Conference Paper

Urinary S-Phenylmercapturic Acid (S-PMA) Level as Biomarkers of Exposure to Benzene in Informal Shoes Industrial Workers, Cibaduyut Bandung

Puri Wulandari, Bambang Wispriyono, Laila Fitria, Haryoto Kusnoputranto, Syafran Arrazy, and Bayu Rizki Sanjaya

Department of Environmental Health, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia

Abstract

Urinary S-PMA is a biomarker that is most specific and sensitive to benzene exposure at any concentrations because it is not influenced by the exposure of other substances. The objective of this study was to analyze the association between urinary SPMA and individual characteristics in workers exposed to benzene. This study used cross-sectional design in five informal shoes industry in Cibaduyut. Urinary S-PMA level in 60 workers was determined using LC-MS/MS and individual characteristics data were collected by interview using questionnaires. The association between urinary S-PMA level and individual characteristics were analyzed using correlation (age and working time) and independent T-test (type of job, working hours per day, smoking status, and alcohol intake). The urinary S-PMA level from 33% workers was above BEI ACGIH (>25 µg/g creatinine). Types of job and working hours per day showed significant associations with urinary S-PMA level (p-value 0.036 and 0.033, respectively). Therefore, workers' urinary S-PMA level indicates the presence of benzene exposure in the workplace.

Keywords: benzene; urinary S-phenylmercapturid acid; shoes industrial

Corresponding Author:
Bambang Wispriyono
bwispri@ui.ac.id

Received: 16 November 2017
Accepted: 15 December 2017
Published: 8 Januray 2018

Publishing services provided by Knowledge E

Selection and Peer-review under the responsibility of the ICGH Conference Committee.

1. INTRODUCTION

The development of informal shoes industry is growing very rapidly and chemicals such as organic solvents are used widely and freely. Organic solvents contained in shoe glue consist of benzene, xylene, ethyl benzene, toluene and n-hexane [13]. Benzene is one of the aromatic hydrocarbon compounds that have many uses for human life, especially for industries such as the rubber industry, oil refining, the footwear industry,

chemical industry, pharmaceutical industry, solvent paints, lubricants, detergents and pesticides, as well as components of crude oil [2, 3].

The use of benzene as a solvent in the industry both in developed countries and developing countries have started to be limited. This is because the benzene has effect of similar to human carcinogens [16–18]. However, occupational health problems have not been controlled, especially in developing countries [7, 12]. In addition, exposure to benzene is still found in air pollutants, such as burning wood/ forest, motor vehicle emissions, coal burning, smoke cigarettes, and gasoline fumes while charging at the fuel station [2, 11, 27]. Approximately 10 kg/ton benzene of manufacturing activity are released to the environment during production, distribution, and storage [5].

Workers exposed to benzene may be at risk of developing hematologic disorders [5, 21, 25, 30], cancers (such as acute and chronic lymphocytic leukemia, non-Hodgkin lymphoma, multiple myeloma, myelodysplastic syndrome and aplastic anemia) [4, 23, 29, 31, 33], chromosomal changes [37], as well as neurotoxicity disturbances [2]. The mechanism of the toxicity of benzene to produce immunotoxic effects may be associated with chromosomal damage, oxidative stress and DNA alteration [32]. Benzene can also damage the immune system by changing levels of antibody [28, 35].

Exposure to benzene is rapidly absorbed by the human body through the inhalation route, which makes exposure to benzene in the form of vapor the primary source of exposure [8]. In the process of metabolism in the liver, benzene produces some metabolites, i.e., phenol, catechol, hydroquinone, trans, trans-muconid acid (t.t-MA), and S-phenylmercapturic acid (SPMA) [19, 20]. Urinary SPMA is considered the most specific and sensitive biomarker for benzene exposure both at high and low concentrations because SPMA in urine is not influenced by other than exposure to benzene exposure than other benzene metabolites [14, 22, 26].

The level of individual susceptibility to exposure to benzene depends on the individual characteristics such as gender, age, smoking habits, lifestyle, working time, physical activity (exercise), nutrition status, health conditions, differences in the level of metabolism in the body, and working environment [24, 30]. Studies that measure the exposure through biomarker monitoring are important because biomarkers could describe the intensity of exposure during certain time intervals. Objectives of this study to analyze the correlation between urinary S-PMA level to the individual characteristics of workers.

