

Neurological Symptoms of Occupational Exposure to Toluene and Xylene.

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Abstract

The neurological symptoms of simultaneous exposure to toluene and xylene were investigated in a group of 78 paint workers. According to the low and high urinary hippuric and methylhippuric acids, three methods were used to determine the general characteristics of subjects, subjective symptoms and the risk of developing such symptoms from chemicals. Since, considering one chemical exposure gave deviated results, the simultaneous exposure of toluene and xylene resulted in more reliable outcomes.

Key words : Hippuric acid, methylhippuric acid, neurological symptoms, toluene, xylene

บทคัดย่อ

การศึกษาอาการทางระบบประสาทที่เกิดจากการได้รับโทลูอีนและไซลีนในคนงานผลิตสีจำนวน 78 คน จากการเก็บปัสสาวะ และสัมภาษณ์อาการทางระบบประสาทตลอดจนข้อมูลทั่วไปของกลุ่มตัวอย่าง พบว่ามีการขับถ่าย ฮีพพิวริก และ เมทิลฮีพพิวริก ในปัสสาวะระดับต่าง ๆ กัน การวิเคราะห์ได้จัดกลุ่มตัวอย่างออกเป็น 3 รูปแบบ ตามความเข้มข้นของฮีพพิวริก และ เมทิลฮีพพิวริก จากการศึกษาพบว่าในโรงงานมีสารเคมีหลายชนิดที่เกิดจากกระบวนการผลิต และคนงานก็ได้รับสารเคมีเหล่านั้น ดังนั้นถ้าผู้วิจัยสนใจศึกษาสารเคมีเพียงชนิดเดียวจะได้ผลของอาการทางระบบประสาทที่เกิดจากการสัมผัสสารที่ศึกษาลดเคลื่อนจากความเป็นจริง

คำสำคัญ : กรดฮีพพิวริก, กรดเมทิลฮีพพิวริก, อาการทางระบบประสาท, โทลูอีน, ไซลีน

Introduction

Toluene and xylene have been widely used as solvents and their health effects were recognized as acute and chronic neurological symptoms of the central nervous system (Sullivan and Ert, 1991). Toluene and xylene are absorbed through the lungs and the skin, metabolized and excreted mainly as hippuric and methylhippuric acids, respectively in urine (Dossing *et al.*, 1983). Coexposure of these two solvents are very common in the industry (Huang *et al.*, 1994).

The objective of this study is to investigate the neurological symptoms of simultaneous exposure to toluene and xylene in both exposed and non-exposed workers in two paint factories. There were three methods used for grouping 78 workers according to their urinary levels of hippuric and/or methylhippuric acids and the adjusted odds ratio of developing neurological symptoms among these three groups were assessed and compared.

Material and method

A cross-sectional study of exposed workers to toluene and xylene was undertaken in two paint manufacturing factories. Urine samples of 78 exposed and non exposed workers, were collected before shift on the first working day and at the end of shift on the second working day. Urine specimens were frozen and subsequently analyzed for hippuric acid (HA), ortho, meta, para-methylhippuric acid (MHA) and creatinine. The method of Carvelho et al. (1991) was modified for the determination of HA and MHA concentrations by a gas-liquid chromatography (Shimadzu, model GC-14B, Japan) using a DBTM-1 capillary column (30 m x 0.53 mm I.D., J&W Scientific, Folsom, California, USA.) and a flame ionization detector with an oven temperature of 200 °C, injector and detector temperature of 250 °C and a flow rate of 10 ml/min helium. The creatinine level was determined by Jaffe reaction as adopted by Palanuvej (1988).

All workers were interviewed by trained graduate students using a questionnaire designed to determine general characteristics of the subjects and subjective symptoms. The general characteristics contain a detail information on sex, age, working duration, marital status, education, alcohol consumption, smoking, proximity of residence to place using toluene or xylene and the use of personal protective equipment (PPE). The subjective symptom questionnaire was modified from Hogstedt et al. (1984) which were separated into two sections. The first section contains a review of 17 symptoms occurring anytime in the previous month and the second section contains 8 symptoms existing while working at the same period of time.

