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Spatial and seasonal variability of urinary trihalomethanes concentrations in urban settings

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ABSTRACT

A complex network of sources and routes of exposure to disinfection by-products (DBP), such as trihalomethanes (THM) has been driving the wide variability of daily THM intake estimates in environmental epidemiological studies. We hypothesized that the spatiotemporal variability of THM exposures could be differentially expressed with their urinary levels among residents whose households are geographically clustered in district-metered areas (DMA) receiving the same tap water. Each DMA holds unique drinking-water pipe network characteristics, such as pipe length, number of pipe leaking incidences, number of water meters by district, average minimum night flow and average daily demand. The present study assessed the spatial and seasonal variability in urinary THM levels among residents ($n=310$) of geocoded households belonging to two urban DMA of Nicosia, Cyprus, with contrasting water network properties. First morning urine voids were collected once in summer and then in winter. Results showed that the mean sum of the four urinary THM analytes (TTHM) was significantly higher during summer for residents of both areas. Linear mixed effects models adjusted for age, season and gender, illustrated spatially-resolved differences in creatinine-adjusted urinary chloroform and TTHM levels between the two studied areas, corroborated by differences observed in their pipe network characteristics. Additional research is warranted to shed light on the contribution of spatially-resolved and geographically-clustered environmental exposures coupled with internal biomarker of exposure measurements towards better understanding of health disparities within urban centers.

1. Introduction

Potable water disinfection is a widely practiced public health intervention to reduce the risk of waterborne infections, but it may also lead to the formation of a suite of compounds, collectively called disinfection by-products (DBP) (Brown et al., 2011; Chowdhury et al., 2009). The four trihalomethanes (THM), namely, chloroform (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM) and bromoform (TBM) comprise the only DBP class currently regulated in the European Union, because they have been associated with increased risk of developing malignancies (i.e. bladder cancer) and adverse pregnancy outcomes (EU Council, 1998; Patelarou et al., 2011; Richardson et al., 2007; Villanueva et al., 2004). However, since the putative causal agent or combination of agents of adverse health effects in the DBP mixture is currently unknown, THM may only serve as a surrogate of this agent or combination of agents in disinfected water. The ubiquitous human exposure to a mixture of putative agents, exhibiting general mutagenicity and potential carcinogenicity by all routes has urged the IARC to consider disinfected water in its priority list for evaluation during 2015–2019 (*IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, 2014).

The choice of external THM exposure measurements (in tap water) has for quite a while dominated over the use of biomarkers of exposure in several environmental epidemiological studies (Makris and Andra, 2014). Whole blood and exhaled breath have been used as biospecimen for measurements of THM exposures with mixed success (Gordon et al., 2006; Rivera-Núñez et al., 2012). THM levels in urine have been measured and moderately correlated with the intake of the compounds through drinking water and occupation (Cammann and Hübner, 1995; Caro and Gallego, 2007; Polkowska et al., 2006, 2003). Tap water THM

Abbreviations: BDCM, Bromodichloromethane; BMI, Body mass index; BrTHM, Brominated trihalomethanes; DBCM, Dibromochloromethane; DBP, Disinfection by-products; DMA, District-metered area; GM, Geometric mean; ICC, Intraclass correlation coefficient; LOD, Limit of detection; LOQ, Limit of quantification; TBM, Bromoform; TCM, Chloroform; THM, Trihalomethanes; TTHM, Total trihalomethanes; UDWDS, Urban drinking water distribution system

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measurements have been characterized by a wide variation between and within water distribution systems (Summerhayes et al., 2011; Włodyka-Bergier et al., 2014). The situation is further complicated when one considers multiple noningestion exposure THM sources, such as showering, swimming, bathing and various activities of household cleaning (Villanueva et al., 2007; Whitaker et al., 2003).

The water boards of major EU cities divide their urban drinking water distribution system (UDWDS) into district metered areas (DMA), which are smaller autonomous sub-networks with distinct geographical boundaries that are easier to manage. Improved assessment of environmental exposures at various urban scales, particularly those at the small-area level could greatly facilitate the assessment of health disparities in urban settings (Voigtländer et al., 2014). Small-area health disparities are considered to be primarily driven by differences in individual exposure to small-area resources and stressors (Voigtländer et al., 2014). It is often the case that health disparities among neighborhoods within the same city are larger than reported health inequalities between cities (Jonker et al., 2013; Pickett and Pearl, 2001).

Since several tap water uses or activities (i.e. showering, bathing, swimming, mopping, dishwashing) have been associated with elevated THM exposures and THM levels in tap water are influenced by water distribution network characteristics, we hypothesized that inclusion of DMA clusters into THM exposure assessment studies could shed additional light on the effects of small-area characteristics on individual health. These geographically-distinct urban DMA (one in the north and the other located south of the city) have been historically receiving the same tap water treated in a single water treatment plant, but they are differentiated with respect to the following UDWDS characteristics: pipe length, number of pipe leaking incidences, number of water meters by district, average minimum night flow and average daily demand (Pieri et al., 2014). It was speculated that household distance from the main chlorination tank and the number of pipe leaking incidences may also influence the formation of THM within UDWDS (Pieri et al., 2014; H. Wang et al., 2012; Z. Wang et al., 2012).

The objective of this study was to assess the relative contribution of spatial and seasonal characteristics on the magnitude and variability of THM exposures using urinary THM measurements among residents of two DMA in Nicosia, Cyprus.

