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Article

Toxic Effects of Methanol among Illegally Dispatched Workers at Aluminum CNC cutting process in Small-scale 3rd tier Subcontractor Factories of Smartphone Manufacturers in the Republic of Korea

Chung Won Kang MD[1], Hyunjoo Kim MD, PhD[1]*, Kyoung Seok Shin MD[2], Jia Rhu MD[3], , Kyounghee Jungchoi, MD, PhD[3], Key Hwan Lim MD, PhD[4], and Jin-Ha Kim MD[4]

[1] Department of Occupational and Environmental Medicine, Ewha Womans University Mokdong Hospital, Seoul, Korea; scmfer@hanmail.net, hyunjoo@ewha.ac.kr
[2] Center for Bio-environmental Science, Seegene Medical Foundation, Seoul, Korea; i.medicine@hotmail.com
[3] Department of Occupational and Environmental Medicine, Medical College, Ewha Womans University; jiyajiya000@gmail.com, jungchoikh@gmail.com
[4] Department of ophthalmology, College, Ewha Womans University; Limkh@ewha.ac.kr, jinhakim11@gmail.com
* Correspondence: hyunjoo@ewha.ac.kr; Tel.: +82-2-2650-5314

Abstract: An outbreak of occupational methanol poisoning occurred in small-scale 3rd tier factories of large-scale smartphone manufacturer, in the Republic of Korea, in 2016. To investigate the working environment and the health effect of the methanol exposure among co-workers of the methanol poisoning cases, we performed a cross sectional study on 155 workers at the five aluminum CNC cutting factories. Air and urinary methanol concentration were measured by gas chromatography, and health examination included symptoms, ophthalmological examinations and neurobehavioral tests. Multiple logistic regression analyses controlled for age and sex were conducted for revealing association of employment duration with symptoms. Air concentrations of methanol in factory A and E were ranged from 228.5 to 2220.0 ppm. Mean urinary methanol concentrations of the workers in each factory were from 3.5 mg/L up to 91.2 mg/L. The odds ratios for symptom of deteriorating vision and CNS increased, according to the employment duration, after adjusting for age and sex. Four cases with injured optic nerve and two cases with decreased neurobehavioral function were founded among co-workers of the victims. This study showed that the methanol exposure under poor environmental control not only produce eye and CNS symptoms but also affect neurobehavioral function and optic nerve.

Keywords: Methanol exposure; toxic effects; subcontractor manufacturing; dispatched workers; visual defect; neurobehavioral function

1. Introduction

Methanol, widely used in various processes for long period after 1900's, is a light, volatile, colorless, flammable liquid with a distinctive odor very similar to that of ethanol. The first case of the occupational methanol poisoning was known as a 1901 report of a man who became blind after periodic exposure to varnish dissolved in methanol, and the use of methanol to clean his face and arms over a period of 3 years [1]. The first epidemiologic study was performed by Greenburg et al. They studied 19 workers employed in the manufacture of "fused collars". Concentrations of methanol in the work room were measured to be 29 to 33 mg/m3, and a "strong odor" of solvent was perceptible. The shortest period that any of these workers had spent fusing collars was 9 months, and the longest was 2 years. No CNS or visual anomalies in any of these workers were reported [2].

Chronic and acute exposures to methanol vapors have been studied at or near the limits of allowable methanol vapor exposure. The current occupational limits of 200 ppm in air averaged over 8-or 10-hour days and 40-hour weeks were established in 1948. 250 ppm averaged over 15 minutes for short-term exposure limit, in 1976, and 6000 ppm for the immediately dangerous concentration to life and health, in 1994 [3]. The more recent epidemiological study on the effect of occupational methanol exposure were conducted by Frederick et al. (1984). NIOSH published a study of teacher aides who worked at or near spirit duplicators that used a 99% methanol duplicator fluid for about 3 years. A health questionnaire survey was conducted and suggested that chronic effects may occur when methanol concentrations exceed the TLV of 260 mg/m3. However additional clinical investigations did not proceed to further define the effects [4].

