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Lifetime risk of urothelial carcinoma and lung cancer in the arseniasis-endemic area of Northeastern Taiwan

Tse-Yen Yang [a,b], Ling-I Hsu [b], Hui-Chi Chen [b], Hung-Yi Chiou [c], Yu-Mei Hsueh [c], Meei-Maan Wu [c,d], Chi-Ling Chen [e], Yuan-Hung Wang [f,g], Ya-Tang Liao [b,h], Chien-Jen Chen [a,b,i,*]

[a] Graduate Institute of Life Sciences, National Defense Medical Center, Taipei, Taiwan
[b] Genomics Research Center, Academia Sinica, Taipei, Taiwan
[c] School of Public Health, Taipei Medical University, Taipei, Taiwan
[d] Graduate Institute of Oncology, National Taiwan University, Taipei, Taiwan
[e] Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan
[f] Division of Urology, Department of Surgery, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan
[g] Graduate Institute of Clinical Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan
[h] Management Office for Health Data, China Medical University and Hospital, Taichung, Taiwan
[i] Graduate Institute of Epidemiology and Preventive Medicine, College of Public Health, National Taiwan University, Taipei, Taiwan

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ABSTRACT

Arsenic in drinking water has been shown to increase the risk of urothelial carcinoma and lung cancer. However, the lifetime risk of developing urothelial carcinoma and lung cancer caused by exposure to arsenic in drinking water has not been reported. This study aimed to assess the lifetime risk of urothelial carcinoma and lung cancer caused by arsenic exposure from drinking water and cigarette smoking habit for residents living in the arseniasis-endemic area in Northeastern Taiwan. We recruited 8086 residents in 1991–1994 and monitored them for their newly developed types of cancers, identified by computerized linkage with the national cancer registry profile. There were 37 newly diagnosed urothelial carcinoma cases and 223 new lung cancer cases during the follow-up period (until 2007). The lifetime (35–85 years old) cumulative risk of developing urothelial carcinoma from an arsenic concentration in the drinking water of <10, 10–99, and 100+ μg/L was 0.29%, 1.07% and 3.43%, respectively. The corresponding probabilities were 7.42%, 8.99% and 17.09% for the lifetime risk of developing lung cancer. Cigarette smoking was associated with an increased risk of urothelial carcinoma and lung cancer, showing the hazard ratio (95% confidence interval) of 2.48 (1.27–4.82) and 3.44 (2.00–5.90) after adjusting for the arsenic concentration in drinking water. After adjusting for cigarette smoking, the hazard ratio (95% confidence interval) of developing urothelial carcinoma caused by the arsenic concentration in drinking water of <10, 10–99 and 100+ μg/L was 1.0 (the reference group), 2.18 (0.59–8.01), and 8.71 (2.49–30.48), respectively. The corresponding figures were 1.0 (the reference group), 1.14 (0.80–1.61), 1.84 (1.28–2.65) for lung cancer. Synergistic effects on the development of urothelial carcinoma and lung cancer existed between the arsenic exposure level and cigarette smoking. It is suggested that people who have had a high exposure to arsenic in drinking water should stop smoking cigarettes to lower their lifetime risk of urothelial carcinoma and lung cancer.

1. Introduction

An increased risk of urinary tract cancer (specifically urothelial carcinoma) and lung cancer has been well documented to be associated with the arsenic concentration in drinking water in ecological studies (Chen et al., 1985, 1988; Chen and Wang, 1990; Wu et al., 1989), a case-control study (Chen et al., 1986) and cohort studies (Chiou et al., 1995, 2001; Chen et al., 2004, 2010a, 2010b) in Taiwan. Arsenic has been classified as a group 1 carcinogen by the International Agency for Research on Cancer (IARC, 2004a). The U.S. Environmental Protection Agency lowered the maximum allowable contamination level of arsenic in drinking water from 50 to 10 μg/L (Carlson-Lynch et al., 1994) based on the cancer mortality in the arseniasis-endemic area in Southwestern Taiwan (Chen et al., 1992; Morales et al., 2000).

A high arsenic concentration in drinking water is widespread in several countries, such as Argentina (Pou et al., 2011; Steinmaus et al., 2006), Bangladesh (Chen and Ahsan, 2004), Chile (Smith et al., 1998; Fraser, 2012), India (Guha Mazumder, 2008), and

* Corresponding author. Address: Genomic Research Center, Academia Sinica, No. 128, Section 2, Academia Rd., Nankang, Taipei 11529, Taiwan. Tel.: +886 2 2789 9402; fax: +886 2 2788 2043
E-mail address: chencj@gate.sinica.edu.tw (C.-J. Chen).

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Table 1
Incidence rate and adjusted relative risk of urothelial carcinoma by the arsenic concentration in drinking water, cumulative arsenic exposure and cigarette smoking habit at enrollment.