2. Methods

2.1. Study population and design

The present work was conducted as part of a larger cross-sectional study of human exposures to THM in the city of Nicosia, Cyprus; the recruitment and sampling activities took place during summer 2012 and winter 2013 (Charisiadis et al., 2014). Randomized recruitment of participants took place within the geographical borders of two pre-selected DMA areas (herein referred to as area 1 and area 2) with contrasting UDWDS characteristics. The selection of these two DMA out of the total of 24 DMA for the city of Nicosia was based on a risk-hierarching algorithm that classified area 1 with a higher frequency of pipe leaking incidences and higher average night water flow (indicative of pipe leaking-induced water losses and pipe age) than those for area 2 (detailed description in Pieri et al., 2014). After obtaining individual written consents, the residential addresses in both areas were geocoded and face-to-face interviews were performed with each participant in their household. Recorded demographic characteristics, lifestyle factors and water consumption habits, were previously described by Charisiadis et al. (2014). The study protocol was approved by the Cyprus National Bioethics Committee.

2.2. Sample collection and analyses

Urine sample collection was conducted twice, during July–early September 2012 (season 1, summer) and during January–early March 2013 (season 2, winter). In both occasions first morning void samples were collected in 60 ml polypropylene vials. Participants were given written instructions for collecting the sample without leaving headspace and preserving the samples in the freezer, until their collection and transportation to our laboratory facilities by our personnel. Before the analysis, all samples were stored in deep freezers at -80°C. Because of the absence of chlorine to quench and pH levels being <6, no need was warranted to add preservatives to urine samples. The urine samples were analyzed for TCM, BDCM, DBCM, and TBM with a modified protocol of U.S. EPA method 551.1-1 (Charisiadis and Makris, 2014). Concentrations below the limit of detection (LOD) were assigned to $\frac{1}{2}$ LOD and values below the limit of quantification (LOQ) were assigned to $\frac{1}{2}$ LOQ. More specifically, for the summer sampling the LOD (LOQ) values were: 94 (282) ng L^{-1}, 46 (136) ng L^{-1}, 31 (94) ng L^{-1}, and 40 (120) ng L^{-1} for TCM, BDCM, DBCM, TBM, respectively. Similarly, the values for the winter sampling were: 27 (80) ng L^{-1}, 11 (32) ng L^{-1}, 24 (71) ng L^{-1}, and 13 (40) ng L^{-1}. Pooled urine samples with negligible THM levels were fortified to a final concentration of 700 ng L^{-1} and used for quality control. For the summer sampling the recoveries were 103%, 100%, 98% and 92% for TCM, BDCM, DBCM, and TBM, respectively, while the mean surrogate recovery was 82%. The winter sampling recoveries were 103% for TCM, 105% for BDCM, 102% for DBCM and TBM, with 85% mean surrogate recovery. The intra- and inter-day variability of the analytical measurements were always $<3.5\%$, with the average total THM recoveries in pooled urine matrix were 95–101% with 4% average relative standard deviation, for the summer measurements. For the winter sampling the intra- and inter-day variability were always $<4.5\%$, with 94–110% average THM recoveries (for the 700 and 1000 ng L^{-1}) (standard deviation of 5%) in pooled urine matrix. Urinary creatinine was determined by the picric acid based spectrophotometric method (Jaffe method) (Angerer and Hartwig, 2010).

2.3. Statistical analyses

Descriptive statistics, including the calculation of geometric and arithmetic means, standard deviations, median values and percentiles, were performed for the urinary concentrations of all THM analytes and for important covariates (gender, age, BMI). Total THM (TTHM) and brominated THM (BrTHM) were defined as the sum of TCM, BDCM, DBCM, TBM, and the sum of BDCM, DBCM and TBM, respectively. Urinary THM concentrations were creatinine-adjusted to account for the urinary dilution (creatinine levels reported in the supplementary information) and log-transformed (natural logarithm) to meet the normality criterion due to skewness. The *t*-test was used to evaluate differences between paired summer and winter log-transformed values of the study participants for each THM analyte and one-way intraclass correlation coefficient (ICC) was calculated to assess the between-season reproducibility of the measurements. The statistical analyses were performed for the pooled study population and sorted by area. Linear mixed effects models were constructed to account for the between- and within-subject random variability in the urinary THM measurements; thus, the association between the creatinine-adjusted log-transformed THM concentrations and fixed effects covariates, such as, age, BMI, gender, area and season was assessed (Peretz et al., 2002). Correlations between the creatinine-adjusted urinary concentrations of all compounds and the corresponding tap water levels measured in the households of each participant were assessed with the Spearman coefficient for both seasons in the pooled sample and for each area separately. The statistical analyses were performed with R with the packages ‘nlme’, ‘lme4’, ‘lmerTest’ and ‘irr’ (Bates et al., 2014; Gamer et al., 2012; Kuznetsova et al., 2014; Pinheiro et al., 2014; R. Core Team, 2013).

3. Results

3.1. Study population

A total of 310 adults (≥ 18 years) participated in this study (154 participants from area 1 and 156 from area 2) (Table 1). A greater proportion of females (61%) was observed, while the male to female ratio was similar for both areas (0.66 in area 1 and 0.63 in area 2). The average BMI and age of the study participants was 26 kg m^{-2} and 50 years, respectively. The majority of participants from both areas were married (75% in area 1 and 82% in area 2) with similar educational background (Table 1). Area 1 is located in the old part of the city, and characterized by an older pipe network system, 22 km long, 2489 registered water meters, and 2.9 pipe leaking incidences per km (Charisiadis et al., 2014; Pieri et al., 2014). Area 2 has a newer and longer (136 km) pipe network compared to area 1 with 7694 water meters and a lower frequency of pipe leaking incidences (1.1 km^{-1}). The greater pipe network length of area 2 was accompanied by a 3 × greater daily average