The Influence of Lipid Lowering on Soluble Tumor Necrosis Factor Receptor I in Patients with Angina Pectoris

Wykretowicz A, Deskur-Smielecka E, Furmaniuk J, Smielecki J
Wysocki H

Homepage:

www.kup.at/jcbc

Online Data Base Search for Authors and Keywords
The Influence of Lipid Lowering on Soluble Tumor Necrosis Factor Receptor I in Patients with Angina Pectoris

A. Wykretowicz, J. Smielecki, J. Furmaniuk, E. Deskur-Śmielecka, H. Wysocki

Inflammation plays an important role in the pathogenesis of atherosclerosis. It has been suggested that the beneficial effects of hydroxy-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors may derive from their anti-inflammatory properties.

**Aim** of the study was to determine levels of soluble tumor necrosis factor receptor I (sTNF-RI) in patients with hypercholesterolaemia and angina pectoris, in a group of asymptomatic subjects (n = 20) with elevated serum cholesterol levels and in a control group (n = 20). Furthermore, we wanted to investigate the possible influence of 3-month treatment with simvastatin on plasma concentrations of sTNF-RI.

**Results:** Baseline concentrations of sTNF-RI in plasma were significantly higher in patients with hypercholesterolaemia and angina pectoris compared to the control group (1259 ± 90 pg/ml vs. 913 ± 98 pg/ml, p = 0.0366). Baseline sTNF-RI levels in hypercholesterolaemic subjects (1004 ± 92 pg/ml) were not significantly different from those in patients with angina pectoris or controls. In both study groups simvastatin had no effect on plasma sTNF-RI concentrations (patients with angina pectoris: 1259 ± 90 pg/ml vs. 1206 ± 117 pg/ml, hypercholesterolaemic subjects: 1004 ± 92 pg/ml vs. 929 ± 66 pg/ml).

**Conclusions:** (1) Patients with hypercholesterolaemia and angina pectoris have increased soluble tumor necrosis factor receptor I plasma levels in comparison with healthy subjects. (2) 3-month therapy with simvastatin has no effect on sTNF-RI concentrations in hypercholesterolaemic patients with, or without, ischaemic heart disease. J Clin Basic Cardiol **2005; 8:** 65–8.

**Key words:** simvastatin, soluble tumor necrosis factor receptor I, sTNF-RI, hypercholesterolaemia

---

**Material and Methods**

The study population consisted of 20 patients with stable angina pectoris and serum cholesterol levels above 200 mg/dl (AP group) and 20 asymptomatic subjects, with total serum cholesterol concentrations exceeding 250 mg/dl (HC group). Healthy subjects with serum cholesterol levels below 250 mg/dl served as the control group (C group). Patients were only enrolled in the study if they had been on a low-fat, low-cholesterol diet (American Heart Association step I diet) and had not been taking any cholesterol-lowering drugs for at least 6 months. The exclusion criteria were a recent history of myocardial infarction (≤ 6 months), unstable angina pectoris, diabetes mellitus, active inflammatory disease, congestive heart failure, renal or hepatic impairment or pregnancy. The characteristics of each study group are summarised in Table 1.

**Table 1. Characteristics of the study population**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AP group (n = 20)</th>
<th>HC group (n = 20)</th>
<th>C group (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57.5 ± 8.5</td>
<td>55.2 ± 2.1</td>
<td>42.0 ± 8.0</td>
</tr>
<tr>
<td>Sex, m/f (n)</td>
<td>13/7</td>
<td>6/14</td>
<td>5/4</td>
</tr>
<tr>
<td>Smokers</td>
<td>7</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>(past or current) (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of myocardial infarction (n)</td>
<td>14</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>14</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

AP group: patients with hypercholesterolaemia and angina pectoris; HC group: asymptomatic subjects with hypercholesterolaemia; C group: control group

---

Received: July 9th, 2003; accepted October 25th, 2004.
From the Department of Cardiology-Intensive Therapy, University School of Medical Sciences, Poznań, Poland
Correspondence to: Andrzej Wykretowicz, MD, PhD, Department of Cardiology-Intensive Therapy, University School of Medical Sciences in Poznań, ul. Przybysza 49, 60-355 Poznań, Poland, E-mail: awykret@pikardio.pl
This investigation was approved by the local Ethics Committee and all patients included gave their written informed consent to participate in the study.

Study Design
Peripheral blood samples were taken from each subject after an overnight fast for evaluation of serum lipid profiles and soluble tumor necrosis factor receptor I levels. Patients in the AP and HC groups received 20 mg simvastatin daily in addition to their habitual medication. No other changes in treatment were allowed during the study period. After 3 months treatment with simvastatin, blood samples were again taken for assessment of serum lipid profiles and sTNF-RI concentrations.

Lipid Profiles
Serum levels of total cholesterol, HDL cholesterol and triglycerides were determined by standard enzymatic methods. LDL cholesterol concentrations were calculated using the Friedewald formula.

Levels of Soluble Tumor Necrosis Factor Receptor I
The concentrations of sTNF-RI in serum samples were determined by the quantitative sandwich enzyme immunosay technique (R&D Systems, Minneapolis, USA).