Three methods were used to categorized 78 workers according to their urinary hippuric and/or methylhippuric acids level at the end of shift. The first method used levels of urinary hippuric acid to divide workers into two groups; the first group (n=15) had hippuric acid level more than 1.6 g/g creatinine (ACGIH, 1998)(High HA) and the second group (n=63) had hippuric acid level less than or equal to 1.6 g/g creatinine (Low HA). In the second method, workers were divided into a group (n=48) having methylhippuric acid (MHA) and another group (n=30) not having methylhippuric acid (No MHA) in urine. The third method divided the 48

workers having urinary methylhippuric acid (MHA) into two groups, the first group (n=13) had hippuric acid level more than 1.6 g/g creatinine (MHA+High HA) and the second group (n=35) had hippuric acid level less than or equal to 1.6 g/g creatinine (MHA+Low HA). The adjusted odds ratio of neurological symptoms among paint workers with high urinary metabolite levels over those with low urinary metabolite levels were analyzed by logistic regression on the IBM compatible personal computer using SPSS/PC⁺ software. Chi-square was also used to analyze the data.

Results

The general characteristics of 78 subjects were summarized in terms of sex, age, working duration, education, illness with medication, alcohol consumption, smoking, proximity of residence to a place using toluene or xylene and the PPE used in table 1.

Table 1 The general characteristics of 78 subjects.

Variables	Total	Method #1		Method #2		Method #3	
		Low HA	High HA	No MHA	MHA	MHA+ Low HA	MHA+ High HA
N	78	63	15	30	48	35	15
Sex(male/female)	52/26	49/14*	3/12	23/7	29/19	27/8*	2/13
Age, years (SD)	31.8 (7.2)	30.7 (6.0)	36.3 (1.0)	31.1 (5.5)	32.2 (8.2)	30.5 (6.5)	36.8 (10.5)
Working duration, months	67.9 (62.2)	54.5 (36.6)	124.5 (105.3)	52.0 (44.5)	77.9 (69.7)	55.9 (27.9)	137.2 (107.6)
%Education (\leq 12 years)	73.1	68.3	93.3	40.0	93.8	91.4	100
%Illness with medication	17.9	17.5	20.0	23.3	14.6	11.4	23.1
%Alcohol consumption	58.4	62.9	40.0	56.7	59.6	65.7	38.5
%Smoking	29.5	34.9	6.7	33.3	27.1	34.3	7.7
%Living close to sources	12.8	14.3	6.7	16.7	10.4	11.4	7.7
%PPE used	40	48.3*	6.7	22.2*	50.0	68.6*	0

* p<0.05

In method #1, subjects in low HA group were significantly different from those in high HA group in sex and %PPE used. For method #2, subjects without MHA and with MHA in urine were not statistically different except for PPE used. In method #3, Those two groups (MHA+Low HA and MHA+High HA) were significantly different for sex and PPE used. In method #1 and #3, it is interesting to note that subjects with low level of urinary metabolites wore PPE greater and had shorter working duration than those with high level of urinary metabolites.

Table 2 Urinary hippuric and methylhippuric acids in workers in these three methods.

Method no.	Group	HA (g/g creatinine)		MHA (g/g creatinine)	
		Mean (SD)	Range	Mean (SD)	Range
Method #1	Low HA	0.69(0.44)	0.0-1.58	0.06(0.08)	0.0-0.38
	High HA	2.87(0.91)	1.66-4.63	0.29(0.44)	0.0-1.82
Method #2	No MHA	0.64(0.52)	0.0-2.17	0.0(0.0)	0.0
	MHA	1.40(1.15)	0.12-4.63	0.17(0.26)	0.01-1.82
Method #3	MHA+Low HA	0.81(0.45)	0.12-1.58	0.11(0.08)	0.01-0.38
	MHA+ High HA	3.01(0.90)	1.66-4.63	0.33(0.45)	0.11-1.82

Considering the levels of urinary hippuric and /or methylhippuric acids in these three methods (Table 2), the results showed that workers had low urinary hippuric acid would also have low level of methylhippuric acid and those having high urinary hippuric acid would have high level of urinary methylhippuric acid.

