The Anti-Inflammatory Effects of Atorvastatins in Patients Suffering Metabolic Syndrome

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Abstract

Introduction: Inflammation plays a key role in all stages of atherosclerosis. Both humoral and cellular mechanisms have been proposed to participate in the onset and/or progression of atherosclerotic lesions, and postulates for the involvement of auto antibodies against oxidative modified LDL, phospholipids and circulating immune complexes have met with considerable experimental support.

Aim of study was to point on anti-inflammatory effect of atorvastatins in metabolic syndrome patients.

Materials and methods: Study included 46 patients who fulfilled criteria for MetS and they have atorvastatin therapy in dose of 10 mg/day. Serum samples were taken for measurement concentrations of: glucose, triglycerides (tg), total cholesterol (ch), high-density lipoprotein (HDL-C) cholesterol, low-density lipoprotein (LDL-C) cholesterol, factor for coronary diseases (CHD), index of atherosclerosis (IA), circulate immune complexes (CIC), C-reactive proteins (CRP) and C4 component of complements (C4) before and after four weeks of atorvastatin therapy.

Results: Four weeks atorvastatin therapy in dose of 10 mg per a day have significantly decreased concentration of total cholesterol (p<0.008), LDL-C (p<0.005) and index of atherosclerosis (p<0.018). Additionally concentration of acute markers of inflammation CRP (p<0.008) and C4 (p<0.034) were significantly decreased.

Conclusion: Atorvastatins have very potent anti-inflammatory effects on atherosclerotic plaques in metabolic syndromes.
In the past decade, there has been an upsurge of interest in the role of immune mechanisms in the development and regulation of atherosclerosis and its complications (11). Both humoral and cellular mechanisms have been proposed to participate in the onset and/or progression of atherosclerotic lesions, and postulates for the involvement of auto antibodies against oxidative modified LDL, phospholipids and circulating immune complexes have met with considerable experimental support (12-15).

The aim of study was to point on anti-inflammatory effect of atorvastatins in metabolic syndrome patients.

**MATERIAL AND METHODS**

Study included 46 patients who fulfilled criteria’s for MetS and they received atorvastatin 10mg/day. Serum samples were taken for measurement concentrations of: glucose, triglycerides (tg), total cholesterol (ch), high-density lipoprotein (HDL-C) cholesterol, low-density lipoprotein (LDL-C) cholesterol, factor for coronary diseases (CHD), index of atherosclerosis (IA), circulate immune complexes (CIC), C-reactive proteins (CRP) and C4 component of complements (C4) at the start of study. All measurements were repeated after 4 weeks of therapy.

All analyses were performed using the Statistical Package for the Social Science (SPSS), statistical software for Windows, Version 12.0 (SPSS Inc., IL, USA). The difference were assessed by Student’s t-test and Pearson’s correlation test. Probability (p) less than 0.05 and 0.01 was considered significantly different and less than 0.001 highly significantly different.

**RESULTS**

Table 1 summarizes serum concentrations of glucose, cholesterol (ch), triglycerides, HDL-C, LDL-C, factor for coronary diseases (CHD), index of atherosclerosis (IA) before and after 4 weeks of atorvastatins therapy.

**DISCUSSION**

Recent studies indicate that statins have salutary physiologic effects within weeks. In conjunction with lowering total and low-density lipoprotein (LDL) cholesterol, statins may improve endothelial functions (16), decrease platelet aggregability and thrombus deposition (17) and reduce vascular inflammation (18). The observation that statins reduce the risk of cardiovascular events even in the absence of a significant decrease of blood cholesterol levels, supports the relevance of the potential “pleiotropic” function of this drug class (19). The REVERSAL trial suggests several potential mechanisms for the greater benefit observed with an intensive treatment regimen. Most atherogenic lipoproteins were reduced to a greater extent in the intensive treatment by atorvastatin, including levels of LDL-C, total cholesterol, and triglycerides. However, factors other than greater LDL-C-reducing efficacy may also have influenced the results, including the differential effect on inflammation. Approximately, all in vitro and in vivo studies uniformly support anti-inflammatory roles of statins which highlight the relationship between the extent of reduction in CRP or other inflammatory markers and the effect on the progression of atherosclerosis.

**CONCLUSION**

Atorvastatins have very potent anti-inflammatory effects on atherosclerotic plaques in metabolic syndromes.

<table>
<thead>
<tr>
<th>Levels</th>
<th>Baseline</th>
<th>4 weeks therapy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIC</td>
<td>1.02 ± 0.74</td>
<td>1.12 ± 1.04</td>
<td>p&lt;0.008</td>
</tr>
<tr>
<td>CRP</td>
<td>1.57 ± 0.81</td>
<td>1.11 ± 0.64</td>
<td>p&lt;0.008</td>
</tr>
<tr>
<td>C4</td>
<td>0.41 ± 0.10</td>
<td>0.38 ± 0.11</td>
<td>p&lt;0.034</td>
</tr>
</tbody>
</table>

**Table 2. Concentration of CRP, CIC and C4 component of complement**

Parameters of inflammation, circulate immune complexes (CIC), C-reactive protein (CRP) and C4 component of complements, are presented in table 2.

Four weeks therapy by 10 mg atorvastatins significantly decreased concentration of total cholesterol (p<0.008), LDL-C (p<0.005) and index of atherosclerosis (p<0.018). Concentration of acute markers of inflammation also were significantly decreased, CRP (p<0.008) and C4 (p<0.034).
**Sažetak**

**Uvod:** Inflamacija igra značajnu ulogu u svim stadijumima ateroskleroze. Značajna je uloga i humoralnog i celularnog imunskog odgovora u početku i/ili progresiji aterosklerotskih lezija kroz auto-antitijela na oksidisani LDL frakcije, fosfolipide i cirkulišuće imune komplekse.

**Cilj rada:** bio je da se ukaže na antiinflamatorni efekat atorvastatin u pacijenata sa metaboličkim sindromom.

**Materijali i metode:** Studija je obuhvatila 46 pacijenata koji su ispunjavali kriterijumne za metabolički sindrom i koji su započeli terapiju atorvastatinom u dozi od 10 mg/dnevno. Uzorci seruma za određivanje koncentracija: glikemije, triglicerida (tg), ukupnog holestera (chol), holesteroljska frakcija visoke gustine (HDL-C), holesteroljska frakcija male gustine (LDL-C), faktora za koronarna oboljenja (CHD), indeks ateroskleroze (IA), C-reaktivnog proteina (CRP), cirkulišućih imunskih kompleksa (CIC) i C4 komponente komplemente (C4) suzeti su bazalno i nakon četiri nedjelje te terapije atorvastatinom.

**Rezultati:** Četiri nedjelje terapije atorvastatinom u dozi od 10 mg/dnevno dovelo je do značajnog smanjenja koncentracije chol (p<0.008), LDL-C (p<0.005) i IA (p<0.018). Značajno su bile smanjene i koncentracije reaktanata akutne faze CRP (p<0.008) i C4 (p<0.034).

**Zaključak:** Atorvastatin ima snažno antiinflamatorno djelovanje na aterosklerotske lezije u metaboličkom sindromu.