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# Assessment of Activated Partial Thromboplastin Time Level in Patients with Acute Myocardial Infarction Receiving Fixed-Dose Intermittent Intravenous Heparin Therapy

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## Abstract

***Introduction-*** Heparin is one of the current and necessary medications in acute myocardial infarction (MI). Given the narrow therapeutic dose and unpredictable pharmacokinetics of heparin, its anticoagulant effect should be measured precisely. Despite the widespread utilization of heparin in intermittent fixed doses and weight-independent IV administration, our data about the range of aPTT as a monitoring marker are quite limited. Thus we prepared this study to measure if the custom method fills the target therapeutic range.

***Methods-*** This cross-sectional study was performed on 144 patients admitted to our department with acute MI in 2004, who received heparin 5000 units q4h and had daily aPTT checked on three consecutive days. We chose the second day samples for this study, and the data were gathered by a checklist and analyzed with SPSS software.

***Results-*** 12.5% of patients had aPTT levels in the therapeutic range, 6.2% of patients had a mean aPTT level above therapeutic range and remarkably, 81.3% of patients never achieved the therapeutic range. Our results also demonstrated that older age and female sex are associated with higher aPTT levels, and smoking unlike diabetes is associated with lower aPTT levels.

***Conclusion-*** Despite tolerability by patients and staff, the above findings necessitate reconsideration in the dose and interval of customary heparin administration (5000 unit IV q4h) and changing to continuous infusion method or use of low molecular weight heparins ***(Iranian Heart Journal 2007; 8 (2): 22-25).***

**Key words:** partial thromboplastin time ■ myocardial infarction ■ heparin

Administration of heparin in the acute phase of myocardial infarction is an inevitable part of the treatment plan.[1,2] Reducing risk of infarction and cardiac mortality in patients with unstable angina, prevention of deep venous thrombosis, pulmonary embolism, ventricular thrombus formation and cerebral embolization, and establishing and maintaining the patency of the infarct-related artery in patients with myocardial infarction are among the beneficial effects of heparin.[3]

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ischemic/embolic events. The dominant routine test to monitor heparin is "activated partial prothrombin time", aPTT. The test is sensitive to the inhibitory effect of heparin on thrombin and factors X and IX.[7]

Although reactions of various trademarked kits to heparin are remarkably different, the widely accepted therapeutic range for all these reactions is 1.5 – 2.5 times that of control level, which is about 45 – 75 seconds.[8] There have been different ways to administrate heparin, but the commonly used ways are continuous intravenous infusion and subcutaneous injection. The most important advantage of intravenous infusion to intermittent methods is the lower risk of hemorrhage.[8] The latter needs an infusion pump, and the subcutaneous route is mostly used for low molecular weight heparins. Because of some restrictions using these methods, a widespread use is not possible.

This research aimed to assess the effectiveness of heparin administration with a dose of 5000 units q4h intravenously and determine if this method could achieve a therapeutic level of anticoagulant effect according to aPTT, having advantages of heparin with minimum risk of hemorrhage. Taking a brief look at the amount of aPTT tests requested in cardiology departments emphasizes the importance of this research.

**Term definitions:**
Diabetes: FBS more than 120mg/dl or previous history of taking glucose-lowering drugs.
Hypertension: Blood pressure ≥140/90mmHg or previous history of taking BP lowering drugs.
Hyperlipidemia: Cholesterol ≥200mg/dl and or triglyceride ≥ 200mg/dl.

## Methods

Collecting data among patients with a diagnosis of acute myocardial infarction in 2004, we chose 144 patients with hospitalization of more than four days and consistent medical records. The subjects had the following criteria:
1- typical ST elevation in at least two contiguous leads,
2- elevated enzymes proving myocardial infarction, and
3- heparin administrated q4h 5000 units intravenously.
Selected data were age, sex, risk factors of diabetes, hyperlipidemia, hypertension, smoking and aPTT. Heparin administration was checked according to nursing records, i.e. every 4 hours and the same for all patients at 4, 8,12,16,20 and 24 hours.
The first day aPTT was omitted because of probable contiguity of heparin administration and taking sample or streptokinase administration in some patients. Because second and third day aPTT checks showed no significant difference in paired sample T-test ($P<0.7$), only second day aPTTs were considered in the statistical analysis.

## Results

Among 144 patients, 43 were female (29.9%) and 101 male (70/1%). The youngest patient was 25 and the eldest 87 years old. The average age was $59 \pm 13$ and the median 61.

**Table I. Patient characterisitics**

| | Number |
|---|---|
| Total patients | 144 |
| Male | 101 |
| Female | 43 |
| Diabetes | 34 |
| Smoking | 47 |
| Hypertension | 61 |
| Hyperlipidemia | 59 |

Among 144 studied patients, 117 patients (81.3%) never achieved therapeutic range by aPTT levels and only 18 patients (12.5%) achieved therapeutic range and 9 patients (6.2%) reached above the therapeutic range (Table II). Mean aPTT for the whole group was $38.7 \pm 23$ seconds.