Subjective symptoms included in the questionnaire consisted of 17 and 8 neurological symptoms occurring anytime and at work respectively in the previous month of the interview. After controlling for age, sex, illness, alcohol consumption, smoking, living close to source of toluene and xylene, PPE used and number of hour sleep, the adjusted odds ratio were rather high for headache, tired, irritation and loss of muscle strength. Considering only toluene exposure in method #1, the adjusted odds ratio of neurological symptoms of workers with high urinary HA over those with low urinary HA were significantly different for irritation and loss of muscle strength in legs or feet. The risk of developing irritation and loss of muscle strength in legs or feet for workers with high urinary HA was 10.3 and 11.5 times of those with low urinary HA respectively. For method #2, the adjusted odds ratio of workers exposed to xylene

(methyhippuric acid detected in urine) developed loss of muscle strength in legs or feet was 6.3 times of those without xylene exposure (methylhippuric acid not detected in urine). In method #3, coexposure of toluene and xylene led to very high adjusted odds ratio of 74.18 for loss of muscle strength in legs or feet, 10.2 for loss of muscle strength at work and 6.97 for irritation probably due to accumulation of toluene and xylene after long term exposure.

Table 3 Adjusted odds ratio of neurological symptoms among paint workers with high urinary metabolite levels over those with low urinary metabolite levels.

Symptom	Method #1	Method #2	Method #3
	OR (SE)	OR (SE)	OR (SE)
Headache	0.766 (0.923)	2.237 (0.692)	1.214 (1.157)
Irritation	10.271* (1.109)	1.031 (0.612)	6.976* (1.333)
Loss of muscle strength in legs or feet	11.481* (1.940)	6.266* (1.486)	74.18* (3.770)
Symptoms at work			
- Headache	2.660 (0.974)	0.691 (0.666)	0.2060 (1.458)
- Tired easily	1.706 (0.861)	0.415 (0.650)	3.5492 (1.358)
- Irritation	2.924 (1.032)	1.096 (0.647)	2.722 (1.596)
- Loss of muscle strength	2.408 (1.311)	1.096 (0.647)	10.310* (2.935)

* p < 0.05

Discussion

Evaluation of paint workers exposed to several kinds of solvents especially toluene and xylene was investigated. When considering only toluene exposure, the symptoms associated with urinary hippuric acid were statistically significant for irritation and loss of muscle strength in legs or feet. If the exposure was confined to xylene, the symptoms associated with xylene exposure was significant only for loss of muscle strength in legs or feet. However, paint workers are exposed to toluene and xylene simultaneously. When considering coexposure of toluene and xylene, workers having MHA and high level of HA in urine had significant greater risk of

irritation, loss of muscle strength in legs or feet and, loss of muscle strength at work than those having MHA and low level of HA in urine.

When considering only toluene exposure, worker exposed to high level of toluene would also exposed to high level of xylene and eventually had high levels of urinary hippuric and methylhippuric acids. On the other hand, regarding xylene exposure, those exposed to xylene would also exposed to toluene simultaneously and might have high levels of those two metabolites. Therefore, the study of workers exposure to more than one chemical simultaneously should consider the risk of developing neurological symptoms from all chemicals involved and other variables affected to the outcome at the same time to get reliable results.

This study may have deviations due to the following reasons:

1. Subjects were categorized into subgroups according to their urinary hippuric and/or methylhippuric acids at the end of shift; therefore, number of subjects in each subgroup could not arrange to have similar number.
2. All subjects have their plan, schedule and frequency of work followed the schedule set forth by a foremen; sample collection and interview of subject may have influence on their work.
3. The neurological symptoms used are not specific to toluene and xylene exposure and could occur from other courses.

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