J. Environ. Res. 33 (1): 27-38

RISK RATIO OF BENZENE, TOLUENE, ETHYLBENZENE AND XYLENE (BTEX) EXPOSURES AND THEIR RELATIONS TO BIOLOGICAL PARAMETERS OF GASOLINE WORKERS IN BANGKOK, THAILAND

อัตราความเสี่ยงต่อการรับสัมผัสเบนซีน โทลูอีน เอทิลเบนซีน และไซลีน (บีเทค) และความสัมพันธ์ต่อพารามีเตอร์ทางชีวภาพของพนักงานสถานบริการน้ำมันเชื้อเพลิงในกรุงเทพมหานคร ประเทศไทย

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received : October 21, 2010 accepted : April 10, 2011

Abstract

Gasoline station is a common source of volatile organic compounds (VOCs) emissions around its perimeter. In order to conduct a monitoring of the VOC's emission, measurements of biological markers of blood benzene, toluene, ethylbenzene and xylene (BTEX) in gasoline-station workers are recommended. The purposes of this study were to evaluate exposure risk ratio (110 gasoline station workers from 11 gasoline stations in Bangkok Metropolitan area compared to 10 office workers in the same station as control group) and to determine the relations between blood BTEX and biological parameters of the gasoline workers. Results showed that blood BTEX levels of gasoline workers were significantly higher than controls (independent t-test, $p<0.001$). Most measurements of toluene, ethylbenzene and xylene (TEX) in female workers were significantly higher exposed levels than in men (independent t-test, $p<0.01$). The highest risk ratio of BTEX environmental exposures was benzene. In addition, blood benzene was the most significantly correlated to toluene (partial correlation=0.704, $p<0.001$), but was not related to all biological parameters in this study.

Keywords: volatile organic compounds, BTEX, risk ratio, relation

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บทคัดย่อ

สถานบริการน้ำมันเชื้อเพลิงเป็นแหล่งแพร่กระจายของสารอินทรีย์ระเหยง่าย การตรวจตัวชี้วัดทางชีวภาพของเบนซีน โทลูอีน เอทิลเบนซีน และไซลีน (บีเทค) ในเลือดเป็นที่ยอมรับในการตรวจติดตามการแพร่กระจายของสารอินทรีย์ระเหยง่าย วัตถุประสงค์ของการศึกษาครั้งนี้เพื่อหาค่าอัตราความเสี่ยงต่อการรับสัมผัสสาร (ของพนักงานสถานบริการน้ำมันเชื้อเพลิง จำนวน 110 คน จากสถานบริการน้ำมัน 11 แห่ง ในพื้นที่กรุงเทพมหานคร เปรียบเทียบกับกลุ่มควบคุมซึ่งเป็นพนักงานในสำนักงานที่ตั้งอยู่บริเวณเดียวกัน จำนวน 10 คน) และหาความสัมพันธ์ระหว่าง ปริมาณบีเทคในเลือดและพารามิเตอร์ทางชีวภาพของพนักงานสถานบริการน้ำมันเชื้อเพลิง ผลการศึกษาแสดงให้เห็นว่าปริมาณบีเทคในเลือดของพนักงานสถานบริการน้ำมันเชื้อเพลิงมีค่าสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (independent t-test, $p<0.001$) ระดับการสัมผัสโทลูอีน เอทิลเบนซีน และไซลีน ในพนักงานหญิงมีค่าสูงกว่าพนักงานชาย อย่างมีนัยสำคัญทางสถิติ (independent t-test, $p<0.01$) ค่าอัตราความเสี่ยงต่อการรับสัมผัสสารบีเทคในสิ่งแวดล้อม คือ เบนซีน นอกจากนี้ปริมาณเบนซีนในเลือดมีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติมากที่สุดกับปริมาณโทลูอีน (partial correlation= 0.704, $p<0.001$) แต่ไม่มีความสัมพันธ์กับพารามิเตอร์ทางชีวภาพทั้งหมดในการศึกษานี้

คำสำคัญ: สารอินทรีย์ระเหยง่าย, บีเทค, อัตราความเสี่ยง, ความสัมพันธ์

Introduction

VOCs are environmental pollutants associated with gasoline vapor emissions and motor vehicle exhaust and can be found in a wide variety of commercial, industrial and residential products[1,2]. The four major compounds of VOCs are BTEX.