	No. of participants[a]	No. of cancer cases	Person-years of follow-up	Incidence rate (per 100,000 person-years)	Adjusted relative risk[b,e]	Adjusted relative risk[b,e]
Cigarette smoking habit						
No	4797	14	60,640	23.09	1.00 (referent)	1.00 (referent)
Yes[c,e]	3275	23	38,542	59.68	2.48 (1.27–4.82)*	2.35 (1.20–4.60)*
Arsenic concentration (μg/L)[d]						
<10	2285	3	28,254	10.62	1.00 (referent)	(Not included)
10–99	2997	9	36,754	24.49	2.18 (0.59–8.01)	
100+	1594	17	19,341	87.90	8.71 (2.49–30.48)***	
*Cumulative arsenic exposure (μg/L * y)*[d]						
<500	2757	4	34,257	11.68	(Not included)	1.00 (referent)
500–4999	2968	11	36,438	30.19		2.46 (0.78–7.72)
5000+	1154	16	13,691	116.86		9.36 (3.03–28.92)***

[a] One participant without birthdate and 13 participants had urothelial carcinoma before enrollment.
[b] Relative risk estimated using the Mantel-Cox method.
[c] Relative risk adjusted for arsenic concentration in drinking water or cumulative arsenic exposure.
[d] Relative risk adjusted for cigarette smoking habit.
[e] $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

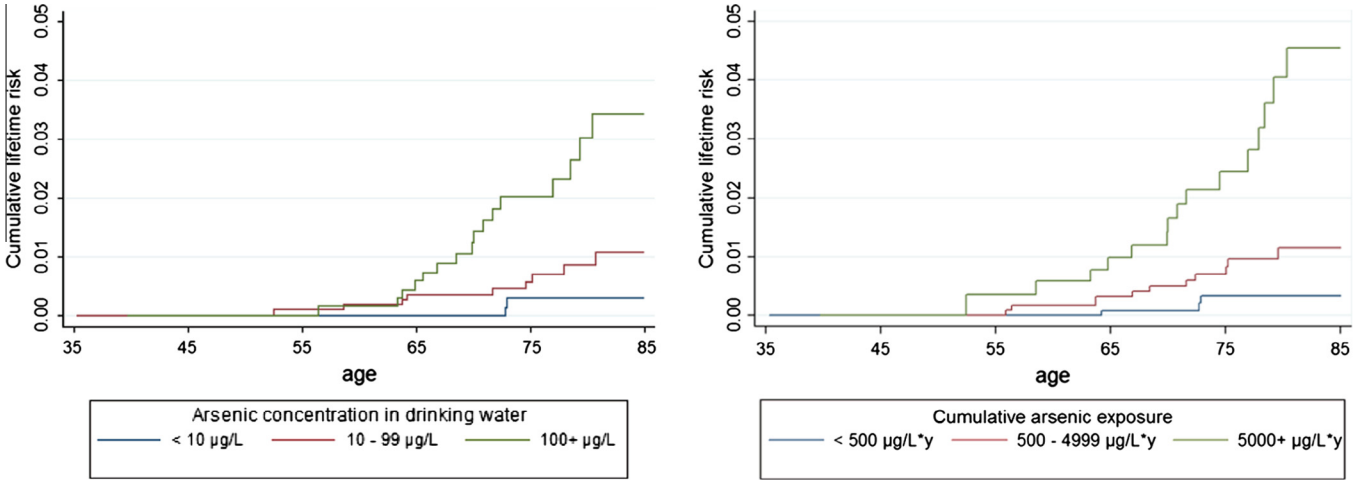

Fig. 1. Lifetime cumulative risk of urothelial carcinoma by the arsenic concentration in drinking well water (left) and cumulative arsenic exposure (right).

Taiwan (Morales et al., 2000; Chiou et al., 2001). Several studies in Argentina (Hopenhayn-Rich et al., 1998) and Chile (Smith et al., 1998; Ferreccio et al., 2000) have also found significant associations between arsenic in drinking water and a risk of urinary cancer and lung cancer. However, the lifetime cumulative risk of developing urothelial carcinoma and lung cancer has never been assessed previously. The synergistic effect of cigarette smoking and exposure to arsenic in drinking water on the development of lung cancer has recently been documented (Chen et al., 2004). However, the synergistic effect on urothelial carcinoma remains to be elucidated.

The specific aims of this study included (1) an estimation of the lifetime cumulative risk of urothelial carcinoma and lung cancer caused by arsenic exposure levels, and (2) the assessment of the synergistic effect of cigarette smoking and exposure to arsenic in drinking water on the development of urothelial carcinoma and lung cancer.

2. Materials and methods

2.1. Study cohort

The study cohort was recruited from residents living in four townships of the Lanyang Basin located in Northeastern Taiwan. They had consumed well water since the 1940s until the public water supply system was implemented in early 1990s (Chiou et al., 1997, 2001). Overall, 8102 residents from 4586 households in 18 villages of the study area participated in the baseline home interview from 1991 to 1994. Because the national identification numbers were used for the computerized linkage with the national cancer registry profile, 16 participants with missing or incorrect numbers were excluded. In total, 8086 participants were included in this analysis.

Information collected using the structured questionnaire included demographic characteristics, cigarette smoking status, and residential and well water consumption history. All participants signed written informed consents forms to participate in this study, which was approved by the Institutional Review Board of the College of Public Health, National Taiwan University. Data on the arsenic concentration in the drinking water for 6888 participants (85.1%) were determined using well water samples collected from study households. This data for the other 1198 residents (14.9%) were unavailable. The concentration of arsenic in the drinking water was determined using hydride generation combined with flame atomic absorption spectrophotometry, which had a detection limit of 0.15 μg/L. The arsenic concentrations in the water samples ranged from "undetectable" to higher 3000 μg/L. In addition to the arsenic concentration in drinking