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Vijaya A. Anand
Department of Biochemistry,
MIET Arts and Science College,
Gundur, Tiruchirappalli-07,
Tamilnadu, India

Tel: 91+9842525830

Pragmatic Aspect of C-Reactive Protein Alone and in Combination with Lipid Profile in Patients with Coronary Artery Disease

[1]A. Vijaya Anand, [2]S. Kalavathy, [3]M. Chenniappan, [4]P. Sampath Kumar, [1]N. Manoharan, [4]S. Sheik Abdulla, [5]R. Chandrasekar and [6]B. Hari Krishnan

The present study was designed to evaluate the association of inflammatory marker C-reactive protein (CRP) alone and in combination with lipid profile in the prognosis of coronary artery disease (CAD) since the cardio vascular disease (CVD) is considered to be a multifactorial disease driven by inflammatory reactions. One hundred and fifty patients were recruited for the study, of which, 75 belongs to control and 75 were test group. For the entire study population CRP and lipid profile were measured. Among the patients with complication (test group), there was a significant elevation in the levels of CRP and lipid profile than the control. It was also found that a combination of measurement of CRP with total cholesterol (TC) or low-density lipoprotein (LDL) cholesterol testing may proven to be even a better marker of risk response in patients with CAD.

Key words: Cardiovascular disease, inflammation, biomarkers, total cholesterol

[1]Department of Biochemistry, MIET Arts and Science College, Tiruchirappalli, India
[2]Department of Botany, Bishop Heber College, Tiruchirappalli, India
[3]Ramakrishna Nursing Home Cardiac Care Unit, Tiruchirappalli, India
[4]Department of Biochemistry, SASTRA University, SRC, Kumbakonam, India
[5]Department of Environmental Biotechnology, Bharathidasan University, Tiruchirappalli, India
[6]Department of Biochemistry and Biotechnology, Annamalai University, Annamalainagar, India

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INTRODUCTION

It is awesome to note that the death rates in the cardiovascular diseases (CVD) are incredibly increasing. This is due to the fact that the markers that are in existence fail to introspect the facts in detail. The Framingham study showed that 35% of cases of coronary artery disease (CAD) were in people with normal total cholesterol (TC) levels (Castelli, 1996). These findings point out the need for markers that better predict cardiovascular risk. In the most recent years, special importance is being laid on inflammation in the pathogenesis of atherosclerosis and its complication. Inflammation also regulates the production of the acute phase proteins such as C-reactive protein (CRP), fibrinogen and serum amyloid A (Gabay and Kushner, 1999; Uhlar and Whitehead, 1999). The serum concentration of CRP can increase >1000-fold upon inflammation and with a half-life of 19 h, CRP is a very stable downstream marker of the inflammatory process (Black *et al*., 2004). Because CRP is such a sensitive indicator of the inflammatory process, it has been extensively studied whether plasma concentrations of CRP and other circulating inflammatory proteins (e.g., fibrinogen, interleukin-6) have predictive value in the pathogenesis of CVD.

Many clinical and population studies, with cross-sectional and nested case control designs, proved these inflammatory mediators to be predictors of CVD (Danesh *et al*., 1998; Koenig *et al*., 1999; Ridker *et al*., 1998a, 2000). Most clinical studies report that CRP is an independent predictor of risk of atherosclerosis (Libby and Ridker, 2004), cardiovascular events (Black *et al*., 2004), atherothrombosis (Pepys and Hirschfield, 2001), hypertension (Sesso *et al*., 2003) and myocardial infarction (Ridker *et al*., 2002), even after considering other cardiovascular risk factors such as age, smoking, obesity, diabetes, hypercholesterolemia and hypertension. However, the prognostic value of CRP in combined with lipid profile in patients with CVD and its application in secondary prevention, have been investigated recently. The content of this study details about the assessment of the prognostic value for CRP alone, as well as in combination with various blood lipids in patients with CAD.

MATERIALS AND METHODS

Patients: The study population consisted of 75 patients (test group) with a mean age of 62.3±8.1 years, admitted to the Ramakrishna Hospital Cardiac Care Unit. The control group included 75 patients with mean age of 59.1±6.8 years, who entered the one day hospitalized health check program, were included in this study. The present study included the taking of a full medical history, physical examinations, blood chemistry and an electrocardiogram. The diagnosis of CVD was based on a history of ischemic chest pain and characteristic ECG changes. All patients gave written informed consent before the study. This study was carried out from April 2005 to September 2007.

Biochemical parameters and assay: Samples for the analysis of CRP and lipid profile were obtained in the fasting state. The venous blood samples were drawn into pyrogen-free blood collection tubes without additive. The serum was collected after centrifugation at 3500 rpm for 3 min and then stored at -70° C until analyzed. CRP was measured by using immunoturbidometry method. Estimation of TC, serum triglycerides (TG) and high-density lipoprotein (HDL) cholesterol, were performed colorimetrically by using commercial kits. The value of low-density lipoprotein (LDL) cholesterol and very low-density lipoprotein cholesterol (VLDL), were calculated using Friedwald's equation. The value of TC/HDL cholesterol ratio and LDL/HDL cholesterol ratio were calculated by TC/HDL cholesterol and LDL/HDL cholesterol, respectively.

