Effects Of Diacetyl Vapor Inhalation On Airway Reactivity To Methacholine (MCh) In Vitro In Rats

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RATIONALE. “Popcorn workers lung” is a fixed obstructive pulmonary disease caused by inhalation of artificial butter flavoring during the manufacture of microwave popcorn. Previous investigations have implicated one of the components of butter flavoring, the α-diketone flavoring, diacetyl, as an inhalation hazard in the workplace. Prior studies in rats demonstrated that inhalation of diacetyl vapor for 6 h elicited dose-dependent damage to the airway epithelium of the nose, larynx, trachea and intrapulmonary airways. A number of other inhaled toxicants which cause epithelial damage, such as ozone, result in hyperreactivity to MCh in the isolated, perfused trachea (IPT) preparation. Therefore, we hypothesized that diacetyl-induced epithelial damage results in hyperreactivity to MCh in the IPT. METHODS. Male rats were exposed by inhalation for 6 h to diacetyl vapor (60, 100, 200, 300, 360 ppm); controls were exposed to air. Eighteen hours after exposure, tracheas were removed and placed on holders for perfusion at a constant rate with modified Krebs-Henseleit solution while measuring inlet minus out pressure difference, an index of tracheal diameter. Methacholine was added in stepwise-increasing cumulative concentrations to the tracheal lumen to induce contractile responses. RESULTS. Compared to air-breathing controls, diacetyl inhalation increased reactivity to MCh of tracheas removed from animals that had been exposed to 200 ppm of the vapor. The remaining exposures had no effect on reactivity to MCh. CONCLUSION. These findings indicate that the morphological damage occurring in the epithelium of rats following select diacetyl exposure may be accompanied by an increase in reactivity to MCh in the IPT preparation. This could reflect the consequences of epithelial damage and the greater penetration of MCh across the airway wall to reach the smooth muscle. Such an increase in reactivity to inhaled MCh was not observed in in vivo studies of the effects if inhaled diacetyl vapor on lung resistance and compliance. Thus, the IPT method may be an advantageous model for investigating the No Observable Adverse Effect Level (NOAEL) for diacetyl vapor. However, it is not understood why the increase in reactivity was restricted to the one exposure condition.

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