HIGH LEVELS OF HIPPURIC ACID IN THE URINE OF THAI PRESS WORKERS

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Abstract. Toluene is an important toxic volatile agent found in many modern industrial processes. Toluene exposure is of particular concern because of the ongoing exposure of thousands of workers in industrial plants and recent research has indicated that toluene/exposure can result in chronic toxicity. The monitoring and control of toluene exposure among at-risk workers is necessary. Urine hippuric acid determination is a helpful test monitoring groups of at-risk workers. In this study, urine samples were obtained from 20 control subjects and 48 press workers from a factory in Bangkok. Each subject gave a specimen of urine; each specimen was analyzed for hippuric acid level by the Ohmori method. The average urine hippuric acid level in the control group was 0.23 ± 0.15 mg/gCr (range = 0.05 - 0.58 mg/gCr) while that of the experimental group was 0.37 ± 0.37 mg/gCr (range = 0.06 - 0.18 mg/gCr). A significant higher urine hippuric acid level among the press workers was found (p = 0.03). Based on this study, the prevention of exposure to toluene among high-risk workers is recommended.

INTRODUCTION

Volatile solvent, particularly toxic agent such as benzene and toluene, constitute significant potential threats to human health in both occupational and environmental settings. Toluene is a common toxic volatile substance, found in many industrial processes in the present day. It is deemed a hazardous chemical agent and human pollutant.

Toluene exposure is of particular concern: thousands of workers in the industrial plants are at risk of developing the central nervous system depression and memory impairment that are associated with asymptomatic exposure (Hayden *et al*, 1977). Symptoms, if they occur, include headache, dizziness, fatigue, muscular weakness, drowsiness, poor co-ordination, a staggering gait, paresthesia, collapse, and coma (Hayden *et al*, 1977).

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Toluene can be measured in the blood, although blood levels are not widely used as the biomarker for toluene exposure because they decline very rapidly after exposure has ended; the initial half-life of toluene is 2-3 hours (Carlsson, 1982; Ikeda, 1999). Hippuric acid, the major metabolite of toluene, can be recovered from urine; determination of the urine hippuric acid level allows the monitoring of at-risk groups of workers (Hjelm *et al*, 1988; Inoue *et al*, 1997; Alvarez-Leite *et al*, 1999). Lauwerys and Buchet (1988) proposed that 2.5 grams of hippuric acid per gram of creatinine in urine be the maximum permissible level to be applied in the screening of workers. In developing countries, awareness of the public health impact of exposure to volatile solvents is growing, although few of these countries have introduced policies and regulations that combat the problem effectively. Owing to the recent industrialization of Thailand, a developing country in Southeast Asia, many occupations are now at-risk of exposure to volatile solvent.

Surprisingly, there have been no report

about monitoring of toluene exposure among high-risk workers in Thailand. A number of occupational group as press workers, are at-risks; these workers have direct contact with toluene in the course of their daily work and specific control measures have yet to be established in Thailand. This pilot study aimed to determine the difference between the urine hippuric acid level of non-exposed subjects and that of press workers.

MATERIALS AND METHODS

Subjects

Sixty-eight healthy subjects were included in this study. The first study group was of 48 press workers from a factory in Bangkok. These workers required to work everyday. The second control group was of 20 subjects who were at low risk of toluene exposure. All were residents in an area free of any nearby factories; all were interviewed about possible exposure to toluene and none reported any; all had the same eating and drinking habit.

All subjects gave informed consent. The Faculty of Allied Health Science, Chulalongkorn University, approved the study. Each subject provided a urine sample for laboratory analysis.

Hippuric acid analysis

Samples were collected and sent for the estimation of hippuric acid level which was conducted by the Department of Clinical Chemistry, Faculty of Allied Health Science, Chulalongkorn University. Hippuric acid was determined by colorimetry by the standard method of Ohmori *et al* (1977). All analysis were performed by the same practitioners using the same analyzer (SHIMADZU UV 1601) at room temperature.

Statistical analysis

Statistical analysis of the results was by SPSS 7.0 for Windows. The Kolmogorov-Smirnov test was used to check for normal distributions of the results. The unpaired *t*-test was used to compare the values for hippuric acid in the control group and the experimental group. A $p < 0.05$ was regared as statistically significant.

RESULTS

The mean hippuric acid level in the control group was 0.23 ± 0.15 mg/gCr (range = 0.05 - 0.58 mg/gCr). The mean hippuric acid level in the mechanics group was 0.37 ± 0.37 mg/gCr (range = 0.06 - 1.98 mg/gCr). A significant higher urine hippuric acid level among the press workers was observed ($p = 0.03$) (Table 1).

DISCUSSION

Toluene is an aromatic hydrocarbon solvent that is widely used in industry, often as a substitute for the cancer-produced benzene. However, repeated or prolonged contact with liquid toluene may the cause removal of natural

Table 1
Urine hippuric acid levels in control and press workers groups.

Group	Number	Urine hippuric acid level (mg/gCr)	
		Range	Mean
Control	20	0.05 - 0.58	0.23 ± 0.15
Press workers	48	0.06 - 1.98	0.37 ± 0.37

lipids from the skin resulting in a dry, fissured dermatitis; prolonged exposure can result in chronic toxicity, especially of the neurological systems (Yin *et al*, 1987).

International organizations, such as the Agency for Toxic Substances and Disease Registry (ATSDR) (ATSDR, 1999) have documented toluene toxicity and recommended the monitoring of toluene exposure for at-risk groups. The work environment is, in many countries, strictly regulated with regards to the air concentration of toluene. However, in exposure- and risk-evaluation, the biological monitoring of toluene has several advantages over technical assessment of exposure. The peripheral biomarker of toluene exposure, the urine hippuric acid level is a useful monitoring tool for early diagnosis of dangerous exposure and can be used to promote improvements in the work environment (Angerer, 1979; De Rosa *et al*, 1985; Lauwerys and Buchet, 1988; Angerer *et al*, 1997).

In many newly industrialized countries, the rapid growth of industrialization in the absence of good policies and regulations for the management of pollutants has led to an increase in occupational diseases. The monitoring of toxic substances in the workers is necessary. Despite the promotion of pullution control in Thailand, the high level of volatile solvent metabolites of benzene, another common volatile solvent, indicates that ongoing industrial exposure to harmful substances has yet to be addressed (Suwansaksri and Wiwanitkit, 2000).

According to a previous study, the urine hippuric acid level correlated well with the degree of neurological disturbances (Vrca *et al*, 1996). In the present study, we used urine hippuric acid level as a biomarker for toluene exposure. We selected the press workers as the representatives of occupationally exposed workers: they are constantly in contact with toluene during their working time and most of them live in rooms near the workplace. These and the other occupations are forgotten and remain unprotected by environmental control strategies. None was able to recall a past annual health check for urine hippuric acid level.

We had expected to find a difference between the urine hippuric acid level of the occupational exposed group and the non-exposed group. Comparing the average urine hippuric acid levels of the press workers with that of the control group, the press workers had a significantly higher levels. This result agrees with that of a previous study (Vrca *et al*, 1997), which indicated high urine hippuric acid level among high-risk workers. Luckily, the urine hippuric acid among our subjects was lower than the maximum permissible level.

Forgotten high-risk workers can be found in Thailand, monitoring of toluene exposure in these workers is important. Protective equipment such as gloves and masks, are necessary and should be provided. Based on this study, we recommended that the prevention of exposure to toluene among high-risk workers be adopted as public health policy. We also recommended using urine hippuric acid determination for the monitoring of toluene exposure in these workers. Annual check of urine hippuric acid is recommended.

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