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Effects of a 3-month course of rosuvastatin in patients with systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is associated with a highly increased cardiovascular risk. Statins can reduce this risk, but may possess additional anti-inflammatory effects that are relevant for the treatment of SLE. In a preliminary study, we investigated the effects of a 3-month course of rosuvastatin on lipids and markers of inflammation using a randomised cross-over design.

The study was approved by the institutional medical and ethical committee and written informed consent was obtained from all subjects. Based upon a previous, representative study,¹ a sample size of 14 patients would be necessary to demonstrate a 25% reduction in C-reactive protein (CRP) levels (power = 80%). A dropout level of 35% (n = 5) was estimated.² Patients with stable SLE (n = 19) were randomly assigned to receive rosuvastatin 10 mg or no treatment during 3 months and were treated vice versa after a wash-out period of 3 months. Fifteen patients completed the study. CRP was measured by Synchron LX20 (Beckman Coulter, Fullerton, USA); antinuclear antibodies (ANA) by Colorzyme ANA-Ro (ImmunoConcepts, Sacramento, USA). Patients had stable, chronic disease characterised by mean (SD) baseline CRP levels of 5.2 (1.9) mg/l and positive ANA in 68% of patients. Levels of total cholesterol, low-density lipoprotein cholesterol and apolipoprotein B levels (5.36 (0.25) mmol/l, 3.46 (0.21) mmol/l and 0.913 (0.051) g/l, respectively) were lowered by 28%, 40% and 30%. Levels of high-density lipoprotein cholesterol, triglycerides, apolipoprotein A1 and lipoprotein(a) were not changed, and neither were levels of CRP, erythrocyte sedimentation rate, C1q, C3, C4, double-stranded DNA antibodies, interleukin (IL) 1 β , IL6, IL8, IL10, IL12p70, tumour necrosis factor α , 24 h urine protein or 24 h microalbumin, creatinine clearance or the clinical SLE Disease Activity Index (SLEDAI) score.

This preliminary study shows potent lipid-lowering effects of rosuvastatin in patients with SLE, but no large anti-inflammatory effects. These negative findings were not to be expected.¹⁻⁴ Considering data from others, the results are not likely to be related to an intrinsic lack of anti-inflammatory properties of rosuvastatin, nor to the dose regimen used or the study duration.⁵ One way to explain the negative results would be to assume that the lack of drug effect is disease specific. Indeed, the only other recently completed trial which investigated statin intervention in SLE also showed no CRP inhibitory effect.⁶ Possibly, statin-induced apoptosis could contribute to an immune reaction compensating anti-inflammatory effects,⁷ or statin-induced shifting of Th1 to Th2 immunological responses leading to B-cell reactivity could induce production of pathogenic autoantibodies.⁸⁻⁹ Furthermore, corticosteroid use may mask anti-inflammatory effects.⁶ Owing to the sample size, no subanalysis could be performed in our study between patients using or not using corticosteroids. The patients in our study had

overall mild disease activity. In contrast, the only positive study reporting anti-inflammatory effects of statins in SLE was a small case series in patients with active, severe disease.¹⁰ As such, it must be emphasised that our study only aimed to explore large anti-inflammatory effects of statin intervention in patients with stable, chronic SLE. Statin treatment in patients with stable SLE may be useful for lipid-lowering purposes, but current evidence for large pleiotropic, anti-inflammatory effects is limited.

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