Receptor For Advanced Glycation End-products Blockade Improves Endothelial Dependent Vascular Function In Atherosclerotic Mice

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Abstract

Atherosclerosis is a progressive inflammatory disease that is present in large vessels in the body. We hypothesized that either adiponectin treatment or soluble Receptor for Advanced Glycation Products (sRAGE) treatment would rescue the decreased endothelial function of aortae in apolipoprotein-E knockout (ApoE-/-) mice, a murine model of atherosclerosis. We examined endothelial-dependent vasorelaxation to acetylcholine (ACh) in aortae removed from ApoE-/- and control wild (WT) mice. Relaxation to ACh was blunted in ApoE-/- compared with WT controls while endothelial-independent vasorelaxation to sodium nitroprusside (SNP) was comparable. sRAGE improved ACh-induced vasorelaxation in ApoE-/- mice without affecting dilator response to SNP.

Adiponectin treatment did not show significant improvement of endothelial function in aortae of ApoE-/- mice. Dilation to ACh was significantly attenuated after administration of nitric oxide (NO) synthase inhibitor N^G-monomethyl L-arginine in WT mice, which indicates that vasodilation to ACh was NO mediated while L-NMMA did not further inhibit endothelial-dependent vasodilation in ApoE-/- mice. Immunostaining showed RAGE to co-localized with the endothelium in murine aortae. These results suggest that AGE/RAGE signaling may play a pivotal role in processes that lead to endothelial dysfunction in atherosclerosis.