Int J Clin Exp Med 2013;6(4):294-297
www.ijcem.com /ISSN:1940-5901/IJCEM1303006

Brief Communication

Alterations in prothrombin time and activated partial thromboplastin time in patients with acute myocardial infarction

Haseeb A Khan[1], Abdullah S Alhomida[1], Tamader Y Al Rammah[2], Samia H Sobki[3], Mohammad S Ola[1], Adnan A Khan[1]

[1]Department of Biochemistry, College of Science, King Saud University, Riyadh, Saudi Arabia; [2]College of Health and Rehabilitation Sciences, Princess Nora Bint Abdulrahman University, Riyadh, Saudi Arabia; [3]Division of Clinical Biochemistry, Department of Pathology, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

Received March 8, 2013; Accepted March 26, 2013; Epub April 12, 2013; Published April 30, 2013

Abstract: Prothrombin time (PT) and activated partial thromboplastin time (aPTT) respectively measures the extrinsic and intrinsic pathways of coagulation and are used to determine the bleeding or clotting tendency of blood. We compared PT and aPTT levels in acute myocardial infarction (AMI) patients and normal subjects. There were significant increases in PT levels in patients with STEMI (15.98 ± 0.96 s), NSTEMI (16.03 ± 0.97 s) and chest pain (15.02 ± 0.54 s) as compared to control group (8.86 ± 0.08 s). The level of aPTT in control subjects was 31.35 ± 0.48 s. Patients with STEMI (40.79 ± 1.83 s), NSTEMI (41.33 ± 2.06) and chest pain (37.84 ± 1.66 s) showed significantly higher levels of aPTT. There was a significant correlation between PT and aPTT levels. Both PT and aPTT were significantly correlated with age however there was no correlation between these coagulation markers and gender or body mass index. In conclusion, both PT and aPTT are significantly increased in AMI patients on anticoagulation therapy. The elevations in PT values were more than 2.5-fold greater than aPTT suggesting a high potential of PT for predicting blood clotting tendency in patients receiving anticoagulation therapy.

Keywords: Acute myocardial infarction, PT, aPTT, biomarker

Introduction

Hemostatic function has been linked to the pathogenesis of the complications of coronary artery disease including recurrent myocardial infarction [1]. Significant elevation in fibrinopeptide A in the early phase of myocardial infarction identifies patients with increased risk for subsequent cardiac death [2]. However, the use of fibrinopeptide A as a marker of fibrin formation is limited by the very short half-life of the compound, by artifact due to sample acquisition, and by extremely long turnaround times. Elevations in plasma concentrations of cross-linked fibrin degradation products, reflecting an increased fibrin turn-over, could be a marker of risk for complications of myocardial infarction [3]. A soluble fibrin bedside test has been found to be useful, particularly for the early identification of patients with unstable angina with a nondiagnostic electrocardiogram [4]. Plasma levels of soluble fibrin were found to be significantly higher in AMI patients than in controls with strongest predictor value of soluble fibrin for myocardial infarction at a young age [5]. Ardissino et al [6] found a U-shaped relationship between plasma prothrombin fragment 1+2 levels and the risk of developing the primary end point; thus, after an episode of acute coronary syndrome, both high and low levels of thrombin generation are predictors of an increased risk of an unfavorable outcome.

Prothrombin time (PT) and activated partial thromboplastin time (aPTT) respectively measures the extrinsic and intrinsic pathways of coagulation and are used to determine the bleeding or clotting tendency of blood. In this

Table 1. Characteristics of subjects

Group	Age (y)	M/F ratio	BMI (kg/m^2)
Control	54.85 ± 10.14	3.6	27.64 ± 3.78
STEMI	56.21 ± 12.65	4.8	28.97 ± 4.80
NSTEMI	61.98 ± 10.83	3.3	28.81 ± 5.04
Chest Pain	53.83 ± 13.75	2.9	32.27 ± 9.63

Values are means ± standard deviation.

investigation, we compared PT and aPTT levels in acute myocardial infarction (AMI) patients and normal subjects.

Patients and methods

This study was conducted on 67 AMI patients and 25 patients with chest pain, admitted to Prince Sultan Cardiac Center, Riyadh and King Khalid University Hospital, Riyadh, Saudi Arabia. The AMI patients were classified into STEMI (N=28) and NSTEMI (N=39). Mean ages of STEMI, NSTEMI and chest pain patients were 56.21 ± 12.65 y, 61.98 ± 10.83 y and 53.83 ± 13.75 y, respectively. All the AMI patients received aspirin (80-300 mg) together with multiple drug regimens. Seven of the chest pain patients did not receive aspirin. We also included 54 age- and gender-matched controls for comparison. The characteristics of subjects are given in **Table 1**.

