HS-CRP LEVELS IN MYOCARDIAL INFARCTION PATIENTS IN RELATION TO CARDIAC MARKERS

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ABSTRACT: Studies have provided strong evidence for the importance of primary or secondary inflammatory processes in the pathogenesis of atherosclerosis. A growing number of studies report that inflammation plays a crucial role in the cell biology of atherosclerosis. The aim of the study was to know the relationship between hs-CRP and cardiac markers in acute myocardial infarction patients. This case control study was conducted at the department of Biochemistry and department of Medicine, JSS Medical College, Mysore, Karnataka. The study protocol was approved by Research Ethics Committee of JSS Medical College. A total 60 subjects were included in the study in the age group of 50-68 years. CK-MB, LDH, AST and hs-CRP were estimated. There was a statistically significant difference between the hs-CRP levels of two groups. Cardiac marker values were significantly higher in cases compared to controls. But there was no correlation between cardiac markers and hs-CRP levels in cases. The CRP measurement has a lot of advantages. Firstly it is a stable compound and secondly it can be measured at any time of the day without regards to biological clock. In contrast to results for cytokines such as IL-6, no circadian variation appears to exist for hsCRP. Thus, clinical testing for hsCRP can be accomplished without regard for time of day. In conclusion we would like to say that hs-CRP levels could be used as risk assessment, diagnostic and prognostic marker in myocardial infarction patients.

Key words: hs-CRP, myocardial infarction, cardiac markers.

INTRODUCTION

Recent studies have provided strong evidence for the importance of primary or secondary inflammatory processes in the pathogenesis of atherosclerosis(1,2). A growing number of studies (3) report that inflammation plays a crucial role in the cell biology of atherosclerosis. Pathologic and immunohistochemical staining studies (4,5) have clearly shown a preponderance of inflammatory cells in the ruptured plaques of patients who have died of acute coronary syndromes. Inflammation, manifested by elevated serum levels of C-reactive protein (CRP) measured by high-sensitivity CRP assay (hs-CRP) is associated with an increased risk of cardiovascular events (6,7).C-reactive protein, as a marker of chronic inflammation, is induced by interleukins 1 and 6 (8,9). It is well recognized that myocardial damage promotes the synthesis of CRP and the level of this CRP has been reported to be associated with poor prognosis after acute myocardial infarction (AMI). However, CRP is primarily synthesized and secreted rapidly in liver 6 h after an acute inflammatory stimulus (10). Creatine kinase - MB is widely recognized as the leading cardiac serum marker, especially since the advent of CK-MB mass assays. The determination of CK-MB mass has proven to be more specific for myocardial necrosis than the long-standing CK-MB activity and CK-MB inhibition assays. Based on above data, we investigated the relationship between hs-CRP and cardiac markers in acute myocardial infarction patients.

MATERIALS AND METHODS

This case control study was conducted at the department of Biochemistry and department of Medicine, JSS Medical College, Mysore, Karnataka. The study protocol was approved by Research Ethics Committee of JSS Medical College. A total 60 subjects were included in the study in the age group of 50-68 years. The subjects selected were given a proforma with information on known factors such as smoking, alcohol, previous history of hypertension, diabetes mellitus, life style, diet and family history of CHD. A written informed consent was taken from the subjects before collecting the samples. Individuals with concomitant systemic diseases (thyroid disorders, acute infections, stroke, diabetic ketoacidosis, rheumatic diseases, chronic liver diseases, renal disorders, cancer and sepsis) and subjects who were critically ill or with ongoing or recent (<1 month) infectious diseases as well as patients with surgical procedure in last 3 months were excluded from the study. Estimation of CRP was done with serum sample by using RX Daytona analyzer (11). Sample reacts with specific antiserum to form a precipitate which is measured turbidimetrically at 340 nm. Venous blood samples were collected under strict aseptic precautions with informed consent of the patients and control subjects. The estimation of creatine kinase-MB (12), lactate dehydrogenase (13) and aspartate transaminase (14) was done.

