Automotive gasoline-Induced Epigenetic Modifications and Genotoxic Effects in Occupationally Exposed Workers

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Introduction: Automotive gasoline is a complex mixture composed of polycyclic aromatic hydrocarbons (PAHs) and various additives. It was recently classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC). Among its components, benzene (PAH) already previously classified as a Group 1 human carcinogen stands out due to its hematotoxic and neurotoxic effects and its significant concentration in gasoline (approximately 1% v/v). Given this, individuals working at fuel stations are potentially exposed to its carcinogenic effects, making it essential to understand benzene's biological interactions to prevent adverse health outcomes. **Materials and Methods:** This cross-sectional study was conducted between 2014 and 2016 with workers from fuel stations located in the Central and Southern zones. A total of 217 individuals participated, divided into three groups: Group 1 (n = 74), exposed only via inhalation; Group 2 (n = 74), exposed via both inhalation and dermal contact; and a control group without occupational exposure (n = 69). All participants were over 18 years old and signed an informed consent form. Socioeconomic and clinical data were collected using structured questionnaires. Urine samples were collected to measure the exposure biomarker trans,trans-muconic acid (t,t-MA), and blood samples were used for genotoxicity analysis (comet assay) and epigenetic assessments (DNA methylation profiling of LINE-1, Alu, MGMT, PARP-1, and MSH3 via pyrosequencing). **Results:** The results showed that most exposed individuals were male, non-white, had low educational attainment, and reported family incomes of up to three minimum wages. Approximately 16.9% of the exposed participants had urinary t,t-MA levels above 0.5 mg/g creatinine, exceeding the limit established by Brazilian regulations. Exposed workers showed significantly higher levels of genotoxic damage compared to the control group, although these levels were not correlated with urinary t,t-MA concentrations. Regarding global DNA methylation, LINE-1 methylation levels were higher in Group 2, while Alu hypomethylation was observed in both exposed groups, more pronounced in Group 1. For DNA repair genes, the MGMT promoter region was hypomethylated in Group 2. Individuals exposed to benzene with genotoxic damage showed lower MGMT methylation levels compared to those without damage. Additionally, PARP-1 and MSH3 were more methylated in Group 1 than in the control group or Group 2. **Conclusion:** In conclusion, urinary t,t-MA levels were not effective predictors of genotoxic effects or hematological changes, suggesting that this biomarker may not adequately reflect the harmful effects of occupational gasoline exposure. In contrast, the observed epigenetic alterations were sensitive to exposure route and may indicate non-genotoxic mechanisms of toxicity. These findings highlight that DNA methylation profiles are a promising approach for biomonitoring and preventing damage related to occupational exposure to automotive gasoline, given their sensitivity to environmental factors and potential reversibility.

Keywords: Epigenetics; DNA Methylation; Benzene; Occupational Exposure; Gas Stations;
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