Original Article

Occupational Exposure to Benzene and Changes in Hematological Parameters and Urinary Trans, Trans-Muconic Acid

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Abstract

Background: For its toxicity, benzene exposure is one of the main health concerns for high risk occupations like gasoline station workers. However, there is little knowledge about the effect of benzene metabolites on hematological parameters.

Objective: To evaluate the correlation between the urinary level of trans, trans-muconic acid (t, t-MA), a benzene metabolite, and some hematological parameters in gasoline workers.

Methods: We studied 102 gasoline station workers from 11 gasoline stations in Pathumwan district, central area of Bangkok, Thailand. Their blood and urine samples were analyzed for some hematological parameters and urinary t, t-MA analysis by high performance liquid chromatography (HPLC).

Results: We found an inverse correlation between urinary t, t-MA concentration and hemoglobin level ($r = 0.281$, $p<0.05$), hematocrit ($r = 0.264$, $p<0.05$). Those with higher urinary t, t-MA had a significantly ($p<0.05$) lower eosinophil counts than those with lower exposure. No significant correlation was found between urinary t, t-MA level and other white blood cell parameters and platelets count.

Conclusion: Exposure to benzene would cause bone marrow depression presenting as drop in hemoglobin, hematocrit and eosinophil counts.

Keywords: Hematologic tests; Benzene; Occupational exposure; Muconic acid

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Introduction

Benzene is well-known carcinogen with relative hematotoxicity.[1,2] Several studies showed high prevalence of cancer, chromosomal damage and leukemia in those with exposure to petrol and its products.[3-6] However, there was inconsistency in hematotoxic outcomes of industrial plant workers.

Biomonitoring of gasoline station workers who are directly exposed to benzene, is an important measure for the prevention and protection of occupational intoxication. The most important biomarkers of benzene exposure are benzene in exhaled air, in blood, and in urine and its metabolites. Urinary trans, trans-mu-

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For more information on exposure of gasoline station workers to BTEX compounds see www.theijoem.com/ijoem/index.php/ijoem/article/view/133/279

For more information on exposure of petroleum depot workers to BTEX compounds see www.theijoem.com/ijoem/index.php/ijoem/article/view/110/232

TAKE-HOME MESSAGE

- Benzene is an important carcinogen used in many industries. Inhalation of this substance can cause both acute and chronic toxicity.
- Many at risk occupations like workers in gasoline stations are at high risk of exposure benzene.
- Urinary t, t-MA, a benzene metabolite, is used to monitor benzene exposure.
- High level of urinary t, t-MA is associated with drop in Hb, Hct and eosinophil count.

conic acid (t, t-MA), one of the benzene metabolites, is a useful biomarker for biomonitoring of benzene exposure.[7,8] Historically, a complete blood count (CBC) has been recognized as an easy and readily available screening tool for assessing the hematotoxicity of benzene.[9] Several studies found no significant association between hematological profile and benzene exposure.[10-13] Usual symptoms of benzene intoxication have been described earlier; they include headache, dizziness and fatigue.[14-16] There are however, scarce information about hematological effects of exposure to benzene or its metabolites.[17-18] We conducted this study to evaluate the correlation between urinary level of t, t-MA, a benzene metabolite, and blood cell indices in a group of gasoline station workers in Bangkok, Thailand.

Table 1: Urinary t, t-MA level and some hematological parameters in gasoline workers

Parameter	Mean±SD	References*
Urinary t, t-MA (mg/gCr)	1.45±2.42	0.5†
Hemoglobin (g/dL)	14.15±1.62	13.0–17.0
Hematocrit (%)	41.93±4.14	39.0–51.0
MCV (fL)	81.93±8.58	80.0–98.0
WBC (×10^9/L)	7.86±1.62	5–10
Neutrophils (%)	52.84±10.50	40–75
Lymphocytes (%)	34.05±7.68	20–45
Monocytes (%)	5.73±1.62	2–10
Eosinophils (%)	6.04±5.25	1–6
Basophils (%)	0.42±0.50	0–1
Platelets (×10^3/L)	256.44±66.25	150–400

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Materials and Methods

One hundred and two gasoline workers were included in this study. They worked in 11 gasoline stations in Pathumwan district, central area of Bangkok, Thailand. They were healthy and had been working there for more than six months. All subjects signed informed consent forms which approved by the Ethical Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University before the study.

Venous blood samples were drawn from participants and collected in EDTA tubes. For each worker, urine sample was collected in glass bottle eight hrs after beginning his work shift.

Laboratory analyses

All blood samples were analyzed for hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), white blood cell count (WBC), counts of neutrophils, lymphocytes, monocytes, eosinophils, basophils, and platelets. The analysis was performed at the Department of Clinical Microscopy, Faculty of Allied Health Sci-

ences, Chulalongkorn University by an automated hematology analyzer (Technicon H*3 RTC).