**Table II. Results of aPTT by number and frequency of patients.**

| Patients | aPTT (sec) | Freq. % |
|---|---|---|

| | | | |
|---|---|---|---|
| | 117 | 45< | 81.3 |
| | 18 | 45-74 | 12.5 |
| | 9 | >75 | 6.2 |
| Total | 144 | 38.7 ± 23 | 100 |

Mean aPTT was 37.4 ± 24.6s in males and 42 ± 20s in females. The mean female aPTT was 5 seconds longer, but this was not statistically meaningful (P<0.27). For an evaluation of the effect of age on therapeutic response, the patients were divided into two groups of less than 60 years old and more than 60; T-test showed there was a meaningful difference between the two groups (P=0.001, Table III ).

**Table III. Comparison of mean aPTT in two age groups.**

| Age group | Frequency | mean | SD |
|---|---|---|---|
| <60 | 70 | 32.3 | 16.5 |
| >60 | 74 | 44.9 | 27 |

Pearson's correlation test between two variables of age and aPTT showed that increasing age had a meaningful correlation with aPTT (P<0.007). Chi-square test showed no meaningful difference between aPTT of patients with one of the risk factors of hyperlipidemia, hypertension and diabetes; there was, however, a meaningful relation between aPTT and smoking, such that aPTT level in smokers was lower than that in non-smokers (p=0.007).

## Discussion

The customary method of heparin administration is more affordable for patients and staff. For patients it is a convenient method because comparatively there is no need to be still, immobile or supine for a lengthy period of time for continuous infusion or have frequent subcutaneous injections, and for staff because there is no need for extra justification of heparin IV doses. Besides the mentioned factors, low cost, simplicity and comfort are other causes of acceptance of this method both for patients and staff, but the question is if this method is efficient enough to achieve therapeutic goals.

The main objective of this research was to evaluate the customary method of heparin administration in cardiac patients. The findings of the research revealed that efficacy of this method of heparin administration based on aPTT monitoring was severely under question, since more than 80 percent of patients never achieved expected therapeutic range by aPTT.

The results at first glance suggested that timing and/or dosing of heparin administration should be reconsidered. The other remarkable point was that patient indices in dose adjustment were not taken into consideration. One very important such index is patient weight,[7,9] while practically all patients received a fixed dose. Finally not using infusion method and eventually no standard nomogram to adjust dose and infusion speed based on aPTT leaves no chance to adjust dosage, so daily aPTT checks are practically useless except for instances of over-prolonged aPTT due to excess heparin.

Another objective of this research was to study the effect of factors like age, sex and blood sugar on patient anticoagulant responses. Our results similar to other trials have demonstrated that low body weight, older age,[6,12] and female sex were associated with higher aPTTs and that smoking[6,12,13]

unlike diabetes was associated with lower aPTTs. Therefore, for achieving optimal results from heparin administration, we offer some recommendations:

1- Administration of heparin based on patients' body weights, not a global single dose.
2- Administration of heparin by continuous infusion method and dose adjustment according to aPTT results.
3- It seems that because of labor, instrumental and paraclinical overhead charges by the two above-mentioned methods lead us to more attractive and recommended method of using low molecular weight heparin subcutaneously with higher clinical efficacy and reliable rapid therapeutic leveling.[3,14] This method may at first seem expensive but in the long term, it could bring remarkable and reasonable cost savings.[14]

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# Comparison of Selenium, Zinc, Copper, TNF-a and IL-6 Serum Levels and Erythrocyte GSH-PX Activity in Patients with Acute and Chronic Coronary Artery Disease

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Abstract

*Background*- **Selenium (Se) is part of the enzyme glutathione peroxidase (GSH – Px) that plays an important role in the antioxidant defense of the body. Evidence has demonstrated that populations with low intake of selenium in the diet have a 2-3 fold risk of ischemic heart disease. Positive statistically significant correlations have been found between trace element concentrations (Cu, Zn, Se) of heart tissue with physiological parameters (CO: cardiac output, EF: ejection fraction) of the heart. Increased plasma concentration of TNF-α has been found in patients with coronary artery disease. Stressed myocardium activates pro-inflammatory cytokines, such as TNF-α, which produce abnormalities in myocyte contractile function. This study was done to determine the circulating levels of Cu, Zn, Se, IL- 6, TNF - α, and erythrocyte GSH - PX activity in two groups of patients with chronic coronary artery disease (CCAD), acute myocardial infarction (AMI) and normal individuals (IHD-free).**

*Methods*- **Patients were divided into two groups: 25 with chronic CAD (CCAD) and 25 with acute myocardial infarction (AMI). The control group was 50 normal individuals that did not have any symptoms for IHD, and was gender and age-matched with the patients. Blood samples were collected during the first hours after the onset of chest pain in the acute MI group. Serum levels of Se, Cu, and Zn were determined by atomic absorption spectrometry, TNF-α and IL-6 were measured with ELISA and erythrocyte GSH-PX activity with Paglia and Valentine methods.**

*Results*- **In both groups of patients, there was a significant reduction of Se in the serum (82.36±11.31 micg/l in CCAD, 74.08±11.31 in AMI vs. 105±32.52 in control group, P-value=0.03). No**