A Comparative Analysis of the Level of High Sensitive C-Reactive Protein in People with and without Hypertension

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Abstract

Background:
High sensitive C-reactive protein (hs-CRP) is an available measured serum marker for detecting blood vessel inflammation and endothelial dysfunction. It has been demonstrated that these two mechanisms have a pivotal role in the pathogenesis and progression of hypertension. We conjecture and confirm in this study that the level of hs-CRP is higher in hypertensive patients.

Methods:
We enrolled 77 hypertensive patients with the following distribution in the case group (male: 27.7%, female: 72.3%, mean age: 58.1 years, mean systolic blood pressure: 15.4 mm Hg, mean diastolic blood pressure: 90.4 mm Hg) and 77 matched normotensives, in the control group. Patients with heart failure, renal failure (cr >2mg/dl,) diabetes mellitus, infective disorder, severe systemic disorder and malignancies were excluded. Blood pressure was measured using the same digital Richter sphygmomanometer (ceo124 Ri-fit.) The hs-CRP was measured using CRP HS ELISA (enzyme immunoassay for quantitative determination of CRP in human serum). The normal range was 0.068–8.2 mg/l. Finally, the data were analyzed using SSPS-10 software.

Results:
The mean levels of hs-CRP in the case and control groups were 4.29 and 2.43 respectively (p value <0.001).

Conclusion:
Our study showed that the level of hs-CRP was elevated in the hypertensive patients, which reflected the role of the inflammatory process in the pathogenesis of hypertension. ***(Iranian Heart Journal 2012; 13(3):27-32).***

Keywords: hs-CRP■Low-grade inflammation■Hypertension

Received November 2012; Accepted for publication December 2012

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Introduction

Increase in the concentration of acute phase reactants comprises a major pathophysiologic phenomenon accompanied by inflammation and tissue injury (1). Changes in the levels of acute phase reactants largely result from the effects of the inflammatory process. Cytokines are primarily produced by macrophages and monocytes. Some of the major cytokines relevant to acute phase response are interlukin-6 (Il_6), interlukin-1(IL_1), tumor necrosis factor – alpha (TNF-α), and interferon gamma. These proteins influence acute phase protein production in hepatocytes (2). One of these acute phase reactants is C-reactive protein (CRP), which is produced predominantly by hepatocytes under the influence of IL_6 and TNF-α (3).

Ever since the introduction of the inflammatory process in the creation of cardiovascular disease (e.g. vascular atherosclerosis, hypertension, etc.) , the relationship between CRP and these disorders has been evaluated in many studies. Data from more than 30 epidemiologic studies have shown a significant association between elevated serum concentrations of CRP and the prevalence of underlying atherosclerosis, the incidence of first cardiovascular event in individuals at risk for atherosclerosis, and the risk of recurrent cardiovascular events among patients with established diseases (4).

In recent years, the role of the inflammatory process in the pathogenesis of hypertension (HTN) has been suggested. Consequently, the relationship between CRP and HTN can be evaluated (5). The possible predictive value of serum CRP for the development of HTN was evaluated in an analysis from the women's health study in the United States with a baseline blood pressure below 140/90 mm Hg and no history of HTN. Serum CRP was measured at baseline, and the women were followed up for a median of 7 years: HTN developed in 11.5%, and there was a progressive increase in the rate of developing HTN with increasing value of serum CRP (serum CRP>3/5 $^{mg}/_{L}$versus < 0/4 $^{mg}/_{L}$) (6).

The association between serum CRP and HTN could be related in part as follows: 1) correlation between elevated CRP and arterial stiffness (7); 2) association between serum CRP and metabolic syndrome, one of whose criteria is HTN (8) and 3); the possibility that CRP may directly contribute to reduced nitric oxide synthesis in endothelial cells, leading to increased vascular resistance (9).

In recent years, the term "high sensitive CRP (hs-CRP)" has been used widely. One common misunderstanding has been the incorrect belief that hs–CRP is different in some way from CRP. The fact is that hs-CRP only denotes the utilization of an assay designed to measure very low levels of CRP, i.e. the so-called low-grade inflammation (10, 11). The low-grade and acute inflammation states differ from each other in several ways. For instance, the latter occurs in response to infection and tissue injury (12) and the former is induced in response to metabolic stress (13).

In one study, it was suggested that low-grade inflammation causes endothelial dysfunction and impaired nitric oxide availability, leading to an increased production of oxidative stress (14). Also, the relationship between this form of inflammation and obesity, a major risk factor of HTN, has been evaluated before (15).

HTN is usually divided into the two major categories of primary (90-95%) and secondary (5-10%). In the latter type of HTN, a more discrete mechanism can be identified (e.g. renovascular disease, endocrine disorders, etc.); as a result, in this setting, the control of HTN can be accomplished as a result of the treatment of these underlying disorders. In contrast, in primary HTN, a single reversible cause cannot be identified (7). It is possible that factors may be able to predict the future

development of primary HTN; therefore, preventive intervention might delay the presentation of primary HTN.

