Acute and subacute pulmonary toxicity and mortality in mice after intratracheal instillation of ZnO nanoparticles in three laboratories

Inhalation is the main pathway of ZnO exposure in the occupational environment but only few studies have addressed toxic effects after pulmonary exposure to ZnO nanoparticles (NP). Here we present results from three studies of pulmonary exposure and toxicity of ZnO NP in mice. The studies were prematurely terminated because interim results unexpectedly showed severe pulmonary toxicity. High bolus doses of ZnO NP (25 up to 100µg; ≥1.4mg/kg) were clearly associated with a dose dependent mortality in the mice. Lower doses (≥6µg; ≥0.3mg/kg) elicited acute toxicity in terms of reduced weight gain, desquamation of epithelial cells with concomitantly increased barrier permeability of the alveolar/blood as well as DNA damage. Oxidative stress was shown via a strong increase in lipid peroxidation and reduced glutathione in the pulmonary tissue. Two months post-exposure revealed no obvious toxicity for 12.5 and 25µg on a range of parameters. However, mice that survived a high dose (50µg; 2.7mg/kg) had an increased pulmonary collagen accumulation (fibrosis) at a similar level as a high bolus dose of crystalline silica. The recovery from these toxicological effects appeared dose-dependent. The results indicate that alveolar deposition of ZnO NP may cause significant adverse health effects.

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