Occupational methanol poisoning seems to disappear into the mists of history with the establishment of these exposure limit values for methanol as well as the settlement for the regulations on occupational health and safety, especially in developed countries. Most of the methanol poisonings recently reported in the articles were due to non-occupational exposure of methanol, mainly by ingestion or intentional inhalation, i.e. abuse [5]. Only a few accidental poisonings due to occupational inhalational or dermal exposure were reported among non-manual workers such as laboratory workers [6] and a consultant [7].

However an outbreak of occupational methanol poisoning occurred in the manufacturing industry in the Republic of Korea in 2016. Two cases worked for several months at aluminum CNC cutting process in a small-scale 3rd tier subcontractor factory of large-scale smart-phone manufacturing companies [8]. An acute poisoning case who had worked just for several days at the same process in another company were found in a week after the first case reported. The 4th case were reported one month later, near the district where the former cases occurred [9]. Furthermore, another two cases had been poisoned at the above factories were reported in September, 2016 [10].

The special health examination for protecting their co-workers from methanol exposure and revealing the cause of this outbreak of occupational poisonings were performed according to the order of the Ministry of Labor and Employment to the employers. This study aimed to investigate the working environment and the health effect of the methanol exposure among co-workers of the poisoning cases.

2. Materials and Methods

2.1. Study population

This retrospective observational study includes 155 workers were checked up the special health examination just after the outbreak of occupational methanol poisonings. They worked at the aluminum CNC cutting process in five small-scale factories named A to E according to the order of the investigation date, located in Bu-cheon city, Kyoung-gi province, the Republic of Korea. The factory A where two cases of sub-chronic poisoning occurred and the factory B, C and D supplied aluminum buttons to the same parent company which was also a 2nd tier subcontractor of large-scale smartphone manufacturing companies. The factory E where an acute poisoning case was found did for another 2nd subcontractor of the same smartphone companies. All the workers who existed at the factory during the day when the hospital staff visited the factories to collect urine samples were participated.

2.2. Exposure assessment

From 22th to 26th Jan in 2016, Environmental samplings and analyses were conducted by labor inspectors affiliated with Bu-cheon district office of the Korea Labor and Employment. Factory A and E used methyl alcohol. Since the factory B, C, and D changed the cooling agent from methanol to ethanol just before the environmental sampling after hearing that methanol poisoning had occurred at the same process, ethanol levels were measured. The workplace air concentration of methanol and

methanol-containing proportion in bulk sample were analyzed using gas chromatography by the laboratory of Korea occupational safety and health (KOSHA). The results were informed to the occupational physician of the hospital, which performed the special health examination.

From 25th to 29th Jan in 2016, the work through survey on each factory and interviews with the employers or managers by an occupational physician were conducted and urine from 146 workers for biological monitoring sampled. Most of urine sampled not the end of the shift, except for day shift workers in factory E. The sampling had to conduct before shut down the factory A and E. The others already stopped to use methyl alcohol. Urinary methanol levels were measured by Seegene medical foundation, Seoul, Korea. GC was performed on an Agilent 7890 series gas chromatograph (Agilent Technologies) with a flame ionization detector. The system was equipped with an CombiPaL Headspace Sampler. A 60m × 0.250 mm × 1.4 um DB-624(Agilent Technologies) column was used. To 10 ml headspace vials, 3 ml of either calibration, urine samples were added. Vials were capped quickly to avoid loss of analyte by volatilization and transferred to the autosampler.

2.3. Special health examination

The special health examination was conducted at the department of occupational and environmental medicine of a university hospital from 26th Jan to 12th Feb. 2016. The examination included work history, symptoms, ophthalmological examination and neurobehavioral function. The structured symptom questionnaire for special health examination based on KOSHA guideline was used to collect the data on workers symptom systematically. In this questionnaire, methanol exposure related symptoms were regarded as follows; (1) My eyesight is worse than before. (2) I feel headaches, (3) I feel dizzy, (4) I have become more forgetful, (5) I am anxious and restless, (6) My head feels numb or I feel as though I am drunk, and (7) I find it hard to concentrate.

