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Toluene Exposure and its Association to Hippuric Acid and Non-Systematic Symptoms among Outdoor Workers in Urban Area, Bangkok, Thailand

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Abstract: Volatile Organic Compounds (VOCs) are mainly from motor vehicle emissions which cause of serious problems of air pollution in Bangkok Metropolitan, Thailand. Toluene is the most abundance of aromatic hydrocarbon found in ambient air. This study aimed to evaluate toluene exposures and its association to non-systematic symptoms among outdoor workers in Pathumwan District, central Bangkok. A cross-sectional study was conducted in urban area of Bangkok during September 2012 to March 2013. Two hundred and eighty seven outdoor workers of security guardsmen, motorcycle drivers and street venders were included in this study for interviewing and urine collection. Thirty six ambient air samples were collected for toluene analyses by Gas Chromatography with Flam Ionized Detector (GC/FID). The results showed that average ambient air toluene was 91.1 μg/m^3 which street vender was the highest exposed as well as average hippuric acid level was 0.4 g/gCr. Non-systematic symptoms prevalence of workers were headache, dizziness, weakness and throat irritation at 42.5, 16.6, 36.6 and 15.3%, respectively which they were highest in street venders. Toluene exposure level was significantly associated to hippuric acid ($p = 0.001$) and non-systematic symptoms of dizziness and throat irritation ($p<0.01$). However, hippuric acid was not associated to any non-systematic symptoms. There were trended higher toluene exposures at roadside area of street venders and motor cycle drivers than security guardsmen in university area as well as non-specific symptoms. There were the associations between ambient air toluene level and urinary biomarker of hippuric acid and non-systematic symptom of dizziness.

Key words: Toluene, hippuric acid, non-systematic symptom, outdoor worker, dizziness

INTRODUCTION

Toluene is formed during the combustion of organic materials and widely used as a solvent in paints, varnishes, pesticide formulations, printing inks, dyes, adhesives, sealants, cleaning agents, nail polish and for chemical extractions (Alberta Environment, 2005). Volatile Organic Compounds (VOCs) constitute one of the most important major air pollutant in the atmospheric. Toluene is the most abundance of aromatic hydrocarbon found in ambient air and can also adversely affect to human health (US EPA, 1994) especially, urban area which vehicle exhaust was considered to be the dominant source (Ameno *et al*., 1992; Al-Khulaifi *et al*., 2014). Toluene is rapidly absorbed into the bloodstream by inhalation exposure. Once absorbed, it is rapidly distributed to white adipose tissue, adrenals, skin, kidneys, liver, lung and brain (WHO, 1985; EPA, 1993). Hippuric acid is the primary urinary metabolite of toluene can be used as an indicator of toluene exposure (Duydu *et al*., 1999; Bahrami *et al*., 2005). It is well established that neurotoxicity and neurobehavioural deficits are the principal effects of long-term inhalation exposure to toluene in both humans and experimental animals (Brugnone *et al*., 1995; ATSDR, 2000) but insufficient information on possible exposure to other chromosome-damaging agents (IARC, 1999; EPA, 2005; Tunsaringkarn *et al*., 2011). Most human carcinogens are genotoxic but all of genotoxic agents have not been carcinogenic in human. Rapid increasing population as well as motor vehicle number per year which most them use biofuel as gasohol and biodiesel, Light Petroleum Gas (LPG) as government policies leading to serious problem of outdoor workers in Bangkok such as mortality, hospital admissions cardiovascular and respiratory disease, asthma attacks, acute bronchitis, respiratory

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symptoms and restrictions in activity (Kampa and Castanas, 2008; WHO, 2014). The global burden of disease estimated that outdoor air pollution was account for 1.4% of total mortality, 0.5% of all Disability-Adjusted Life Years (DALYs) and 2% of all cardiopulmonary disease (Ezzati *et al*., 2002; WHO, 2002; Cohen *et al*., 2004). The WHO estimates indicated that 81% of the attributable deaths from air pollution (WHO, 2002). Outdoor workers in urban area are also directly exposed to toluene in atmosphere. It should have risk of long-term effects on non-systematic symptoms. This study aimed to evaluate toluene in ambient air and its association to hippuric acid and non-systematic symptoms among outdoor workers in Urban Area, Central Bangkok, Thailand.

