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Original Research

Correlation between Blood Cell Parameters and BTEX Exposure among Gasoline Station Workers

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Abstract
This study evaluated the correlation between red and white blood cell parameters and BTEX exposure among a cross-sectional survey involving 105 gasoline workers of 11 stations in Bangkok in 2009. Blood BTEX levels were evaluated by gas chromatography with flame ionized detector (GC-FID) which represented BTEX exposure. Blood benzene, toluene, ethylbenzene and xylene levels were 284.9, 201.3, 178.7 and 105.5 µg/L which benzene level was strong correlated to toluene and xylene levels (Linear regression, $p < 0.001$ and $p = 0.001$). Blood cell parameters should present adverse affects of the exposure. The results of this study showed that toluene, ethylbenzene and xylene levels were associated with abnormal red blood cells (Logistic regression, $p < 0.05$, $p < 0.05$ and $p < 0.05$, respectively). In addition, toluene was also associated with hematocrit level of gasoline workers (Linear regression, $p < 0.05$). But blood benzene level was not shown association with any blood cell parameters. In conclusion, red blood cell parameters may be the sensitive biomarker determinants than white blood cell parameters for BTEX exposure among gasoline workers. Toluene, ethylbenzene and xylene had potential affect to red blood cell morphology.

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INTRODUCTION

Volatile organic compounds (VOC), associated with the exposure to motor vehicle exhaust and/ or gasoline vapor emissions, are pollutants of great concern due to their toxicity [1, 2]. Benzene, toluene, ethylbenzene and xylene known as the BTEX group which is important fraction found in urban air [3, 4, 5, 6]. BTEX is known as toxic and genotoxic substances [7, 8]. Benzene-rich additives are used as the anti-knock agents but benzene concentration limit in gasoline 3.5% for Thailand [9] but in industrialized country such as North America and Europe reduced benzene in gasoline about 1% [10, 11]. Benzene can vaporize from gasoline tank and filling stations which also tend to increase though other components (toluene, ethylbenzene and xylene, etc) [12]. There were reported health adverse effects of BTEX on hematological, neurological, immunological, respiratory systems and carcinotoxicity [13]. The previous study showed ambient BTEX level has also been increases in gasoline station of urban areas in Thailand which could have serious implications for human health and the environment [14, 15, 16, 17, 18]. This study evaluated correlation between blood BTEX and blood cell parameters of gasoline station workers who have risk to expose between their work shifts.

MATERIALS AND METHODS

Study population

A cross sectional surveyed in 105 gasoline workers at 11 gasoline stations in Bangkok, Thailand. Which were performed by interview with blood collection in 2009. All workers were healthy, age more than 18 and worked more than 6 months. The informed consent was obtained from all participants before the study which this protocol was approved by the Ethical Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University.

Blood collection and analyses

The 2 ml of venous blood samples were collected from participants using plastic heparinized vacuum blood tube during the 6-8 hours shift work and stored at -20^{o}C.

Blood BTEX levels were determined by GC-FID using modified HS-SPME technique [19]. The quantity of blood BTEX analysed under relative intensity of chromatographic signal for 40 minutes. The Limit of Detection (LOD) of benzene was 10.00 µg/L (ppb) and the average coefficient of determination (r^2) was 0.999657.

Count blood cells were done by automated hematology analyzer Technicon H*3 RTC at Department of Clinical Microscopy, Faculty of Allied Health Sciences, Chulalongkorn University. All blood cell parameter were red blood cell parameters (hemoglobin, Hb: hematocrit, Hct: mean corpuscular volume, MCV, abnormal RBC and abnormal hemoglobin typing), white blood cell parameters (white blood cells count, WBC: neutrophils, N: lymphocytes, L: monocytes, Mo; eosinophils, Eo: basophils, Ba) and platelets.

Statistical analyses

Descriptive statistic [mean and standard deviation (SD)] was used to analyze all parameters. The association between BTEX; between hematological parameters and BTEX level were assessed by Linear and Logistic regression analyses. A statistically significant difference was accepted at a *p*-value of *< 0.05.* The results of all laboratory examinations were carried out using the SPSS 17.0 for Windows Program.

RESULTS

Characteristics of gasoline station workers

One hundred and five gasoline station workers had mean age, BMI, work duration, smoking, alcohol and coffee drinking at 29.9 years, 23.2 kg/m^2, 5.3 years, 34.3%, 60.0% and 61.9% respectively (Table 1).