Several studies reported on occupational exposure to VOCs from gasoline vapor emissions including their toxicities via inhalation, dermal contact and ingestion[3,4]. In addition, high concentration of VOCs can lead to adverse health effects of acute and chronic effects, as benzene was classified as human carcinogen[5,6]. Therefore any biological monitoring for the estimation of chemical composition in worker's tissue and body fluid samples were recommended[7,8]. Such occupational practices are especially valuables as they indicate potentially harmful exposures[9]. Previous studies of Yimrungruang et.al.[10] and Wiwanitkit[11] reported that the gasoline worker was classified as a high risk occupation due to direct contact with benzene in ambient air. Among BTEX, benzene is the smallest molecule with short half life in blood circulation as demonstrated in the distribution by route of exposure in study of human autopsies on individuals dying shortly after exposure. Traces benzene levels were found in the brain, with lower levels in the fat, blood, kidneys, and liver[12]. Rana and Verma[13] reported that benzene induces multiple myeloma in petrochemical workers, while Liu[7] found that exposure to certain VOCs either in a group or individual may influence certain biochemical liver test. Uzma et al.[14] revealed that there was a significant toxic

effect of solvents and air pollutants on gasoline workers who exposed for longer duration.

Therefore, any biological monitoring of workers who are closely associated with chemical exposures is crucial and essential in order to estimate risks. It was our main objective to investigate if there is any gender factor involved in the BTEX exposures in gasoline workers in Bangkok.

Materials and Methods

Population Study

A cross sectional survey was conducted by collecting blood samples from 110 gasoline workers (80 men, 30 women) from 11 gasoline stations and 10 office workers for a control purpose (6 men and 4 women in the same gasoline station) during April to June 2009, in Pathumwan District area, Bangkok. All subjects were healthy and had worked for more than six months. They were provided the consent form before the study. Permission to conduct the biological monitoring for human subjects in this study was approved by the Ethical Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University.

Blood Collection

Two mL of venous blood samples were collected from subjects during their work shift performed during work shift 6-8 hr, using glass heparinize vacuum blood tube (Vacutest Lithium Heparin 4 mL of S.E. Supply LTD., PART). Blood samples were stored at -20 °C until BTEX analysis.

Biological Analysis

The following biological analyses; hematological tests [hemoglobin, hematocrit, white blood cell (WBC)], kidney function tests [blood urea nitrogen (BUN), blood creatinine], liver function tests [alkalinephosphatase (ALP), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT)] and serum cholinesterase (SChE), were performed at Department of Clinical Microscopy, Faculty of Allied Health Sciences, Chulalongkorn University under standard laboratory quality control process.

Blood BTEX Analysis

The BTEX analysis was performed using the headspace-solid phase microextraction (HS-SPME) technique of Tunsaringkarn et al.(15). 0.2 gm of sodium chloride was added to 0.5 mL of blood sample in glass bottle with cap, and vortexed for 15 sec, controlled and absorbed by SPME (solid phase microextraction) in water bath at 50°C with sonication for 20 min. The treated

sample was then injected in gas chromatograph (GC, Varian CP 3800) at temperature 220°C using flame ionization detector at 220°C (column CP-SIL5 CB, splitless). The samples were put in the oven for 10 min at the starting temperature of 50°C. The temperature was increased at 5°C per minute until 90°C was reached. Then, again the temperature was increased at 30°C per minute until 250°C was reached and stayed for 17 min. The quantity of blood benzene was analysed under relative intensity of chromatographic signal for 40 min. The limit of quantitations (LOQs) which is equal to ten times of standard deviation at minimum concentration (LOQ = 10 SD)[16] were carried out. LOQs for benzene, toluene, ethylbenzene and xylene were 33.30, 16.70, 66.70 and 33.30 μg/L (ppb) respectively. Average coefficient of determination (r^2) was 0.99 for four chemicals (m-and p- xylene appeared at the same peak).

Statistical Analysis

Descriptive statistical analysis was used for data on the characteristics and concentration of blood biological markers of gasoline workers. Exposure risk ratio of benzene obtained were compared to the Biological Exposure Indices (BEI). While, the linear regression was used to analyze the partial correlation of blood BTEX and relations between blood BTEX and biological parameters of gasoline workers. All the statistical analyses were performed using SPSS 17.0 for Windows Program.

Result

Characteristics of Gasoline Workers and Controls

The majority of gasoline workers (80/110) were men with mean age of 29.8 yr. Of all gasoline workers monitored in this study, 33.6% having cigarette smoking and 59.1% having alcohol drinking habit. While, all[10] controls were non smokers, mean age 29.1 yr with 50.0% alcohol drinking habit. However, gender, age and alcohol drinking habit showed no significant difference between groups except cigarette smoking (independent t-test, $p<0.05$).

Blood BTEX and Risk Ratio

Average blood BTEX levels in worker groups (of 286.60, 205.51, 186.76 and 113.79 μg/L, respectively), were signifi cantly higher than in the control groups (of 27.28, 47.71, 49.75 and 43.03 μg/L, respectively) (independent t-test, $p<0.001$) (Table 1). In addition, blood toluene, ethylbenzene and xylene levels in female workers were significantly higher than men

(independent t-test, $p<0.01$) except for benzene. The exposure risk ratios were ranged from 2.64 to 10.51, for xylene, ethylbenzene, toluene and benzene.

