Bisphenol A and other environmental risk factors for prostate cancer in Hong Kong

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ABSTRACT

Background: Environmental exposures are contributing factors to prostate cancer etiology, but these remain unclear. We aimed to document the associations between environmental risk factors and prostate cancer in Chinese, with special reference to bisphenol A (BPA).

Methods: We recruited 431 newly diagnosed prostate cancer cases and 402 age-matched controls from Prince of Wales Hospital in Hong Kong. We obtained each participant's clinical data and epidemiological information on chronic BPA exposure and other environmental risk factors (e.g., dietary habits, occupation and shift work) using a standard questionnaire. A new assessment tool of environmental BPA exposure was developed and replicated. Multiple logistic regression analysis was performed to examine odds ratio (OR) and 95% confidence interval (95% CI) for the association of prostate cancer with a novel cumulative BPA exposure index (CBPAI) and other environmental risk factors.

Results: Weekly consumption of deep fried food (OR = 1.85, 95% CI: 1.15–2.95) and pickled vegetable (OR = 1.87, 95% CI: 1.07–3.28) was significantly associated with excessive prostate cancer risk. Prostate cancer was positively associated with nightshift work (OR = 1.76, 95% CI: 1.07–2.89) and it was negatively associated with green tea drinking (OR = 0.56, 95% CI: 0.34–0.91). There was a positive exposure-response relationship between CBPAI and prostate cancer, with the greatest and significant risk in the high versus reference category (OR = 1.57, 95% CI: 1.01–2.44).

Conclusions: Frequent consumption of deep fried food and pickled vegetable, non-habitual green tea drinking and nightshift work are the contributing risk factors to prostate cancer in Hong Kong Chinese. More importantly, this study provides the first epidemiological evidence on carcinogenicity of BPA on the human prostate.

1. Introduction

Prostate cancer is the leading cancer incidence in Hong Kong and many other countries (Hsing and Chokkalingam, 2006; Registry, 2016; Sim and Cheng, 2005). Only advancing age, race, and family history of prostate cancer are the established risk factors (Hsing and Chokkalingam, 2006), but these known risk factors cannot explain the accelerating age-standardized incidence rate of prostate cancer in Hong
Kong population. Clearly, environmental exposures are contributing factors to prostate cancer etiology but these remain unclear. Environmental xenoestrogen bisphenol A (BPA) is widespread. Geographic variations in age-standardized incidence rates of prostate cancer were positively correlated to the detection rate of urinary BPA between Chinese and Western populations (He et al., 2009; Soto and Sonnenschein, 2010). Estrogen-like BPA has been linked to prostate cancer risk in animals but its evidence in human is scare. Excess risk of prostate cancer has been reported in occupations requiring night shift work whilst the findings were mixed, probably due to the small case numbers and inadequate exposure assessment on shift work (Davis and Mirick, 2006; Kolstad, 2008). There are other putative environmental factors and lifestyle-related risk factors, including Westernized dietary habits, physical inactivity, tobacco smoking, alcohol drinking, androgens, and inflammation, that have been implicated in the etiology of prostate cancer (Hsing and Chokalingam, 2006); but the epidemiological evidence about their roles in the occurrence of prostate cancer was inconsistent. Most of the previous epidemiological studies on the associations between non-BAP environmental risk factors and prostate cancer were conducted in Western countries, and there is lack of knowledge among Chinese population in Hong Kong.

This study aimed to provide an overall picture of risk factors in Hong Kong Chinese men by documenting a wide range of environmental exposures including a detailed exposure assessment on chronic BPA exposure that has never been investigated in epidemiological studies. Moreover, our investigation is the first to explore a possible exposure-response relationship between cumulative BPA exposure and prostate cancer risk.

2. Methods

2.1. Study design and the subjects

In this case-control study, eligible cases were Chinese men aged 35-84 years who were newly confirmed as primary prostate cancer (International Classification of Disease, version 10; code C61) by histology. During August 2011 and November 2016, all eligible cases registered in the Department of Surgery and Clinical Oncology from one regional hospital of New Territories East Cluster were invited to participate in this study, covering around 10% of overall prostate cancers in Hong Kong. Controls were randomly selected from the same hospital and frequency matched in 5-year age groups to the cases. Controls were diagnosed with a variety of diseases including diseases of hepatobiliary and pancreatic, colorectal, urinary stone, and circulatory system but without a physician diagnosed history of cancer or benign prostate hyperplasia. Overall, the response rate was 88% for cases and 73% for controls. Lack of interest was the main reason for the nonparticipation in cases (82%) and controls (83%). The protocol of this case-control study was obtained from the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committees. Written informed consent was received from each participant prior to the interview.