2. METHOD

This study was conducted at five industries located in two areas, namely Bandung City (Cibaduyut Wetan and Cibaduyut Kidul Urban Villages) and Bandung Regency (Cangkuang Kulon and Sukamenak Villages). This study used cross sectional design and aimed to measure the level of benzene exposure, using urinary S-PMA level with individual characteristics. The selection of industry was based on inclusion criteria such as: industry had been established for minimum one year, had the number of workers of minimum 10 people, shoes making process was conducted in workplace or in industry owner house, not in workers' house. Study samples were then selected based on inclusion and exclusion criteria. Workers inclusion criteria were male, minimum age18 years, and not performing or receiving blood donors in the last one year. The exclusion criteria were refusal of urinary and/or blood sample collection, refusal of being interviewed, being ill (fever/influenza), being unavailable in workplace when the study was conducted, and urinary creatinine level was less than 30 mg/dL or more than 300 mg/dL.

Workers' urinary samples were collected once, which was in the end of working shift. Urinary SPMA level in 60 workers was determined by using LC-MS/MS [1]. Individual characteristic data (age, working time, working hours per day, type of job, smoking status and alcohol intake) were collected by interview. Bivariate data is analyzed by T-test and correlation. Differences were regarded as significant at $P < 0.05$. This study had passed ethical study procedure and was declared eligible to be conducted by Committee of Experts for Research and Ethics Research, Faculty of Public Health Universitas Indonesia on 1st June 2016, under the No. 170/UN2.F10/PPM.00.02/2016.

3. RESULTS

Urinary SPMA level showed the amount of exposure to benzene for each worker. Data of urinary S-PMA level of obtained workers were not normally distributed. Table 1 showed that mean of the urinary S-PMA level of the workers was 26.07 ± 40.57 µg/g creatinine standard deviation (Table 1).

According to Table 2, there was no significant association between urinary S-PMA level with the variables of age and working time. Variable of age and working time affected urinary S-PMA level by 1.8% and 5.0%, respectively. In Table 3, there was significant association between urinary S-PMA level with the type of job (p value 0.036) and working hours per day (p value 0.033).

Table 1: Descriptive Statistics of Urinary S-PMA Level.

Variable	Mean	Median	SD	Min-Maks	95% CI	n (%)
S-PMA level (µg/g creatinine)	26.07	10.54	40.57	0.18 - 211.82	15.59 – 36.55	
Variable	Mean	Median	SD	Min-Maks	95% CI	n (%)
>25 µg/g creatinine						20 (33.3)
≤ 25 µg/g creatinine						40 (66.7)

Table 2: Correlation Analysis of Urinary S-PMA Level with Benzene Concentration, Age and Working Time.

Variable	Mean	SD	r	P value
Age	36.92	12.55	0.133	0.311
Working time	13.80	12.89	0.223	0.087

4. DISCUSSION

Urinary S-PMA levels in the shoe industry workers were still below normal limits (<25 µg/g creatinine. Low levels of S-PMA urine might be due to the loss of compound due to the evaporation process or because of contamination. This not only occured in the measurement of S-PMA but also occurred in the other benzene metabolites (t, TMA,

Table 3: Independent Samples T Test Analysis Between Urinary S-PMA.

Level and Individual Characteristic					
Variable	N	Mean	SD	SE	p value
Type of job					
- Gluing	35	35.32	49.56	8.37	0.036
- Non-gluing	25	13.12	16.37	3.27	
Working hours per day					
- >8 hours	50	21.11	25.47	3.60	0.033
- ≤ 8 hours	10	50.88	80.24	25.37	
Smoking status					
- Yes	46	20.84	25.53	3.76	0.070
- No	14	43.25	69.27	18.51	
Alcohol intake					
- Yes	11	26.30	26.02	7.85	0.983
- No	49	26.02	43.38	6.19	

phenol, hydroquinone, catechol) during the measurement using urine samples [1]. The results of other studies in the shoe industry in China showed that workers exposed to high concentrations of benzene will have S-PMA levels >25 µg/g creatinine more than the workers exposed to benzene at low concentrations [22].

In this study there was no significant association between age and working time with urinary SPMA level. This is because urinary S-PMA level is also very influenced by life style, such as smoking habits seen by differences in smoking intensity and the number of cigarettes consumed per day and/ or alcohol intake [14, 34].

