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No Sex Differences in Inflammatory Response and Vascular Function During Low Estrogen Phase

Sara E. Mascone, Catalina A. Chesney, Lauren E. Eagan, Sushant M. Ranadive. University of Maryland, College Park, Maryland.

Acute inflammation increases pro-inflammatory cytokine production and reduces nitric oxide bioavailability, resulting in impaired vascular function. Estrogen has both anti-inflammatory and pro-vasodilatory properties. During the high estrogen, mid-luteal phase of the menstrual cycle, sex differences in vascular function and inflammatory responses to induced inflammation have been observed in premenopausal women as compared with age-matched men. **PURPOSE:** To evaluate sex differences in vascular responses to induced inflammation- with a reduced influence of estrogen concentration. **METHODS:** In a double-blind crossover sham-controlled study of 15 women (21±3y) and 15 men (21±2y), we assessed pro-inflammatory interleukin-6 concentration ([IL-6]) and vascular function via brachial artery flow mediated dilation (FMD) at baseline (BL), 24 hours (24H), and 48 hours (48H) after influenza vaccine administration. Women were studied when circulating estrogen levels are typically low (early follicular phase or placebo pill phase of oral contraceptive pills) and similar between sexes. **RESULTS:** Following induced inflammation, both sexes exhibited an increase in [IL-6] at 24H (BL v 24H: women p=0.0024; men p=0.0029) that returned to near baseline levels by 48H (BL v 48H: women p=0.64; men p=0.30; [IL-6] (pg/mL): women BL: 0.54 ± 0.5, 24H: 1.12 ± 0.6, 48H: 0.57 ± 0.3; men BL: 0.39 ± 0.2, 24H: 1.07 ± 0.7, 48H: 0.58 ± 0.2). There were no sex differences in FMD or [IL-6] at any time point (FMD: sex p=0.062, time p=0.30, interaction p=0.25; FMD (%): women BL: 8.33 ± 4.8, 24H: 6.40 ± 4.4, 48H: 9.05 ± 5.5; men: BL: 5.25 ± 2.9, 24H: 6.14 ± 2.1, 48H: 6.71 ± 1.1; [IL-6]: BL: p=0.74, 24H: p=0.57, 48H: p=0.66). Though, women exhibited significantly lower resting brachial artery diameter (BL D; p<0.0001 all time points) than men (BL D (mm): women BL: 3.22 ± 0.4, 24H: 3.18 ± 0.4, 48H: 3.19 ± 0.4; men BL: 4.07 ± 0.6, 24H: 4.24 ± 0.4, 48H, 4.22 ± 0.4). However, there were no sex differences in allometrically scaled FMD (sex p=0.11, time p=0.20, interaction p= 0.072; Scaled FMD (%): women BL: 6.39 ± 3.7, 24H: 4.32 ± 3.8, 48H: 6.92 ± 3.7; men BL: 7.03 ± 3.9, 24H: 8.71 ± 4.2, 48H: 8.69 ± 4.3). **CONCLUSION:** When estrogen concentrations are low, women show similar inflammatory responses and vascular function as compared with age-matched men.

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