Table 1. Characteristics of gasoline station workers

Characteristic	Mean or Percentage	SD
Age (years)	29.9	9.3
BMI (kg/m^2)	23.2	4.9
Work duration (years)	5.3	6.4
Cigarette smoking (%)	34.3	-
Alcohol drinking (%)	60.0	-
Coffee drinking (%)	61.9	-

Table 2. Blood BTEX levels and their association

Compound	Mean (µg/L)	SE	Linear regression results[a]			Partial correlation
			Coefficient	95% CI	*p-value*	
Benzene	284.9	10.4	-	-	-	-
Toluene	201.3	12.4	0.700	0.460 to 0.715	0.000	0.681
Ethylbenzene	178.7	16.1	0.340	0.089 to 0.352	0.331	0.321
Xylene	105.5	9.8	0.365	0.124 to 0.604	0.001	0.346

[a]Adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking

Table 3. Association between blood benzene level and hematological parameters of gasoline station workers

Red Blood Cell Parameters	Reference[c]	Mean	SD	Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Hemoglobin (gm%)	13.0 – 17.0	14.1	1.7	-0.081	-0.005 to 0.002	*0.424*
Hematocrit (%)	39.0 – 51.0	41.8	4.5	-0.053	-0.011 to 0.006	*0.600*
MCV (ft)	80.0 – 98.0	81.9	8.9	0.008	-0.016 to 0.018	*0.941*
				Logistic regression results[b]		
				Coefficient	95% CI	*p-value*
Abnormal RBC (%)	-	27.6	-	0.992	0.992 to 1.001	*0.168*
Abnormal Hb (%)	-	45.8	-	0.994	0.994 to 1.002	*0.369*
White Blood cell parameters				Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Total WBC	5.0 – 10.0	7.8	1.6	-0.968	-0.004 to 0.002	*0.335*
Neutrophils	40.0 – 75.0	52.9	10.5	-0.108	-0.031 to 0.010	*0.301*
Lymphocytes	20.0 – 45.0	34.0	7.7	0.149	-0.004 to 0.025	*0.148*
Monocytes	2.0 – 10.0	5.7	1.6	0.001	-0.003 to 0.003	*0.995*
Eosinophils	1.0 – 6.0	6.0	1.6	-0.005	-0.013 to 0.008	*0.605*
Basophils	0.0 – 1.0	0.4	0.5	0.011	-0.001 to 0.001	*0.918*
Platelets	150.0 – 400.0	256.6	66.4	0.074	-0.081 to 0.173	*0.476*

Independent variable: benzene
[a]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking
[b]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking
[c]Standard reference laboratory of Faculty of Allied Health Sciences, Chulalongkorn University

Table 4. Association between blood toluene level and hematological parameters of gasoline station workers

Red Blood Cell Parameters	Reference[c]	Mean	SD	Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Hemoglobin (gm%)	13.0 – 17.0	14.1	1.7	-0.189	-0.005 to 0.000	*0.068*
Hematocrit (%)	39.0 – 51.0	41.8	4.5	-0.213	-0.015 to 0.000	***0.039***
MCV (ft)	80.0 – 98.0	81.9	8.9	0.084	-0.009 to 0.021	*0.427*
				Logistic regression results[b]		
				Coefficient	95% CI	*p-value*
Abnormal RBC (%)	-	27.6	-	-0.006	0.989 to 0.999	***0.012***
Abnormal Hb (%)	-	45.8	-	-0.002	0.995 to 1.001	*0.234*
White Blood cell parameters				Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Total WBC	5.0 – 10.0	7.8	1.6	-0.124	-0.004 to 0.001	*0.233*
Neutrophils	40.0 – 75.0	52.9	10.5	-0.030	-0.020 to 0.015	*0.788*
Lymphocytes	20.0 – 45.0	34.0	7.7	0.134	-0.004 to 0.021	*0.206*
Monocytes	2.0 – 10.0	5.7	1.6	-0.013	-0.003 to 0.002	*0.904*
Eosinophils	1.0 – 6.0	6.0	1.6	-0.088	-0.013 to 0.005	*0.419*
Basophils	0.0 – 1.0	0.4	0.5	0.099	0.000 to 0.001	*0.363*
Platelets	150.0 – 400.0	256.6	66.4	0.028	-0.042 to 0.176	*0.226*

