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Levels of selected urinary metabolites of volatile organic compounds among children aged 6-11 years ☆

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ABSTRACT

Data from National Health and Nutrition Examination Survey for the years 2011–2012 were used to evaluate variability in the observed levels of 20 urinary metabolites of volatile organic compounds (VOCs) by age, gender, and race/ethnicity among children aged 6–11 years. Exposure to environmental tobacco smoke was positively associated with the levels of selected metabolites of acrylonitrile, 1,3-butadiene, cyanide, and propylene oxide in a dose-response manner. Levels of the selected metabolites of acrolein, acrylonitrile, 1,3-butadiene, styrene, toluene, and xylene decreased with increase in age. Levels of 1-bromopropane decreased with number of rooms in the house but the reverse was true for 1,3-butadiene, carbon-disulfide, and N,N-dimethylformamide. Levels of most of the 20 metabolites did not vary with gender. Non-Hispanic white children had higher adjusted levels of N-Acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA), N-Acetyl-S-(N-methylcarbamoyl)-L-cysteine (AMCC), and phenylglyoxylic acid (PGA) than non-Hispanic black children. Non-Hispanic white children had statistically significantly higher adjusted levels of N-Acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine (GAMA), trans, trans-Muconic acid (MU), and N-Acetyl-S-(N-methylcarbamoyl)-L-cysteine (AMCC) than non-Hispanic Asian children but statistically significantly lower levels of N-Acetyl-S-(n-propyl)-L-cysteine (BPMA) than non-Hispanic Asian children. Non-Hispanic Asian children had the lowest levels of 13 of the 20 metabolites among four major racial/ethnic groups but highest levels for three metabolites. For selected metabolites of acrolein, acrylamide, acrylonitrile–vinyl chloride–ethylene oxide, benzene, 1,3-butadien, crotonaldehyde, cyanide, ethylbenzene–styrene, and toluene, children had statistically significantly higher levels than nonsmoking adults. These results demonstrate how vulnerable children are to being exposed to harmful chemicals like VOCs in their own homes.

1. Introduction

Volatile organic compounds (VOC) are numerous ubiquitous, naturally occurring as well as man-made chemicals. They have high vapor pressure at room temperatures because of their low boiling points. Paints, pesticides, deodorizers, cleaning and degreasing agents, personal care products, and solvents are a few of the common sources of exposure to VOCs (Sexton et al., 2005). Humans can be exposed to quite a few VOCs like benzene, toluene, xylenes, and other from environmental tobacco smoke (Chambers et al., 2011). Benzene concentration has been reported to be about 45 μg/cigarette in the mainstream smoke and about 10 times of that in the sidestream smoke (Korte et al., 2000). Other sources of exposure to VOCs include automobile exhausts and even office devices like printers and photocopiers (Kowalska et al., 2015). St Helen et al. (2014) conducted a study in which change in the levels of nine VOC metabolites in urine among 14 individuals exposed to second hand smoke for one hour in the backseat of a car was measured. As compared to the baseline, post-exposure levels of N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine (MHBMA3) increased 2.1 fold; levels of N-Acetyl-S-(phenyl)-L-cysteine (PMA) and methylating agents (MMA) increased 1.6 fold; and levels of N-Acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA) increased 1.3 fold (St Helen et al., 2014).

Many VOCs have adverse health effects and have the potential to cause harm to the environment. For example, benzene may induce drowsiness, dizziness, rapid or irregular heartbeat, headaches, tremors, confusion, unconsciousness, and even death at very high levels of exposure (http://www.bt.cdc.gov/agent/benzene/basics/facts.asp). Eating foods or drinking beverages which