Due to the influence of race and environmental factors such as diet and smoking in the development of HTN and their different prevalence in numerous countries depending on the prevalent life style, the association between hs-CRP and cardiovascular events has been separately evaluated in different populations such as Nigerians (16), Kashmiris, and Indians (17). In this study, we tried to compare the level of serum hs-CRP in hypertensive and normotensive individuals as a sample of the Iranian population.

Methods

This study was performed on patients referring to Ekbatan Hospital Clinic, Hamedan, Iran, for blood pressure control, between 2010 and 2011. A total of 154 patients were divided into two matched groups based on their blood pressure as follows: the case group comprised 77 patients with blood pressure more than 140/90 mm Hg recorded in at least two separate clinic–based measurements after ruling out secondary causes and the control group contained 77 normotensive individuals with blood pressure of 100-120/70-80 mm Hg.

Patients with congestive heart failure, chronic kidney disease (Cr>2), diabetes, infective disease, malignancies, and chronic inflammatory disease were excluded from this study. Both groups were matched, based on their age, sex, body mass index and other cardiovascular risk factors.

In all the individuals, blood pressure was measured in seated position with digital Richter sphygmomanometer (Ceo124 Ri-ft) after a 5-10 minute relaxation period. After that peripheral blood was drawn and then CRP was measured by CRP HS ELISA (enzyme immunoassay for quantitative determination of CRP in human serum). In this method, the normal range of hs-CRP was 0.068-8.2 $^{mg}/_{L}$.

As a result of the matching between the two groups, fasting blood sugar (FBS), lipid profile, blood urea nitrogen (BUN), and creatinine were measured simultaneously in all the individuals. Additionally, both groups were matched based on their body mass index. Finally, all the data were analyzed using SSPS-10 software.

Results

The 77 hypertensive patients in the case group were comprised of 27.7% males and 72.3% females at a mean age of 58.1 years. The control group comprised 28.2% males and 71.8% females at a mean age of 57.4 years.

In the case group, the mean systolic and diastolic blood pressures were 150.4 mm Hg and 90.4 mm Hg, respectively. These means in the control group were 108 and 74 mm Hg, respectively (Table 1). The body mass index in the case group was 24.2 versus 23.7 in the control group (p value >0.05). The means of total cholesterol, triglycerides, low-density lipoprotein (LDL), and high-density lipoprotein in the case group were 168 $^{mg}/_{dl}$, 137 $^{mg}/_{dl}$, 84 $^{mg}/_{dl}$ and 31.2 $^{mg}/_{dl}$, respectively. These data in the control group were 153$^{mg}/_{dl}$, 129$^{mg}/_{dl}$, 81$^{mg}/_{dl}$ and 34.3$^{mg}/_{dl}$, respectively (p value >0.05). The mean level of creatinine was 0.7$^{mg}/_{dl}$ in both groups.

The mean levels of hs-CRP in the case and control groups were 4.29 $^{mg}/_{l}$ and 2.43$^{mg}/_{l}$, respectively. Although these levels were within the normal range (0.068- 8.2 $^{mg}/_{dl}$) , there was a significant analytical difference between the two groups (Table 2) (p value <0.001).

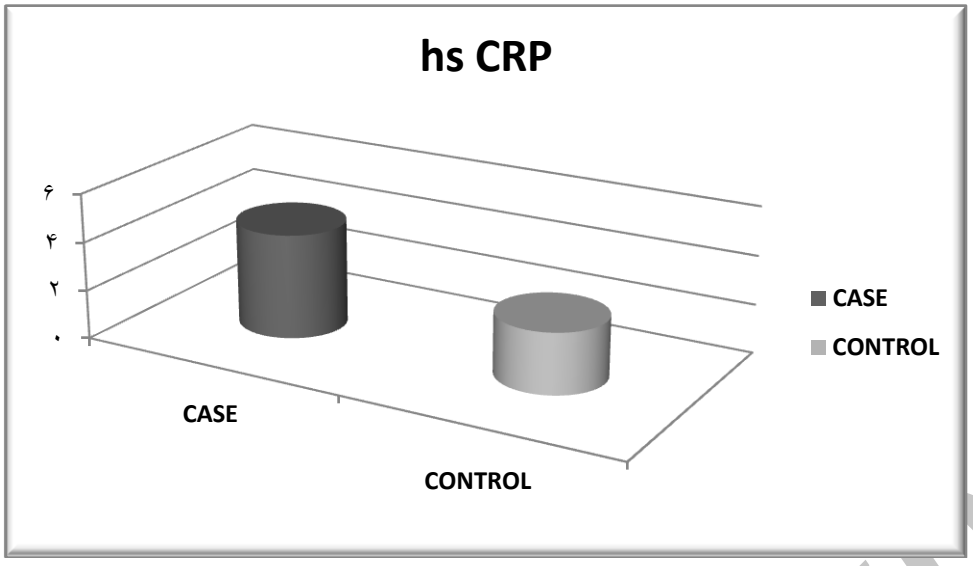

Figure 2: hs-CRP level in case and control groups (mg/L)

