Silica Exposure Alters Mouse Lung Mechanics through Inflammation and Type II Cell Hyperplasia.

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Chronic exposure to crystalline silica leads to the development of small airway disease. We speculate that early release of inflammatory mediators contributes to this process. To test this, we examined the effects of silica on pulmonary inflammation and lung function. C57bl/6J mice were treated i.t. with silica (1 mg/kg Min–U–Sil 5) or PBS. Seven days after silica, diffuse alveolitis, lipoproteinosis, and fibrin deposition were observed in the lungs of treated mice. Total protein and cell content in bronchoalveolar fluid (BALF) increased 2–fold following silica treatment. The cellular infiltrate consisted of neutrophils and macrophages. Both "free silica" and silica engorged macrophages were also observed in BALF. Expression of cyclooxygenase–2, a key enzyme in eicosanoid production, surfactant protein–D, a collectin important in regulating lung inflammation, and inducible nitric oxide synthase were upregulated in the lung following silica exposure. Proliferating cell nuclear antigen was also upregulated in the alveolar epithelium. This was correlated with increased expression of the Type II cell marker, proSP–C, suggesting that silica induces Type II cell hyperplasia. The effects of silica on lung function were assessed by measuring responsiveness to inhaled methacholine using a SCIREQ flexiVent. In both control and silica treated mice, quasi–static compliance, which reflects the elastic static recoil pressure at the level of the alveoli, decreased upon challenge with methacholine. These effects were significantly greater in animals exposed to silica suggesting a loss in lung elasticity. Taken together, these data suggest that early inflammatory changes may be important in structural and functional alterations in the lung following exposure to silica.

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