Effects of Benzene Exposure on Hematological Parameters Shoe-Manufacturing Workers in Bogor, West Java

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Abstract

Benzene is pollutant well-known to be a carcinogen. Recent studies have shown that low-level benzene exposure can affect the hematological system. The present study examined the relationship between low-level benzene inhalation exposure and neutrophil counts in shoe-manufacturing workers. Segmented-neutrophil counts were measured in blood samples from 78 benzene-exposed workers in Bogor.

Benzene exposure was measured according to S-phenylmercapturic acid (SPMA) concentrations in urine samples. Demographic data, exposure, and blood test data were analyzed using Pearson's chi-square test. The results showed that the average age of the study population was 29 years (range 18–56 years). The average SPMA concentration was 1.618 µg/g creatinine but the SPMA concentration varied considerably. No correlation was found between neutrophil counts and other characteristics of the subjects.

The odds ratios (ORs) indicates that the workers even with low SPMA concentrations were at risk of having abnormal segmented-neutrophil counts. The workers with fair SPMA concentrations were 4.5 times more likely to have abnormal segmented-neutrophil counts. These data suggest that low-level benzene exposure may be hemotoxic. A longitudinal study with direct measurements of workers' benzene exposure is needed to confirm the toxicity of low-level benzene exposure.

Clinical article (J Int Dent Med Res 2019; 12(2): 837-841)

Keywords: Benzene, Inhalation Exposure, S-phenyl-N-acetylcysteine, Neutrophils, Workers.

Received date: 11 February 2019 **Accept date:** 19 March 2019

Introduction

Benzene a pollutant of concern to public health because of it is a human carcinogen, as classified by the International Agency for Research on Cancer (IARC)[1]. Exposure to benzene can lead to problems in the hematopoietic system[2]. It is also a potent toxin, suppressing bone marrow, and accordingly, benzene exposure can lead to serious adverse hematological effects, such as pancytopenia and aplastic anaemia[3]. Benzene exposure can also cause abnormal blood-cell production in the bone marrow, which suppresses the production of red blood cells (RBCs), white blood cells (WBCs), and platelets[2].

Individuals may be exposed to benzene through inhalation, ingestion, or skin contact, but the main route of exposure is inhalation of contaminated air, which can reach benzene concentrations as high as 50%[2]. Environmental sources of benzene include vehicle-exhaust emissions, evaporation losses during handling, distribution and storage of petrol, and smoking tobacco[4,5]. Occupational exposure to benzene occurs primarily in the petrochemical industries (upstream and downstream), coke ovens and steel plants, chemical and associated industries (pharmaceutical, pesticide, lubricants, dyes, paints, soap), shoe manufacturing, and in laboratories[2]. Once absorbed into the body, benzene is distributed via the blood to fat tissue, bone marrow, and urine[6]. Then it metabolizes to benzene oxide before forming either S-phenylmercapturic acid (SPMA) or trans,trans-muconic acid (t,t-MA) in the liver and lungs[7]. SPMA and t,t-MA are the most commonly used biomarkers for occupational benzene exposure[8-10]. Urinary SPMA concentrations are the most sensitive biomarker to measure inhalational benzene exposure because they are not affected by other sources of exposure[11].

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As working conditions have gradually improved, the potential adverse effects from even lower benzene exposures have drawn increased attention. Neutrophil counts and average platelet volume have been reported to change with exposure to 7.8–8.2 ppm of benzene in the air[12]. Recently, studies have examined the effects of benzene at even lower concentrations of <1 ppm. RBCs, WBCs, and neutrophil counts were reported to be lower than normal at benzene concentrations of 0.25 ppm[13].

This study sought to examine the effects of occupational benzene exposure on the neutrophil counts in shoe-manufacturing workers.

Materials and methods

Ethics Statement

Written informed consent was obtained from subjects before enrollment. This study was approved by the Faculty of Public Health, Universitas Indonesia Ethics Committees No. 222/UN2.F10/PPM.00.02/2018.

Study Design & Population

This study was conducted in Sukajaya Village, Tamansari Sub-District, Bogor District, West Java, from March to May 2018 and had a cross-sectional design. The study population consisted of 78 workers from informal shoe-manufacturing workshops which have been exposed to inhalation benzene from using glue.

The informal shoe-manufacturing workshops had been in operation for at least 1 year and had at least five workers. The workers were male, ≥ 18 years old, and had worked in the same position at the workshop for at least 1 year. Questionnaires collected information regarding exposure history, medical history, lifestyle factors, occupational activities, and other personal information.

