Research Article

Aysun Çetin, İhsan Çetin*, Semih Yılmaz, Ahmet Şen, Gök土耳其 Savaş, Behzat Çimen and Ahmet Öztürk

Oxydative stress markers and cytokine levels in rosuvastatin-mediated hypercholesterolemia patients
Rosuvastatinle Tedavi Edilen Hiperkolesterololemili Hastalarda Oksidatif Stres Belirteçleri ve Sitokin Düzeyleri

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Abstract

Background: Limited research is available concerning the relationship between oxidative stress and inflammation parameters, and simultaneously the effects of rosuvastatin on these markers in patients with hypercholesterolemia. We aimed to investigate the connection between cytokines and oxidative stress markers in patients with hypercholesterolemia before and after rosuvastatin treatment.

Methods: The study consisted of 30 hypercholesterolemic patients diagnosed with routine laboratory tests and 30 healthy participants. The lipid parameters, interleukin-1 beta (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), paraoxonase-1 (PON1) and malondialdehyde (MDA) levels in controls and patients with hypercholesterolemia before and after 12-week treatment with rosuvastatin (10 mg/kg/day), were analyzed by means of enzyme-linked immunosorbent assay.

Results: It was found that a 12-week cure with rosuvastatin resulted in substantial reductions in IL-1β, IL-6 and TNF-α and MDA levels as in rising activities of PON1 in patients with hypercholesterolemia. Before treatment, the PON1 levels were significantly negatively correlated with TNF-α and IL-6 in control group, while it was positively correlated with TNF-α in patients.

Conclusion: Our outcomes provide evidence of protected effect of rosuvastatin for inflammation and oxidative damage. It will be of great interest to determine whether the correlation between PON1 and cytokines has any phenotypic effect on PON1.

Keywords: Hypercholesterolemia; Rosuvastatin; Cytokines; Antioxidants; Oxidative stress.

Öz

Amaç: Hiperkolesterololemili hastalarda oksidatif stres ile inflamasyon parametreleri arasındaki ilişkiye ve rosuvastatinin bu belirteçler üzerindeki eş zamanlı etkilerine ilişkin sınırlı sayıda araştırma mevcuttur. Rosuvastatin tedavisi öncesi ve sonrasında hiperkolesterololemili hastalarda sitokin ve oksidatif stres belirteçleri arasındaki ili̇kiiyi araştırmayı amaçladık.

Gereç ve Yöntem: Çalışma, rutin laboratuvar testleri ile tanı konulan otuz hiperkolesterolomik hastayı ve 30 sağlıklı katılmaya kapsamaktadır. Kontroller ve 12 haftalık rosuvastatin (10 mg/kg/gün) tedavisi öncesi ve sonrası hiperkolesterololemili hastalarda lipid parametreleri, interlökin-1...
Introduction

Hypercholesterolemia, which means elevation in plasma cholesterol levels, increases the risk of atherosclerosis and cardiovascular disease [1]. Peripheral vascular disease, myocardial infarction, coronary artery disease and stroke associated with hypercholesterolemia take the first place among the causes of morbidity and mortality. Previous studies found that decreased hypercholesterolemia severely reduces the number of foam cells [2]. Imaging techniques approved that reduction in cholesterol levels might upgrade regression of atherosclerosis in humans [3].

Clinical studies have shown a correlation between lipid metabolism and inflammation. The patients with hypercholesterolemia have been reported to experience significant changes in serum cytokine levels. Moreover, it has been displayed that atherosclerosis can be considered as ongoing immune reaction and inflammatory response of increased inflammatory disease [4]. This inflammation is associated with interleukin-6 (IL-6), the main stimulator of the formation of acute phase proteins. On the other hand, tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β) have profound effects on formation and development of atherosclerosis and impact subgroups of acute phase proteins [5].

