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Interactions of a high-fat Western diet and crystalline silica inhalation on airway epithelial ion transport and airway reactivity

Janet A. Thompson, Michael L. Kashon, Walter S. McKinney, Jeffrey S. Fedan

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Abstract

Silicosis, an irreversible occupational lung disease caused by crystalline silica inhalation, is a serious health risk for silica-exposed workers. NIOSH reports that Appalachian coal miners have higher rates of obesity and metabolic dysfunction (MetDys) compared to the general U.S. adult population. MetDys is a risk factor for lung function impairment, pulmonary hypertension, and asthma. Consumption of a high-fat Western diet (HFWD) is associated with obesity and MetDys. In this study, we investigated the effects of, and determine interactions between, HFWD-consumption and silica-exposure on airway epithelial ion transport and smooth muscle reactivity in the F344 rat. Six-week-old male F344 rats were fed either a HFWD [40.6% fat (19.5% lard), 40.6% total carbohydrate (20% sucrose), 14.8 % protein] or standard rat chow (STD) [6.2 % fat, 44.2 % carbohydrate (grain sources), 18.6 % protein] for the duration of the study. Following 16 weeks of diet-consumption, inhalation exposure to respirable crystalline silica (Min-U-Sil 5®, 15 mg/m^3, 6 h/d, 5 d/wk, for 39 d) or filtered air began, with endpoint experiments conducted at 0, 4, and 8 wk post-exposure. Airway epithelial ion transport maintains airway surface liquid osmolarity and depth required for effective cilia motility and clearance of xenogens. Changes in ion transport were determined *ex vivo* by measurement of transepithelial potential difference (V_t), short-circuit current (I_{SC}) and transepithelial resistance (R_t) in rat tracheal segments mounted in Ussing chambers, and administered the ion transport inhibitors amiloride (Na^+ channel blocker; apical), 5-nitro-2-(3-phenylpropylamino) benzoic acid (NPPB; Cl^- channel blocker; apical), and

ouabain (Na^+, K^+-pump blocker; basolateral). Airway hyperresponsiveness is associated with obesity and pulmonary diseases such as asthma and COPD; thus, the isolated perfused trachea apparatus was employed to ascertain whether silica or HFWD altered airway smooth muscle reactivity to serosal or mucosal applied methacholine (MCh). HFWD-consumption had no effect on basal V_t. Silica exposure increased Na^+ transport at 0 wk, decreased basal I_{SC} at 4 wk, and reduced Cl^- channel and Na^+, K^+-pump activity at both 4 wk and 8 wk compared to STD+AIR controls. HFWD-consumption caused a reduction in Cl^- transport and Na^+, K^+-pump activity at 4 wk, while increasing R_t in response to ouabain at 0 wk and NPPB at 8 wk compared to STD+AIR. HFWD+SIL increased basal I_{SC} at 0 and 4 wk, caused reduction in Cl^- transport and Na^+, K^+-pump activity at 4 wk, while reducing $R_t$in response to ouabain at 4 wk compared to STD+SIL. No significant changes in tracheal reactivity to MCh were observed. In conclusion, HFWD and silica altered epithelial ion transport, but the combined effects of HFWD+SIL were not synergistic.

This is the full abstract presented at the Experimental Biology meeting and is only available in HTML format. There are no additional versions or additional content available for this abstract.