All workers were checked up visual acuity and color vision test by Han's method and fundus photography. 36 workers who complained worsened eyesight or showed abnormal findings of the fundus photography were examined visual field (30-2 SITA-standard strategy, Humphrey visual field analyzer HFA750i; Carl Zeiss Meditec Inc., Dublin, CA, USA)

Simple reaction and symbol digit substitution was tested on 90 workers by Korean computerized neurobehavioral test system [11]. The reason why all workers could not be received neurobehavioral test was that the workers, who visited to the hospital just after 12 hours fixed night shift work, could not meet the prerequisites for testing.

2.4. Statistical analysis

SPSS 22.0 statistical package was used. The descriptive statistics were calculated for explaining the characteristics of the study population and the exposure of methanol. Multiple logistic regression analyses were conducted for revealing association of employment duration with symptoms, controlling for age and sex.

2.5. Ethical consideration

The study was approved by the institutional review board of Ewha Womans University Mok-dong Hospital. (Approval no. 2016-05-048-002)

3. Results

More male workers (67.9%) than female workers (30.3%) worked at five small scale factories. Most frequent age group was twenties (49.7%), followed by thirties (32.3%) and forties (18.1%). Alcohol drinker was 51.0%. They worked as aluminum CNC cutting machine operators (60.0%), inspectors measuring size (16.1%), visual inspectors (7.7%) and managers (16.1%). Their duration of

employment was relatively short ; 19.4% for less than 1 month, 38.1% for from one to three months, 42.6% for more than three months. 80% of the study population were illegally dispatched workers and only 20% of those were permanent workers. The proportion of the migrant workers was 41.3% (Table 1).

Table 1. Characteristics of co-workers of methanol poisoning cases (n=155)

Unit : %

Characteristics		**Frequency**	**(%)**
Sex	Male	108	(69.7)
	Female	47	(30.3)
Age	<29	77	(49.7)
	30-39	50	(32.3)
	40 ≤	28	(18.1)
Alcohol drinking	no	76	(49.0)
	yes	79	(51.0)
Company	A	29	(18.7)
	B	44	(20.6)
	C	37	(28.4)
	D	13	(8.4)
	E	32	(20.6)
Migrant workers	no	91	(58.7)
	yes	64	(41.3)
Type of employment	permanent	31	(20.0)
	dispatched	124	(80.0)
Process	machine operating	93	(60.0)
	measuring size	25	(16.1)
	visual inspection	12	(7.7)
	management	25	(16.1)
Duration of employment	<1 month	30	(19.4)
	1-3 months	59	(38.1)
	4 months≤	66	(42.6)

Regarding characteristics of factories, the numbers of the involved dispatch agencies were ranged from two to four in each factory and the proportions of dispatched workers were from 62.2 to 100%. Those of migrant workers, from 3.4 to 69.2%. The number of the aluminum CNC cutting machines in each factory varies from 29 to 66. All the machines were open-mode which methanol easily vaporized and disseminated in the factory E. Almost all machine, 24 of 29, were open -mode in the factory A. There were more closed machines than the opened in the other factories than in factory A and E. Environmental samplings were conducted during the routine operations in the factory A and E which used 99.9% of methanol as cooling agent for aluminum CNC cutting machines. The air concentration of methanol ranged from 1030.1 to 2220.0 ppm in the factory A and from 228.5 to 417.7 ppm in the factory E. Ethyl alcohol levels of the factory B, C and D were measured and their

levels ranged from 22.5 to 128.7 ppm. Mean air concentrations of methanol in the factory C and D were slightly higher than reference value of 2 mg/L. The factory B showed 8.6 ± 16.2 mg/L of methanol in urine because their workers used still 30% of methanol containing coolant. In the factory A, mean 7.9 ± 7.1 mg/L of methanol in the urine were detected ,although their urine sampled one day after shut down. Mean 91.2 ± 85.8 mg/L of methanol in urine did among workers in the factory E (Table2).

