GENOMIC DNA METHYLATION ALTERATIONS DUE TO METAL-RICH AIR PARTICLE EXPOSURE: POTENTIAL LINKS WITH INFLAMMATION AND COAGULATION MARKERS

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Background and Aims: DNA methylation alterations have been proposed as a novel molecular mechanisms linking inhalable particular matter (PM) exposure to cardiovascular effects. However, data showing relations among PM exposure, DNA methylation and cardiovascular-related outcomes, such as inflammation and blood coagulation, are limited. We investigated global DNA methylation, inflammation and coagulation markers in foundry workers with well-characterized exposure to a wide range of metal-rich PM.
Methods: We recruited 63 male workers (mean age 44 years) in an electric-steel plant in Italy. Individual exposure to PM with diameter<10 µm (PM10) and its metal components was estimated using work-area measurements and time spent in each area. DNA methylation analysis of Alu and LINE-1 was performed trough bisulfite-pyrosequencing on blood DNA obtained on two different work days. We measured PT, aPTT, t-PA antigen, D-dimer, and CRP. Endogenous thrombin potentials (ETPs) were assessed with (TM+) or without (TM-) soluble thrombomodulin, but without exogenous triggers. Covariate-adjusted linear mixed-effect regression was used to evaluate associations between PM or metal exposure and methylation; and between methylation and coagulation/inflammation markers.
Results: Workers were exposed to a wide range of PM10 (between 73-1220 • g/m3) and metal components (PM10 metal content between 2%-94%). PM10 showed a negative association with Alu (• =-0.18, p=0.05) and LINE-1 (• =-0.37, p=0.04) methylation. Zinc had a marginal negative association with Alu methylation (• =-0.17, p=0.06). Aluminum was negatively associated with LINE-1 methylation (• =-0.19, p=0.04). Lower Alu methylation was associated with activated coagulation and inflammation, as indicated by shorter PT (• =-0.18, p=0.02), and increased ETP TM+ (• =87.17, p=0.03), ETP TM- (• =144.82, p=0.02), and CRP (• =0.58, p=0.01). No associations were found with other markers.
Conclusions: We found novel associations of coagulation markers with Alu repetitive element methylation. DNA methylation was associated with specific metal components, suggesting a possible common path linking PM exposure, methylation, and blood coagulation.