Independent variable: toluene; [a]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking; [b]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking; [c]Standard reference laboratory of Faculty of Allied Health Sciences, Chulalongkorn University

Table 5. Association between blood ethylbenzene level and hematological parameters of gasoline station workers

Red Blood Cell Parameters	Reference[c]	Mean	SD	Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Hemoglobin (gm%)	13.0 – 17.0	14.1	1.7	-0.070	-0.003 to 0.002	*0.513*
Hematocrit (%)	39.0 – 51.0	41.8	4.5	-0.110	-0.009 to 0.003	*0.308*
MCV (ft)	80.0 – 98.0	81.9	8.9	0.163	-0.003 to 0.020	*0.131*
				Logistic regression results[b]		
				Coefficient	95% CI	*p-value*
Abnormal RBC (%)	-	27.6	-	-0.005	0.990 to 1.000	***0.036***
Abnormal Hb (%)	-	45.8	-	-0.003	0.994 to 1.000	*0.061*
White Blood cell parameters				Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Total WBC	5.0 – 10.0	7.8	1.6	-0.104	-0.003 to 0.001	*0.332*
Neutrophils	40.0 – 75.0	52.9	10.5	-0.052	-0.017 to 0.011	*0.641*
Lymphocytes	20.0 – 45.0	34.0	7.7	0.173	-0.002 to 0.018	*0.113*
Monocytes	2.0 – 10.0	5.7	1.6	0.068	-0.003 to 0.001	*0.526*
Eosinophils	1.0 – 6.0	6.0	1.6	-0.096	-0.010 to 0.004	*0.391*
Basophils	0.0 – 1.0	0.4	0.5	0.000	-0.000 to 0.001	*0.997*
Platelets	150.0 – 400.0	256.6	66.4	0.045	-0.106 to 0.069	*0.679*

Independent variable: ethylbenzene; [a]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking; [b]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking; [c]Standard reference laboratory of Faculty of Allied Health Sciences, Chulalongkorn University

Table 6. Association between blood xylene level and hematological parameters of gasoline station workers

Red Blood Cell Parameters	Reference[c]	Mean	SD	Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Hemoglobin (gm%)	13.0 – 17.0	14.1	1.7	-0.080	-0.005 to 0.002	*0.456*
Hematocrit (%)	39.0 – 51.0	41.8	4.5	-0.144	-0.016 to 0.003	*0.181*
MCV (ft)	80.0 – 98.0	81.9	8.9	0.136	-0.007 to 0.032	*0.212*
				Logistic regression results[b]		
				Coefficient	95% CI	*p-value*
Abnormal RBC (%)	-	27.6	-	-0.008	0.985 to 0.999	***0.029***
Abnormal Hb (%)	-	45.8	-	-0.003	0.992 to 1.001	*0.149*
White Blood cell parameters				Linear regression results[a]		
				Coefficient	95% CI	*p-value*
Total WBC	5.0 – 10.0	7.8	1.6	-0.124	-0.005 to 0.001	*0.246*
Neutrophils	40.0 – 75.0	52.9	10.5	0.023	-0.021 to 0.026	*0.839*
Lymphocytes	20.0 – 45.0	34.0	7.7	0.172	-0.003 to 0.030	*0.115*
Monocytes	2.0 – 10.0	5.7	1.6	-0.039	-0.004 to 0.003	*0.716*
Eosinophils	1.0 – 6.0	6.0	1.6	-0.312	-0.019 to 0.005	*0.236*
Basophils	0.0 – 1.0	0.4	0.5	-0.051	-0.001 to 0.001	*0.651*
Platelets	150.0 – 400.0	256.6	66.4	0.100	-0.078 to 0.210	*0.364*

Independent variable: xylene; [a]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking; [b]Model were adjust for age, BMI, work duration, cigarette smoking, alcohol drinking and coffee drinking; [c]Standard reference laboratory of Faculty of Allied Health Sciences, Chulalongkorn University

Blood BTEX levels and their association

Blood benzene, toluene, ethyl benzene and xylene were 284.9, 201.3, 178.7 and 105.5 µg/L respectively (Table 2). Blood benzene was strongly and positively associated with toluene (Linear regression, $p < 0.001$) and xylene (Linear regression, $p = 0.001$).

Association between blood BTEX levels and hematological parameters

Most of hematological parameters among gasoline station workers were in reference ranges as shown in Table 3, 4, 5 and 6. Where the results found that there were 27.6% abnormal red blood cells (RBC) and 45.8% abnormal hemoglobin (Hb) typing.