MATERIALS AND METHODS

Study sites: The study was carried out in 32 samples from 16 monitoring sites consist of 10 sites of motorcycle drivers and street venders on the main roadsides of Rama road 1, Phyathai road, Henrydunant road and 6 sites of security guardsmen in Chulalongkorn University which all sites are in Pathumwan area, central Bangkok, Thailand. Main study sites of roadsides were located at Community Pharmacy Clerkship (CPC), Bangkok Bank Public Company Limited (BBL), Krung Thai Bank Public Company Limited (KTB), Siam Commercial Bank Public Company Limited (SCB), Faculty of Science (FS) and study sites in university were located at Satit Chula (SC), university entrance-exit gate 1-4 and checkpoint behind Faculty of Science as shown in Fig. 1.

Population study: Total of 287 outdoor workers were included by random in this study including 76 security guardsmen of university, 76 motorcycle drivers and 135 street venders. All inclusion criteria of workers were healthy, age over 18 years old, work period >3 months and signed consent from and interviewed the characteristics of age, weight, height, period of employment, working hour a day, working day a week and non-systematic symptoms at last 3 months. This research was approved by the Ethical Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University (COA No. 089/2012).

Ambient air sample collection and analyses: Total of 32 ambient air monitoring study sites were collected for 8 h working time of workers during September 2012 to March 2013. Ambient air samples were collected by active charcoal tube with flow rate 100 mL min^{-1} for toluene analyses by GC/FID (Tunsaringkarn *et al*., 2012). Sample tubes were kept at 4°C during transportation to the laboratory and were stored in a refrigerator until further analysis.

Fig. 1: Study site map; ● motercycle drivers and street venders at roadsides; ★ security guards in university

The charcoal tube was extracted with Carbondisulphide (CS) and the sample solution was then analyzed by Gas Chromatography (GC) with an FID detector (Varian, CP3800) and column RP Amide Discovery C16 (25 m×4.0 mm with 0.5 μm packing). The initial oven temperature was set to 40°C, increased at a rate of 10°C min^{-1} 100°C and held at that temperature for 2 min; FID temperature was set at 225°C. The carrier gas was he pushed at a flow rate of 1.0 mL min^{-1}. Toluene levels was analyzed under the relative intensity of chromatographic signal for 20 min. Quantification was performed using the External Calibration Method. The coefficients of toluene determination (R^2) ranges were 0.991-0.999. Each sample was analyzed by triplicate.

Urinary sample collections and analyses: The cross-sectional study of 287 urine samples of all outdoor workers were collected by glass bottle after 8 h working time (8.00 am to 15.00 pm). Urine samples were kept at 4°C during transportation to laboratory, stored at -20°C and later analyzed for Creatinine (Cr) (Slot, 1965), hippuric acid (Ogata and Taguchi, 1987). All urinary samples were analyzed at a standard Spacial Laboratory, Bangkok, Thailand. Urinary creatinine concentrations were accepted between 0.3 and 3.0 g L^{-1} (ACGIH, 2010) as the World Health Organization (WHO) has adopted guideline. All measured values were corrected by urinary Cr concentrations for clinical chemistry analysis (Barr *et al*., 2005).

Statistical analysis: All data were statistically analyzed using the SPSS 17.0 for Windows Software. Descriptive statistics was used to understand the characteristics, exposures and urinary biomarkers concentrations. The comparison of ambient air toluene and urinary biomarkers of hippuric acid were done using independent t-test. The association between ambient air VOCs levels and urinary biomarkers of outdoor workers were assessed by Linear Regression Model. A statistically significant difference was accepted at $p<0.05$ as other medical studies.

RESULTS

Characteristic, ambient air toluene, hippuric acid of outdoor workers: Average age, BMI, period of employment, working hour a day and working day a week of all workers were 40.3 years, 24.5 kg/m^2, 8.5 years, 10.8 h and 6.5 days, respectively (Table 1). Age and period of employment of security guardsmen were significantly higher than motorcycle drivers ($p<0.05$) and period of employment of security guardsmen was significantly higher than street venders ($p<0.01$). Working hour a day of security guardsmen was higher than motorcycle drivers ($p<0.01$) and was higher than street venders ($p<0.05$). While working day a week of security guardsmen was higher than street venders ($p<0.05$). Average ambient air toluene was 91.1 μg/m^3 while hippuric acid of all workers was 0.4 g/gCr.