Benzene Exposure Assessment

A urine spot sample (20–50 ml) was collected at the end of a work shift. All samples were coded and stored in a cooler box. They were then delivered to the laboratory, where analyses were performed without knowledge of their origin. SPMA concentrations were then measured from the urine samples using liquid chromatography (LC)-MS/MS in the Regional Health Laboratory of DKI Jakarta.

Hematological Assessment

Blood samples were taken of approximately 3-mL-volume, were coded, and were delivered within 3 h after collection to the Regional Health Laboratory of DKI Jakarta for processing. The samples were maintained at room temperature for 30 min and were then mixed well for blood-cell counts. WBC counts were measured using a cell counter which was calibrated daily. Neutrophil counts were measured on the basis of the total-WBC counts and the differential counts.

Statistical Analysis

All analyses were performed with Mplus *Version 8.1*. The normality of the distributions was assessed by the Kolmogorov–Smirnov test. Demographics, exposure, and blood component variables were analyzed using Pearson's chi-square test for categorical variables. SPMA concentrations were categorized by quartile, whereas segmented-neutrophil counts were categorized by the standard.

Results

The average age of the study population was 29 years (range 18–56 years). The average SPMA concentration was 1.618 µg/g creatinine, and 68 workers were in the normal range of segmented-neutrophil counts. Most workers had been making shoes for 1–25 years working an average daily shift of 11.24 h per day (Table 1). These lifestyle factors are summarized in Table 1.

The workers had various SPMA concentrations, and only three workers had abnormal segmented-neutrophil counts and very high SPMA concentrations. Other characteristics and neutrophil counts were also analyzed by Pearson's chi-square correlations, but most subjects had normal segmented-neutrophil counts. Six workers who did not engage in regular sports activity had abnormal segmented-neutrophil counts. A person exposed to benzene can cause health problems, one of which is an abnormality of the number of neutrophils. Neutrophils are a type of white blood cell that forms in the bone marrow, which is a very important cell to fight infections - especially infections caused by bacteria.

Variables	n	%	Mean ± standard deviation	Minimum–Maximum
SPMA (µg/g creatinine)			1.618 ± 2.29	0.045–10.24
Very high (>1.843)	19	24.4		
High (0.6871–1.843)	20	25.6		
Fair (0.21176–0.6870)	20	25.6		
Low (<0.21175)	19	24.4		
Segmented-neutrophil counts (%)			65.81 ± 4.931	52.00–78.00
Abnormal	10	12.8		
Normal	68	87.2		
Age			29.88 ± 8.339	18–56
>29 years	36	46.2		
18–29 years	42	69.2		0
History of infection				
Yes	27	34.6		
No	51	65.4		
Body mass index				
Abnormal	24	30.8		
Normal	54	69.2		
Habitual sports				
Not regularly	25	32.1		
Regularly	53	67.9		
Daily duration of work			11.24 ± 1.974	6–16
>11 h	41	52.6		
≤11 h	37	47.4		
Years of work			6.74 ± 5.694	1–25
>5 years	33	42.3		
1–5 years	45	57.7		

Table 1. Descriptive Characteristics of the Study Subjects

No correlation was found between neutrophil counts and other characteristics. The odds ratios (ORs) indicate that workers with even low SPMA concentrations were at risk of having abnormal segmented-neutrophil counts. The workers with within-normal-range SPMA concentrations were at 4.5 times elevated risk of having abnormal segmented-neutrophil counts. Table 2 lists the Pearson's correlations between segmented-neutrophil counts and characteristics of the study subjects.

Discussion

In the present study, SPMA concentrations were measured as a biomarker of inhalational benzene exposure. SPMA concentrations can be measured in urine samples[14]. The American Conference of Governmental Industrial Hygienists (ACGIH) also recommends urinary SPMA as a biomarker to measure inhalational benzene exposure[15]. SPMA is a metabolite of benzene that enters the body through respiratory pathways at both high and low concentrations, though this metabolite is not affected by the benzene derived from sorbic acid in food[11].

Urine samples were obtained at the end of a work shift, under the assumption that this sample would indicate benzene exposure since the beginning of the workday and over the previous several days. The average SPMA concentration was 1.618 µg/g creatinine, and the lowest concentration was 0.045 µg/g and the highest was 10.24 µg/g. This value is still far below the threshold of the Biological Exposure Indices (BEI) recommended by the ACGIH (25 µg/g creatinine).

