

Atorvastatin therapy improves endothelial-dependent vasodilation in patients with systemic lupus erythematosus

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The aim of the presented study was to investigate the efficacy of atorvastatin in improving endothelium-dependent arterial dilation in systemic lupus erythematosus (SLE) patients with and without conventional risk factors for atherosclerotic disease.

Conventional risk factors alone seem not to explain the high, intense and premature development of CHD patients with SLE. Chronic inflammation, antiphospholipid antibodies, chronic use of glucocorticosteroids, cytokines, homocysteine and anti-oxidized low density lipoprotein (LDL) antibodies, may strongly influence the prevalence of CHD among SLE patients. Clinical data demonstrate that endothelial dysfunction is remarkable at initial stages of the disease in SLE patients. Improvement of endothelial dysfunction could theoretically minimize atherosclerotic complications.

Besides the hipolipemiant effect statins have also pleiotropic effects, such as anti-inflammatory, immune modulator and anti-thrombogenic, effects which contribute to the improvement of endothelial function.

A total of 91 patients with SLE were included in the study. Inclusion criteria were: female sex, SLE according to the American College of Rheumatology revised classification criteria,

disease diagnosis =1 yr, age >18 yrs and regular menstruation. Exclusion criteria included: current or past use of hypolipemic drugs in the last six months, menopausal status, diabetes mellitus, serum creatinine > 1.2 mg/dl, pregnancy, smoking status (last 12 months), family history of CHD, skeletal myopathic disease and/or elevated creatinine phosphokinase (CK), hepatic disease and cyclosporine use.

Patients were divided in two groups: intervention group – 64 patients who received atorvastatin 20 mg/day during 8 weeks and a control group – 24 SLE patients followed in the same period without atorvastatin. At baseline and after 8 weeks, all 88 participants underwent complete clinical examination, brachial artery ultrasound and blood sampling for laboratory analysis. Mean age was 32 ± 8 yrs and mean disease duration was 8.9 ± 4.8 yrs. None of the patients had confirmed coronary or cerebrovascular event. 81.8% of the patients were on regular use of prednisone, 61% were on regular use of chloroquine diphosphate and 52% were receiving additional immunosuppressive agents. Intervention and control groups did not differ significantly regarding most of the demographic and risk factor variables.

At baseline, no significant difference in FMD was observed between the group of 50 patients

with risk factors for CHD and the group of 38 patients without risk factors ($P=0.79$).

At the end of 8 weeks, there was a significant increase in FMD in the 64 patients receiving atorvastatin (3.8% vs 6.9%, $P<0.001$). The analysis of subgroups of 26 patients with and 38 patients without dyslipidaemia showed both groups achieved a significant increase in the FMD after atorvastatin ($P=0.006$), with no statistical difference between the 2 subgroups.

Atorvastatin treatment was associated with a significant increase in brachial artery baseline diameter (baseline 2.79 ± 0.30 mm vs 8th week 2.92 ± 0.40 mm, $P<0.001$). No significant difference in brachial artery baseline diameters was seen for patients in the control group. Patients receiving atorvastatin had a significant decrease of total cholesterol, LDL-cholesterol, triglycerides and homocysteine level but atorvastatin did not significantly affect serum levels for HDL-cholesterol and lipoprotein-a.

A significant decrease in SLEDAI (Systemic Lupus Erythematosus Disease Activity Index) mean scores was observed for patients in the intervention group at the end of the study (4.47 ± 5.0 vs 3.08 ± 3.6 , $P<0.001$) while patients in the control group experienced significant increase in their mean disease activity scores.

No significant difference in the dose of oral prednisone was observed between baseline and the end of the study for both, intervention and control groups.

No significant difference was observed in the increase in FMD after 8-week atorvastatin therapy in patients with and those without chloroquine.

The duration of the study was not suitable to evaluate long-term adverse effects associated with atorvastatin use. Only six patients had mild and transitory adverse effects related to atorvastatin use, none of them justifying discontinuation of the therapy.

This is the first study to evaluate the effect of atorvastatin on endothelial dysfunction in SLE patients and showed that an 8-week period atorvastatin treatment was associated with significant improvement in FMD, homocysteine serum levels reduction and decrease in SLEDAI scores. Atorvastatin improved endothelial function measured by brachial artery ultrasound independently on the presence of risk factors for CHD. These findings suggest that atorvastatin may be useful to prevent atherosclerotic cardiovascular complications in SLE and maybe other connective tissue disease. Nevertheless long-term multicentric studies are necessary to precisely define the recommendation for statins in SLE patients. □



Comment on the paper:

Ferreira GA, Navarro TP, Telles RW, et al – Atorvastatin therapy improves endothelial-dependent vasodilation in patients with systemic lupus erythematosus: an 8 weeks controlled trial. *Rheumatology* 2007; 46:1560-1565