

Population-Based Case-Control Study of Chinese Herbal Products Containing Aristolochic Acid and Urinary Tract Cancer Risk

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Background.—Consumption of Chinese herbs that contain aristolochic acid (eg, Mu Tong) has been associated with an increased risk of urinary tract cancer.

Methods.—We conducted a population-based case-control study in Taiwan to examine the association between prescribed Chinese herbal products that contain aristolochic acid and urinary tract cancer. All patients newly diagnosed with urinary tract cancer (case subjects) from January 1, 2001, to December 31, 2002, and a random sample of the entire insured population from January 1, 1997, to December 31, 2002 (control subjects), were selected from the National Health Insurance reimbursement database. Subjects who were ever prescribed more than 500 pills of nonsteroidal anti-inflammatory drugs and/or acetaminophen were excluded, leaving 4594 case patients and 174 701 control subjects in the final analysis. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated by using multivariable logistic regression models for the association between prescribed Chinese herbs containing aristolochic acid and the occurrence of urinary tract cancer. Models were adjusted for age, sex, residence in a township where black foot disease was endemic (an indicator of chronic arsenic exposure from drinking water [a risk factor for urinary tract cancer]), and history of chronic urinary tract infection. Statistical tests were two-sided.

Results.—Having been prescribed more than 60 g of Mu Tong and an estimated consumption of more than 150 mg of aristolochic acid were independently associated with an increased risk for urinary tract cancer in multivariable analyses (Mu Tong: at 61–100 g, OR = 1.6, 95% CI = 1.3 to 2.1, and at >200 g, OR = 2.1, 95% CI = 1.3 to 3.4; aristolochic acid: at 151–250 mg, OR = 1.4, 95% CI = 1.1 to 1.8, and at >500 mg, OR = 2.0, 95% CI = 1.4 to 2.9). A statistically significant linear dose-response relationship was observed between the prescribed dose of Mu Tong or the estimated cumulative dose of aristolochic acid and the risk of urinary tract cancer ($P < .001$ for both).

Conclusions.—Consumption of aristolochic acid-containing Chinese herbal products is associated with an increased risk of cancer of the urinary tract in a dose-dependent manner that is independent of arsenic exposure.

► Patients, the lay press, and, to some extent, physicians believe that if something is natural, it cannot do you harm. Studies such as this one demonstrate the fallacy of this view. These authors found that consumption of aristolochic acid-containing Chinese herbal products was linked to an increased risk of urothelial carcinomas. Importantly, this was in a dose-dependent manner—the more you

took, the higher the risk. The major limitation in this study is that smoking was not controlled for since it was unknown. This raises the possibility that patients who consumed more of these herbs were more likely to smoke.

I am not a huge fan of herbal remedies not because I do not think they work, but because they have the potential to cause harm. Multiple drugs have been found to be effective; yet the risks outweigh the benefits. The unregulated nutraceutical market is likely to be promoting products as safe that have long-term adverse effects. In the past, I have thought that these drugs were harmless. No longer.

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