ORIGINAL ARTICLE

Received: August 2016
Accepted: October 2016

Cancer Risk Analysis of Benzene and Ethyl Benzene in Painters

Bahram Harati[1], Seyed Jamaleddin Shahtaheri [2]*, Ali Karimi[1], Kamal Azam[3], Alireza Ahmadi[5], Maryam Afzali Rad[1], Ali Harati[6]

1. Department of Occupational Health Engineering, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
2. Department of Occupational Health Engineering, School of Public Health, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran.
3. Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
4. Department of Occupational Health Engineering, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
5. Department of Occupational Health Engineering, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.
6. Department of Occupational Health Engineering, School of Public Health, Islamic Azad University, Boroujerd Branch, Boroujerd, Iran.

***Corresponding Author:**
Seyed Jamaleddin Shahtaheri, Professor of Occupational Health Engineering, School of Public Health, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran.
Tel: (+98)2142933133
Email: shahtaheri@tums.ac.ir

BCCR
2016; 8(4): 22-28
www.bccrjournal.com

ABSTRACT

Background: Several effects of volatile organic compounds (VOCs) have been recognized such as toxic and carcinogenic human health effects. To evaluate cancer risk of benzenes, air samples were taken from the working environment of automobile painters in Tehran following inhalation exposure.

Methods: To perform this study, a cross-sectional study was performed in 2016. Sampling was carried out by active pump sampler using the NIOSH method 1501. A total of 40 samples of BTEX were analyzed by Gas Chromatography-Flame Ionization Detector (GC-FID). Finally, estimated terms of Chronic Daily Intake (CDI) was performed for cancer risk and Exposed Concentration (EC) for non-cancer.

Results: The 4-week average benzene, toluene, ethyl-benzene, and xylene exposure levels in exposed subjects were 0.775 ± 0.12, 1.2 ± 2.08, 45.8 ± 8.5, and 42.5 ± 23.9 ppm, respectively. The results of the study indicated that among all BTEX compounds, toluene had the lowest concentration. The mean cancer risk for workers exposed to benzene and ethyl benzene was estimated at 3.21×10-2 and 3.63×10-2, respectively. The non-carcinogenic risk of exposure to BTEX compounds was higher than the reference hazard level of one. Statistical tests showed a significant difference between concentrations of pollutant in the breathing zone of workers according to age and duration of employment (P<0.001).

Conclusion: This study suggests that exposed workers exposed workers are influenced the actual cancer and non-cancer risk (exposed to BTEX compounds) compared to those who were not exposed. Exposure to benzene and ethyl benzene would increase the risk of cancer in painters working in automobile manufacturing factories.

Keywords: Cancer risk, Compound BTEX, Automobile manufacturing, Painters

Introduction

Exposure to solvents occurs in a variety of workplaces and community settings, including oil refineries and petrochemical facilities, plastics manufacturing, paint manufacturing processes and building maintenance[1]. The importance of aromatic chemicals produced by anthropogenic activities in the workplace was recognized about 50 years ago[2]. Volatile organic compounds (VOCs) are present in the workplace and urban settings to parts per million (ppm) caused by gasoline evaporative emissions from different vehicles[3, 4]. VOCs such as benzene, toluene, ethyl benzene and xylene (BTEX) are considered as predominant pollutants in areas near the large cities and have adverse effects on both humans and the environment[3, 5]. The BTEX compounds can be emitted during various oil and paint activities processes[6-9]. BTEX can be produced by industries and are the most prevalent hazardous air pollutants in urban areas[10]. The BTEX compounds are carcinogenic and neurotoxic[11], classified as precedence pollutants ordered by the Environmental Protection Agency (EPA)[12]. [Benzene is widely used in the United States and ranks in the top 20 chemicals for production volume][13]. Benzene is an important environmental contaminant present worldwide[14]. Benzene is considered a carcinogenic substance, according to several international organizations, such as the International Agency of Research on Cancer (IRAC) (1982), American Conference of Governmental Industrial Hygienists (ACGIH) (2003) and EPA (2002). Benzene can also affect the hematopoietic system[15-17]. Although benzene is known to have toxic effects on the central nervous system (CNS) at high concentrations, chronic exposure to low concentrations of benzene can lead to adverse health effects such as decreased numbers of erythrocytes and leukocytes[15, 18, 19]. Toluene has adverse health effect and can affect the central nervous system. Ethyl benzene and xylene can have neurological effects[20, 21]. Natalie reported that ethyl benzene is a very ototoxic chemical[22]. More organizations worldwide suffer from a retract of chemicals in need of human health risk assessment[23]. In some instances, several governmental organizations have calculated cancer potency values for a certain chemical[24]. Health risk assessment for exposure to chemical substances is usually performed to evaluate the health damage[25]. For public health purposes, information of the relationship between exposure to chemical substances and their related health risk is essential[26]. The aim of this study was to conduct risk analysis for cancer and non-cancer of benzene, toluene, ethyl benzene, and xylene (BTEX) in an automobile manufacturing.