Non-systematic symptoms of outdoor workers: Non-systematic symptoms of all outdoor workers were headache, dizziness, weakness and throat irritation at 42.5, 16.6, 36.6 and 15.3%, respectively (Table 2). All symptoms were highest in street vender group.

Association between ambient air toluene and hippuric acid and non-systematic symptoms and association between hippuric acid and non-systematic symptoms of outdoor workers: The ambient air toluene was significantly associated to hippuric acid ($p = 0.001$) and

Table 1: General characteristic, ambient air toluene exposure and of hippuric acid among outdoor workers

	Mean±SD			
Parameters	Security guardsman (n = 76)	Motorcycle driver (n = 76)	Street vender (n = 135)	Average
Age (years)	43.5±0.4*	37.9±0.80*	39.4±0.80	40.3±2.90
BMI (kg/m^2)	24.5±0.4	24.4±0.20	24.8±0.10	24.5±0.20
Period of employment (years)	12.8±0.1*, **	7.0±0.20*	5.7±0.20**	8.5±3.80
Working hour per day (h)	10.5±0.3**	12.0±0.10**, †	10.1±0.10†	10.8±1.00
Working day per week (days)	6.4±0.1*	6.6±0.10	6.1±0.10*	6.5±0.20
Ambient air toluene (μg/m^3)	31.7±4.3	88.5±76.0	157.1±77.4	91.1±57.6
Hippuric acid (g/gCr)	0.3±0.3	0.3±0.30	0.5±0.50	0.4±0.10

*,†Significant difference between worker group at $p<0.05$; **significant difference between worker group at $p<0.01$

Table 2: Non-systematic symptoms among outdoor workers

	n (%)			
Non-systematic symptoms	Security guardsman (n = 76)	Motorcycle driver (n = 76)	Street vender (n = 135)	Total (n = 287)
Headache	17 (22.4)	29 (38.2)	76 (56.3)	122 (42.5)
Dizziness	5 (6.6)	9 (11.8)	34 (25.2)	48 (16.6)
Weakness	15 (6.6)	30 (19.7)	61 (25.9)	106 (36.6)
Throat irritation	8 (10.5)	10 (13.2)	29 (21.5)	44 (15.3)

Table 3: Association between toluene exposures, hippuric acid and non-systematic symptom parameters of outdoor workers

		Linear regression model results#		
Independence parameters	Dependence parameters	Standardize coefficient	95% CI	p-values
Toluene	Hippuric acid	0.311	0.001-0.004	0.001
	Headache	0.000	0.000-0.001	0.059
	Dizziness	0.000	0.000-0.001	0.006
	Weakness	0.000	-0.003-0.002	0.636
	Throat irritation	0.000	0.000-0.001	0.002
Hippuric acid	Headache	0.020	-0.173-0.218	0.818
	Dizziness	0.034	-0.111-0.165	0.696
	Weakness	0.024	-0.169-0.222	0.790
	Throat irritation	-0.116	-0.221-0.046	0.197

Adjust by age, BMI, period of employment, working hours a day and working days a week

non-systematic symptoms of dizziness ($p<0.01$) and throat irritation ($p<0.01$) (Table 3). In addition, ambient air toluene was nearly significantly associated to headache symptom ($p = 0.059$). However, hippuric acid was not associated to any non-systematic symptom of outdoor workers.