Table 2. Characteristics of the working conditions and the exposure to organic solvents in the five factories

Factory	A	B	C	D	E
Working conditions					
Number of involved dispatch agency	2	4	3	3	2
Proportion of dispatched workers (%)	69.0	83.7	62.2	92.3	100
Proportion of migrant workers (%)	3.4	40.9	45.9	69.2	59.4
Organic solvent exposure					
Number of CNC–cutting machines (open mode/total)	24/29	17/49	18/54	3/25	66/66
Methyl alcohol in bulk sample (%)	99.9	30.0	0	0	99.9
Air concentration (ppm)	Methyl alcohol	Ethyl alcohol	Ethyl alcohol	Ethyl alcohol	Methyl alcohol
cutting machine 1	1656.3	93.7	22.5	94.6	347.9
cutting machine 2	2220.0	18.9	34.4	128.7	228.5
cutting machine 3	1030.1		23.0		417.7
cutting machine 4					252.9
size measurement 1	2052.2	94.0			231.1
size measurement 2	1103.5				
Number of urine sample	24	44	37	11	30
Urinary methanol concentration (M(SD), mg/L)	7.9(7.1)	8.6(16.2)	3.5(3.0)	4.7(6.8)	91.2(85.8)

Workers with deteriorating vision were 29.7%. The odds ratios for deteriorating vision among workers with 2-3 months employment and those more than 3 months were 2.242 (95% C.I., 0.345-4.044) and 3.487 (95%C.I., 1.164-10.449) respectively, compared to workers with less than one month of employment duration in multiple logistic regression analysis controlling for age and sex. Workers with CNS symptoms were 31.6%. The odds ratios for CNS symptom were 2.775 (95% C.I., 0.808-9.528) and 4.611 (95% C.I., 1.377-15.440), respectively (Table 3).

The results of visual acuity and color vision test did not suggest methyl alcohol induced eye problems. However, we found four cases with visual field defect and two cases with abnormal neurobehavioral test. Two cases with optic nerve abnormality detected by ophthalmoscopy had worked in the factory B and C. Another two cases with decreased neurobehavioral function were found also in the factory B and C (Table 4)

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Table 3. Association of employment duration with methanol exposure related symptoms: multiple logistic regression analysis

Duration of employment	n	case	Crude OR (95% C.I)	Adjusted OR (95% C.I)[1]
Deteriorating vision	155	46		
<1 month	29	5	1	1
1-3 months	58	12	1.252(0.395-3.971)	2. 242(0.354-4.014)
4- months≤	68	29	3.569(1.216-10.476)	3.487 (1.164-10.449)
CNS Symptoms	155	49		
<1 month	29	4	1	1
1-3 months	58	18	2.250(0.742-6.825)	2. 775 (0.808-9.528)
4- months≤	68	27	3.537(1.211-10.326)	4.611 (1.377-15.440)

[1] Adjusted for age and sex

Table 4. Abnormal clinical findings by the special health examination

	Age/sex	Factory	Entry date	Symptoms	Ophthalmological findings	Neurobehavioral test(delayed > 90percentile)
1	M/26	C	14th Feb 2014	Headache, dizziness, difficulty in memory and concentration	Visual filed defect Abnormal optic nerve	Normal
2	F/29	B	2nd Oct 2015	None	Visual field defect Abnormal optic nerve	Delayed Simple reaction time
3	F/36	C	26th Nov 2015	None	Visual field defect	N/A
4	M/20	A	15th Jan 2016	Sickness absence due to eye, skin, cardiopulmonary, CNS symptoms	Visual field defect	Normal
5	M/33	C	06th Jan 2016	None	Not applicable	Delayed simple reaction time and symbol digit substitution time
6	M/50	B	15th Jan 2014	None	Not applicable	Delayed simple reaction time and symbol digit substitution time