Methods

This was a cross-sectional study conducted in 2016 in an automobile manufacturing company . The study population consisted of 40 painters aged 25 to 54 years who were exposed over periods of 2 to 16 years. Consent form was completed for all participants before their participation in the research.

Sampling and analysis of BTEX

Sampling and analysis of BTEX compounds in air inhaled were carried out by NIOSH method number of 1501. A total of 40 samples were collected in the workplace. Air was aspirated at a known flow rate through the sampling tubes, containing activated coconut shell charcoal, to collect air samples in the workplace and ambient air. Low volume samplers were used for collecting samples at a flow rate of 100 mL/min. Pumps with stable low flow rates (10 to 200 mL/min) were preferable for long period sampling (up to 8 hours). After collection, cartridges were extracted with CS2 (2 mL). Chemical analyses were performed using VARIAN c-3800 gas chromatography (GC) coupled with FID. The maximum

concentrations of benzene, toluene, ethyl-benzene, and xylene in the working environment were 1.7, 8.7, 62, and 74 ppm, respectively. The period of exposure to BTEX ranged between 1 to 20 years.

Cancer and non-cancer risk calculation

The breathing zone exposures were estimated in terms of Chronic Daily Intake (CDI) (mg/kg/day) for cancer risk assessment using the equations below:

$CDI = (CA \times IR \times ET \times EF \times ED)/ (BW \times AT)$

$Cancer\ risk = CDI \times CSF_i$

CDI (mg/kg/day) = Chronic Daily Intake

CA (mg/m^3) = Contaminant Concentration in Air

IR (m^3/h) = Inhalation Rate (0.875 m3/h assumed for adult)

ET (h/day) = Exposure Time (8 h/day for workers)

EF (day/years) = Exposure Frequency (350 day/ years assumed for workers)

ED (years) = Exposure Duration (30 years for workers)

BW (kg) = Body weight (60.54 kg, average body weight of workers)

AT (day) = Averaging Time (70 years× 365 for cancer or ED × 365 for non-cancer)

CSF_i $(mg/kg/day)^{-1}$ = inhalation cancer slope factor

A cancer risk of $>10^{-6}$ was considered as carcinogenic effects of concern, a value $\leq 10^{-6}$ was considered as an acceptable level.

Exposed Concentration (EC) for non-cancer:

Risk assessment for non-cancer risk was expressed by Hazard Quotient (HQ) calculated according to the following equation:

$EC = (CA \times ET \times EF \times ED)/ AT$

$HQ = EC/ Rfc$

Rfc ($\mu g/m^3$ or ppb) = Represent exposure concentration

HQ>1 indicates adverse non-carcinogenic effects of concern and a value HQ of ≤1 was considered as an acceptable level.

Statistical analysis

The obtained data were analyzed using the statistical package for social science (SPSS) version 22. The mean concentration of pollutants in personnel and related standard threshold limit value (TLV) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) were compared using t-test. A p value <0.05 was considered as statistically significant.