2.2. Data collection and specification of risk factors

Trained interviewers carried out personal interview for participants using a standardized questionnaire covering detailed information on education level, smoking habits, alcohol drinking, dietary habits, supplements intake, physical activity, history of benign diseases in gynecological system, family cancer history of first-degree relatives, occupation, shift work, and environmental exposure to BPA. Clinical information of cases on medical diagnosis and histological findings were extracted from hospital records. A smoker referred to one who had ever smoked > 400 cigarettes in lifetime (Tse et al., 2009). Dietary habits and supplement intake were assessed using a reduced version of the Block Food Frequency Questionnaire over 5 years’ period before the diagnosis or recruitment (Block et al., 1990). Night shift work was defined as ever worked night shift (any hour from midnight to 5 am) more than once a month for > 1 year (ILO, 1990).

2.3. Development of assessment tool for BPA exposure

Around 90% of human exposure to BPA is from food in which BPA may migrate from plastic food containers, coated food cans, and plastic bottled water (Hill et al., 1979). We asked each participant to report on the habitual use of specific type of food or beverage container including what the container is made of, the frequency of use (e.g., daily, weekly, etc.), the handling practice (e.g., for storing hot water, heating by microwave), and years of usage.

We developed a new BPA assessment tool based on literature review (method 1, in Supplement I) to reconstruct each participant’s past exposure to BPA according to a master list of food or beverage container under different handling processes (Supplement I). The purpose of the BPA assessment tool was to rank specific items of food or beverage containers in terms of concentrations of BPA according to the literature review. The following steps demonstrated the method of obtaining a novel cumulative BPA exposure index (CBPAI) for our study participants. First, we assigned an exposure score (0 = no exposure, 1 = low exposure, 2 = moderate exposure, 3 = high exposure) according to evidence in the literature to rate the intensity of BPA exposure for each item of food or beverage container included in the master list. Second, we combined the assigned exposure score with behavioural data on the frequency and years of consumption of such container item (in Supplement I) to generate a cumulative BPA exposure index score of each participant following a semi-quantitative approach that was commonly adopted in exposure assessment of working environment (Olsson et al., 2011): multiplying the square of exposure score by the frequency (per week) and years of use for each type of container under specific handling practice, then summed over all types of containers in a lifetime (ΣBPA intensity × frequency of use × net years of using specific container). An alternative cumulative BPA exposure index (CBPAI) was calculated using a similar approach but without square of exposure score (ΣBPA intensity × frequency of use × net years of using specific container). A higher value of cumulative BPA exposure index indicates a higher level of chronic BPA exposure.

To measure how well the reliability of the newly developed assessment tool, we invited two experts (Hartle JC, Leung KS) in environmental hygiene and food safety to blindly rate the exposure score of BPA based on the same master list and using the same rating scale. We compared the expert’s rating results with those rated based on the literature review (i.e., the newly developed assessment tool) and high agreement was obtained with interclass correlation coefficient (ICC) of 0.86 and 0.90, which indicates a good replication of our newly developed assessment tool on evaluation of environmental BPA exposure via ingestion (Table 1). The ICC for the rating results between the two expert raters (JH, KSL) was 0.94. Such a high agreement between the two expert raters provided further evidence on robustness of the newly developed assessment tool of BPA exposure.

2.4. Statistical analysis

Chi-square tests or independent t-tests were used to compare various risk factors between cases and controls. Unconditional logistic regression model was performed to estimate the associations of potential risk factors with prostate cancer using the following strategies. Basically, two models were built to obtain odds ratio (OR) and 95% confidence interval (95% CI). In the initial ‘base’ model, we estimated the ‘base’ effect of each potential environmental risk factor by adjustment of age at interview, marital status, and employment status that were the statistically significant socio-demographic factors identified from the univariate analysis (Table 1). In addition to the socio-demographic variables included in the ‘base model’, the following non-BPA...
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