Inflammation may start due to increased oxidative damage to macromolecules. Previous studies found that oxidative stress is an underlying pathomechanism of atherosclerosis [6]. Recently, new evidences have established that oxidative stress has significant impact on starting and progression of atherosclerosis [7, 8]. Also, the decreased antioxidant capacity and increased oxidative stress are likely to promote the elevated risk of a cardiovascular disease [9]. Lipid peroxidation is well established as oxidative stress index in tissues and cells. Elevated lipid peroxidation levels have been connected with many diseases [10]. Malondialdehyde (MDA) is extensively used as an index of lipid peroxidation [11]. Paraoxonase-1 (PON1) is an element of this oxidative mechanism, and has drawn attention as a protein responsible for one of the components of antioxidant features of High Density Lipoprotein (HDL) [12]. It is proposed that oxidative stress related with decreased activities of PON1 has been found in patients with hypercholesterolemia [13].

Previous studies showed that statins have been favorite therapy means as lipid lowering drugs and are extensively used for the medication of hypercholesterolemia [14]. Statins are implemented in wide range of immuno-modulating and anti-inflammatory activities [15]. One of the members of statin family is rosuvastatin. Compared to other statins, chemical and pharmacokinetic properties of rosuvastatin submit a very restricted penetration to extra hepatic tissues with a lower risk of toxicity [16]. Rosuvastatin might at the same time apply an inhibiting impact on inflammation parameters [17].

As mentioned above, inflammation may start due to increased oxidative damage [6] and incessant persistent inflammation could culminate in the inception and progression of atherosclerosis. The patients with hypercholesterolemia have been reported to experience significant changes in serum cytokines levels [2–4]. Moreover, clinical experiments propose that statins possess direct anti-inflammatory effects and antioxidative stress independent of their influences on plasma cholesterol levels [7, 14, 18, 19]. Rosuvastatin is a novel statin with a long half-life, more potency in lipid lowering and humble liver metabolism than other statins [20]. We know little about the mechanism(s) underlying the antiinflammatory and antioxidative impacts of rosuvastatin. Considering these aspects, we hypothesized that the inflammatory and oxidative stress markers may be altered by hypercholesterolemia; and hypercholesterolemia treatment with rosuvastatin may restore this condition. On the other hand, the relationship between inflammatory and oxidative stress markers may be differentiated by treatment in patients with hypercholesterolemia. However, there is restricted number of studies related to the influences of rosuvastatin simultaneously on inflammation and oxidative stress markers in patients with hypercholesterolemia. Therefore, in this study, we aimed to measure IL-1β, IL-6, TNF-α, MDA, PON1 levels in patients with hypercholesterolemia before and after treatment with rosuvastatin.
Methods

Study population and design

The study group included 30 patients aged 18–65 diagnosed with hypercholesterolemia and 30 healthy subjects who were examined and treated at the clinic of Medicine Faculty of Erciyes University in Kayseri, Turkey. Erciyes University Ethics Committee approved the study protocol by (15-03-2013/96681246-103). Low density lipoprotein (LDL) limit was determined in compliance with the European Society of Cardiology [21].

Patients, who applied to the cardiology outpatient clinic and received an indication for statin therapy by cardiologists according to current guidelines, were included in study. According to current guidelines, it is recommended that calculation of the patient’s 10-year risk of atherosclerotic cardiovascular disease (ASHV) and life-long risk of ASHV be carried out by using a special scoring method. For patients with age ≥21 and LDL ≥ 190 (without ASKV risk estimation), high-intensity statin therapy is recommended for primary prevention [22]. Patients were given information about the research and they, by signing, certified the informed consent form according to Helsinki Declaration. The subjects with renal failures, coronary artery diseases, liver diseases, immune system diseases, diabetes, systemic diseases hypertension; and for any reason, the ones receiving treatment with medications such as lipid-lowering drugs, using alcohol and cigarettes were excluded from the study. Patients with similar age and gender distribution and 30 healthy volunteers, who had no systemic diseases and were nonsmokers and did not use any drugs whose body mass index was in the range 18.5–24.9 kg/m², were included in study.

Rosuvastatin (10 mg/kg/day) was applied to all ill participants for 12-weeks. Before and after treatment with rosuvastatin, concentrations of serum lipids, serum IL-1β, IL-6, TNF-α, MDA and PON1 levels were quantified. Dietary and exercise treatments were carried out; in addition, the patients were suggested not to change their lifestyle.