These results are in accordance with research on 110 petrochemical workers that showed an average SPMA concentration of 1.40 µg/L (µg/g creatinine)[16]. Another study focused on 158 Bulgarian petrochemical workers found an average SPMA concentration of only 0.24 µg/L (µg/g creatinine)[17].

These SPMA concentrations are also below the BEI limit recommended by ACGIH. The benzene exposure indicated by SPMA concentrations may be less than the BEI limit because it is set according to total benzene exposure, whereas SPMA only correlates to inhaled benzene[11]. A research conducted on Cibaduyut workers on shoe-manufacturing has an average urine SPMA concentration above the biological exposure index value (BEI)[22]. Thus, the presence of SPMA indicates that workers have been exposed to only small concentrations of benzene through inhalation.

The benzene concentration in the glue used by the shoe-manufacturing workshops was not measured in the present study. However, another study found that EHA-Bond and Gold Bond brands have benzene content of only 1.34%–1.52% while their toluene contents are 73.72% and 76.79%[18]. Both brands of glue were used in the shoe-manufacturing workshops in the Sukajaya Village, which indicate that the glue used in shoe manufacturing has only low concentrations of benzene.

Variables	Segmented neutrophil counts (%)				Total		Crude odds ratio (95% confidence interval)	p value
	Abnormal		Normal					
	n	%	n	%	n	%		
SPMA (μg/g creatinine)								
Very high (>1.843)	3	15.8	16	84.2	19	100	3.375 (0.318–35.789)	0.313
High (0.6871–1.843)	2	10.0	18	90.0	20	100	2.0 (0.166–24.069	0.585
Fair (0.21176–0.6870)	4	20.0	16	80.0	20	100	4.5 (0.455–44.546)	0.198
Low (<0.21175)	1	5.3	18	94.7	19	100	(Reference)	
Age								
>29 years old	4	11.1	32	88.9	36	100	0.75 (0.194–2.898)	0.745
18–29 years old	6	14.3	36	85.7	42	100		
History of infection								
Yes	2	7.4	25	92.6	27	100	0.43 (0.085–2.186)	0.48
No	8	15.7	43	84.3	51	100		
Body mass index								
Abnormal	3	12.5	21	87.5	24	100	0.959 (0.226–4.077)	1.0
Normal	7	13.0	47	87.0	54	100		
Habitual sports								
Not regularly	6	24.0	19	76.0	25	100	3.868 (0.981–15.247)	0.067
Regularly	4	7.5	49	92.5	53	100		
Daily duration of work								
>11 h	3	8.1	34	91.9	37	100	0.429 (0.102–1.797)	0.317
≤11 h	7	17.1	34	82.9	41	100		
Years of work								
> 5 years	2	6.1	31	93.9	33	100	0.298 (0.059–1.510)	0.177
1–5 years	8	17.8	37	82.2	45	100		

Table 2. Pearson's Chi-Square Correlations between Segmented-Neutrophil Counts and Characteristics of the Study Subjects

Neutrophils are the most abundant WBCs, and deficiencies in these cells, regardless of whether they are inherited or acquired, can lead to severe infections[19]. Studies have suggested that neutrophils are more sensitive to benzene exposure than lymphocytes[12,13]. In this study, most of the workers (87.2%) had normal segmented-neutrophil counts, but even low benzene exposure increased the risk of having a lower segmented-neutrophil count. The ORs indicate that workers with very high SPMA concentrations were at 3.375 times greater risk of having abnormal segmented-neutrophil counts, and workers with fair SPMA concentrations were approximately 4.5 times more likely to have abnormal segmented-neutrophil counts. This suggests that with low benzene exposure, as indicated by low SPMA concentrations, workers were at greater risk of having an abnormal segmented-neutrophil count.

SPMA concentrations can also be affected by benzene concentrations in the air[20]. The ventilation in the workshop space affects the benzene concentration in the air[21]. Some of the workshops have good ventilation systems, with doors always open, which should minimize benzene exposure. Despite that the workers experiences low benzene exposure to benzene as indicated by the SPMA biomarkers; the long-term accumulation of benzene exposure could eventually increase the workers' cancer risk[1]. Therefore, shoe-manufacturing workshops should have good air circulation with open windows and doors, even though the amount of benzene exposure is relatively low for industrial environments.

Conclusions

In summary, this study found that low-level benzene exposure may interfere with the production of segmented neutrophils. Although low-level benzene exposure may not cause serious diseases (e.g., aplastic anemia), evidence of adverse effects on the hematological system is increasing. Thus, the careful application of safety procedures in the work environment and health monitoring are needed for the long-term health of workers.

Declaration of Interest

The authors report no conflict of interest.

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