does not suffer from reagent to reagent variability. It is a useful indicator where over heparinization or under heparinization is suspected and APTT results are awaited.

APTT is the test of choice in monitoring heparin therapy.

DISCUSSION

In the present study, ACT results were significant in low dose heparin therapy. Compared with APTT (gold standard) it gave sensitivity of 64.25%. Thus ACT cannot be substituted for APTT in monitoring heparin therapy, though it has its own advantages and applications. During the year 1993 2001, many research studies[11,12,13,14,15,17,18,19] on cardiology patients focused on studying the

COMPARISON OF ACT AND APTT IN MONITORING LOW DOSE HEPARIN THERAPY

			APTT
ACT		Prolong n=42	Not prolong n=8
	Prolong n=30	27	3
	Not prolong n=20	15	5

Table 4

results of low dose heparin therapy used ACT as the monitoring test. In these cases heparin therapy was given to these patients to keep the ACT as low as 130 sec to as high as 200 sec. A study was carried out using heparin bonded extracorporeal circuits during prolonged lung assist. This study was carried out on goats. In this study, ACT was used as the monitoring test and was maintained around 130 sec by systemic infusion of small doses of heparin[11]. A patient was kept on percutaneous cardiopulmonary support system (PCPS) for impaired right ventricular function. During this time period, patient was given low dose heparin therapy and his ACT level was maintained around 150 sec[12]. In a study low dose heparin therapy (0.50.8g/hr) was given to increase ACT to 1.5 2.0 times its normal value[13]. In another case report ACT was kept around 150 sec to monitor heparinization[14]. A study was carried out on one hundred and three (103) patients undergoing coronary intervention and used ACT to monitor low dose heparin in these patients[15]. 'The ACT is a bedside clotting test that is most useful for monitoring highdose heparin anticoagulation, such as during cardiopulmonary bypass surgery, can also be used when an immediate measure of heparin anticoagulation is required at the bedside, such as with extracorporeal membrane oxygenation (ECMO), haemodialysis, cardiac catheterization, and vascular surgery[16].

In our study ACT gave uniform results. Tests were carried out on the bedside and results were obtained within minutes. It supports the view that ACT may be a bedside test and gives uniform results. ACT is an alternate test available, though it does not have a significant value, to monitor heparinization in low dose heparin therapy when APTT is readily available. ACT can be introduced as a bedside test to monitor heparin therapy, as it is a useful indicator, when over or underheparinization is suspected and APTT results are awaited. All these studies in which ACT has been used to monitor low dose heparin therapy show the confidence in the test.

Our study is in confirmation with a study, which concludes that 'ACT is a simple test of adequacy of anticoagulation that can be performed at the bedside on whole blood in a reasonable time period and does not require a sophisticated piece of equipment or operator skill'[9].

CONCLUSION

ACT is a useful bedside test to monitor heparin therapy. It is a useful indicator when over or under heparinization is suspected and APTT results are awaited. However due to low sensitivity and specificity, ACT cannot substitute APTT in routine monitoring of heparanization.

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