DNA Damage in Children Exposed to Arsenic in Utero and During Early Childhood: Application of Salivary and Urinary Biomarkers

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Abstract

Early life exposure to inorganic arsenic is associated with a wide range of chronic disease and cancers later in life. Arsenic-induced oxidative damage is believed to play a crucial role in arsenic carcinogenesis. Our previous study on the consequences of arsenic exposure in utero was conducted in pregnant women living in arsenic contaminated areas in Southern Thailand. Arsenic exposed newborns had significantly higher levels of arsenic in cord blood, and a set of genes associated with various biological pathways, including cell signaling, inflammation and stress responses. To gain a better understanding of the mechanism through which arsenic induces toxicity in children, assessment of arsenic exposure and its effect on oxidative DNA damage and repair were conducted in the same cohort of children who prenatally exposed to arsenic and continued to live in the same arsenic-contaminated areas.

A follow-up study was carried out in 40 arsenic-exposed and 40 matched-control children at the age of 5-7 years old. To address the need for biological specimens that can be acquired with minimal discomfort to children, non-invasive urinary and salivary based assays were employed for assessing arsenic exposure and potential health effects. Arsenic exposure, assessed as arsenic concentrations in drinking water and in various biological samples (saliva, urine, fingernails and toenails) by ICP-MS, was significantly higher in arsenic-exposed children. Arsenic levels in saliva showed significant positive correlations with other biomarkers of arsenic exposure, including arsenic accumulation in nails (r = 0.56, P < 0.001) and arsenic concentration in urine (r=0.50, P < 0.05). Oxidative DNA damage was measured as 8-hydroxydeoxyguanosine (8-OHdG) by HPLC-MS/MS. Levels of salivary 8-OHdG in exposed children were significantly higher (4-fold, P<0.01), whereas levels of urinary 8-OHdG excretion and salivary hOGG1 expression were significantly lower in exposed
children (3-fold, P<0.05), suggesting a defect in *hOGG1* that resulted in ineffective cleavage of 8-OHdG.

From these findings, it is clear that children exposed to arsenic *in utero* through early childhood resulted in increased DNA damage and decreased DNA repair capacity which may pose a life-long health risk. In addition, this study shows the usefulness of non-invasive urinary and salivary-based assays for genotoxicity as tools for human biomonitoring in terms of arsenic biomarkers of exposure and biological effects.

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