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contain benzene may also cause similar symptoms (http://www.bt.cdc.gov/agent/benzene/basics/facts.asp). Long term health effects of exposure to benzene include anemia, leukemia, and excessive bleeding (http://www.bt.cdc.gov/agent/benzene/basics/facts.asp). Adverse health risks of exposure to selected VOCs have been studied and reported, among others, by Batterman et al. (2014), Carwile et al. (2014), Cristofori et al. (2015), Guyton et al. (2014), Lash et al. (2014), Lerner et al. (2014), Ruckart et al. (2013, 2014), Singthong et al. (2014), Vlaanderen et al. (2014), and Yang et al. (2014). In a review of cancer and non-cancer risk estimates of chemicals in mainstream cigarette smoke, 1,3-butadiene was identified with the highest cancer risk index of $3.02^{*}10^{-4}$/cigarette/day and acrolein was identified with the highest non-cancer risk index of 172/cigarette/day because of its respiratory effects (Fowles and Dybing, 2003). Burns et al. (2008) also identified acrolein with the highest non-cancer response index per mg nicotine. Cristofori et al. (2015) reported haloalkenes to be highly nephrotoxic in vivo and in vitro. A positive association between occupational exposure to benzene and risk of multiple myeloma, acute lymphocytic leukemia, and chronic lymphocytic leukemia was reported by Vlaanderen et al. (2011). Tetrachloroethylene exposure during pregnancy above sample median was associated with 2.38 times the risk of stillbirth and 1.35 times the risk of placental abruption (Carwile et al., 2014). Economic costs at superfund sites for health conditions like birth defects, urinary tract disorders, diabetes, eczema and skin conditions, anemia, speech and hearing impairments among children, and stroke among VOC exposed populations was estimated at $330 million per year (Lybarger et al., 1998).

Maternal exposure to benzene and trichloroethylene above 5 parts per billion was associated with elevated risk of neural tube defects (Ruckart et al., 2013). In a 4-year longitudinal study among six primary schools, sick building syndrome was found to be associated with exposure to VOC (Norbäck et al., (1990)). In a study of 85 neonates, maternal exposure to VOCs was shown to be associated with adverse immune status of the child as measured by percentages of interferon-gamma-producing type 1 T cells (Lehmann et al., 2002). In a study of 26 Hispanic children, a positive association between bothersome or more severe asthma and same day breath concentrations of benzene was discovered (Delfino et al., 2003). In a case-control study of children aged 6 months to 3 years with and without the diagnoses of asthma, cases had significantly higher levels of exposure to VOCs than controls (Rumchev et al., 2004). VOC exposure among children indoors at home and in personal samples was found to be well above health benchmarks for several compounds (Adgate et al., 2004). Positive association between prenatal exposure to styrene, ethylbenzene, octane, 1-butanol, tridecane, and o-xylene and wheezing during early infancy was reported (Franck et al., 2014).

Data on selected VOCs in blood and/or air have been reported among others by Ashley et al. (1994), Bonanno et al. (2001), Chambers et al. (2011), Churchill et al. (2001), Jia et al. (2012), Kim et al. (2006), Lin et al. (2008), Sexton et al. (2005), and Su et al. (2013). Levels of VOCs and their metabolites and/or the analytical methods to detect them in urine, based on mostly small sample sizes, have been reported among others by Alwis et al. (2012), Barbieri et al. (2004), Carmela et al. (2009), Ding et al. (2009), Protano et al. (2012), Reska et al. (2010), and Schettgen et al. (2008, 2009). Wilson (2015) has reported the use of electronic nose technologies to detect the presence of certain VOCs in human breath.

For the first time, the US National Health and Nutrition Examination Survey (NHANES) for the years 2011–2012 released data in public domain for 28 metabolites of urinary VOCs as listed in Alwis et al. (2012) for a representative sample of US population. Thus, the objective of this study was to use data from 2011 to 2012 NHANES to evaluate the variability in the concentration levels of selected VOC metabolites by age, gender, race/ethnicity, and smoking status (or exposure to second hand smoke). This analysis will be restricted to children aged 6–11 years. Since, exposure to second hand smoke has been found to be associated with increased levels of certain VOC metabolites in urine (St Helen et al., 2014), it is hypothesized that children exposed to second hand smoke at home will have statistically significantly higher levels of selected VOC metabolites in urine than children not exposed to second hand smoke at home. In addition, in a limited analysis, VOC levels among children will also be compared to VOC levels among nonsmoker adults.

