Analysis of Distribution and Clearance of Silicon Nanowires After Pulmonary Exposure In Rats

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Rationale: The occupational health community is concerned that pulmonary exposure to wire-shaped nanomaterial causes chronic lung disease (e.g., fibrosis). We have shown that intratracheal instillation (IT) of silicon nanowires (SN) induces an acute inflammatory lung response in a rat model. The goal of this study was to assess lung distribution and clearance of SN up to1 month after IT as it relates to inflammation and the potential to develop fibrotic lung disease. **Methods:** SN were synthesized by a vapor-liquid-solid method with silane as the silicon precursor and gold as the catalyst (~20-30 nm diameter; ~15 μm length; 20 nm gold nanoparticle catalyst at one end). SN were isolated, suspended in a physiologic dispersion medium (DM, phosphate-buffered saline + 0.6 mg/ml rat serum albumin + 0.01 mg/ml dipalmitoyl phosphocholine), and sonicated. Sprague-Dawley rats received 10, 25, 50, or 100 μg of SN, or DM alone (vehicle control) via IT. Bronchoalveolar lavage was performed on right lungs at 1, 3, and 7 days after exposure to assess lung inflammation, and the left lungs were preserved at time points up to 28 days for morphometric analysis of tissue distribution and clearance of SN. **Results:** Lung inflammation observed at the highest dose had resolved within 1 week. In rats treated with 100 μg of SN, lung burden on day 28 was found to be ~18% of the total burden on Day 1. From Day 1 to Day 28, nearly 100% of the SN were located in the alveolar region. On day 1, ~70% of the burden was located in alveolar macrophages (AMs), ~20% was in alveolar tissue (AT), and ~10% was in alveolar airspaces (AA). By day 7, ~90% of SN was located in AMs, ~10% was in AT, and there were no SN observed in AA. The SN that remained on day 28 were contained within AMs only. Despite the lack of a persistent inflammatory response and increased pulmonary clearance of SN, there was a significant increase in alveolar wall thickness due to an elevation in connective tissue thickness in this region on day 28 when compared to day 1. **Conclusions:** Inflammation due to SN exposure that resolved within 1 week correlated with movement of SN from AA and AT into AMs and the overall clearance of SN from the lungs. Because SN clearance is substantial over time at the administered doses, increases in alveolar tissue thickness may not lead to fibrotic disease.

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