Simvastatin modulates aortic intima-media thickness in an animal model of systemic sclerosis

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Systemic sclerosis (SSc) is a multisystem autoimmune disease characterized by vasculopathy and organ fibrosis. Although many previous studies highlighted microvascular alterations in SSc, a growing body of evidence exists for structural and functional abnormalities in the macrovascular circulation. Recent reports shows that in SSc patients macrovasculopathy occurs preferentially at the forearm and aorta (Liu et al, 2011). Aim of the study was therefore to evaluate the effect of simvastatin administration on aortic intima-media (IM) thickness and ratio in a murine model of systemic sclerosis. SSc–like illness was induced in BALB/c mice by daily subcutaneous injections of HOCl as an oxidant stress for 6 weeks. Mice (n=24) were randomized in three arms to treatment with either HOCl (n=10), HOCl plus simvastatin (n=9); or vehicle alone (n=5). Simvastatin treatment was initiated 30 minutes after HOCl subcutaneous injection (40 mg/kg) continuing daily for the 6 weeks. Thoracic aorta was evaluated by histological methods. IM thickness and ratio were measured for statistical analysis. In HOCl treated mice aortic IM thickness was significantly higher than controls, showing an increase of 104% ($p<0.0001$). Treatment with simvastatin diminished this increase by 92% ($p<0.0001$). Simvastatin treated animals had a significantly thinner intima layer (-9%, $p<0.0001$) and media layer (-197%, $p<0.0001$) compared to HOCl group. IM ratio was also decreased in HOCl treated mice compared to controls (0.75 vs 1.74, $p<0.0001$) and significantly increased by simvastatin administration (1.61 vs 0.75, $p<0.0001$). Administration of simvastatin moderates the increase of IM thickness in this animal model of SSc. Further analysis on IM ratio suggests that aortic media layer is thickened in HOCl treated animals and this increase can be prevented by simvastatin.

References:
Liu et al (2011). *Arthritis Care Res (Hoboken).* 63, 579-87