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Association between urinary arsenic profiles and DNA hypomethylation in a case-control study of urothelial carcinoma

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Inorganic arsenic is a well-known human carcinogen and commonly found in groundwater, surface waters, rice, grains and fish. Recently, many studies suggested the effect of DNA methylation on the carcinogenesis. However, the medication of DNA methylation on arsenic exposure related UC risk was limitedly explored. Therefore, we want to construct a hospital-based case-control study to explore the interaction of inorganic arsenic exposure and DNA methylation level on UC risk. We recruited 178 UC patients and 356 controls between 2011 and 2017. Urine samples were analyzed to measure urinary arsenic profiles including total arsenic, percentages of Inorganic Arsenic (InAs%) Monomethylarsonic (MMA%) and Dimethylarsinic Acid (DMA%). In addition, blood 5-methyl-2'-deoxycytidine levels were measured as a proxy for DNA methylation. Multivariate logistic regression was applied to estimate the risk for UC. In the results, the average concentrations of total arsenic were, respectively 26.12±0.97 ppb and 20.75±1.32 ppb in UC patients and control groups. There were significantly dose-response relationships of total arsenic, InAs% and DMA% on increased UC risk after adjusting for other risk factors. For DNA methylation, people with Q1 levels of DNA methylation had significantly 2.10-fold UC risks compared to those with Q5 levels of DNA methylation. The levels of InAs% and DMA% were significantly associated with the levels of DNA methylations. Furthermore, people with high InAs% and low DNA methylation (Q1) or low DNA% and low DNA methylation had the highest UC risks. Environmental inorganic arsenic explore may resulted in increased risks of UC through the modification of DNA methylation.

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