The diagnosis of myocardial infarction required the presence of at least two of the following criteria: (i) history of characteristic prolonged (≥ 30 min) pain or discomfort, (ii) creatine kinase (CK) levels exceeding twice the upper limit of normal (or CK-MB ≥ 50% of total CK) and (iii) presence of new Q waves or new abnormal ST-T features [7]. Patients with STEMI were classified on the basis of (i) continuous chest pain upon presentation, refractory to nitrates, and lasting ≥ 30 min, (ii) ST-segment elevation of ≥ 0.2mV in ≥ 2 contiguous precordial leads, or ≥ 0.1mV in ≥ 2 contiguous limb leads, or new left bundle branch block on admission electrocardiogram, and (iii) presentation within the first 12 h from index pain. Patients with NSTEMI were required to have angina-like chest pain at rest in the last 24 h lasting ≥ 5 min, with associated ST segment depression of ≥ 0.1 mV in ≥ 2 contiguous leads upon presentation [8]. The patient exclusion criteria included recent surgery, active infection, chronic inflammatory diseases, significant hepatic or renal dysfunction and malignancy. The protocol of this study was approved by our Institutional Review Board (IRB) for human studies and all the patients signed informed consent.

The blood coagulation markers, PT and aPTT were measured by DiaPlastin and DiaClin kits (DiaMed GmbH, Switzerland). The data were evaluated by one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test using SPSS statistical package version 17. Pearson's and Spearman's tests were used for correlation analysis of continuous and categorical variables respectively. *P* values < 0.05 were considered as statistically significant.

Results and discussion

There were significant increases in PT levels in patients with STEMI (15.98 ± 0.96 s), NSTEMI (16.03 ± 0.97 s) and chest pain (15.02 ± 0.54 s) as compared to control group (8.86 ± 0.08 s) (ANOVA F=33.93, P<0.001) (**Figure 1**). The level of aPTT in control subjects was 31.35 ± 0.48 s. Patients with STEMI (40.79 ± 1.83 s), NSTEMI (41.33 ± 2.06) and chest pain (37.84 ± 1.66 s) showed significantly higher levels of aPTT (ANOVA F=10.61, P<0.001) (**Figure 1**). Schwartz et al [9] screened 223 patients with suspected acute coronary syndrome and observed that 29 (13%) and 23 (10%) had international ratio (INR) and aPTT values respectively beyond the reference range. Salamonson have shown that patients who reached the therapeutic aPTT threshold within 24 hours after heparin treatment weighed significantly less than those who did not reach the therapeutic threshold within the stipulated time suggesting that a non-weight based heparin regimen is ineffective in the rapid achievement of therapeutic aPTT [10]. Pearson product moment correlation showed negative correlations between aPTT and the day of onset of recurrent angina and target vascular revascularization, and positive correlations for myocardial infarction and death in ACS patients treated with unfractionated heparin [11]. Activated partial thromboplastin time tended to be prolonged in the group with physical training, while it was shortened in the control group [12]. Granger et al [13] have noticed an unexpected direct relationship between the aPTT and the risk of subsequent reinfarction.

There was a significant correlation between PT and aPTT levels (Pearson correlation coeffi-