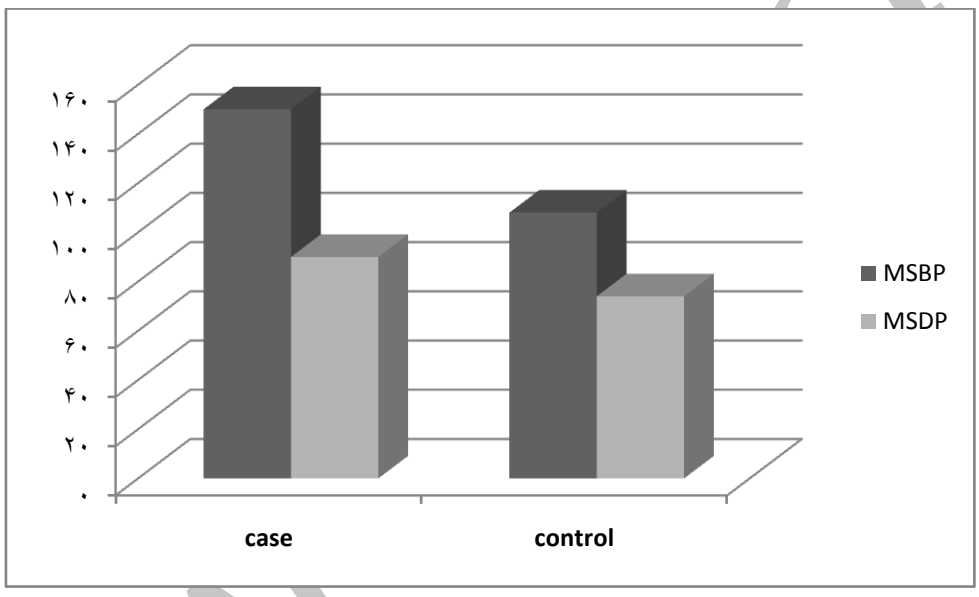

Figure 1: Mean systolic and diastolic blood pressures in case and control groups (mmHg)

Discussion

HTN is one of the most common cardiovascular problems; and among all the risk factors of atherosclerosis, it is more common than diabetes and hyperlipidemia. In addition, HTN is associated with a greater risk of heart failure, left ventricular hypertrophy, ventricular arrhythmia, ischemic (and hemorrhagic) stroke, and chronic renal failure. Nowadays, with increasing population age and rate of obesity in developed countries, there is a rise in the number of hypertensive patients. Therefore, timely diagnosis and even anticipation of HTN are cost effective.

Serum hs – CRP is one of the suitable markers for low-grade inflammation evaluation. This marker rises subsequent to metabolic stresses, which are accompanied by endothelial dysfunction and lead to peripheral vascular remodeling, decreased compliance, and vascular stiffness. All of these pathological alterations give rise to increased peripheral vascular resistance and after a period of time, primary hypertension. With low-grade inflammation markers such as serum

hs-CRP, the primary stages of endothelial dysfunction can be revealed and probable HTN occurrence can be diagnosed.

Korean (24) showed that serum hs-CRP level was not a risk factor in the rural population over 50 years of age. Nevertheless, due to different life style, daily activity, and diet between rural and urban populations, this study cannot be generalized. Another study (25) reported that serum hs-CRP was a strong predictor of HTN occurrence in normal or prehypertensive people in comparison to other inflammatory markers such as interleukin 6, TNF- α, and angiotensin II.

Given the role of serum hs-CRP in HTN, researchers have studied the effect of hypertensive medications on the serum hs-CRP level, prevention of HTN, and its complications. Valsartan is known to decrease blood pressure and hs-CRP levels (26). Aspirin and statins have same effects on the serum hs-CRP level and could prevent HTN, but this claim requires further research.

Although the existing literature contains only a small number of studies that have demonstrated the direct effect of serum hs-CRP lowering on the improvement of cardiovascular diseases, other interventions such as body weight reduction, cigarette smoking cessation, and Aspirin (and statins) consumption are believed to be associated with reduced cardiovascular events and serum hs-CRP level, indicating an indirect role of hs-CRP lowering.

It should be emphasized that interference on a wide range of physiologic and pathologic conditions and life style may be associated with increased pre-inflammatory markers such as the serum hs-CRP level. It is, therefore, advisable that confounding factors be taken into consideration. In our study, we tried to reduce these factors as much as possible so as to obtain more reliable results.

Conclusion

Our findings showed that the level of hs-CRP was elevated in the hypertensive patients, which reflected the role of the inflammatory process in the pathogenesis of HTN.

Conflict of Interest

The authors have no conflict of interest to declare.

Sources of Support

This study was approved and funded by the Deputy Directorship of Research and Technology, Hamadan University of Medical Sciences (registration number; 23564).

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