Other factors that affect urinary S-PMA level is the type of job and working hours per day. This type of job investigated in this study was workers gluing and workers non gluing. Gluing has higher risk of exposure to benzene because the job is widely using shoe glue, while non-gluing type is dealing more with administrative work. Most workers in the informal shoes industry work hours more than 8 hours per day, which result in workers spending more time in the workplace. This is because the manufacturer of shoes are employing handmade technique which takes longer time in the manufacturing process.

Other studies showed that urinary S-PMA level was significantly higher on workers who smoked than those who did not [14, 34]. However, this study showed that there was no difference between the mean of urinary SPMA level and smoking status. This was because all workers were placed in one room, so that workers who did not smoke might have had inhaled smoke from workers who smoked. Smoking can affect both S-PMA metabolites, t, t-MA, hydroquinone, catechol, and phenol. The metabolite levels can reach five times higher in smokers than non-smokers. Smoking can be considered as the main source of benzene intake. Among the chemical compounds contained in cigarette smoke, benzene is the most powerful leukemogenic agent [10].

Alcohol intake can affect urinary S-PMA level [6], but this study showed that no significant mean difference urinary S-PMA level between workers who consumed alcohol and those who did not. It might be because alcohol-consuming workers only drank occasionally.

Unlike smoking who was practiced daily, alcohol consumption was not routinely done.

Alcoholic drinks contain ethanol. When consumed, ethanol intake and exposure to benzene in the body result in the formation of liver isoenzymes of cytochrome P-450 (CYP2E1). As a result, ethanol can increase the toxicity of benzene by increasing the rate of formation of benzene metabolites [36].

5. CONCLUSION

Individual characteristics such as age and working time can affect urinary S-PMA level. Studies that measure the exposure through biomarker monitoring are important to do, because biomarkers could describe the intensity of exposure during certain time intervals. Urinary SPMA can be used for biological monitoring in the workplace environment, so as to minimize health risks in the work environment and to ensure safety for workers' health. Further researches can analyze the relationship between the levels of urinary S-PMA with occupational health due to benzene exposure.

ACKNOWLEDGMENT

We would like to thank this our research sponsor namely Direktorat Riset dan Pengabdian Masyarakat Universitas Indonesia (DRPM UI/ Directorate Research and Community Service, University of Indonesia) under the scheme Universitas Indonesia's Internationally-Index's Publication for Post Graduate Student Grant Research (Hibah Publikasi International Terindeks untuk Tugas Akhir Mahasiswa), 2016 No. 1961/ UN2.R12/HKP.05.00/2016.

References

[1] Arnold, S. M., J. Angerer, P. J. Boogaard, M. F. Hughes, R. B. O'Lone, S. H. Robison, and A. R. Schnatter. 2013. "The Use of Biomonitoring Data in Exposure and Human Health Risk Assessment: Benzene Case Study." Critical Reviews in Toxicology. 43 (2): 119–153.

[2] ATSDR (Agency for Toxic Sustances and Disease Registry). 2007. Toxicological Profile for Benzene. Atlanta,

[3] GA: US Departement of Human and Health Services. Available from http://www.atsdr.cdc.gov/toxprofiles/tp3-c8.pdf.

[4] Baan, R., Y. Grosse, K. Straif, B. Secretan, F. El Ghissassi, V. Bouvard, L. Benbrahim-Tallaa, N. Guha, C. Freeman, L. Galichet, V. Cogliano. 2009. A Review of Human Carcinogens. Part F. "Chemical Agents and Related Occupations." The Lancet Oncology. 10 (12): 1143–1144.

[5] Bahadar, H., S. Mostafalou, & M. Abdollahi. 2014. "Current Understandings and Perspectives on NonCancer Health Effects of Benzene: A Global Concern." Toxicology and Applied Pharmacology. 276 (2014): 83-94.

[6] Carrieri M, G. B. Bartolucci, M. L. Scapellato, G. Spatari, D. Sapienza], L. Soleo, P. Lovreglio, G. Tranfo, M. Manno, A. Trevisan. 2011. "Influence of Glutathione S-Transferases Polymorphisms on Biological Monitoring of Exposure to Low Doses of Benzene." Toxicology Letters. 213 (2012) 63– 68.

[7] Elci O. C., G. Yener, R. Ucku. 2007. "Working condition and related neuropsychatric problems among shoemakers in Turkey:Do child workers differ from others?." Occupational and Environmental medicine. 11 (1): 9–13.

[8] EPA (Environmental Protection Agency). 2002. Toxicological Review of Benzene (Noncancer Effects). [report no. EPA/635/R-02/001F]. Washington (DC): US Environmental Protection Agency.