Statistical Analysis
Data analysis utilised standard descriptive techniques. The t-test for paired variables was used for within-group comparisons and the unpaired t-test was employed for between-group comparisons. A p-value < 0.05 was considered significant. All data are expressed as means ± SEM.

Results
Serum Lipid Profiles
The serum concentrations of total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides are shown in Table 2. Total and LDL cholesterol concentrations decreased significantly after 3 months of therapy with simvastatin in both study groups. No changes were observed in the HDL cholesterol and triglycerides levels.

Serum Concentrations of Soluble Tumor Necrosis Factor Receptor I
The baseline concentrations of sTNF-RI were significantly higher in patients with angina pectoris than in healthy subjects (1259 ± 90 pg/ml vs. 913 ± 98 pg/ml) (Fig. 1). There were no significant differences between the hypercholesterolaemic subjects and the control group for baseline sTNF-RI levels (1004 ± 92 pg/ml vs. 929 ± 66 pg/ml).

Discussion
Tumor necrosis factor plays a pivotal role in the inflammatory response. It exerts its effects by binding to two distinct receptors designated TNF-RI and TNF-RII on the target cell surface [16, 17]. Both receptor types exist in a circulating soluble form, resulting from a proteolytic cleavage of their extracellular domains from the cell membrane [18, 19]. The biological role of the soluble tumor necrosis factor receptors is not clear. They may bind and inactivate circulating tumor necrosis factor and thus protect cells from the effect of this agent [20, 21]. It has been also suggested that soluble tumor necrosis factor receptors may serve as a biological reservoir for tumor necrosis factor, binding and stabilising it with subsequent controlled, slow release of this factor into the circulation [22, 23]. Soluble tumor necrosis factor receptors are present in human serum, but their levels increase markedly in acute infection or inflammation [24, 25]. Elevated soluble tumor necrosis factor receptor II levels have been recently reported both in patients with congestive heart failure [26] and angiographically proven coronary heart disease [27].

Our study was designed to evaluate sTNF-RI levels in hypercholesterolaemic patients presenting with or without the symptoms of angina pectoris. We observed significantly higher sTNF-RI levels in patients with angina pectoris in comparison with the control group. This finding is in keeping with previous studies demonstrating activation of the tumor necrosis factor system in patients with ischaemic heart disease [27] and indicates that sTNF-RI, in addition to sTNF-RII, may be a potential immunologic marker of coronary heart disease. In contrast, there were no significant differ-

![Figure 1. Concentrations of soluble tumor necrosis factor receptor I (sTNF-RI) in patients with angina pectoris and hypercholesterolaemia (AP group), in asymptomatic subjects with hypercholesterolaemia (HC group) and in the control group (C group)](image)

Table 2. Serum lipid profiles in the study population before and after 3-months treatment with simvastatin

<table>
<thead>
<tr>
<th></th>
<th>Before therapy</th>
<th>AP group After therapy</th>
<th>p</th>
<th>Before therapy</th>
<th>HC group After therapy</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>277 ± 8</td>
<td>207 ± 8</td>
<td>&lt; 0.0001</td>
<td>298 ± 9</td>
<td>221 ± 4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>42 ± 2</td>
<td>44 ± 2</td>
<td>n.s.</td>
<td>55 ± 3</td>
<td>57 ± 2</td>
<td>n.s.</td>
</tr>
<tr>
<td>% HDL cholesterol</td>
<td>14 ± 1</td>
<td>21 ± 1</td>
<td>0.0002</td>
<td>18 ± 1</td>
<td>26 ± 1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>195 ± 8</td>
<td>126 ± 7</td>
<td>&lt; 0.0001</td>
<td>214 ± 8</td>
<td>137 ± 4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>triglycerides</td>
<td>199 ± 11</td>
<td>186 ± 20</td>
<td>n.s.</td>
<td>160 ± 19</td>
<td>164 ± 24</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

AP group: patients with hypercholesterolaemia and angina pectoris; HC group: asymptomatic subjects with hypercholesterolaemia
In conclusion, we found that soluble tumor necrosis factor receptors play a significant role in the inflammatory response. Further detailed studies are required to fully understand the mechanisms of action of statin drugs in the context of other components of the immune system.

References:


Mitteilungen aus der Redaktion

Besuchen Sie unsere zeitschriftenübergreifende Datenbank

☑ Bilddatenbank ☑ Artikeldatenbank ☑ Fallberichte

e-Journal-Abo

Beziehen Sie die elektronischen Ausgaben dieser Zeitschrift hier.

Die Lieferung umfasst 4–5 Ausgaben pro Jahr zzgl. allfälliger Sonderhefte.

Unsere e-Journale stehen als PDF-Datei zur Verfügung und sind auf den meisten der marktüblichen e-Book-Readern, Tablets sowie auf iPad funktionsfähig.

☑ Bestellung e-Journal-Abo

Haftungsausschluss


Bitte beachten Sie auch diese Seiten:

Impressum    Disclaimers & Copyright    Datenschutzerklärung