ORIGINAL ARTICLE

To Identify the Role of C-Reactive Protein in Predicting the Response of Thrombolytic Therapy in Acute Myocardial Infarction

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ABSTRACT

Objectives: To identify the role of c-reactive protein in predicting the response of thrombolytic therapy in acute myocardial infarction.
Study design: Cross sectional study.
Setting: Department of Medicine, Nawaz Sharif Social Security Hospital Lahore.
Duration of study: This study carried out from February 2011 to January 2012.
Subjects and methods: Sixty patients were included in this study. Information of patients like age, symptoms, myocardial infarction distribution, symptoms according their sex, thrombolytic therapy, correlation between CRP-1 and time duration and CRP-2 and time duration.
Results: The age range was 37-70 years, most common age group was 51-60 years, 26(43%) patients. Forty (67%) were males and 20(33%) were females. Chest pain, sweating, dyspnea and vomiting were the main symptoms at presentation, among them chest pain and sweating were the most common, 30(50%) patients. Inferior wall MI was the most common, 25(45%) patients. Successful thrombolysis was seen in 39(65%) patients and 21(35%) patients failed to respond. There was significant correlation between duration of symptom onset and plasma CRP levels (P value <0.05).
Conclusion: It is concluded that C-reactive protein has prognostic value for outcome of the disease in patients with acute myocardial infarction and plasma C-reactive protein begins to rise 4-6 hours after onset of symptoms in acute myocardial infarction.
Key words: C-reactive protein, acute MI, thrombolytic therapy

INTRODUCTION

Ischemic heart disease is the leading cause of death worldwide. It is associated with high patient morbidity and mortality. The inflammation plays a key role in the pathogenesis of atherosclerosis and plaque formation. The chronic inflammatory process can lead to an acute clinical event by the induction of plaque rupture and thus leading to acute coronary syndrome[1,2].

Approximately half of all individuals who present with an acute coronary event do not have any of the conventional risk factors, such as smoking, diabetes and hypertension[3]. In recent years, new insights have revolutionized our understanding of potential inflammatory markers as risk factors for underlying cardiovascular disease[4]. The serum inflammatory markers are elevated in patients with acute coronary syndrome[5]. In particular, C-reactive protein has received great attention as one of these novel atherogenic markers[6,7]. Serum C-reactive protein is one of these inflammatory markers and is very sensitive marker for acute inflammatory reactions[8].

Thrombolytic therapy and acute coronary intervention has reduced mortality significantly after acute myocardial infarction. Thrombolytic therapy reduces mortality by improving myocardial perfusion and reducing the incidence of life threatening arrythmias[9]. Many non-invasive markers, like resolution of chest pain, St-segment elevation and biochemical assays are used to assess the success of thrombolytic therapy[10]. Serum C-reactive protein is one of these biochemical markers that help to predict the efficacy of thrombolytic therapy in patients with acute myocardial infarction[11].

METHODOLOGY

Sixty patients of acute myocardial infarction who were given thrombolytic therapy were included in the study. The diagnosis of acute myocardial infarction was made on clinical parameters and ECG criteria, ECG changes with St-segment elevation 2mm or more in consecutive two chest leads and 1mm or more in consecutive two limb leads. The ECG changes were noted before starting thrombolysis. The baseline sample for C-reactive protein (CRP-1) was taken before starting thrombolysis. The time

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duration between onset of symptoms and start of thrombolysis was also noted. The thrombolysis was done with streptokinase infusion, 1.5 million units diluted in 100ml normal saline, intravenously over one hour. The ECG was repeated after six hours of completion of thrombolysis and, changes were noted and compared with ECG changes before thrombolysis. Now second sample for C-reactive protein (CRP-2) was taken after six hours of completion of thrombolysis. About 5ml blood was taken in non-anticoagulated vial for each sample. Both samples were sent to laboratory for analysis. The serum levels of C-reactive proteins were checked qualitatively with latex agglutination method.

The positive samples for C-reactive proteins were checked quantitatively by dilution method. The results of both samples, CRP-1 and CRP-2 were noted. The normal serum CRP value was 6mg/L. The values above this were positive and below were negative. According to ECG findings after thrombolysis, all patients were divided into two groups.

Group A: was considered as successful group to thrombolysis, in whom ECG changes were settled.

Group B: was considered as unsuccessful group to thrombolysis, in whom ECG changes remained same as before thrombolysis. Now the both values of C-reactive protein, CRP-1 and CRP-2 were compared in both groups group A and group B.

Data analysis: The findings were recorded on a proforma and data was analyzed according to SPSS version 16. The following variables were included in my study like age, sex, clinical symptoms, Time duration between onset of symptoms and start of thrombolysis, types of myocardial infarction, association of heart failure with myocardial infarction. The patients were divided in group A and B. The nominal variables were recorded as frequencies/percentages. The numerical data was recorded as Mean±SD. Independent sample t test and paired sample t test, were used for analysis of numerical data. Pearson Chi-square test was used for correlation (cross tabulation) among different nominal variables.

