

Full Length Research Paper

The relationship and diagnostic value of C-reactive protein (CRP) and high-sensitivity- reactive protein (hsCRP) for myocardial infarction

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Accepted 23 August, 2011

Atherosclerosis is the main cause of myocardial infarction (MI) and inflammation is considered as a main cause of atherosclerosis. Inflammatory indicators such as C-reactive protein (CRP) are considered as a diagnostic marker for MI in recent years. We studied the relationship between seropositivity to CRP and high-sensitivity- reactive protein (hsCRP) with MI and compared their relationship and diagnostic values. All sera of patients and control cases were examined by a commercial quantitative ELISA kit for measuring hsCRP and by a non-quantitative latex agglutination kit for detecting CRP, simultaneously. Results were analyzed by chi-square statistic test in SPSS software version 16. About 62.0% of patients were positive for CRP and 100% positive for hsCRP but in control group, seropositivity rate was 6.6% for CRP and 52.6% for hsCRP. Mean titer of hsCRP in patients was 23.2 but 6.3 mg/l in control group. We found significant relationship between CRP and MI (P=0.004) and with hsCRP with MI (P=0.002). hsCRP and CRP have significant relationship to MI as diagnostic indicators and hsCRP is more sensitive than CRP but regarding to their false positive and negative values, and for decreasing their accuracy, it is recommended to perform both simultaneously.

Key words: C-reactive protein (CRP), high-sensitivity- reactive protein (hsCRP), myocardial infarction.

INTRODUCTION

Acute myocardial infarction (MI) is one of the common causes of morbidity and mortality. Atherosclerosis is the main cause of coronary arteries obstruction by thrombosis (Brek et al., 1990; Ridkler et al., 1997). In recent years, incidence of MI as a very important health problem has increased worldwide especially in developed and also in developing countries (Brek et al., 1990). Several risk factors are introduced for atherosclerosis

that is main cause of MI such as obesity, diabetes, stress, smoking, hypertension, hyperlipidemia, and chronic inflammation due to different causes such as infection (Brek et al., 1990; Ridkler et al., 1997). Too many studies have been done for revealing the role of these risk factors and their mechanisms on predisposing MI. Inflammation as a risk factor for atherosclerosis is a subject for several studies performed in recent years. Most of these studies showed chronic inflammation is a certain cause for atherosclerosis (Ross, 1999; Semeri et al., 1992; Thompson et al., 1995; Torres and Ridker, 2003; Veleska et al., 2005) and some predisposing factor can intensify inflammation of coronary arteries that must

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be revealed in the future (Ross, 1999; Danesh et al., 2000). Infections may be one of these factors (Roivainen et al., 2000; Kiechls and Mary, 2001). There are several indicators for inflammation such as C-reactive protein (CRP) and IL-6 (Ridker, 1999). Role of CRP as an indicator for MI was studied by several researchers (Ridker et al., 2000; Veleska et al., 2005) hsCRP is a very sensitive measuring of CRP concentration by ELISA method. High concentration of hsCRP is reported in about half of MI cases and some researchers believe that even a little increase in hsCRP concentration (≥ 3 mg/L) can be an indicator for risk of acute cardiovascular accidents (Veleska et al., 2005). Prognostic value of this indicator for unstable angina is controversial but clinical trials on patients who had Percutaneous Coronary Intervention (PCI) showed that increased inflammation has a significant relationship with severity in clinical situation and complications (Veleska et al., 2005; Harris et al., 1999). The aim of this study was to evaluate and compare of relationship and diagnostic value of CRP and hsCRP in the patients with MI in the first 12 h.

MATERIALS AND METHODS

This study is performed in Heshmat Hospital, Rasht, Iran. The patients have been diagnosed based on clinical symptoms, ECG, and echocardiography. Sera of first 12 h of patients were collected and stored in -20°C . Demographical information was taken by asking close relatives and referring to medical record. Control group was selected in the same range of patients age and sex in the individuals who referred to a private diagnostic laboratory for routine check up and had not history of heart diseases. For all serum samples, CRP test was examined by using a commercial semi quantitative latex agglutination diagnostic kit (HUMAN, Germany) and hsCRP was measured by using a commercial quantitative ELISA kit (Accu Bind, Monobind Inc company, USA). According to the company recommendations, titers of hsCRP ≥ 3 mg/L were considered as positive. All results were analyzed by Chi-square test using SPSS software version 16.