Results

History of workers

Forty pollutants-exposed workers, aged 25 to 54 years (mean 34.22 ± 6.85), who were exposed over periods of 2 to 16 years (mean 6.9 ± 4.13), working 8-10 h/day, in the automobile manufacturing factories in Tehran, Iran were considered for evaluation. The information from workers is summarized in **Table 1.**

BTEX in breathing air zone

Forty air samples were collected from 20 painters (two samples from each painter). Duration of the time for taking all samples was 120 hours (3 hours per sample). These samples were collected during different working hours due to the different air pollution throughout a working shift. The 4-week average exposure levels of benzene, toluene, ethyl-benzene, and xylene in exposed subjects were 0.775±0.12, 1.2±2.08, 45.8±8.5 and 42.5±23.9 ppm, respectively (**Table 2**).

Comparing concentrations of BTEX to recommended standard level showed that the concentration of benzene in the breathing zone of painters was significantly higher than TLV-TWA recommended by ACGIH ($p<0.05$). The concentrations of toluene, ethyl-benzene, and xylene were lower than

Table 1. Demographic data of workers (n=40)

Variables		Frequency (percentage)	BMI	Marital status		Smoking status	
				Married	Single	Yes	No
Age group	20-29 years	11(27.5 %)	26.01±3.6	9(22.5%)	2(5%)	5(12.5%)	6(15%)
	30-39 years	17(42.5%)	24.73±3.1	16(40%)	1(2.5%)	6(15%)	11(27.5%)
	40-49 years	11(27.5%)	26.91±5.02	11(27.5%)	0(0%)	4(10%)	7(17.5%)
	Older than 50 years	1(2.5 %)	23.31	1(2.5%)	0(0%)	0(0%)	1 (2.5%)
Experience	Less than 5 years	18 (45 %)	24.89±3.5	15(37.5%)	3(7.5%)	9(22.5%)	9(22.5%)
	5-10 years	14 (35 %)	24.96±3.7	14(35 %)	0(0 %)	5(12.5%)	9(22.5%)
	10-15 years	7 (17.5 %)	29.05±3.7	7(17.5 %)	0(0 %)	0(0 %)	7(17.5%)
	15-20 years	1 (2.5%)	25.06	1(2.5%)	0(0 %)	1(2.5%)	0 (0 %)

Table 2. Exposure levels of BTEX by categories, in workers exposed to BTEX in Tehran, Iran

Duration of sampling	Benzene		Toluene		Ethyl-benzene		Xylene	
	Mean ±SD	Range	Mean ±SD	Range	Mean ±SD	Range	Mean ±SD	Range
Current day levels (ppm)	0.69±0.14	0.54 - 0.83	2.29±3.2	0.4 - 6.08	40.6±2.08	39 - 43	35.1±27.6	4.05 - 57
Four-week average (ppm)	0.775±0.12	0.54 - 0.86	1.2±2.08	0 - 6.08	45.8±8.5	39 - 60	42.5±23.9	4.05 - 67

the standard level of TLV-TWA recommended by ACGIH. The results demonstrated the statistically significant difference between the concentrations of benzene in the breathing zone of workers and the permitted levels of 0.5 ppm (P=0.004) (**table 3**).

Cancer risk and non-cancer assessment

Cancer risk assessment of automobile manufacturing factories painters was determined using the Chronic Daily Intake (CDI) for cancer and Exposed Concentration (EC) for non-cancer. The mean cancer risk for workers exposed to benzene and ethyl benzene was estimated to be 3.21×10-3 and 3.63×10-2 respectively (**Table 4**). The CDIs for benzene and ethyl benzene were 0.1176 and 9.450 mg/kg/day, respectively. The ECs for benzene, toluene, ethyl benzene, and xylene were 8.136, 14.86, 653.81 and 606.73 mg/m3, respectively. The cancer risks for benzene and ethyl benzene in painters in automobile manufacturing factories were above the acceptable limit of 10-6. The non-cancer risks of workers' exposure to BTEX compounds for benzene, toluene, ethyl benzene, and xylene were ratios of 271.23, 3.112, 6538.1 and 768.01, respectively.