RESULTS

In this study total 60 patients of acute myocardial infarction, receiving thrombolytic therapy with streptokinase were included. Out of these 60 patients 4(7%) patients were having age upto 40 years (2 patients of 37 years and 2 of 40 years). Majority of them were among 41-60 years of age groups. Twenty patients (33%) were having age from 41-50 years and 26 patients (43%) were having their ages between 51-60 years. Only 10 patients (17%) were having ages between 61-70 years (Table 1). Out of total 60 patients, 20 patients (33%) were females and 40 (67%) were males (Table 2).

Among these symptom groups, chest pain and sweating were the most common symptoms in males, 17 patients (57%) out of 30 patients in this symptom group. While vomiting and vertigo were the most common symptoms in females 4 (67%) patients out of 6 patients in this symptom group. Correlation study between males and females for symptom groups showed no significant correlation between sex and symptoms. The P value is 0.06 (Table 3).

In this study, there were seven types of myocardial infarctions. Among them, acute inferior wall MI was the most common, 25 (42%) patients out of total 60 patients. Next most common types were acute anterior wall MI and acute anterolateral wall MI, 10 (17%) and 13 (21%) respectively. Lateral wall MI and inferior wall with right ventricular infarcts were the least common types of infarcts in this study, only 2 (3%) patients in each type. Acute anteroseptal MI and acute inferoposterior wall MI were 4 (7%) patients in each type (Table 4).

Successful thrombolysis based on ECG changes was observed in 39(65%) patients out of the total. In 21(35%) patients unsuccessful thrombolysis was considered whose ECG changes remained same as before thrombolysis. The baseline C-reactive protein was positive in 39(65%) patients and negative in 21(35%) patients out of total 60 (Table 5).

Majority of patients having positive baseline C-reactive protein came between 3-4 and 5-6 hours after starting symptoms, 15(25%) and 9(7%) respectively, out of 39 patients. Fifteen (25%) patients came after 6 hours of starting symptoms, all of them were having positive baseline C-reactive protein. Only in 5(8%) patients, baseline C-reactive protein was positive who came within two hours of starting symptoms. Majority of patients having baseline C-reactive protein negative came within 2 hours after starting symptoms, 17(28%) out of 21(35%) patients. Only 4(7%) patients were having baseline C-reactive protein negative who came between 3-4 hours of starting symptoms (Table 6). There was also significant correlation between C-reactive protein after thrombolysis (CRP-2) and time duration (time between onset of symptoms and start of thrombolysis). The P value is 0.00. C-reactive protein after thrombolysis (CRP-2) was positive only in 19(32%) patients and was negative in 41(68%) patients. Majority of patients having positive CRP values after thrombolysis came after 6 hours of starting symptoms, 13(22%) out of 19(32%) patients. Only 6 patients had negative CRP-2 who came between 5-6 hours and after 6 hours after starting symptoms, 4(7%) and 2(3%) respectively (Table 6).

The mean value of C-reactive protein before thrombolysis (CRP-1) was 15.95±19.87 in successful group to thrombolysis. The mean value of C-reactive protein after thrombolysis (CRP-2) was 1.23±7.69 in patients having successful and unsuccessful thrombolysis. There was significant difference in mean values of C-reactive protein before and after thrombolysis in patients having successful thrombolysis with significant P value of 0.000. The paired difference between mean values of C-reactive protein before and after thrombolysis was 14.72±19.31. There was no significant difference in mean values of C-reactive protein before and after thrombolysis in patients having unsuccessful thrombolysis (P value=0.086). The paired difference between mean values of C-reactive protein before and after thrombolysis was 0.76±19.50 (Table 7).

There was significant correlation between basal C-reactive protein (CRP-1) and response of thrombolytic therapy with significant P value of 0.002. Out of 39 patients having successful thrombolysis, 20(51%) patients had baseline C-reactive protein positive and negative in 19(49%) patients. Out of 21 patients having unsuccessful thrombolysis, 19(90%) patients had positive baseline C-reactive protein and only 2(10%) patients had negative basal C-reactive protein. The predictive value of baseline C-reactive protein for thrombolytic response was 63.3% (Table 8). There was also very significant correlation between C-reactive protein after thrombolysis (CRP-2) and response of thrombolytic therapy with significant P value of 0.000. Out of 39 patients having successful thrombolysis, only 1(3%) patient had positive C-reactive protein after thrombolysis and 38 patients (97%) had negative C-reactive protein after thrombolysis. While out of 21 patients having unsuccessful thrombolysis, 18(86%) patients had positive C-reactive protein after thrombolysis and only 3(14%) patients became negative. The predictive value of C-reactive protein for response of thrombolytic therapy was 93.3% (Table 8).