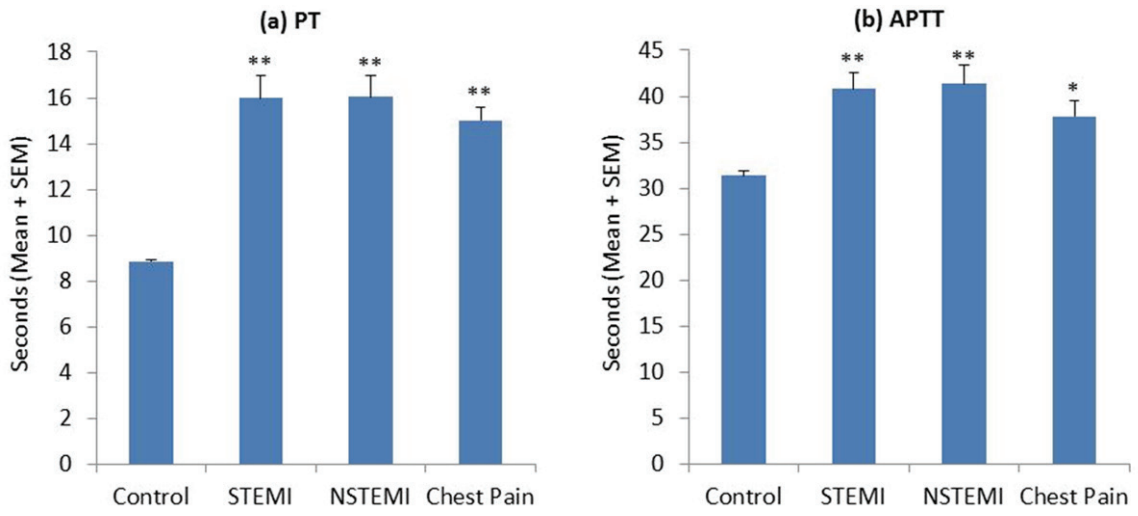

Figure 1. Blood coagulation markers in different groups. *P<0.01 and *P<0.001 versus control group using Dunnett's multiple comparison test.

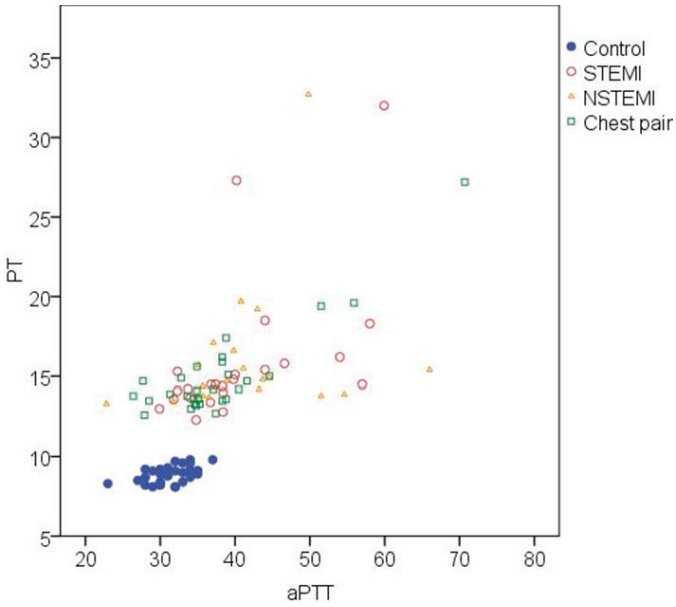

Figure 2. Correlation between PT and aPTT (correlation coefficient=0.620, P<0.001, Pearson's test).

Table 2. Correlations between coagulation markers and age, gender and BMI

	PT		aPTT	
Group	R	P	R	P
Age	0.364	0.000*	0.343	0.000*
Gender	-0.079	0.302	-0.120	0.115
BMI	0.032	0.725	-0.020	0.825

*Statistically significant.

cient, R=0.620, P<0.001, **Figure 2**) indicating a mutual interaction between the intrinsic and extrinsic pathways of blood coagulation. The percent increases in PT in the patient groups were as follows: STEMI (80.36%), NSTEMI (80.92%) and chest pain (69.52%). However, the percent increases in aPTT in the patient groups were not as profound as PT and were as follows: STEMI (30.11%), NSTEMI (31.83%) and chest pain (20.71%). The ratios of percent increases (PT/aPTT) in the patient groups were found to be 2.67-fold (STEMI), 2.54-fold (NSTEMI) and 3.35-fold (chest pain), indicating that PT is comparatively more sensitive in predicting the response to anticoagulant therapy. Both PT and aPTT were significantly correlated with age however there was no correlation between these coagulation markers and gender or BMI (**Table 2**) suggesting that age of the patient should be taken into account while interpreting these markers.

In conclusion, both PT and aPTT are significantly increased in AMI patients on anticoagulation therapy. The elevations in PT values were more than 2.5-fold higher than aPTT suggesting a greater responsive potential of PT for predicting blood clotting tendency in patients receiving anticoagulation therapy. Further studies are warranted to determine the correlation between PT and soluble fibrin while achieving the set ref-

erence ranges for the management of AMI patients.

Acknowledgments

This study was supported by National Plan for Science and Technology (NPST) Program by King Saud University Project Number 08-BIO571-02. We are thankful to Dr. Shahid Habib and Dr. Abdulrahman Al Moghairy for clinical observations. The technical assistances of the nursing staff of King Khalid University Hospital and Prince Sultan Cardiac Center, Riyadh for sample collection and patient care are gratefully acknowledged.

Address correspondence to: Dr. Haseeb A Khan, Department of Biochemistry, College of Science, Bld 5, Rm 1B20, King Saud University, P.O. Box 2455, Riyadh 11451, Saudi Arabia. E-mail: khan_haseeb@yahoo.com, haseeb@ksu.edu.sa

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