Statistical analysis: Statistical analysis was performed with SPSS 12 statistical software package. Data were recorded on a pre-designed proforma and managed on spreadsheet. All the entries were checked for any error. Descriptive statistics for quantitative variables were computed by mean and standard deviation. Means in the two groups were compared by Student's t-test. In this study, $p<0.05$ has been considered as statistically significant.

RESULTS

The present study demonstrates that considerable variability is observed between control and test group. Among the patients with complication the baseline mean CRP concentration increased significantly ($p<0.001$) than the control (Table 1). The mean level of CRP in control is found to be 0.5±0.3 and in test group 1.3±0.7 (patients with CAD).

Table 1: Baseline clinical characteristics

Variables	Control group (n = 75)	Test group (n = 75)
Age (years)	59.1±6.8	62.3±8.1
Sex (male/female)	54/21	46/29
Systemic hypertension (%)	17(23)	42(56)
Diabetes mellitus (%)	21(28)	34(45)
Smoking consumption (%)	28(37)	39(52)
Alcohol consumption (%)	8(11)	16(21)
Oral hypoglycemic (%)	19(25)	28(37)
Insulin (%)	2(3)	6(8)
Antihypertensive (%)	17(23)	42(56)
Lipid lowering drugs (%)	Nil(0)	54(72)

The mean levels of TC in control is found to be 159.5±28.3 and in test group 199.5±36.5. The mean levels of TG in control is found to be 135.6±60.4 and in test group 167.8±78.5. Thus, there is a significant increase of TC ($p<0.001$) and TG ($p<0.01$) levels in test group than the control. The mean levels of HDL cholesterol in control is found to be 39.7±7.0, in the test group 41.9±8.1. The mean levels of LDL cholesterol or bad cholesterol in control is found to be 92.7±25.3, in the test group 124.9±36.8. Significant increase ($p<0.001$) was noted in the mean level of LDL cholesterol in test group. The mean level of VLDL cholesterol in control is found to be 27.0±12.1, in the test group 33.1±15.6. The elevated level of CRP and lipid profile seems to be a strong indicator of CAD risk. The mean levels of TC/HDL cholesterol ratio in control is 4.0±0.7 and in test group 5.4±1.2. The mean levels of LDL/HDL cholesterol ratio in control is 2.3±0.7 and in test group 3.4±1.1.

DISCUSSION

Atherosclerosis is an inflammatory disease and it was thought that circulating factors associated to inflammation might be predictors of CVD in general populations. In 2003, despite the lack of consistent epidemiological data, the Centers for Disease Control and Prevention (CDC) and the American Heart Association (AHA) concluded that it is reasonable to measure CRP, a sensitive circulating marker of inflammation, as an adjunct to the measurement of established risk factors in order to assess the risk of CAD (Pearson *et al*., 2003).

The results of the present study indicate that an elevated CRP level is a strong indicator of cardiovascular events. CRP plasmatic levels might increase in patients with acute coronary syndrome (ACS). Elevated CRP plasmatic concentrations carry out a prognostic significance, both in subjects with ST elevation ACS (Brunetti *et al*., 2006) and with unstable angina - non-ST elevation ACS (Sabatine *et al*., 2002; Zebrack *et al*., 2002). Moreover, increased levels of CRP could be detected also in subjects with risk factors for CVD such as hypertension (Lakoski *et al*., 2005) or diabetes (Kahn *et al*., 2006).

Based in part on these data, high-sensitivity assays for CRP have become existing in standard clinical laboratories. However, clinical application of CRP testing will depend not only on demonstration of independent predictive value, but also on demonstration that addition of CRP testing to traditional screening methods improves cardiovascular risk prediction. The most important findings of the present study is that the patients with a combination of elevated levels of CRP and TC or LDL cholesterol showed the highest risk compared to the measurement of only one of these marker. Results of the present study also suggest that the atherogenic metabolic disturbance may be adequately reflected by the variation in the TC/HDL cholesterol and LDL/HDL cholesterol ratio.

The concurrent assessment of CRP and blood lipids, representing two different pathophysiological features of atherosclerosis, may be superior in identifying patients at high coronary risk. Findings from Multiple Risk Factors Interventional Trail (MRFIT) demonstrated a direct positive association between CRP and CAD mortality in men followed over a 17 year period (Kuller *et al*., 1996). Similar positive association between CRP and future coronary events in apparently healthy men was also demonstrated by Physician's Health Study (PHS) data set (Ridker *et al*., 1998b). Blake and Ridker (2001) indicated that CRP was the single most powerful predicator of cardiovascular risk in all of the inflammatory and lipid markers. In this multivariate analysis, matched for age and smoking and adjusted for other cardiovascular risk factors, found that only CRP and TC/HDL cholesterol ratio were independent predictors of future cardiovascular risk. Furthermore, available studies suggest that the concentration of CRP testing with traditional lipid screening may significantly improve cardiovascular risk prediction, particular when LDL cholesterol is low (Blake and Ridker, 2001).

CONCLUSION

CAD is multifactorial in etiology. Among a variety of serum biomarkers of CAD risk, CRP is one of the most supported by research and clinical utility. The present findings suggest that the measurement of CRP with lipid profile might be useful for risk stratification in patients with CAD. Modifying the risk factors or maintaining a healthy lifestyle, such as losing excess weight, no smoking and regular exercise, can be recommended as ways to reduce CRP and lipid profile levels and the risk of CAD.

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