Statistical analysis:

Independent Student's *t*-test was used for comparison between two groups and values expressed as mean± standard deviation. A *p*-value of <0.05 was considered as statistically significant. As values were non-parametric spearman's correlation was done.

RESULTS

The cardiac markers such as CK-MB, LDH, AST and hs-CRP levels of controls and cases are shown in table 1.There was a statistically significant difference between the hs-CRP levels of two groups. But there was no correlation between cardiac markers and hs-CRP levels in cases.

Table 1: Creatine Kinase - MB, Lactate dehydrogenase, aspartate transaminase and hs- CRP levels in cases and controls

	Control (30) (Mean ± SD)	Cases (30) (Mean ± SD)
Age (yrs)	52± 10	59± 10
Hs-CRP (mg/L)	0.687± 0.41	18.29± 16.58***
LDH (U/L)	280.6± 45.5	1057± 534.8***
CK-MB (U/L)	12.3± 2.72	79.44± 53.09***
AST (U/L)	23.67± 6.99	88.08± 73.02***

*** = Very Highly Significant (p < 0.001)

DISCUSSION

More than 20 large prospective trials have shown that the inflammatory biomarker high-sensitivity C-reactive protein (hs-CRP) is an independent predictor of future cardiovascular events it predicts risk of incident hypertension and diabetes (15).

Several studies from both the United States and Europe indicate that elevated levels of hs-CRP among apparently healthy men and women are a strong predictor of future cardiovascular events (16-19). A long-term predictive value of elevated hs-CRP levels has been found in patients with documented coronary artery disease and angina (20, 21) and in individuals with multiple risk factors (22). hsCRP not only predicts first myocardial infarction but also recurrent events(23, 24, 25). In most of these studies, effect of hsCRP on vascular risk remained highly significant after adjustment for traditional risk factors typically used in global risk assessment programs. In our study we found that hsCRP levels were significantly higher in patients with myocardial infraction patients as compared to healthy individuals.

CK is the enzyme responsible for catalyzing the transfer of high-energy phosphate from creatine phosphate to adenosine triphosphate. CK is known to rise within 4–8 h after an acute MI and to decline to normal levels within 3–4 days. In our study we found statistically significant increase in CK-MB and LDH-1 levels in cases.

The CRP measurement has a lot of advantages. Firstly it is a stable compound and secondly it can be measured at any time of the day without regards to biological clock. In contrast to results for cytokines such as IL-6, no circadian variation appears to exist for hsCRP. Thus, clinical testing for hsCRP can be accomplished without regard for time of day (26).

In conclusion we would like to say that hs-CRP levels could be used risk assessment, diagnostic and prognostic marker in myocardial infarction patients.

REFERENCES

1. DeJong SC, Stehouwer CD, van den Berg M, Vischer UM, Rauwerda JA, Emeis JJ (1997). Endothelial marker proteins in hyperhomocysteinemia. Thromb Haemost. 78: 1332–7.
2. ECAT Angina pectoris Study Group. ECAT angina pectoris study: Baseline associations of haemostatic factors with extent of coronary arteriosclerosis and other coronary risk factors in 3000 patients with angina pectoris undergoing coronary angiography. Eur Heart J 1993; 14: 8–17.
3. Pasceri V, Chang J, Willerson JT, et al (2001). Modulation of C-reactive protein-mediated monocyte chemoattractant protein- 1 induction in human endothelial cell by anti-atherosclerosis drugs. Circulation; 103:2531–2534
4. Burke AP, Farb A, Malcom GT, et al (1997). Coronary risk factors and plaque morphology in men with coronary disease who died suddenly. N Engl J Med; 336:1276–1282
5. Burke AP, Tracy RP, Kologie F, et al (2002). Elevated C-reactive protein values and atherosclerosis in sudden coronary death: association with different pathologies. Circulation; 105: 2019–2023
6. Shak PK (2000). Circulating markers of inflammation for vascular risk prediction: are they ready for prime time? Circulation; 101:1758–1759
7. Mueller C, Buettner HJ, Hodgson JM, et al (2002). Inflammation and long-term mortality after non-ST elevation acute coronary syndrome treated with a very early invasive strategy in 1042 consecutive patients. Circulation; 105:1412–1415
8. Biasucci LM, Liuzzo G, Caligiuri G et al (1996). Episodic activation of the coagulation system in unstable angina does not elicit an acute phase reaction. Am J Cardiol; 77: 85–7.
9. Ikeda U, Ohkawa F, Seino Y et al (1992). Serum interleukin 6 levels become elevated in acute myocardial infarction. J Mol Cell Cardiol; 24: 579–84.

