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Estrogen Deficiency and Diet Differentially Regulate Goblet Cell Count and Inflammation in Gut

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Estrogen is known to regulate many processes in women that protect them from inflammation prior to menopause. Upon menopause and estrogen deficiency, many women experience increased risk for inflammatory-based chronic diseases that can be comorbid with weight gain. Our lab has previously shown increased weight gain in ovariectomized (OVX) animals, gut microbiota alterations like obese models, and increased intestinal inflammation. 4-Vinylcyclohexene dioxide (VCD) is an injectable chemical used to induce menopause and decrease estrogen production. However, the extent to which VCD is like OVX and how VCD may interact with high-fat diets is not well understood. **PURPOSE:** The purpose of this study was to investigate the effect of estrogen deficiency, via VCD injection, in animals fed diets that contains high (22.5%) and low (1%) amounts of omega-6 fatty acids (LA). **METHODS:** Forty 4-month-old C57BL/6J female mice were fed a chow diet and injected with either VCD or oil (control). After 4 weeks of injections, mice were fed either 22.5% or 1% LA diets for an additional 4 weeks until sacrifice; estrous stage was noted at time of sacrifice. Colon samples were collected and preserved in 3% paraformaldehyde 2% sucrose solution for immunohistochemistry. Tissue staining included (1) Periodic acid–Schiff (PAS) to observe goblet cells and (2) the inflammatory marker cyclooxygenase-2 (COX-2). **RESULTS:** Unlike OVX, VCD-injections did not cause significant weight gain in either 22.5% (35.9±6.4 vs 34.5±4.7, oil vs VCD) or 1% (34.5±5.9 vs 33.4±4.7, oil vs VCD) LA groups. Control animals had higher numbers of goblet cells, the highest noted in 22.5% LA fed animals. Contrary to this, VCD-injected animals had less goblet cells irrespective of diet consumed. COX-2 expression was highest in control animals fed 22.5% LA diet. VCD-injected animals on either diet had a similar expression of COX-2 but appears less than control animals fed 22.5% LA diet. **CONCLUSION:** VCD did not increase weight gain as normally seen with OVX, however it did reduce the number of goblet cells present in gut which could not be rescued with 22.5% LA. VCD-injected animals on either diet did not express the same amount of inflammation as control animals fed 22.5% LA diet. Our data indicate that high-fat diets combined with VCD injections may not behave the same as OVX procedures.

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