Arsenic methylation and bladder cancer risk

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摘要

Abstract

Background. To date the mechanism of arsenic detoxification in humans remains unclear. Data are especially lacking on low-level arsenic exposure. We hypothesize that arsenic methylation ability, defined as the ratios of MMA(V)/inorganic arsenic (primary arsenic methylation ability) and DMA(V)/MMA(V) (secondary arsenic methylation ability), may modify the association between cumulative arsenic exposure and the risk of bladder cancer. In this study we investigated the relationship among arsenic methylation ability, cumulative arsenic exposure, and the risk of bladder cancer in a hospital-based case-control study in southwestern Taiwan.
Methods. From January 1996 to December 1999 we identified 49 patients with newly-diagnosed cases of bladder cancer at the National Cheng-Kung University (NCKU) Medical Center; controls consisted of 224 fracture and cataract patients selected from the same medical center. The levels of four urinary arsenic species (As(III), As(V), MMA(V), and DMA(V)) were determined in all subjects by using the high-performance liquid chromatography hydride-generation atomic absorption spectrometry (HPLC-HGAAS). Cumulative arsenic exposure was estimated by using published data collected in a survey from 1974 to 1976.
Results. Compared to a cumulative arsenic exposure≦2 mg/L-year, cumulative arsenic exposure>12 mg/L-year was associated with an increased risk of bladder cancer (multivariate odds ratio, 4.23; 95 percent confidence interval, 1.12 to 16.01), in the setting of a low secondary arsenic methylation ability (≦4.8). Compared to women, smoking men (multivariate odds ratio, 6.23; 95 percent confidence interval, 1.88 to 20.62) and non-smoking men (multivariate odds ratio, 3.25; 95 percent confidence interval, 0.95 to 11.06) had higher risks of bladder cancer. Given the same level of primary arsenic methylation ability, smoking men (multivariate odds ratio, 9.80; 95 percent confidence interval, 2.40 to 40.10) and non-smoking men (multivariate odds ratio, 4.45; 95 percent confidence interval, 1.00 to 19.84) had a higher risk of bladder cancer when compared to women. With the same level of secondary arsenic methylation ability, both smoking men (multivariate odds ratio,

6.28; 95 percent confidence interval, 1.76 to 22.39) and non-smoking men (multivariate odds ratio, 3.31; 95 percent confidence interval, 0.84 to 12.97) had a higher risk of bladder cancer when compared to women.
Conclusions. Subjects with low secondary arsenic methylation ability (SAM) have a substantially increased risk of bladder cancer, especially when combined with high cumulative-exposure levels. Males in all strata of arsenic exposure and methylation ability are at higher risk of bladder cancer.
Abbreviations used: Arsenite, As(III); arsenate, As(V); monomethylarsonic acid, MMA(V); monomethylarsonous acid, MMA(III); dimethylarsinic acid, DMA(V); cumulative arsenic exposure, CAE; primary arsenic methylation ability, PAM; and secondary arsenic methylation ability, SAM
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