Benzene was not associated with all red and white blood cell parameters (Table 3). Toluene, ethylbenzene and xylene levels were associated with abnormal red blood cells (Logistic regression, $p < 0.05$, $p < 0.05$ and $p < 0.05$ respectively) (Table 4, 5 and 6). Moreover, blood toluene level was showed the significant relation to hematocrit level (Logistic regression, $p < 0.05$).

DISCUSSION

The workers had average age 29.9 years and worked for 5.3 years within normal BMI (18.0-24.9 kg/m^2) [20]. Most of them were alcohol and coffee drinking at 60.0% and 61.9%. 34.3% of worker was smoking but was in low level (less than 10 cigarettes per day). Blood BTEX levels showed that benzene was the highest exposure which benzene and ethylbenzene are accepted as carcinogens [21, 22]. Blood benzene level in this study was lower than the previous study of petrol station workers in Italy [23]. Benzene was strongly related to toluene and xylene levels ($p < 0.001$ and $p = 0.001$). The BEI is a guideline for control of potential health hazards to the worker which its values are neither rigid line between safe and dangerous concentrations nor they are an index of toxicity. But there are much lack BEI of chemical substances especially for human blood levels. It may be appropriate to remove the worker from toxic exposure if there is reason to believe that significant exposure may have occurred. So, it should be concerned of health affects among these workers.

Most of blood cell parameters were in reference ranges but the results of this study found 27.6% abnormal red blood cells which were hypochromic and microcytic cells and 45.8% abnormal hemoglobin typing which were 32.4% E-trait, 42.9% alpha-beta-thal-trait. An abnormal RBC of worker compared to a normal RBC were 1.0 (95% CI = 0.989 to 0.999), 1.0 (95% CI = 0.990 to 1.000) and 1.0 (95% CI = 0.985 to 0.999) times more likely to have toluene, ethylbenzene and xylene exposures respectively. They may effect to RBC morphology while benzene may sensitively effect to genotoxicity as previous studies [24, 25, 26]. The characteristic systemic effect resulting from intermediate and chronic benzene exposure in humans and animals which major types of blood cells are susceptible of red blood cells, white blood cells and platelets is the most noted hematotoxicity. And a common clinical finding is cytopenia, which is a decrease in various cellular elements manifested as anemia, leukopenia, or thrombocytopenia in humans [27]. But this study showed that benzene was not related to all count blood cell parameters. The result was argued from Chinese worker in Shanghai, China which supported the use of the absolute lymphocyte count as the most sensitive indicator of benzene-induced hematotoxicity [28].

Toluene was significantly inversely associated with hematocrit ($p < 0.05$) which it depends on number and size of red blood cells. Lower level of hematocrit should be risk to anemia [29]. This result supported other study [30] which showed that toluene appears to be associated with the hemoglobin rather than the cell membrane. Absorbed toluene in humans and laboratory animal distributions are characterized by preferential uptake in lipid-rich and highly vascular tissues such as the brain, bone marrow, and body fat [31]. Toluene is distributed between the plasma and red blood cells at approximately a 1:1 ratio in humans based on in vitro data and a 1:2 ratio in rats based on in vivo data [32]. In addition, toluene, ethylbenzene and xylene were associated with abnormal red blood cells were additive as previous study [33, 34] but was difference of hematological effect observed in an occupational study of xylene-exposed workers in which no benzene was involved [35].

The BTEX level was not shown the relation to hemoglobin typing. Abnormal typing might be caused by genetic thalassemia carriers that was high prevalence among gasoline workers in Thailand [36]. Information on the developmental toxicity of xylenes in humans is limited to a few occupational studies that are inadequate for assessing the relationship between exposure to xylene and developmental effects due to concurrent exposure to other solvents [37].

No studies are available that directly characterize health hazards and dose-response relationships for exposures to whole mixtures of benzene, toluene, ethylbenzene, and xylenes. All four components is the critical noncancer effect of concern for BTEX mixtures. Benzene can additionally cause hematological effects which may ultimately lead to aplastic anemia, development of acute myelogenous leukemia [38, 39, 40, 41, 42, 43].

This study may conclude that most of hematological parameters showed notable changes of red blood cell morphology. It seems reasonable to conclude that toluene, ethylbenzene and xylenes combination had potential of the red blood cell toxicities.

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