Reduced Function of the Vascular Endothelium via Fatty Acids and the Role of Oxidative Stress

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Received Aug. 21, 2024; Accepted for publication Aug. 26, 2024; Published online Aug. 27, 2024
https://doi.org/10.17161/kjm.vol17.22714

Introduction. Evidence suggests that ascorbic acid improves function of the vascular endothelium via suppression of oxidative stress. Therefore, we tested the hypothesis that ascorbic acid (AA, a water-soluble antioxidant) would prevent lipid-mediated reductions in function of the vascular endothelium via antioxidant properties.

Methods. A 20% IV fat emulsion (Intralipid) was administered for two hours to eight healthy, middle-aged adults (two men/six women) with and without co-infusion of AA (separate visits) in a double-blinded, crossover study design. Endothelium-dependent dilation was assessed via brachial artery flow-mediated dilation and immunocytochemistry was used to assess oxidative stress (nitrotyrosine) and phosphorylated endothelial nitric oxide synthase (eNOS) in cultured human umbilical vein endothelial cells (HUVEC).

Results. Within 20 min of infusion, Intralipid increased plasma fatty acid concentration (+36 ± 18 μmol/L, $P<0.05$) and significantly reduced flow-mediated dilation (-53%, $P<0.05$). In contrast to our hypothesis, co-infusion of AA did not prevent the reduction in flow-mediated dilation (-41%, $P<0.05$). In HUVECs, AA did not prevent the increase in oxidative stress following incubation with lipid (Lipid: +53% vs. Lipid+AA: +35%). An increase in phosphorylated eNOS was observed with incubation of both AA (+28%) and lipid+AA (+24%).

Conclusions. These preliminary findings suggest that increased oxidative stress and impaired function of the vascular endothelium via fatty acids cannot be prevented by ascorbic acid despite increased phosphorylated eNOS.