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Original Article

Prognostic importance of c - reactive protein levels in ischemic heart disease

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ABSTRACT

Objectives: C-reactive protein (CRP) is a highly sensitive marker of inflammation and tissue injury. This study aims to evaluate the changes in the CRP levels in the serum in patients with Ischemic Heart diseases and to evaluate the utility of CRP levels as a diagnostic and prognostic tool of myocardial ischemia and infarction. Methods: We carried out a case-control study over 18 months wherein the study groups are compared with healthy control group with respect to their CRP values on admission, after 48 hours and at the end of one week. Study group included Stable angina group (n=25), Unstable angina (UA) group (n=25) and AMI group (n=50) along with healthy control group (n=25). Results: The mean (± SD) age group in our study groups was matched with the control group. Males dominated the present study groups and control groups. In UA group, majority 80% of patients had raised CRP (1.776± 2.68 mg/dl) compared to control group and stable angina group. In AMI group all patients had a raised CRP (4.752± 4.56 mg/dl) on admission and these values were higher compared to UA group and control group ($p < 0.001$). In UA group 16% and in AMI group 66% developed complication and both these groups had significantly higher CRP levels on admission as compared to those patients who had no complications ($P < 0.001$). The patients who expired also had significantly higher CRP values (9.45 ± 5.435 mg/dl) on admission as compared to those without any complications ($P < 0.001$). Conclusions: Higher the CRP value on admission and 48 hours more is the risk of complications and death. Hence CRP values help in risk stratification and predicting the prognosis.

1. Introduction

Atherosclerotic process has a long pre-symptomatic phase, which begins early in life as 'Fatty Streaks'. Major hypothesis proposed for atherosclerosis- Lipid hypothesis [Virchow's] and vascular injury hypothesis [Ross]. Infectious theory for atherosclerosis has been proposed1 .The study of Van Der Wal et al 2 strongly raises the possibility of inflammation in atherosclerosis. The assessment of inflammatory markers may help in diagnosis and prognostic stratification in acute coronary syndromes3, 4.C-reactive protein (CRP) is a prototypical acute phase reactant. It is a β -globulin synthesized in hepatocytes in response to inflammation. It is a highly sensitive but non-specific marker of inflammation. To study the changes in the C-reactive protein levels in the serum in patients with ischemic heart diseases(IHD), by comparing the CRP levels on admission, after 48 hours and at the end of one weekand to evaluate the utility of CRP levels as a diagnostic and prognostic tool of myocardial ischemia and infarction.

2. Materials and Methods

Design: Case-control study wherein the study groups are compared with healthy control group with respect to their CRP values, including complications during the period of 18 months.

Subjects: Study group included stable angina group (n=25), unstable angina (UA) group (n=25) and acute myocardial infarction (AMI) group (n=50) along with healthy control group (n=25). Standard diagnostic criteria used for selection of patients of stable angina, UA and AMI groups.

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Stable angina pectoris is characterized by chest or arm discomfort that may not be described as pain but is reproducibly associated with physical exertion or stress and is relieved within 5–10 minutes by rest and/or sublingual nitroglycerin[5].

UA is defined as angina pectoris or equivalent ischemic discomfort with at least one of three features: (1) it occurs at rest (or with minimal exertion), usually lasting >10 minutes; (2) it is severe and of new onset (i.e., within the prior 4–6 weeks); and/or (3) it occurs with a crescendo pattern (i.e., distinctly more severe, prolonged, or frequent than previously) [5].

Selection criteria for patients with AMI: (At least two of the following criteria were fulfilled)

1) Prolonged severe ischemic chest pain of ≥20 minutes duration.

2) Diagnostic Electrocardiogram (ECG) new q waves or persistent ST elevations.

3) An increase in cardiac enzymes above normal in at least two consecutive samples6.

Exclusion criteria:

Intercurrent inflammatory or neoplastic conditions likely to be associated with an acute phase response, a left bundle branch block invalidating its ST segments analysis, smokers and those with very high cholesterol levels were excluded.

Test: Passive Agglutination test using RHELAX CAP kits (slide test), on admission, at 48 hrs and at one week.

Statistics:

Data were presented as the mean ± standard deviation (SD). Each group values were compared with the control group values using 'unpaired t test'. Test 'significant' if p values < 0.05.

3. Result

In our study, the mean age (± SD) stable angina group was 58.9 ± 7.72 years, in UA group 62.76 ± 7.699 years and in AMI group 60 ±10.552 years.

In control group mean age (± SD) was 58 ± 6.775 years. Statistically we found no significant difference in mean (± SD) age in study groups and control groups (P > 0.05). In our study, stable angina group included 20 males (80%) and 5 females (20%). Among the UA group, 17 (68%) were males and 8 (32%) were females. In AMI group, 35 (70%) patients were males and 15 (30%) patients were females. Similarly, control group included 18 (72%) males and 7 (28%) females. In each group, there is a similar male predominance and all the study groups are statistically comparable with the control group.

Table no 1 showing CRP values in UA and AMI groups on admission, after 48 hours and after one week and CRP values on admission in stable angina and in control group

Groups	CRP values at admission(mg/dl)		CRP values at 48 hrs(mg/dl)		CRP values at one week(mg/dl)	
	No of patients	Mean ± SD	No of patients	Mean ± SD	No of patients	Mean ± SD
UA	25	1.776 ± 2.680	25	3.60±5.310	25	3.24±8.582
AMI	50	4.752 ± 4.560	38	8.463±6.525	35	1.73±1.189
Stable angina	25	0.048 ± 0.1661				
control	25	0.048±0.1661				

Stable angina vs. control p > 0.005- statistically not significant
Unstable angina vs. Control p< 0.005- statistically significant
AMI vs. Control p< 0.001- statistically significant

Table No.2 showing CRP values in unstable angina with complications (n = 4) and without complications (n = 21).