Determination of lipid profiles

After being fast for an overnight (≥12 h), control and patient groups were asked to give blood samples which were collected in vacutainer BD serum separation tubes comprise a thrombin-based clot activator and polymer gel for serum separation (Becton, Dickinson and Company, Franklin Lakes, NJ, USA). Being let to clot for 30 min., samples were centrifuged at 2000 ×g for 10 min as always. Not only lipemic but hemolyzed samples as well were taken out. The aliquots of samples were stored at −70°C until measurements.

Serum total cholesterol (TC), trigliserid (TG), LDL (using direct LDL kit) and HDL were analyzed by means of Advia 1800 chemistry system (Siemens, Erlangen, Germany).

Determination of cytokines and oxidative stress markers

The serum IL-1β, IL-6, TNF-α and PON1 levels were detected by making use of a commercial enzyme-linked immunoassay kit: For IL-1β (KHC0011, Invitrogen, Waltham, MA, USA), for IL-6 (KHC0061, Invitrogen, Waltham, MA, USA), for TNF-α (EK0525, Boster, Valley Ave Pleasanton, CA, USA) and for PON1 (SK00141-01, AVISCERA BIOSCIENCE, Santa Clara, CA, USA). Micro-plates were washed with micro ELISA washer (BioTek ELx800, Highland Park, Vermont, USA) and optical density was determined with ELISA reader (BioTek ELx800).

Antibodies specific to IL-1β, IL-6, TNF-α and PON1 were pre-coated on the microplates. Briefly, we pipetted standards and samples into the wells; and added biotin-conjugated specific antibodies over them. Then, we added avidin conjugated horseradish peroxidase to the wells after removing any unbound substances. Chromogen reagent was added to the wells and later the plate was let to be incubated. The color development was stopped by using stop solution and the optical density of wells was measured under 450 nm. Coefficient of variation (CV) of intra-assay for IL-6, IL-1β, TNF-α and PON1 were found to be <3%, <3%, <3% and <6%, respectively. Inter-Assay CV for IL-6, IL-1β, TNF-α and PON1 were found to be <9.3%, <7.3%, <7.5% and <12%, respectively.

Determination of malondialdehyde

The serum MDA levels were detected with a mercantile Assay Kit, [Thiobarbituric Acid Reactive Substances] (10009055, Cayman, Ann Arbor, MI, USA). The TBARS Assay was carried out in line with the manufacturer’s instruction, and, concisely, the MDA-thiobarbituric acid (TBA) adduct formed by the reaction of TBA and MDA under acidic conditions and 90–100°C was gauged colorimetrically at 532 nm. Intra-Assay CV for MDA was established to be <7.6%, while inter-Assay CV for MDA was found to be <5.9%.
Statistical analyses were conducted utilizing statistics programs with IBM SPSS Statistics 20.0 (IBM Corp., Armonk, NY, USA). The usual distribution of the data was determined by the Shapiro-Wilk test. The statistics of the variables with normal distribution were given as the mean ± standard deviation (SD) and variables with no normal distribution were verbalized as median (25th–75th percentile) categorical variables were given in numbers. Independent samples of t-test were utilized for normal distributions in the intergroup comparisons. Before treatment - After treatment differences were compared with paired samples t. Variables with no normal distribution were evaluated by using Wilcoxon test and Mann-Whitney U-test. Pearson and Spearman analysis was benefited to examine the relationship between variables. When the p-value was less than 5%, it was accepted as statistically significant.

Results

Anthropometric parameters of the patients and control group are presented in Table 1. No significant differences were noticed between patients and control group in terms of age, gender, weight, height and BMI values (Table 1). In this table, the mean ages of patients were 46.94 ± 9.11 and the controls were 46.26 ± 8.11. Nineteen patients and controls were women and 11 patients and controls were men (Table 1).