Table 1: Age distribution of patients (n=60)

Age Range (years)	n=	%age
< 40	4	7
41-50	20	33
51-60	26	43
61-70	10	17

Table 2: Sex distribution of patients

Sex	n=	%age
Male	40	67
Female	20	33

Male to female ratio 2.0:1

Table 3: Association between symptoms and sex distribution

Symptoms	n=	Male	Female
Chest pain, sweating	30	17(57%)	13(43%)
Chest pain, dyspnea	4	4(100%)	-
Chest pain, Sweating & Vomiting	7	7(100%)	-
Chest pain, dyspnea, sweating & vomiting	11	8(73%)	3 (27%)
Chest pain, sweating & dyspnea	2	2(100%)	-
Vomiting, Vertigo	6	2 (33%)	4 (67%)

P value = 0.06

Table 4: Types of MI (frequency distribution)

Types	n=	%age
Inferior wall MI	25	42
Anterior wall MI	10	17
Anteroseptal MI	4	7
Anterolateral MI	13	21
Lateral wall MI	2	3
Inferoposterior wall MI	4	7
Inferior wall + right ventricular MI	2	3

Table 5: Response of Thrombolytic Therapy (Percentage)

Groups	n=	%age
Group A	39	65
Group B	21	35

Group A = Successful thrombolysis (based on ECG changes)
Group B = Unsuccessful thrombolysis (based on ECG changes)

Table 6: Correlation between CRP-1 and CRP-2 time duration

Duration	CRP-1		CRP-2	
	+ve	-ve	+ve	-ve
Upto 2 hours	5(8%)	17(28%)	-	22(36%)
3-4 hours	15(25%)	4(7%)	6(10%)	13(22%)
5-6 hours	4(7%)	-	-	4(7%)
Above 6 hours	1525%)	-	13(22%)	2(3%)
Total	39(65%)	21(35%)	19(32%)	41(68%)

P value = 0.00
CRP-1 = C-reactive protein before thrombolysis
CRP-2 = C-reactive protein after thrombolysis

Table 7: Response of C-reactive protein (CRP 1 & 2)

CRP	Group A		Group B	
	=n	Mean±SD	=n	Mean±SD
CRP-1	39	15.95±19.87	21	37.81±27.00
CRP-2	39	1.23±7.69	21	37.05±30.04
Paired differen ce		14.72±19.31		0.76±19.50

P value = 0.000 P value = 0.086

Table 8: Correlation between C-Reactive Protein and Thrombolytic Response (Relationship of CRP-1 and CRP-2 to Group A & B**)**

Groups	=n	C-Reactive Protein-1		C-Reactive Protein-2	
		+ve	-ve	+ve	-ve
Group A	39	20(51%)	19(49%)	1(3%)	38(97%)
Group B	21	19(90%)	2(10%)	18(86%)	3(14%)
Total	60	39(65%)	21(35%)	19(32%)	41(68%)

Predictive value of CRP-1 = 63.3% *Predictive value of CRP-2 = 93.3%*
P value = 0.002 *P value = 0.000*

DISCUSSION

This study was conducted to know the predictive value of C-reactive protein for thrombolytic response, comparing CRP values to ECG changes before and after thrombolysis. Sixty patients of acute myocardial infarction, receiving thrombolytic therapy with intravenous streptokinase were enrolled in the study.

No comparable study was found in Pakistan in literature review. However, the study was comparable to Auer[1] which included 25 patients of AMI, having age range 40-86 years, 18(72%) males, 7(28%) females. While in this study 60 patients of AMI were enrolled, having age range 37-70 years, 40(67%) were males and 20(33%) were females, which is quite comparable. In this study the baseline CRP values were significantly higher in patients with AMI than stable CAD (P value 0.001), shortly after the onset of symptoms (12 hours after). While in our study 39 (65%) patients out of 60 were having high titre of C-reactive protein after 4-6 hours of onset of symptoms (P value 0.000). In Auer's study the CRP values were compared in patients with AMI and stable CAD, while in this study CRP values were compared to ECG changes before and after thrombolysis[1].

Zaires[11] study was also comparable to this study in view of association between plasma CRP levels and response of thrombolytic therapy. Three hundred nineteen patients of acute St-segment elevation MI, who were given intravenous thrombolysis, their ECG changes (resolution of ST-segment) after thrombolysis, were compared to plasma CRP values. Those patients having low plasma CRP values, were having higher incidence of resolution of ST-segment elevation (P value <0.05), while there was low incidence of resolution of ST-segment elevation in patients having higher plasma CRP values (P values 0.06). While in this study those patients having complete resolution of St-segment elevation (successful group to thrombolysis) were having significance difference in mean values of CRP before and after thrombolysis (Mean difference value 14.72±19.31, P value 0.00), and there was no significant difference in mean values of CRP in those patients whose St-segment elevation did not resolve completely (unsuccessful to thrombolysis) after thrombolysis (Mean difference value 0.76±19.50, P value 0.086).