All urine samples were analyzed for t, t-MA according to the modified method described by Lee, *et al*,[19] and creatinine levels using creatinine Liquicolor reagent kit (Human, Germany). The measurements were performed at a standard laboratory, Bangkok, Thailand. Acceptable limits for urinary creatinine concentrations were between 0.3 and 3.0 g/L according to the WHO guidelines.[20]

Statistical analyses

Data were analyzed by SPSS® ver 17.0 for Windows®. Continious dat were presented as mean±SD. The mean values of two groups were compared by *Student's t* test for independent variables. A p value <0.05 was considered statistically significant.

Results

The mean±SD of the measured parameters in gasoline workers are presented in Table 1 There were a negative correlation between urinary t, t-MA and both Hb and Hb (r = 0.281, p = 0.004) and Hct (r = 0.264, p = 0.007) (Table 2). Using a cut-off value of 0.5 mg/gCr (the ACGIH BEI level) for urinary t, t-MA level, workers with high level of urinary t, t-MA had a significantly (p<0.05) lower eosinophil counts than those with lower urinary t, t-MA (Table 3).

Discussion

The mean urinary t, t-MA level in the studied gasoline workers was 1.45 mg/gCr—2.9 times more than the upper limit of the ACGIH BEI level, which reflected gasoline workers are at high risk of benzene exposure. This is important as prolonged exposure to benzene may cause chronic bone marrow, hematological, and neurological toxic effects and cancer.[15,21,22] The agency for toxic substances and disease registry (ATSDR) have several cases

Table 2: Correlation between urinary t, t-MA level and and some hematological parameters

Parameter	r	p value
Hemoglobin (g/dL)	-0.281	0.004
Hematocrit (%)	-0.264	0.007
MCV (fL)	0.058	0.559
WBC (×10⁹/L)	0.037	0.714
Neutrophils (%)	0.151	0.130
Lymphocytes (%)	-0.097	0.333
Monocytes (%)	0.016	0.872
Eosinophils (%)	-0.122	0.222
Basophils (%)	0.029	0.774
Platelets (×10³/L)	0.106	0.291

Table 3: Mean±SD of some hematological parameters in gasoline workers with high and low urinary t, t-MA levels

Parameter	High urinary t, t-MA (>0.5 mg/gCr*) (n=67)	Low urinary t, t-MA (≤0.5 mg/gCr*) (n=35)
Hemoglobin (g/dL)	14.20±1.72	14.20±1.36
Hematocrit (%)	41.85±4.58	42.17±3.14
MCV (fL)	83.18±8.02	80.21±8.58
WBC (×10⁹/L)	7.90±1.72	7.77±1.36
Neutrophils (%)	53.58±11.13	51.14±9.47
Lymphocytes (%)	33.72±8.35	34.80±6.51
Monocytes (%)	5.78±1.64	5.66±1.42
Eosinophils (%)	5.09±4.26†	7.97±6.51
Basophils (%)	0.40±0.49	0.43±0.53
Platelets (×10³/L)	256.12±68.10	257.69±65.67

*Based on ACGIH BEI
†Significantly different from the low urinary t, t-MA group (p<0.05).

of well documented benzene toxicity and recommended monitoring benzene exposure for the at risk group.[23] Most of the studied hematological parameters of workers were within the reference range. However, the eosinophil count was a little bit higher than the upper limit of the normal range; the count was significantly lower in workers with high urinary t, t-MA than those with lower urinary t, t-MA (Table 3). Eosinophils are developed and matured in the bone marrow and involved in many biological processes.[24-26] The lower number of eosinophils in those with higher level of urinary t, t-MA may be due to the suppression of benzene on bone marrow.[15,27]

There was a significant ($p<0.01$) negative correlation between urinary t, t-MA level and Hb concentration and Hct ($p<0.01$) which supported some previous studies[28] but refute others.[29] There was no correlation between urinary t, t-MA level and MCV. In addition and were no correlation between urinary t, t-MA and white blood cell parameters or platelets count. Some researchers reported that the absolute lymphocytes count, platelet count, and red blood cell count, and Hct were decreased among exposed workers compared to controls.[30,31] Qu, *et al*,[32] showed a significant decrease in red blood cells, WBC, and neutrophil counts in those exposed to benzene as indicated by their levels of urinary metabolites (S-phenylmercapuric acid and t, t-MA acid). Tsai, *et al*, however, showed no adverse hematological effects after exposure to benzene.[33]

One of the limitations of this study included a lack of detailed exposure history in the studied workers. Furthermore, the low sample size of this study would have reduced the study power.

In conclusions, those exposed to benzene may develop bone marrow depression, as evidenced by drop in Hb and Hct in all workers; lower eosinophils counts in those with higher exposure to benzene (and higher urinary t, t-MA level). Nevertheless, it seems that WBC or platelets count are not sensitive indicators of benzene-induced hematotoxicity.

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Conflicts of Interest: None declared.

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