10. Hon-Kan Yip, Chiung-Jen Wu, Hsueh-Wen Chang et al (2004).Levels and Values of Serum High- Sensitivity C-Reactive Protein Within 6 Hours After the Onset of Acute Myocardial Infarction. CHEST;126(5):1417-1422.
11. Claus et al (1976). Journal of Laboratory and Clinical Medicine, (87 (1);: 120 - 127.

12. Wurburg, U., et al (1976). Clin Chem.; 54: 357.

13. Weisshaar, H.D., et al(1975). Med. Welt. 26: 387.

14. Tietz N W (1987): Fundamentals of Clinical Chemistry ed 3. Philadelphia, WB Saunders Co. pg 372.
15. Ridker PM (2007). C-reactive protein and the prediction of cardiovascular events among those at intermediate risk: moving an inflammatory hypothesis toward consensus. J Am Coll Cardiol.;49(21):2129–38.
16. Ridker PM, Hennekens CH, Buring JE, Rifai N (2000). C reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med.;342:836–43.
17. Ridker PM, Buring JE, Shih J, Matias M, Hennekens CH (1998). Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation.;98:731–3.
18. Danesh J, Whincup P, Walker M, Lennon L, Thomson A, Appleby P, *et al (*2000). Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ;321:199–204.
19. Mendall MA, Strachan DP, Butland BK, Ballam L, Morris J, Sweetnam PM, *et al (*2000). C-reactive protein: relation to total mortality, cardiovascular mortality and cardiovascular risk factors in men. Eur Heart J;21:1584–90.
20. Thompson SG, Kienast J, Pyke SDM, Haverkate F, van de Loo JCW (1995). Hemostatic factors and the risk of myocardial infarction or sudden death in patients with angina pectoris. N Engl J Med;332:635–41.
21. Haverkate F, Thompson SG, Pyke SDM, Gallimore JR, Pepys MB (1997), for the European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study Group. Production of C-reactive protein and risk of coronary events in stable and unstable angina. Lancet;349:462–6.
22. Kuller LH, Tracy RP, Shaten J, Meilahn EN (1996), for the MRFIT Research Group. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study. Am J Epidemiol;144:537–47.
23. Ridker PM, Glynn RJ, Hennekens CH (1998). C-reactive protein adds to the predictive value of total and HDL cholesterol in determining risk of first myocardial infarction. Circulation;97:2007–11.
24. Biasucci LM, Liuzzo G, Grillo RL, Caligiuri G, Rebuzzi AG, Buffon A, *et al (*1999). Elevated levels of C-reactive protein at discharge in patients with unstable angina predict recurrent instability. Circulation;99:855–60.
25. Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, *et al (*1998). C-reactive protein is a potent predictor of mortality independently and in combination with troponin T in acute coronary syndromes. J Am Coll Cardiol;31:1460–5.
26. Meier-Ewert HK, Ridker PM, Rifai N, Price N, Dinges DF, Mullington JM (2001). Absence of diurnal variation of C-reactive protein levels in healthy human subjects. Clin Chem;47:426–30.