It is available to see the study populations clinical and laboratory parameters in Table 2. Before treatment, the mean values of TC, TG and directly measured LDL (D-LDL) levels were significantly lower in control group than in patients (p < 0.001). There were no significant differences between control and patients before treatment in terms of serum HDL (p = 0.058). The mean values of TC, TG and D-LDL levels were lower (p < 0.001) while mean values of HDL were significantly lower in patients before treatment than patients after treatment (p = 0.002). The mean values of D-LDL, TC and TG were higher in patients after treatment than control group (p = 0.007, p < 0.001 and p < 0.001; respectively). There were no significant differences between patients and control after treatment in terms of serum HDL (p = 0.560; Table 2).

Before treatment, the mean levels of IL-1β, IL-6 and TNF-α in patients were found to be higher than those of control group (Figures 1 and 2, p < 0.001). The mean levels of MDA were higher, while the mean values of PON1 were lower in patients before treatment than control group (Table 2, Figure 3; p < 0.001). The mean levels of IL-1β, IL-6 and TNF-α were lower in patients after treatment than patients before treatment (p < 0.001). The mean levels of MDA were lower, while the mean values of PON1 were higher in patients after treatment than patients before treatment (Table 2; Figure 4, p < 0.001). The mean values of IL-1β were significantly higher in patients after treatment than control group (p < 0.001). No significant differences were established between control group and patients after treatment with regard to serum IL-6 and TNF-α. The mean values of MDA were considerably higher in patients after treatment than control group (p < 0.001). The mean values of PON1 were significantly lower in patients after treatment than control group (p < 0.001).

The correlation analyses revealed that HDL levels had significantly negative medium level correlation with TNF-α in control group (r = −0.518; p < 0.003). The PON1 levels had significantly negative medium level correlation with IL-6 and TNF-α in control group (r = −0.432, p = 0.032; r = −0.472, p = 0.008, respectively). The PON1 levels had significantly positive medium level correlation with TNF-α in patients before treatment (r = 0.532, p = 0.002). The D-LDL levels had significantly positive weak level correlation with IL-1β in patients after treatment (r = 0.383, p = 0.037; Figure 5). Other values of correlation coefficient between inflammatory and oxidative markers are shown in Table 3.

Table 1: Basic characteristics of the patients and controls.

<table>
<thead>
<tr>
<th></th>
<th>Patient (n = 30)</th>
<th>Controls (n = 30)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>47.9 ± 9.2</td>
<td>46.2 ± 8.11</td>
<td>0.469</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>19/11</td>
<td>19/11</td>
<td>0.999</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.62 ± 0.1</td>
<td>1.64 ± 0.1</td>
<td>0.497</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.2 ± 9.9</td>
<td>63.9 ± 8.8</td>
<td>0.785</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.7 ± 0.95</td>
<td>23.4 ± 1.1</td>
<td>0.406</td>
</tr>
</tbody>
</table>

Data are expressed as numbers for categorical variables and mean ± SD for continuous variables. F, Female; M, male.