[9] Available from http://www.epa. gov/iris/toxreviews/0276tr.pdf. [Accessed February 15, 2016].

[10] Fustinoni S, M. Buratti, L. Campo, A. Colombi, D. Consonni, A. C. Pesatori, M. Bonzini, P. Farmer, S. Garte, F. Valerio, D. F. Merlo, P. A. Bertazzi. 2005. "Urinary t,t-Muconic Acid, S-Phenylmercapturic Acid and Benzene as Biomarkers of Low Benzene Exposure." Chemico- Biological Interactions. 153–154: 253–256.

[11] Galbraith, D., S. A. Gross, D. Paustenbach. 2010. "Benzene and Human Health: A Historical Review and Appraisal of Associations with Various Diseases." Crit. Rev. Toxicol. 40 (Suppl. 2): 1–46.

[12] Abdallah H. M., A. S. Hussesin, N. M. A. Latif, J. S. Hussein, M. A. Hassanien. 2010. "Ventilatory function and oxidative-antioxidant Status in shoe makers." Researcher. 2 (4): 59–66.

[13] Hodgson, Ernest. 2004. A Textbook of Modern Toxicology Third Edition. New Jersey: John Wiley & Sons, Inc.

[14] Hoet P, E. D. Smedt, M. Ferrari, M. Imbriani, L. Maestri, S. Negri, P. D. Wilde, D. Lison, V. Haufroid. 2009.

[15] "Evaluation of Urinary Biomarkers of Exposure to Benzene: Correlation with Blood Benzene and Influence of Confounding Factors. International Archives of Occupational & Environmental Health." 82 (8): 985–995.

[16] Huff J. 2007. Benzene-induced cancers: "abridged history and occupational health impact." Int J Occup Environ Health. 13(2): 213–21.

[17] IARC (International Agency for Research on Cancer). 2012. "Complete List of Agents, Mixtures and Exposures Evaluated and Their Classification." International Agency for Research on Cancer, Lyon.

[18] Karakitsios, S.P., V. K. Delis, P. A. Kassomenos, G. A. Pilidis. 2007. "Contribution to Ambient Benzene Concentrations in the Vicinity of Petrol Stations: Estimation of the Associated Health Risk." Atmos. Environ. 41: 1889–1902.

[19] Kim S, R. Vermeulen, S. Waidyanatha, B. A. Johnson, Q. Lan, N. Rothman, M. T. Smith, L. Zhang, G. Li, M. Shen, S. Yin, S. M. Rappaport. 2006. "Using Urinary Biomarkers to Elucidate Dose-Related Patterns of Human Benzene Metabolism." Carcinogenesis. 27 (4): 772–781.

[20] Kim S, R. Vermeulen, S. Waidyanatha, B. A. Johnson, Q. Lan, M. T. Smith, L. Zhang, G. Li, M. Shen, S. Yin, N. Rothman, S. M. Rappaport. 2006. "Modeling Human Metabolism of Benzene Following Occupational and Environmental Exposures." Cancer Epidemiology Biomarkers &Prevention, 15 (11): 2246–52.

[21] Lan Q, L. Zhang, G. Li, R. Vermeulen, R. S. Weinberg, M. Dosemeci, S. M. Rappaport, M. Shen, B. P. Alter, Y. Wu, W. Kopp, S. Waidyanatha, C. Rabkin, W. Guo, S. Chanock, R. B. Hayes, M. Linet, S. Kim, S. Yin, N. Rothman, M. T Smith. 2004. "Hematotoxicity in Workers Exposed to Low Levels of Benzene." Science. 306 (): 1774–1776.

[22] Lv, B. H, S. Z. Song, Z. Zhang, Y. Mei, F. L. Ye. 2014. "Urinary S-phenylmercapturic Acid as a Key Biomarker for Measuring Occupational Exposure to Low Concentrations of Benzene in Chinese Workers: A Pilot Study: Erratum." Journal of Occupational and Environmental Medicine. 56 (3): 319-25.