This study is also comparable to Pietela[12] in view of assessing the response of thrombolytic therapy by measuring plasma CRP values. However the comparative parameters in this study were serial cardiac enzymes (CK-MB) and thalium scan, while in my study ECG was the only comparative parameter. The number of patients was only 9, who were given intravenous streptokinase, while in our study 60 patients were enrolled.

According to Dibra[13] CRP levels on admission may predict the efficacy of reperfusion response in patients which AMI, this stands true for my study too. As 38 (97%) patients out of 39 (having successful thrombolysis) with elevated baseline CRP values, got reduction in CRP values, after thrombolysis and 18 (86%) patients out of 21 (those having unsuccessful thrombolysis) failed to have any change in plasma CRP values after thrombolysis). However in this study different combination of reperfusion strategies e.g. stenting plus abciximab, thrombolysis with streptokinase alone and streptokinase plus abciximab were used, while in this study reperfusion was done only with streptokinase.

The current study is also comparable to Berton[14] study in view of knowing the predictive values of C-reactive protein for association of heart failure with acute myocardial infarction. In Berton's study, baseline and subsequent CRP values were higher in patients having associated heart failure with AMI than those patients without heart failure (P value 0.00). This also stands true in the present study as well.

CONCLUSION

It is concluded that the ECG, C-reactive protein is a strong predictor of response of thrombolytic therapy in patients with acute myocardial infarction. C-reactive protein has prognostic value for outcome of the disease in patients with acute myocardial infarction. Plasma C-reactive protein begins to rise 4-6 hours after onset of symptoms in acute myocardial infarction.

REFERENCES

1. Auer J, Berent R, Lassnig E, Eber B. C-reactive protein and coronary artery disease. Jpn Heart J 2002; 43: 607-19.
2. Ross R. Atherosclerosis an inflammatory disease. N Engl J Med 1999; 340: 115-26.

3. Braunwald E. Shattuck Lecture: Cardiovascular medicine at the turn of the millennium: triumphs, concerns and opportunities. N Engl J Med 1997; 337: 1360-9.
4. Gabay C, Kushner I. Acute phase proteins and other systemic responses to inflammation. N Engl J Med 1999; 340: 448-54.
5. Topol EJ. A guide to therapeutic decision – making in patients non-ST-segment elevation acute coronary syndromes. J Am Coll Cardiol 2003; 41: 123-9.
6. Kervinen H, Palosuo T, Manninen V. Joint effects of C-reactive protein and other risk factors on acute coronary events. Am Heart J 2001; 141: 580-5.
7. Ridker PM, Haughery P. Prospective studies of C-reactive protein as a risk factor for cardiovascular disease. J Invest Med 1998; 46: 392-5.
8. Gardezi AR, Sattar A, Ahmed T. Intravenous thrombolytic treatment in acute myocardial infarction. Biomedica 2000; 16: 78-9.
9. Ablij HC, Meinders AE. [Atherosclerosis and inflammation: the role of C-reactive protein] Ned Tijdschr Geneeskd 2003; 147: 15-20.
10. Mujib F, Nadeem MA, Waeem T, Khalid AW, Khan AH. Non-invasive markers of reperfusion following thrombolysis in acute myocardial infarction. Pak J Cardiol 1999; 10: 108-14.
11. Zaires MN, Manousalus SJ, Stefanidis AS, Papadaki OA, Andriko Poulos GK, Olympias CD et al. C-reactive protein levels on admission are associated with response to thrombolysis and prognosis after ST-segment elevation acute myocardial infarction. Am Heart J 2002; 144: 782-9.
12. Pietela K, Harmoinen A, Poyhonen L, Koskinen M, Heikkilo J, Ruosteeroja R. Intravenous streptokinase treatment and serum C-reactive protein in patients with acute myocardial infarction. Br Heart J 1987; 58: 225-29.
13. Dibra A, Mehilli J, Schwaiger M, Schuhlen H, Bollowein H, Braun S et al. predictive value of basal C-reactive protein levels for myocardial salvage in patients with acute myocardial infarction is dependent on the type of reperfusion treatment. Eur Heart J 2003; 24: 1128-33.
14. Berton G, Cardiano R, Palmeri R, Pianca S, Pagliara V, palatine P. C-reactive protein in acute myocardial infarction: association with heart failure. Am Heart J 2003; 145: 1094-101.