Discussion

In the present study, we tried to display that a 12-week treatment with rosuvastatin 10 mg daily improved lipid profile levels and was associated with significant reductions in IL-1β, IL-6, TNF-α and MDA levels, yet significant increase in serum levels of PON1.
Table 2: Biochemical measurement results of the patients and the controls.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patients Before treatment (n=30)</th>
<th>Patients After treatment (n=30)</th>
<th>Controls (n=30)</th>
<th>Comparisons Before treatment-control</th>
<th>After treatment-control</th>
<th>Before treatment After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mg/dL)</td>
<td>269.4±22.1</td>
<td>182.0±25.1</td>
<td>158.9±16.0</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>43.4±7.21</td>
<td>46.1±7.1</td>
<td>47.3±8.24</td>
<td>p=0.058</td>
<td>p=0.560</td>
<td>p=0.002</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>164.2±45.0</td>
<td>140.0±35.4</td>
<td>103.8±40.7</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>D-LDL (mg/dL)</td>
<td>188.9±23.5</td>
<td>104.3±26.1</td>
<td>87.7±12.7</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>IL-1β (pg/mL)</td>
<td>40.2 (37.9–44.3)</td>
<td>38.5 (34.6–42.5)</td>
<td>30.7 (27.6–35.1)</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>47.2±11.6</td>
<td>37.2±9.10</td>
<td>37.1±6.71</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>29 (24.9–32.6)</td>
<td>21.7 (19.3–23.4)</td>
<td>18.8 (15.4–23.1)</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>MDA (µM)</td>
<td>6.4±1.57</td>
<td>4.3±1.12</td>
<td>2.1±0.96</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>PON-1 (ng/mL)</td>
<td>9.87±2.88</td>
<td>17.5±4.67</td>
<td>17.8±6.0</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD or median (25th–75th percentile) for continuous variables. The significance of differences in variables between before-treatment and control or after-treatment and control was tested using independent samples t-test or Mann-Whitney U-test. The significance of differences of variables between before treatment and after treatment were tested using paired samples t-test or Wilcoxon test.
Rupture of coronary plaques and formation of thrombus, the basic mechanism causing acute coronary syndromes, are described in detail by a great lipid core, elevated number of macrophages and T lymphocytes, reduced number of smooth muscle cells [23]. Statins could function through multiple receptors and pathways in their target cells. Besides its consequent suppression of cholesterol biosynthesis, several studies have proved that rosuvastatin may exert more protective influences, requiring the enhancement of endothelial function and stabilization of atherosclerotic plaque [20].

In our study, although we found that there were no significant differences between controls and patients after treatment in respect to D-LDL and HDL levels, it was shown that D-LDL levels decreased by 40–60%, while HDL levels increased by 6.3% in patients with hypercholesterolemia after treatment. The reduction in D-LDL levels is also consistent with European Society of Cardiology 2016 hyperlipidemia guide and previously conducted clinical trials; and there is also a quite great deal of interindividual variation in LDL decrease with the same dose of drug [24]. Poor reaction to statin treatment in clinical studies is, to a certain extent, led by poor concordance, yet it could as well be described by a genetic background necessitating variations in genes because of both statin uptake and cholesterol metabolism in the liver [25, 26]. Moreover, status leading to high cholesterol (e.g. hypothyroidism) ought to be contemplated. To tell the truth, interindividual diversities in statin response permit observing the individual response at the start of therapy.

In this study, we tried to exhibit that a 12-week treatment with rosuvastatin had a close connection with significant decrease in IL-1β, IL-6 and TNF-α levels.

Studies, conducted before, displayed that rosuvastatin exert multiple purpose variations in inflammatory cells; for instance decrease in cytokines on isolated cells, animal models, and patients [18]. TNF-α and IL-6 can initiate a number of intracellular signaling events, and have an important role in the inflammatory cascade and promote vascular inflammation [27]. McGuire et al. suggested that decreases in TNF-α level might be a potential mechanism for anti-inflammatory activity of rosuvastatin [28]. However, how rosuvastatin regulates cytokines expression in patients with hypercholesterolemia is not clear enough. Nevertheless, some scholars proposed that statins could change expression of cellular inflammatory factors via mediating calcium modulating proteins [29]. It was also demonstrated that miR-155 is upregulated in activated immune cells and it attenuates immune responses by regulating cell differentiation (as in Th1 and Tregs) and cytokine secretion (as in TNF-a and IL-6) [18]. On the other hand, some proofs point to the reduced production of mevalonate and isoprenoids, the first yield produced by HMG-CoA reductase [30]. It was also found that the statin-induced downregulation of cytokine production in human umbilical vascular endothelial cells (HUVECs) and peripheral blood mononuclear cells (PBMCs) are regressed by coincubation with mevalonate. This monitoring shows a specific statin influence and a role of the mevalonate-isoprenoid pathway in cytokine production [31]. Experimental studies also suggest that pretreatment with statin significantly reduced levels of proinflammatory cytokines by inhibiting NF-κB expression in myocardial tissue [32]. Therefore, it may be suggested that rosuvastatin reduces the IL-1β, IL-6

![Figure 5: Correlation of direct low density lipoprotein (mg/dL) with interleukin 1-β (pg/mL) in patients after treatment (r = 0.383, p = 0.037).](image)
and TNF-α levels by using above-mentioned pathways. However, the molecular mechanism is not sufficiently clear; and further cellular, experimental and controlled clinical studies on the role of rosuvastatin in prevention of the formation of inflammation in terms of cytokine are required.

