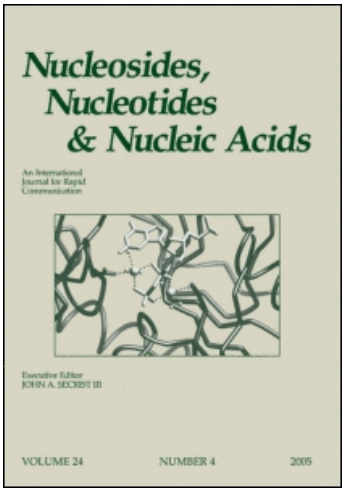

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

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Online publication date: 11 June 2010

To cite this Article Ogata, N. , Fujimori, S. , Oka, Y. and Kaneko, K.(2010) 'Effects of Three Strong Statins (Atorvastatin, Pitavastatin, and Rosuvastatin) on Serum Uric Acid Levels in Dyslipidemic Patients', Nucleosides, Nucleotides and Nucleic Acids, 29: 4, 321 — 324
To link to this Article: DOI: 10.1080/15257771003741323
URL: http://dx.doi.org/10.1080/15257771003741323

Nucleosides, Nucleotides and Nucleic Acids, 29:321–324, 2010

ISSN: 1525-7770 print / 1532-2335 online
DOI: 10.1080/15257771003741323

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EFFECTS OF THREE STRONG STATINS (ATORVASTATIN, PITAVASTATIN, AND ROSUVASTATIN) ON SERUM URIC ACID LEVELS IN DYSLIPIDEMIC PATIENTS

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□ *We have retrospectively investigated the effects of three strong statins, atorvastatin, pitavastatin, and rosuvastatin, on serum uric acid (SUA) levels. SUA levels after a few months of statin treatment were compared with those before treatment in 150 outpatients with dyslipidemia. In the atorvastatin ($n = 62$) and rosuvastatin ($n = 45$) groups, the SUA levels were reduced by 6.5% ($p < 0.0001$) and 3.6% ($p = 0.03$) respectively, but in the pitavastatin group ($n = 43$), the SUA level increased by 3.7% ($p = 0.38$). Because uric acid is considered a risk factor for cardiovascular disorders, atorvastatin or rosuvastatin treatment may be recommended when statins are used in patients at high risk for cardiovascular disorders complicated with hyperuricemia.*

Keywords Statin; uric acid; dyslipidemia; LDL-cholesterol

INTRODUCTION

Several epidemiological studies have shown that serum uric acid (SUA) is a risk factor of cardiovascular disorders.[1] As a result, when treating patients at high risk for cardiovascular disorders, such as those with hypertension and dyslipidemia, medications that do not elevate SUA levels are recommended. The statin atorvastatin reportedly shows SUA-lowering effects.[2] However, rosuvastatin, another strong statin, reportedly shows no SUA-lowering effects.[3] No studies have examined SUA levels with use of pitavastatin. The present study, therefore, investigated the effects of these three strong statins on SUA levels.

SUBJECTS AND METHODS

Subjects comprised 150 dyslipidemic outpatients whose SUA levels were measured before and after treatment with one of three types of strong statins

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during the period between 2003 and 2009. Their treatment was not altered or discontinued and they were not administered a new drug that affects SUA levels during the period of investigation. About 40% of them had hypertension but not were administered diuretic drugs. Medication was atorvastatin (mean dosage: 5.52 mg/day) for 62 patients, pitavastatin (mean dosage: 1.23 mg/day) for 43 patients, and rosuvastatin (mean dosage: 2.53 mg/day) for 45 patients. These are standard medication dosages in Japan. In each patient, LDL-C, triglycerides (TG), HDL cholesterol (HDL-C), blood urea nitrogen (BUN), creatinine, and SUA levels were measured before treatment and the results were compared to those measured after 2–3 months of treatment. Student's paired *t* test was used to analyze significant difference for all measured values compared to baseline levels.