Discussion

Occupational exposures occur in manufacturing industries, such as rubber production, shoe manufacturing, and painting, which use aromatic solvents, containing benzene[1, 27-30]. The distribution of BTEX from automobile manufacturing factories to the workplace mainly depends on the vapor pressure of substances. The result of this study indicated that lower concentration of BTEX attributed to in the breathing zone of workers, toluene concentration detected . The concentration of benzene in breathing zone of painters (0.775 ppm) was higher than the standard level recommended by ACGIH. However,

Table 3. Concentration of BTEX among painters comparison to TLV-TWA (ACGIH)

BTEX compounds	Concentrations ppm (Mean ±SD)	TLV-TWA (ACGIH) (ppm)	P-value
Benzene	0.775±0.12	0.5	0.004
Toluene	1.2±2.08	50	0.0001
Ethyl benzene	45.8±8.5	100	0.0001
Xylene	42.5±23.9	100	0.0001

Table 4. Average life time cancer risk and hazard quotients (HQ) assessments among painters

BTEX compounds	EC (mg/m3)	Non-cancer risk (HQ)	CSFi (mg/kg/day)-1	CDI (mg/kg/day)	Cancer risk
Benzene	8.136	271.23	2.73×10-2	0.1176	3.21×10-3
Toluene	14.86	3.112	-	-	-
Ethyl benzene	653.81	6538.1	3.85×10-3	9.450	3.63×10-2
Xylene	606.73	768.01	-	-	-

concentrations of other pollutants in the breathing zone of painters were lower than the standard level. While, other concentration of pollutant in the breathing zone of painters were lowers than the standard level. A few studies have indicated that benzene is the fundamental component of volatile organic compounds[21,31]. According to this study, the cancer risk of benzene exposure in the breathing zone was higher than the acceptable level of 10-6. Risk assessment is determined as characterization of potential harmful health effects of workers' exposures to different chemical substances[32]. Some studies have been conducted on the assessment risk for cancer[33, 34]. Tunsaringkarn reported that the average lifetime cancer risk of benzene and formaldehyde was higher than the acceptable level of 10-6[31]. Exposure to high concentrations of benzene may have adverse effect for a long-term[21]. Exposure to benzene causes several adverse effects, including decreased numbers of erythrocytes and leukocytes, which is usually found to be the result of aplastic anemia[35- 39]. The International Agency for Research on Cancer (IARC) has reported that exposure to pure benzene or benzene- containing mixtures possibly results in adverse effects on the hematopoietic system[40]. According to this study, cancer risk of ethyl benzene exposures was higher than the acceptable level of 10-6. Nevertheless, Tunsaringkarn reported that cancer risk for exposure to ethyl benzene was in the acceptable range in a gasoline station[21]. The non-carcinogenic risk of exposure to BTEX compounds in the breathing zone was higher than the hazard level of one. This shows that BTEX compounds may possibly have adverse health effects. This study suggests that these workers (exposed to BTEX compounds) are susceptible to actual cancer and non-cancer risk compared to those who are not exposed. The advantages of this study are using rank and prioritizing risks of contaminants in the breathing zone of automobile manufacturing workers. This research demonstrated that, cancer risk analysis can provide valuable information on prevention and control procedures in place. Therefore, in order to control higher exposure to pollutants, alternative methods and management control are recommended.

Acknowledgement

The authors thank the Department of Health Safety Environment (HSE) of automobile manufacturing for supporting this study.

References

1. Jafari MJ, Karimi A, Rezazadeh Azari M. The challenges of controlling organic solvents in a paint factory due to solvent impurity. Industrial health. 2009;47(3):326-32.

2. Tiwari V, Hanai Y, Masunaga S. Ambient levels of volatile organic compounds in the vicinity of petrochemical industrial area of Yokohama, Japan. Air Quality, Atmosphere & Health. 2010;3(2):65-75.

