Electronic-cigarette Vapor Exposure Causes Impaired Left-Ventricular Relaxation and an Inflammatory Response in Male Adolescent Mice

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Objective: Electronic cigarettes (e-cigs) are the most commonly used tobacco product by teens and young adults. The aim of the present study was to determine the potential effects of e-cig vapor exposure on cardiac function in adolescent mice. Materials and Methods: Four-week-old FVB/NJ male mice were separated into three exposure groups: 1) e-cig exposure with nicotine (EC(+)) (20.2 mg nicotine/1 mL 50:50 propylene glycol:vegetable glycerin), 2) e-cig exposure without nicotine (EC(-)), or 3) filtered air exposure (FA) (HEPA filter), and exposed for three months. A puff profile consisting of one 70-mL e-cig vapor puff per minute of exposure was administered for 4 h/day, 5 days/week over the course of three months, and filtered air was administered continuously throughout the 4-hour periods. Cotinine concentration in the serum of mice from either group was determined using a cotinine ELISA. Echocardiography was used to examine global cardiac function after 1, 2, and 3 months of exposure. Following the exposure period, mice were sacrificed within 24 hours of exposure, and heart tissue and serum was collected. Serum was analyzed for 42 cytokines by Ampersand Bioscience's Rodent MAP 4.0 service. Left ventricular (LV) cardiac lysates were examined for protein expression via western blot. Results: The average cotinine concentration in the serum of the EC(+) mice after three months of exposure was 189 ng/mL, while there was not a detectable concentration of cotinine in the serum of EC(-) or FA mice. Echocardiography illustrated significant reduction in the E/A ratio for mitral flow in mice exposed to EC(+) as early as two months into exposure. There were no significant alterations in ejection fraction (%EF), fractional shortening (%FS), or posterior wall thickness (PWT). The cytokine panel showed significant increases in the concentrations of MCP-1, IL-18, and MIP-1β in EC(+) compared to FA, and increases in SCF and VEGF for both EC(-) and EC(+) compared to FA. Cardiac fibrosis was observed via an increase in collagen I levels in LV tissue of EC(+) compared to EC(-) and FA. Additionally, a decrease in phospho-phospholamban and phospho-troponin I was observed in EC(+) LV tissue, suggesting alterations in calcium cycling and myofilament regulation. Conclusions: E-cig exposure causes early signs of impaired cardiac relaxation with no observed systolic dysfunction in adolescent male mice. Fibrosis, alterations in calcium cycling, and inflammation may contribute to the observed dysfunction.