Groups	CRP values at admission(mg/dl) Mean ± SD	CRP values at 48 hrs(mg/dl) Mean ± SD	CRP values at one week(mg/dl) Mean ± SD
Patients with complications (n= 4)	7.2± 2.771	14.4± 5.543	19.2± 13.576
Patients without complications (n= 21	0.743± 0.682	1.543± 1.208	0.2± 0.289

Group with complications vs. group without complications p< 0.001

Table no. 3 showing CRP values in AMI group with complications (n = 33) and those who expired (n = 16) with those without any complications (n = 17).

Group AMI	CRP values at admission (mg/dl)		CRP values at 48 hrs(mg/dl)		CRP values at one week (mg/dl)	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
Patients without complications	17	1.976± 0.591	17	4.517± 0.797	17	1.058± 0.451
Patients with complications	33	6.18± 5.046	21	11.66± 7.369	18	2.367± 1.325
Death	16	9.45± 5.435	04	21.6± 12.080	1	2.1

Group with complications vs. group without complications p< 0.001
Group with death vs. group without complications p< 0.001

4. Discussion

The control group consisted of healthy individuals who were non-smokers.CRP values were undetectable (i.e. values < 0.6 mg/dl) in 23 out of 25 persons (92%) and CRP values were just positive (0.6 mg/dl) in 2 out of 25 persons (8%). The exact cause of the positive CRP values in 8% of the controls could not be established, but it may be because of some undisclosed smoking, alcoholism or some occult inflammation of minor degree, as CRP is not a specific protein. Similarly Berk BC et.al7 in their study found 4 persons out of 32 controls (13%) who had just positive CRP values. And in these cases they proposed the probable cause as arthritis (mainly osteoarthritis).

In our study on stable angina CRP levels was not elevated in 92% of patients and just elevated in 8% of patients. Similarly Berk BC et.al7 in their study found that in 87% stable angina, CRP levels were not raised (< 0.6 mg/dl) and CRP levels were just raised (0.6 mg/dl) in 13% and there were no further increases in the follow-up period.

In contrast with the results in stable angina group, CRP levels were in normal range only in 20% of UA patients and were raised in 80% of patients in our study at admission. Out of these, 40% had the values of 0.6 mg/dl and 16% of patients had the value of 1.2 mg/dl.But after 48 hours maximum i.e. 32% patients had values of 2.4 mg/dl, but again at the end of one week CRP values returned to normal range in 56% patients.

Berk BC et.al7 in their study, in UA group found that CRP levels were raised in 90% of patients and only in 10% CRP values were in normal range. The values ranged between 0.6 mg/dl to 15 mg/dl, but 81% patients had the values between 0.6 – 2.4 mg/dl. There was a similar rise in CRP values after 48 hours and as a response to treatment, majority of patients had normal values at the end of one week.

In our study, CRP levels were raised in all patients of acute myocardial infarction on admission and the levels rose further after 48 hours. On admission, maximum number of patients (62%) had CRP values of 2.4 – 4.8 mg/dl. After 48 hours, 84% patients of AMI had values of 4.8 – 9.6 mg/dl. After one week, the CRP values declined and maximum number of patients 78% had CRP values of 0.6 – 2.4 mg/dl.This shows that there is invariably an acute phase response in cases of AMI, which is because of both myocardial necrosis and inflammation. Luizzo G et.al4 in their study found elevated CRP values in all patients of acute myocardial infarction and found more increased values in those AMI patients, who had previous history of unstable angina.

In UA group, 16% developed complication in the form of myocardial infarction(CRP 7.2 + 2.77 mg/dl on admission) as compared to patients who had no complications, (0.743 + 0.982 mg/dl) (P < 0.001). This may help in risk stratification.

Kesavmurthy CB et.al 3 in their study showed higher CRP values in UA who had adverse cardiac complications (18.8+/-13.1 mg/dl) as compared to those without complications (3.8+/-0.9 mg/dl).They concluded that patients of UA with high CRP values have worst short term prognosis.

In our study, in AMI group 66% patients had complications like CCF, cardiogenic shock and CRP values was high (6.18 + 5.05 mg/dl) as compared to patients who had no complications (1.98+0.591 mg/dl). The patients who expired (32%) also had significantly higher CRP values (9.45 + 5.435 mg/dl) on admission. The peak value above 20 mg/dl can be considered as independent risk factor for death. Similar results were obtained by Ridker PM et.al 8 in their study.

Thus as discussed till now, CRP levels increase significantly in UAand AMI groups as compared to stable angina and control groups and more the levels worst is the prognosis.

5. Conclusion:

Higher the CRP values on admission in UA and AMI, more is the risk of complications and death. Hence CRP values help in risk stratification and predicting the prognosis.

Limitation of the study: The clinical utility of measurements of CRP in the diagnosis and management of acute coronary syndromes remains to be defined. Although in the present study, the 'sensitivity' of the test was high, the 'specificity' might have been unavoidably compromised by the presence of other inflammatory illnesses which are common in the elderly population with acute coronary syndromes.

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