Table 1 Blood BTEX levels and exposure risk ratio in gasoline worker and control groups

Compound	Concentration (μg/L, Mean ± S.E.)			Exposure
	Gasoline Worker	(No./%) (n=110)	Control (n=10)	risk ratio
Benzene	Mean =	286.6 ± 10.4**	Mean = 27.3 ± 15.3**	10.5
	Men: (80/72.7)	275.8 ± 9.9		10.1
	Women: (30/27.3)	315.3 ± 26.8		11.6
Toluene		205.5 ± 13.3**	47.7 ± 12.3**	4.3
	Men:	175.0 ± 11.3*		3.7
	Women	286.9 ± 34.6*		6.0
Ethylbenzene		186.8 ± 16.9**	49.8 ± 12.3**	3.8
	Men:	144.5 ± 11.1*		2.9
	Women:	299.4 ± 49.3*		6.0
Xylene		113.8 ± 11.5**	43.0 ± 17.4**	2.6
	Men:	83.7 ± 9.5*		2.0
	Women:	193.0 ± 29.3*		4.5

* Statistically significant difference between men and women of gasoline worker group at $p< 0.01$

** Statistically significant difference between control and gasoline worker groups at $p<0.001$

Correlations between BTEX

The linear regression analysis indicated that blood benzene level in gasoline workers was significantly associated with toluene, ethylbenzene, and xylene levels (Multiple Linear regression, $p<0.001$) (Table 2). While, benzene levels were correlated with toluene (0.704), ethylbenzene (0.322) and xylene (0.360) (Multiple Linear regression, Partial correlation).

Table 2 Correlation between blood benzene, toluene, ethylbenzene and xylene of gasoline workers

Compound	Mean of Concentration (μg/L), n=110	Linear regression model results*			
		Standardized Coefficients	95% CI	p-value	Partial Correlation
Benzene	286.6				
Toluene	205.5	0.660	0.68 to 1.02	0.000	0.704
Ethylbenzene	186.8	0.296	0.21 to 0.76	0.001	0.322
Xylene	113.8	0.329	0.18 to 0.55	0.000	0.360

*Adjusted for gender, age, smoking, alcohol drinking

Relations between BTEX and Biological Parameters

Blood benzene level in gasoline worker group showed no relationship to all biological parameters (Table 3). Toluene levels were significantly inverse-related to BUN and creatinine and serum cholinesterase levels, while ethylbenzene levels were significantly inverse relation to BUN and creatinine, but xylene level was only significantly inverse relation to BUN (Multiple Linear regression, $p<0.05$).

All BUN, creatinine and serum cholinesterase in men were significantly higher than in women ($p<0.001$, $p<0.001$, $p<0.01$ respectively) (Table 4).

Table 3 Relation between blood benzene toluene, ethylbenzene, xylene and blood biological parameters in gasoline workers

Compound	Linear regression model results*			
	Standardized Coefficients	95% CI	p-value	Relation to Blood Biological Parameters
Benzene	-	-	-	-
Toluene	-0.241	-0.011 to -0.001	0.015	BUN
	-0.016	-0.001 to 0.000	0.030	Creatinine
	-0.226	-2.695 to -0.515	0.023	Serum cholinesterase
Ethylbenzene	-0.236	-0.008 to -0.001	0.018	BUN
	-0.258	-0.001 to -0.000	0.010	Creatinine
Xylene	-0.232	-0.014 to -0.001	0.021	BUN
	-0.202	-0.001 to 0.000	0.202	Creatinine