3. Eisaei HR, Dehrashid A, Shaho S, Khani MR, Hashemi SM. Assessment and control of VOCs emitted from gas stations in Tehran, Iran. Pollution. 2015;1(4):363-71.

4. Singh A, Tomer N, Jain C. Monitoring, assessment and status of benzene, toluene and xylene pollution in the urban atmosphere of Delhi, India. Res J Chem Sci. 2012;2(4):45-9.

5. Franco M, Chairez I, Poznyak T, Poznyak A. BTEX decomposition by ozone in gaseous phase. J Environ Manage.2012;95 Suppl:S55-60.

6. Hippelein M. Background concentrations of individual and total volatile organic compounds in residential indoor air of Schleswig-Holstein, Germany. J Environ Manage.. 2004;6(9):745-52.

7. Roberts SM, James RC, Williams PL. Principles of toxicology: environmental and industrial applications: John Wiley & Sons; 2014.

8. Vainiotalo S, Peltonen Y, Ruonakangas A, Pfäffli P. Customer exposure to MTBE, TAME, C6 alkyl methyl ethers, and benzene during gasoline refueling. Environ Health Perspect. 1999; 107(2): 133–40.

9. Zhao P, Cheng YH, Lin CC, Cheng YL. Effect of resin content and substrate on the emission of BTEX and carbonyls from low-VOC water-based wall paint. Environ Sci Pollut Res Int. 2016;23(4):3799-808.