2. Materials and methods

NHANES data on demographics, body measures, and urinary VOC files for the years 2011–2012 (http://wwwn.cdc.gov/nchs/nhanes/search/nhanes11_12.aspx) for children aged 6–11 years were downloaded and match merged. The laboratory methods used to measure VOCs in urine, as previously mentioned are provided in Alwis et al. (2012) and at http://wwwn.cdc.gov/nchs/nhanes/2011-2012/UVOCS_G.htm#Description_of_Laboratory_Methodology. The sampling plan for NHANES is a complex, stratified, multistage, probability cluster designed to be representative of the civilian, non-institutionalized U.S. population. NHANES provides sampling weights to account for the complex survey design, including oversampling, survey non-response, and post-stratification. All analyses incorporated information on sampling design variables.

Data were available for 28 metabolites of 18 parent VOCs. Specifically, parents and their metabolites for which data were available were (1) acrolein: N-Acetyl-S-(2-carboxyethyl)-L-cysteine (CEMA), N-Acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA); (2) acrylamide: N-Acetyl-S-(2-carbamoylethyl)-L-cysteine (AAMA), N-Acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine (GAMA); (3) acrylonitrile: N-Acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA); (4) acrylonitrile, vinyl chloride, ethylene oxide: N-Acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA); (5) benzene: N-Acetyl-S-(phenyl)-L-cysteine (PMA), trans, trans-Muconic acid (MU); (6) 1-bromopropane: N-Acetyl-S-(n-propyl)-L-cysteine (BPMA); (7) 1,3-butadiene: N-Acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA), N-Acetyl-S-(1-hydroxymethyl-2-propenyl)-L-cysteine (MHBMA1), N-Acetyl-S-(2-hydroxy-3-butenyl)-L-cysteine (MHBMA2), N-Acetyl-S-(4-hydroxy-2-buten-1-yl)-L-cysteine (MHBMA3); (8) carbon-disulfide: 2-Thioxothiazolidine-4-carboxylic acid (TTCA); (9) crotonaldehyde: N-Acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine (HPMMA); (10) cyanide: 2-Aminothiazoline-4-carboxylic acid (ATCA); (11) N,N-dimethylformamide: N-Acetyl-S-(N-methylcarbamoyl)-L-cysteine (AMCC); (12) ethylbenzene, styrene: phenylglyoxylic acid (PGA); (13) propylene oxide: N-Acetyl-S-(2-hydroxypropyl)-L-cysteine (2HPMA); (14) styrene: N-Acetyl-S-(1-phenyl-2-hydroxyethyl)-L-cysteine + N-Acetyl-S-(2-phenyl-2-hydroxyethyl)-L-cysteine (PHEMA), mandelic acid (MA); (15) tetrachloroethylene: N-Acetyl-S-(trichlorovinyl)-L-cysteine (TCVMA); (16) toluene: N-Acetyl-S-(benzyl)-L-cysteine (BMA); (17) trichloroethylene: N-Acetyl-S-(1,2-dichlorovinyl)-L-cysteine (1,2DCVMA), N-Acetyl-S-(2,2-dichlorovinyl)-L-cysteine (2,2,DCVMA), and (18) xylene: N-Acetyl-S-(2,4-dimethylphenyl)-L-cysteine + N-Acetyl-S-(2,5-dimethylphenyl)-L-cysteine + N-Acetyl-S-(3,4-dimethylphenyl)-L-cysteine (DPMA), 2-methylhippuric acid (2MHA), 3-methylhippuric acid + 4-methylhippuric acid (3MHA + 4MHA). Percent values at or above the limit of detection (LOD) varied from $< 0.1\%$ for MHBMA2 to 100% for HPMMA (Supplementary Table S1). There were 8 metabolites for which percent observations < LOD were < 60%. These metabolites were: PMA, MHBMA1, MHBMA2, PHEMA, TCVMA, 1,2DCVMA,