The present research demonstrated the correlation between inflammation and oxidative stress parameters in study groups. It was determined that 12-week treatment with rosuvastatin significantly lowered the MDA levels, while it significantly increased levels of PON1 after treatment. We also established that PON1 levels were significantly negatively correlated with IL-6 and TNF-α in control group, while PON1 levels were significantly positively correlated with TNF-α in the patients before treatment.

People with obvious rise in MDA-modified LDL were demonstrated to be more predisposed to advanced atherosclerosis statin medication having a positive effect on reducing serum MDA levels in human. It was found that rosuvastatin inhibited the elevations of MDA in rats and humans [33]. Bergeanu et al. showed that during 18 weeks of treatment, only PON1 activity was rose substantially from baseline in the rosuvastatin group. Nevertheless, the difference could not reach to be even significance compared directly with atorvastatin [19]. Oxidative stress plays a fundamental role in atherosclerosis basically by inciting endothelial dysfunction and improving proinflammatory processes causing formation of atherosclerotic plaque [34]. Kumon et al. stated that IL-1 and TNF-α downregulated serum PON1 activity [35]. It was also observed that increase in pro-inflammatory cytokines including IL-1, IL-6, and TNF-α caused reduction in serum PON1 activity [36]. In addition, hepatic PON1 mRNA synthesis was downregulated by treatment of IL-1, IL-1β and TNF-α [35, 36].

Consistent with the previous studies, we determined that PON1 levels were significantly positively correlated with TNF-α in the patients before treatment, while PON1 levels were significantly negatively correlated with IL-6 and TNF-α in the control group. Although PON1 is a HDL related with enzyme taking part in the protective mechanisms of HDL [19], it was found that HDL levels increased by 6.3%, while PON1 levels increased by 77.3% in patients with hypercholesterolemia after treatment. Moreover, we did not establish any significant relationships between HDL and PON1 levels after treatment.

In individuals, serum PON1 activity rather than genetic variation in the PON1 gene foresees vascular disease and a study carried out lately exhibits a sound relation of coronary artery disease and angiographic severity with PON1 activity, regardless of age, abnormal glucose regulation, hypertension, HDL-cholesterol and smoking [19]. As a result, reduction in PON1 in serum of patients with hypercholesterolemia could be associated with the rise of these cytokines [19, 34–36]. We suggest that PON1 levels might be changed as part of the inflammatory response as well, and thus seems that this balance is disrupted in patients with hypercholesterolemia. It may be also suggested that serum levels of PON1 is directly capable of suppressing serum levels of TNF-α and IL-1β. It may also be said that PON1 levels, which vary with treatment, are associated with cytokines instead of HDL levels in patients. Therefore, we propose that this condition may be an important mechanism for the action of rosuvastatin.

Nevertheless, the present research has some restrictions such as the insufficient number of participants and our inability to detect the circadian variation of IL-1β, IL-6 and TNF-α. Another limitation is the lack of the patients with hypercholesterolemia who are not separated by phenotypes according to PON1 and arylesterase activity since PON1 activity includes arylesterase activity. Therefore, further research is required to certify and enhance these studies since it is not absolutely clear how treatment with rosuvastatin affects the correlations between PON1 and cytokines in patients with hypercholesterolemia.

Conclusions

Our results provide evidence for the protective effect of rosuvastatin against inflammation and oxidative damage by lowered serum levels of IL-1β, IL-6, TNF-α and MDA, and ascending activities of PON1 in patients with hypercholesterolemia after treatment. On the other hand, correlation between PON1 levels and cytokines may be suggested that lowered serum PON1 levels may be one of the mechanisms underlying the augmented threat of not only oxidative stress but also inflammation process. It will be of great interest to determine other potential causes of correlation between PON1 and cytokines, and to learn whether this has any phenotypic effect on PON1.

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Conflict of interest statement: The authors report no conflict of interest.
References