*Adjusted for gender, age, cigarette smoking, alcohol drinking

Table 4 Blood biological parameter levels in gasoline workers

Blood biological parameter (No./%) (n =110)	Standard Reference[a]	Our Measurement (Mean ± S.E.)	p-value*
Hemoglobin (gm%)		**14.1 ± 0.2**	
Men (80/72.7)	13.0 – 17.0	14.4 ± 0.2	0.000
Women (30/27.3)	12.0 – 15.0	12.9 ± 0.2	
Hematocrit (%)		**41.7 ± 0.4**	
Men (80/72.7)	39.0 – 51.0	42.7 ± 0.5	0.000
Women (30/27.3)	36.0 – 45.0	38.5 ± 0.5	
WBC (x 109/L)		**7.9 ± 0.2**	
Men (80/72.7)	5.0 – 10.0	7.8 ± 0.2	0.794
Women (30/27.3)	5.0 – 10.0	7.9 ± 0.3	
BUN (mg/%)		**11.8 ± 0.3**	-
Men (80/72.7)	6.0 – 20.0	12.4 ± 0.4	0.000
Women (30/27.3)	6.0 – 20.0	9.8 ± 0.5	-
Creatinine (mg/%)		**1.0 ± 0.0**	-
Men (80/72.7)	0.5 – 1.5	1.0 ± 0.0	0.000
Women (30/27.3)	0.5 – 1.5	0.8 ± 0.0	-
SGOT (u/L)		**26.3 ± 1.8**	
Men (80/72.7)	< 40	28.1 ± 2.3	0.026
Women (30/27.3)	< 40	19.8 ± 1.2	
SGPT (u/L)		**30.8 ± 2.5**	
Men (80/72.7)	< 40	34.0 ± 3.1	0.013
Women (30/27.3)	< 40	21.1 ± 2.1	
ALP (u/L)		**71.5 ± 3.7**	
Men (80/72.7)	26.0 – 117.0	78.1 ± 4.6	0.001
Women (30/27.3)	26.0 – 117.0	51.5 ± 3.1	
Serum cholinesterase (u/L)		**9198.5 ± 225.7**	-
Men (80/72.7)	5,320.0 – 12,920.0	9,557.0 ± 267.9	0.003
Women (30/27.3)	4,260.0 – 11,250.0	8,096.0 ± 331.2	-

* Statistically significant difference between men and women of gasoline worker group

[a] Standard reference labolatory of Faculty of Allied Health Sciences, Chulalongkorn University.

Discussions

Our results exhibited that there were relationships between biological monitoring in human body and environmental monitoring data similarly to previous reports [17-19]. Data on monitoring of gasoline workers and controls in our study showed no significant difference on their gender, age and alcohol drinking habit except about one-third of gasoline workers with cigarette smoking habit. The biological data on mean blood BTEX levels in worker groups were significantly higher than in the control groups (which had no direct contact with VOCs). Benzene is known as human carcinogen. While, toluene, ethylbenzene and xylene are non carcinogen. However, have adverse health effects depend on dose and exposure duration[20-23]. Result of average blood benzene levels in gasoline workers found in our study was 5.7 times of the BEI reference[24]. Benzene risk ratio was the highest among the BTEX observed in this study. It demonstrated the high risk of benzene exposure in gasoline workers in Bangkok when compared to other countries[25,26]. Since benzene is a carcinogen agent, the gasoline workers in Pathumwan area, central of Bangkok, who directly exposed to benzene, would have had high risk of cancer development. Recent study of Twaveevong[27] on the ambient VOCs from gas station in Bangkok found that benzene in ambient air was 308-852 $\mu g/m^3$, higher than Time-Weighed-Average (TWA) limit of American Conference of Governmental Industrial Hygienists (ACGIH)[28]: the cancer risk calculation for benzene was ranged from 3.42×10^{-4} to 1.23×10^{-3}).

Blood toluene, ethylbenzene and xylene levels in women workers were significantly higher than in men ($p<0.01$), whereas the blood benzene level did not significantly increase in women workers ($p=0.08$). This might be due to sex difference that women have overall complexity of heart rate dynamics higher than men[29] and half-life of each chemicals[30].

Analysis on the correlation among the BTEX revealed that blood benzene level of workers was the most significantly correlated to toluene. This relation could be implied to the increased health adverse effects such as neurological, hematological and endocrinal effects[23,31].

However, benzene was not shown to have any relations to all biological parameters. Despite the fact that, benzene is a VOC with toxicities including genotoxicity, hematotoxicity, neurotoxicity and carcinogenesis[32-35]. However, for its leukemogenetic effect, it was still not well-described[32.35].

For toluene, ethylbenzene and xylene, they showed inversed-relations to BUN

and creatinine which are in line with previous studies[36-38]. Both BUN and creatinine are the primary parameters used for determining the kidney function. In this study, we found that creatinine were higher in men than women similar to other report [39] and also found in BUN and serum cholinesterase in normal range. For toluene, we found that it was inversely related to serum cholinesterase. This enzyme (present primarily in the liver to break down acetylcholine) can be used to determine risk of liver disease[40]. Acetylcholine is a critical chemical in the transmission of nerve impulses[41-42]. This result showed that toluene might affect liver function and nervous system.

Conclusion

Our findings in this study indicated the high risks among the gasoline workers in Pathumwan area, central Bangkok for potential cancer development caused by exposure to high benzene. Our findings also indicated that the gasoline workers also might have risks on kidney and liver malfunctions, especially in female workers. Health education on hazard exposures and appropriate prevention measures could reduce those risks. Further study on exposure to other hazardous compounds is recommended.

Acknowledgements

This work was funded and supported by the Thai Fogarty ITREOH Center (D43-TW007849 NIH FIC) and College of Public Health Sciences, Chulalongkorn University. The authors would like to thank Dr. Kriangkrai Lerdthusnee for his advice and editing this paper.

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