European Respiratory Society
Annual Congress 2013

Abstract Number: 2180
Publication Number: P4249

Abstract Group: 6.2. Occupational and Environmental Health
Keyword 1: Inflammation **Keyword 2:** Environment **Keyword 3:** Lung injury

Title: The histopathologic damage and glycation injury of C57BL/6 mouse lung due to titanium dioxide particles

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Body: Background: In this study, we examined the associations between TiO2 particle and glycated products associated lung injury. To evaluate the relationship of inflammation and glycation injuries during TiO2 exposures, we examined the content of Advanced glycation end products(AGEs) and related proteins to glycation injuries on the lung tissue specimens and mice serum. Methods: Titanium dioxide particles (TiO2) were administered intratracheally to C57BL/6 mice. The mice were exposed to saline and saline suspensions of 20 mg/ kg of TiO2particles twice a week for 12 weeks. Following exposure with these particles, the lungs were analyzed histopathologically by hematoxylin and eosin (H&E)stain, Glycation injuries were determined by immunohistochemistry (IHC) for AGE, HMGB1 and RAGE in the lung tissues. The serum of mice exposed to TiO2 particles was analysised for evaluating expression of proteins related to Glycation injuries by western blot. Results: The lung tissue specimens of mice exposed to TiO2 showed significantly increased inflammatory changes and AGE expressions compared to the control group but didn’t show significant change in RAGE and HMGB1 expressions compared to the control group. The serum of mice exposed to TiO2 showed there was no significant changes for AGE, HMGB1, S100A12 and CML(carboxy methyl lysine) expressions compared to the control group. Conclusion: Our results showed that 12 weeks exposure to TiO2 particle induced inflammatory changes and increased AGE expression in the lung tissue but not in serum of C57BL/6 mice. After TiO2 particles exposure in mice, Increased AGE expressions might have induce lung parenchymal inflammation.