RESULTS

The total number of 200 serum samples (100 patients and 100 control) examined in this study. Positive rate of CRP in patients and control was 62 and 6.6%. hsCRP was positive in all patients (100.0%) but 52.6% in control cases. Range of hsCRP titer was 3.2 to 30 mg/L in patients but 1.8 to 9.4 mg/l in control cases. Mean of hsCRP titer was 23.2 mg/L in patients but 6.3 mg/L in control group. By considering freedom degree =1 and significant level=0.01 and insurance level=995, statistical analysis of data showed a significant relationship between MI and CRP seropositivity ($P=0.004$) and also with hsCRP seropositivity ($P=0.002$). So regarding to linear quotation, P value and significancy level=0.01, CRP and hsCRP seropositivity was more frequent in patients than control and also high titers of hsCRP was more frequent in patients than control cases. Considering the significant relationship of CRP and hsCRP to MI and by comparing

to correlation quotation of the two tests with MI, and also correlation of CRP with MI was less than correlation of hsCRP with MI (V Cramer quotation=0.583 for CRP versus 0.752 for hsCRP), it can be noted that the diagnostic value of hsCRP is more than CRP for MI.

DISCUSSION

In half of MI cases in which amount of lipid in serum is normal, other indicators such as serum amyloid A, ICAM-1, VCAM-1, homocystein, preinflammatory cytokins such as IL-1 and IL-6, and acute phase proteins especially CRP can be regarded as indicators for MI (Hwang et al., 1997; Ridkler et al., 1997; Ridker et al., 2000; Harris et al., 1999; Ridker et al., 1998; Ridker et al., 1999). It seems that measuring inflammatory indicators other than screening of plasma lipid, is useful for prediction of clinical events (Brek et al., 1990; Ridker, 2003; de Beer et al., 1982). Reports of several prospective and case control studies showed that the above parameters are useful but are not cost benefit because they are complex and expensive, so they can not be usual for clinical management except CRP that is simple, easy to perform, and cost benefit than others (Chew et al., 2001; Daesh et al., 1997; Danesh et al., 2000; de Beer et al., 1982; de Winter et al., 2003; Gottlieb et al., 1986; 1987; Harris et al., 1999; Hwang et al., 1997; Kiechls, and Mary, 2001; Kuller et al., 1997; Lienomen and Saikku, 2003; Liuzzo et al., 1996; 1994; Maseri et al., 1996; Mazzone et al., 1996; Moreno et al., 1994; Ridkler et al., 1997, 1998, 1999; Ridker, 1999). On the other hand, in patients who are suffering from unstable angina, continuing or intensifying of ischemia after a full treatment program, may be an indicator for a bad prognosis (Gottlieb et al., 1986, 1987). After admitting patient in hospital, it is not easy to predict that angina will be treated or will develop to MI, whether the etiology and the cause of instability be revealed (Auer et al., 2002). In the cases that inflammation is the main cause, CRP may reveal the etiology and can be a guide for the management strategy (Auer et al., 2002). It is possible to measure infiltrative inflammatory factors and to detect macrophage in coronary platelets and around ruptured coronary arteries. Increasing the number of neutrophile, lymphocyte, monocyte and increasing concentration of IL-1 are other indicators (Auer et al., 2002) but measuring these factors are not as easy as CRP. Histological investigation Kohchi et al., 1985), measuring tromboxan and leukoterins in peripheral blood (Carry et al., 1992) and activated leukoterins in circulation (Carry et al., 1992; Semeri et al., 1992) are also studied but there are the same problem and they can not be considered as routine as CRP test. CRP is also increased in unstable angina (de Beer et al., 1982; Harris et al., 1999) and in other types of angina (Ridker et al., 2000; Ridker, 2003). Increasing CRP titer is reported in 20% of case 6 h after MI and before increasing titer of myocardial enzymes (de Beer et al., 1982; Harris et al., 1999). In this study we

measured CRP concentration after about 12 h. Inflammatory indicators are not as specific as myocardial enzymes but are very sensitive for inflammation. Acute phase response can be an initial marker for instability in unstable angina cases because increasing in concentration of inflammatory markers is not related to: myocardial cell necrosis, troponin titer, and ischemia (Maseri et al., 1996; Liuzzo et al., 1996) and also to the activation of coagulatory system (Biasucci et al. (1996) as the amount of CRP does not increase significantly after activation of coagulatory system and also will remain in high titer after relieving the complication (Thompson et al., 1995). It must be noted that increasing CRP titer is a short time prognosis indicator for unstable angina (Liuzzo et al., 1994) but is a long time prognosis factor for coronary diseases (Aronow, 2003) and for individuals with multiple risk factors (Moreno et al., 1994). Plaque rupture is mostly related to the number and activity of macrophages that are main inflammatory cell in atherosclerotic plaques not to size of plaques (Moreno et al., 1994).

Conclusion

We found that hsCRP and CRP are useful diagnostic markers for MI, and hsCRP is more sensitive than CRP, but regarding their false positive and negative values, and for decreasing their pitfalls, it is recommended to perform both of them for each case.

ACKNOWLEDGEMENT

The authors are grateful to Dr Mohamadi, and Mrs. Dinparast for their assistance.

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