DISCUSSION

Most of all workers had normal BMI while their work employment was 8.5 years. The motorcycle drivers worked for longest time a day (12.0 h) but street venders was highest exposed to toluene (157.1 μg/m^3). The average toluene (91.1 μg/m^3) in this study was in urban air concentration range 5-150 μg/m^3 which present toluene concentration was higher than previous study in Bangkok 2007 (36.1 μg/m^3) (Laowagul *et al*., 2008). Moreover, this toluene level was higher in the comparison of previous reported data in urban cities of other countries; 4-36 μg/m^3 in Hong Kong (Lee *et al*., 2002), 27 μg/m^3 in Taiwan (Hsieh and Tsai, 2003), 39.2 μg/m^3 in Algeria (Kerbachi *et al*., 2006), 13.0-33.1 μg/m^3 in ITO, Delhi (Kumar and Tyagi, 2006) and 11.52 μg/m^3 in Suzhou, China (Wang *et al*., 2010). It may be higher if it close to industrial emission sources (WHO, 2000). The acute and chronic effects of toluene on Central Nervous System (CNS) are the effects of the most concern (Dann *et al*., 1989; WHO, 2000).

This study found that most of workers had non-systematic symptoms of 42.5% headache, 36.6% weakness, 16.6% dizziness and 15.3% throat irritation which were also found in gasoline station workers (Tunsaringkarn *et al*., 2012). The street vender had the highest of these symptoms while the security guardsman was the lowest symptoms. Ambient air toluene was significantly associated with dizziness ($p<0.01$) and throat irritation symptoms ($p<0.01$). In addition, ambient air toluene was strongly associated with hippuric acid ($p = 0.001$). It can supported that hippuric acid is used as biomarker of toluene exposure (Pagnotto and Lieberman, 1967; Kawai *et al*., 2008) which hippuric acid excretion has been correlated with the Time Weighted Average concentration (TWA) of toluene during the workshift (Duydu *et al*., 1999). But insufficiency of urinary hippuric acid to indicate the low exposures to toluene as previous study (Angerer and Kramer, 1997; Duydu *et al*., 1999). Average hippuric acid concentration of all workers in this study was 0.4 g/gCr which was the same value of press workers from factories in Bangkok (0.37 g/gCr; range 0.06-1.98 g/gCr; Wiwanitkit *et al*., 2002) but higher than gas service station workers in Chonburi Province (0.28 g/gCr; Yimrungruang *et al*., 2008). Moreover, toluene showed the association with non-specific symptoms of dizziness and throat irritation which supported other study including headache, dizziness, fatigue, muscular weakness, drowsiness and incoordination with staggering gait, skin paresthesia, collapse and coma (US EPA, 1980). The previous study of the subjective symptoms were measured with the psychologicalneurological questionnaire (Psychologisch-Neurologischer Fragebogen, PNF) have been reported in a significant dose-response relation (50-100 ppm) and long term exposure (>12 years) which scored significantly higher on a symptom index than shorter exposure (1-12 years) (Ukai *et al*., 1993). About 20% of absorbed toluene dose is excreted unchanged by the lungs which the rest is mainly metabolized to hippuric acid and very small percentage of the toluene is metabolized to cresol (Angerer, 1979). So, hippuric acid can found in urine which occupational worker was limited at 1.6 g/gCr (ACGIH, 2009a, b). This study found hippuric acid was lower than limited level and it was not associated with any symptoms in this study as Kim *et al*. (1989) and Hashim *et al*. (2006) studies found that there were no correlation between hippuric acid concentrations and subjective symptoms and pulmonary function parameters.

However, the air quality guideline could also be based on the odour threshold. The peak concentrations of toluene in air should be kept below the odour detection threshold level of 1 mg/m^3 (0.266 ppm) as a 30 min average as WHO recommended (WHO, 2000).

CONCLUSION

Average ambient air toluene concentration (8 h average) which widespread in the environmental of urban area, Bangkok was 91.1 μg/m^3 (24.2 ppb) with a range of 28.7-142.2 μg/m^3 (7.6-37.8 ppb). Outdoor workers of guardsmen, motorcycle drivers and street venders exposed to considerably higher levels than the general population. Most non-systematic symptoms prevalence of outdoor workers found headache, weakness, dizziness

and throat irritation respectively which dizziness and throat irritation were associated with ambient air toluene exposure. As well as urine hippuric acid was strongly associated with toluene exposure.

However, urine hippuric acid was good an indicator of toluene exposure but did not seem to be a good predictor of non-systematic symptoms of outdoor workers. It should be future studied in large population group.

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