

ADVERSE EFFECTS OF CHRONIC EXPOSURE TO ARSENIC IN KIDNEY EPITHELIAL CELLS

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Abstract: Arsenic exposure is a major public health concern. Accumulating evidence suggests that arsenic exposure is associated with chronic kidney disease (CKD) including kidney cancer. However, the effect of relatively low dose arsenic and the mechanism of arsenic-induced CKD are not well understood. Therefore, the objective of this study was to evaluate the adverse effects of chronic exposure to low dose arsenic on the growth and morphology of kidney epithelial cells, and identify the molecular mechanism underlying this process. HK2 kidney epithelial cells, derived from normal human kidney, were exposed to arsenic for chronic period and the effects on growth, morphology, and gene expression changes were determined. Our data revealed a significant increase in the growth of arsenic exposed HK2 cells as compared to the control HK-2 cells. Additionally, the arsenic exposure also induced morphological changes of EMT and stemness in these cells. The analysis of genes expression further confirmed these changes in arsenic exposed HK-2 cells. In addition to these changes, the increased expressions of pro-fibrotic genes were also observed in arsenic exposed cells. The treatment of arsenic exposed cells with DNA demethylating agent 5-aza-2'-deoxycytidine restored the epithelial morphology and expression of genes in these cells. Therefore, the data of this study suggest that chronic exposure to arsenic can increase the risk of CKD including kidney fibrosis. Additionally, our data suggest an epigenetic mechanism behind the adverse effects of arsenic in kidney epithelial cells. These adverse effects of arsenic can potentially be reversed by epigenetic therapeutics.

Key words: Arsenic, Kidney Cancer, DNA methylation