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High Antioxidant Load Impairs Cutaneous Microvascular Function In Healthy Young Women

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PURPOSE: Human cutaneous circulation is used as a bioassay to assess mechanisms underlying vascular dysfunction in a variety of populations. Local drug interventions (intradermal microdialysis), including Atorvastatin (statin; LOX inhibitor), have been used to elucidate mechanisms underlying microvascular dysfunction in cohorts with accelerated cardiovascular disease risk. Additionally, systemic drugs (e.g., oral salsalate) have been used to further elucidate these mechanisms. However, high antioxidant load from these localized and systemic treatments may impair endothelial function in healthy control groups. **METHODS:** In a randomized placebo control design oral salsalate (1500mg/twice daily/5 days) was used to assess the impact of systemic inflammation on cutaneous vascular function. Two intradermal microdialysis fibers were placed into the ventral forearm skin of eight healthy control women (32±3 yrs). Cutaneous blood flow was measured via Laser-Doppler flowmeter probes placed in local heating units set to a thermoneutral temperature of 33°C. Increasing concentrations of acetylcholine (ACh; Endothelial nitric oxide synthase agonist) from 10^{-10} to 10^{-1} M were perfused with lactated Ringer's (control) or 0.02 mM statin sequentially for 5 min each. Following the dose-response protocol, local skin temperature was increased to 43°C and 28 mM sodium nitroprusside was perfused to elicit maximal cutaneous vasodilation. Brachial blood pressure was measured every 5 min. Cutaneous vascular conductance (CVC) was calculated (red blood cell flux/mean arterial pressure) and normalized as a percentage of the site-specific maximum (%CVC_{max}). **RESULTS:** There was no impact of oral salsalate at either control or local statin sites (p=0.3411). Following salsalate intake, there was a significant reduction in %CVC_{max} at the statin treated site (control 56± 17% vs statin 34± 11% 10^{-5} M, control 65± 17% vs statin 41± 14% 10^{-4} M, control 64± 16% vs statin 41±13% 10^{-3} M ACh; p=0.0078, 0.0045, 0.0069, respectively). **CONCLUSION:** Combination of oral salsalate and localized treatment with statin resulted in attenuated endothelial function. In healthy women, five-day oral salsalate intake and local statin may result in high antioxidant load creating a shift in redox balance leading to impaired endothelial function.

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