[23] Mchale, C.M., L. Zhang, & M. T. Smith. 2012. "Current Understanding of The Mechanism of Benzene-

[24] Induced Leukemia in Humans: Implications for Risk Assessment." Carcinogenesis. 33 (2): 240–252. Pesatori A. C., S. Garte, T. Popov, T. Georgieva, T. Panev, M. Bonzini, D. Consonni, M. Carugno, B. D. Goldstein, E. Taioli, V. Fontana, E. Stagi, P. A. Bertazzi, D. F. Merlo. 2009. "Early Effects of Low Benzene Exposure on Blood Cell Counts in Bulgarian Petrochemical Workers." Med Lav. 100 (2): 83-90.

[25] Qu Q, R. Shore, G. Li, X. Jin, L. C. Chen, B. Cohen, A. A. Melikian, D. Eastmond, S. M. Rappaport, S. Yin, H. Li, S. Waidyanatha, Y. Li, R. Mu, X. Zhang, K. Li. 2002. "Hematological Changes among Chinese Workers with a Broad Range of Benzene Exposure." American Journal of Industrial Medicine. 42 (4): 275–285.

[26] Qu Q, R. Shore, G. Li, L. Su, X. Jin, A. A. Melikian, N. Roy, L. C. Chen, I. Wirgin, B. Cohen, S. Yin, Y. Li, R. Mu. 2005. "Biomarkers of Benzene: Urinary Metabolites in Relation to Individual Genotypes and Personal Exposure." Chemico-Biological Interactions. 153–154: 88-95.

[27] S. M. Rappaport, S. Kim, Q. Lan, R. Vermeulen, S. Waidyanatha, L. Zhang, G. Li, S. Yin, R. B. Hayes, N. Rothman, M. T. Smith. 2009. "Evidence That Humans Metabolize

Benzene via Two Pathways." Environmental Health Perpectives. 117 (6): 946-952.

[28] Ray, M.R., S. Roychoudhury, S. Mukherjee, T. Lahiri. 2007. "Occupational Benzene Exposure from Vehicular Sources in India and Its Effect on Hematology, Lymphocyte Subsets and Platelet PSelectin Expression." Toxicology and Industrial Health. 23 (3): 167-175.

[29] Richardson, D. B. 2008. "Temporal Variation in the Association between Benzene and Leukemia Mortality." Environmental Health Perpectives. 116 (3): 370-374.

[30] Schnatter, A. R., P. J Kerzic, Y. Zhou, M. Chen, M. J. Nicolich, K. Lavelle, T. W. Armstrong, M. G. Bird, L. Lin, H. Fu, R. D. Irons. 2010. "Peripheral Blood Effects in Benzene-Exposed Workers." ChemicoBiological Interactions. 184 (1-2): 174–181.

[31] Schnatter A. R., D. C. Glass, G. Tang, R. D. Irons, L. Rushton L. 2012. "Myelodysplastic Syndrome and Benzene Exposure among Petroleum Workers: An International Pooled Analysis." Journal of the National Cancer Institute. 104 (22): 1724–1737.

[32] Smith, M.T. (2010). "Advances in Understanding Benzene Health Effects and Susceptibility." Annual Review of Public Health. 31: 133–148.

[33] Strom, S. S., Y. Yamamura, H. M. Kantarijian, and J. E. Cortes-Franco. 2009. "Obesity, Weight Gain, and Risk of Chronic Myeloid Leukemia." Cancer Epidemiology, Biomarkers and Prevention. 18 (5): 1501–1506.

[34] Suna S., T. Hirao, F. Asakawa, T. Suzue, T. Mannami, F. Jitsunari. 2008. "Possible Sources of Urinary Benzene among Nonoccupationally Exposed Japanese Subjects." Toxicology and Industrial Health. 24: 155–160.

[35] Uzma N., B. S. Kumar, M. A. Hazari. 2010. "Exposure[Q1] to Benzene Induces Oxidative Stress, Alters the Immune Response and Expression of p53 in Gasoline Filling Workers." American Journal of Industrial Medicine. 00: 1-8.

[36] Wilbur S., D. Wohlers, S. Paikoff, L. S. Keith, O. Faroon. 2008. "ATSDR evaluation of potential for human exposure to benzene." Toxicology and Industrial Health. 24 (5-6): 399–442.

[37] Zhang L., C. M. McHale, N. Rothman, G. Li, Z. Ji, R. Vermeulen, A. E. Hubbard, X. Ren, M. Shen, S. M. Rappaport, M. North, C. F. Skibola, S. Yin, C. Vulpe, S. J. Chanock, M. T. Smith,Q. Lan. 2010. "Systems Biology of Human Benzene Exposure." Chemico-Biological Interactions. 184 (1-2): 86– 93.