10. Mohamed MF, Kang D, Aneja VP. Volatile organic compounds in some urban locations in United States. Chemosphere.

2002;47(8):863-82.
11. Dean BJ. Recent findings on the genetic toxicology of benzene, toluene, xylenes and phenols. Mutat Res. 1985;154(3):153-81.
12. Yadav J, Reddy C. Degradation of benzene, toluene, ethylbenzene, and xylenes (BTEX) by the lignin-degrading basidiomycete Phanerochaete chrysosporium. Appl Environ Microbiol. 1993;59(3):756-62.
13. Smith MT. Advances in understanding benzene health effects and susceptibility. Annu Rev Public Health. 2010;31:133-48 2 p following 148.
14. Rappaport SM, Kim S, Lan Q, Li G, Vermeulen R, Waidyanatha S, et al. Human benzene metabolism following occupational and environmental exposures. Chem Biol Interact. 2010 19;184(1-2):189-95.
15. ATSDR U. Toxicological Profile for Benzene. US Department of Health and Human Services, Agency for Toxic Substances and Disease Registry, Atlanta, GA. 2007.
16. Hayes RB, Dosemeci M, Wacholder S, Travis LB, Rothman N, Hoover RN, et al. Benzene and the dose-related incidence of hematologic neoplasms in China. J Natl Cancer Inst. 1997;89(14):1065-71.
17. Winder C, Stacey NH. Occupational toxicology: CRC Press; occupation toxicology 2nd Edition, Boca Raton London New York Washington, D.C., 2004.
18. Nordlinder R, Ramnäs O. Exposure to benzene at different work places in Sweden. Ann Occup Hyg. 1987;31(3):345-55.
19. Zhang L, Eastmond DA, Smith MT. The nature of chromosomal aberrations detected in humans exposed to benzene. Crit Rev Toxicol. 2002;32(1):1-42.
20. Dennison JE, Bigelow PL, Mumtaz MM, Andersen ME, Dobrev ID, Yang RS. Evaluation of potential toxicity from co-exposure to three CNS depressants (toluene, ethylbenzene, and xylene) under resting and working conditions using PBPK modeling. J Occup Environ Hyg. 2005;2(3):127-35.
21. Tunsaringkarn T, Siriwong W, Rungsiyothin A, Nopparatbundit S. Occupational exposure of gasoline station workers to BTEX compounds in Bangkok, Thailand. Int J Occup Environ Med. 2012;3(3):117-25.
22. Cappaert NL, Klis SF, Baretta AB, Muijser H, Smoorenburg GF. Ethyl benzene-induced ototoxicity in rats: a dose-dependent mid-frequency hearing loss. J Assoc Res Otolaryngol. 2000;1(4):292-9.
23. Moffat I, Chepelev NL, Labib S, Bourdon-Lacombe J, Kuo B, Buick JK, et al. Comparison of toxicogenomics and traditional approaches to inform mode of action and points of departure in human health risk assessment of benzo [a] pyrene in drinking water. Crit Rev Toxicol. 2015;45(1):1-43.
24. Lloyd AC, Denton JE. Technical Support Document for Describing Available Cancer Potency Factors. Secretary for Environmental Protection, California Environmental Protection Agency, 2005.
25. Edokpolo B, Yu QJ, Connell D. Health Risk Assessment for Exposure to Benzene in Petroleum Refinery Environments. Int J Environ Res Public Health. 2015;12(1):595-610.
26. Fromme H, Albrecht M, Angerer J, Drexler H, Gruber L, Schlummer M, et al. Integrated Exposure Assessment Survey (INES): exposure to persistent and bioaccumulative chemicals in Bavaria, Germany. Int J Hyg Environ Health. 2007;210(3):345-9.
27. Verma DK, Tombe Kd. Benzene in gasoline and crude oil: occupational and environmental implications. AIHA J (Fairfax, Va). 2002;63(2):225-30.
28. Wang L, Zhou Y, Liang Y, Wong O, Armstrong T, Schnatter AR, et al. Benzene exposure in the shoemaking industry in China, a literature survey, 1978–2004. Regul Toxicol Pharmacol. 2006;46(2):149-56.
29. Weisel CP. Benzene exposure: an overview of monitoring methods and their findings. Chem Biol Interact. 2010;184(1):58-66.
30. Williams PR, Robinson K, Paustenbach DJ. Benzene exposures associated with tasks performed on marine vessels (circa 1975 to 2000). J Occup Environ Hyg. 2005;2(11):586-99.
31. Tunsaringkarn T, Prueksasit T, Kitwattanavong M, Siriwong W, Sematong S, Zapuang K, et al. Cancer risk analysis of benzene, formaldehyde and acetaldehyde on gasoline station workers. J Environ Engin Ecol Sci. 2012;1(1):1.
32. Staff NRC. Risk assessment in the federal government: managing the process: National Academies Press; 1900.
33. Guo H, Lee S, Chan L, Li W. Risk assessment of exposure to volatile organic compounds in different indoor environments. Environ Res. 2004;94(1):57-66.
34. Morello-Frosch RA, Woodruff TJ, Axelrad DA, Caldwell JC. Air toxics and health risks in California: the public health implications of outdoor concentrations. Risk Anal. 2000;20(2):273-92.
35. Bogadi-Šare A, Zavalić M, Turk R. Utility of a routine medical surveillance program with benzene exposed workers. Am J Ind Med. 2003;44(5):467-73.
36. Fishbeck WA, Townsend JC, Swank MG. Effects of chronic occupational exposure to measured concentrations of benzene. J Occup Med. 1978;20(8):539-42.
37. Liu CS, Tsai JH, Kuo SW. Comparisons of Complete Blood Counts and Urinary Benzene Metabolites After Exposure to Benzene. Mid Taiwan J Med. 2000;5(4):235-42.
38. Neghab M, Rahimian JT, Jahangiri M, Karimi A, Nasiri G, Aghabeigi M, et al. Evaluation of hematotoxic potential of benzene, toluene, xylene, ethyl benzene and n-hexane in petrochemical industries. Safe Prom Inj Prev. 2015;2(4):293-302.
39. Schnatter AR, Kerzic PJ, Zhou Y, Chen M, Nicolich MJ, Lavelle K, et al. Peripheral blood effects in benzene-exposed workers. Chem Biol Interact. 2010;184(1):174-81.
40. Huff J. Benzene-induced cancers: abridged history and occupational health impact. Int J Occup Environ Health.. 2007;13(2):213-21.