RESULTS

Baseline LDL-C levels were 168.7 ± 23.3 mg/dl in the atorvastatin group, 160.8 ± 28.9 mg/dl in the pitavastatin group, and 161.2 ± 22.1 mg/dl in the rosuvastatin group. After treatment, these levels had decreased markedly in all 3 groups, to 109.3 ± 27.7 mg/dl ($p < 0.0001$) for atorvastatin, 109.2 ± 26.5 mg/dl ($p < 0.0001$) for pitavastatin, and 95.2 ± 21.1 mg/dl ($p < 0.0001$) for rosuvastatin. TG levels were decreased in all groups but a significant change was only seen in the rosuvastatin group ($p = 0.04$). Baseline SUA levels were 6.2 ± 1.4 mg/dl and 5.6 ± 1.3 mg/dl in the atorvastatin and rosuvastatin groups, respectively, decreasing significantly to 5.8 ± 1.3 mg/dl (−6.5%; $p < 0.0001$) and 5.4 ± 1.3 mg/dl (−3.6%; $p = 0.03$), respectively. However, in the pitavastatin group, these levels showed an increasing tendency rising from 5.4 ± 1.3 mg/dl to 5.6 ± 1.1 mg/dl (+3.7%; $p = 0.38$; Figure 1). Changes in renal function were evaluated by investigating blood urea nitrogen (BUN) and serum creatinine levels in each group. In the atorvastatin group, BUN and serum creatinine levels decreased significantly from 16.4 ± 4.8 mg/dl to 15.0 ± 4.4 mg/dl ($p = 0.001$) and from 0.82 ± 0.20 mg/dl to 0.81 ± 0.19 mg/dl ($p = 0.04$), respectively, but no significant changes were seen

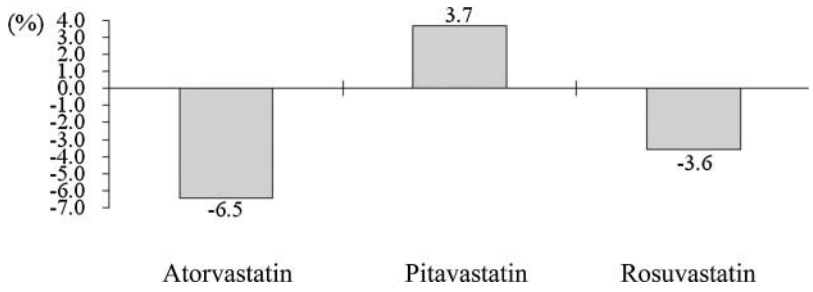

FIGURE 1 Percentage changes in SUA levels.

in the pitavastatin or rosuvastatin groups. However, it is not clear whether these changes are relevant.

DISCUSSION

In the present retrospective study, SUA levels decreased significantly after atorvastatin and rosuvastatin treatment, but tended to increase following administration of pitavastatin. Athyros et al.,[2] who reported on the SUA-lowering effect of atorvastatin, inferred that decreased SUA levels may result from increased renal blood flow associated with improved endothelial function brought about by atorvastatin, which, in addition to hypolipidemic effects, exerts a variety of pleiotropic effects.[4] In another study, Milionis et al.[3] reported that SUA levels decreased with increased FEua (fractional excretion of uric acid) following atorvastatin treatment, and this decrease in SUA levels was considered as uric acid excretion promoted by atorvastatin. The results of our investigation support this conclusion.

Rosuvastatin reportedly shows no SUA-lowering effect.[3] However, the present investigation did find serum uric acid-lowering effects of rosuvastatin when by-patient treatment results were compared to baseline levels. When changes in SUA levels were examined in six patients who changed medication from atorvastatin to rosuvastatin, SUA levels were found to have increased, although not significantly, suggesting that atorvastatin shows greater SUA-lowering effects than rosuvastatin (data not shown). The SUA-lowering effect produced by rosuvastatin was unaccompanied by changes in renal function, presumably indicating that this effect results from a different mechanism than that with atorvastatin. However, details remain unclear, and further investigation is needed to ascertain whether uric acid production or excretion is being affected.

Although this was the first study of pitavastatin and uric acid, unlike other strong statins, SUA levels tended to increase with administration of pitavastatin. We could not examine the dietary habits and BMI of subjects because this study was retrospectively done. SUA levels can be influenced by many factors, such as food, alcohol, drugs, body mass index, etc. Although the SUA changes after statin treatment were relatively small and significant, they might be related by the lifestyle of subjects.

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