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4. Discussion

We found that workers in the small- scale 3rd tier subcontractor factories of large scale smartphone manufacturer exposed to methanol at the maximum air concentration of about ten- fold higher compared to the occupational exposure limit. It is hard to happen in the countries established occupational safety and health system. However, it is possible because subcontracting within the supply chain for electronics manufacture is known to pursue the maximized profit in electronics industry depends on the system of 'cost down' and 'flexibility' [12]. Dispatched labor is eventually prevalent, although it is prohibited by the Korean Labor Standard Law. This phenomenon was accelerated in the case of the multi-layered subcontracting. As seen in this study, 14 dispatch agencies involved in 5 factory for the purpose of providing a smooth workforce to prepare for fluctuating orders and meeting the lowest supply price for large scale smartphone manufacturer. In particular, these factories were run without a holiday ahead of the release of new products during the period of occurring methanol poisonings in 2016. Their workers had to use methanol as a coolant, instead of ethanol, which is less toxic, and does not produce optic neuropathy, because the cost of ethanol is 4 fold expensive compared to that of methanol. Furthermore, they used the cheap open-mode machine, instead of the expensive closed-mode, which can prevent from methanol vapor- disseminating [10].

This study showed that the exposure to methanol vapor at concentrations under poor environmental control not only produce eye and CNS symptoms, but also affect neurobehavioral function and optic nerve among co-workers of methanol poisoning cases. Symptom prevalence of deteriorating vision increased according to the duration of employment. Furthermore, we found four cases of subclinical visual defect. One case was exposed methanol at concentration of 2220 ppm only for several days. The other three cases were supposed to be exposed to relatively low levels of methanol for several months. However, there were no additional case in the factory D irrespective of their workers' 6.2 time higher levels of urinary methanol compared to the occupational exposure limit of the biological exposure index (15 mg/L). It may be because of their short exposure period. This result is consistent with the former studies. According to ACGIH report, there were several occupational methanol poisoning and the related investigations until 1960's as follows; A study indicated severe, recurrent headaches in workers exposed to methanol at concentrations between 200 and 375 ppm [13]. Another study of the wood heel industry found average methanol vapor concentrations ranging from 160 to 780 ppm, with no definitive evidence of injury to the exposed workers [14]. Visual disturbances, including dilated unreactive pupils and dim vision, were reported from airborne methanol concentrations of 1200 to 8300 ppm [15]. One case of chronic methanol poisoning resulted from exposure at 1200 to 8000 ppm for 4 years was reported [16]. These ocular toxicity appears to be caused by formic acid, the metabolite of methanol, directly and not by the metabolic acidosis that accompanies its accumulation. Acidosis can increase toxicity further by enabling greater diffusion of formic acid into cells. Undissociated formic acid specifically targets the optic disc and retrolaminar section of the optic nerve, causing optic disc edema, breakdown of the myelin sheaths and optic nerve lesions [17].

Regarding the effect on central nervous system of methanol, there were significant differences in symptoms according to the duration of employment in this study. This finding suggests that the cumulative levels of exposure played an important role in methanol toxicity. There were two cases with abnormal results of neurobehavioral test in this study, which may reflect that exposure to methanol produce adverse effect on the ability of attention and the perceptual motor speed of the workers. The epidemiological studies published before these neurobehavioral tests had developed, were describing CNS symptoms such as headache and difficulty in concentration. In later studies with the use of various tools for neurobehavioral test, typically decreased neurobehavioral function were demonstrated in workers exposed to organic solvents [18]. Methanol, like other organic solvents, can be expected to harm the white matter in addition to its specific damage to the basal ganglia.

The ocular and CNS effect of methanol mentioned above were observed at relatively low air concentration of methanol compared to the former studies. Moreover, it is known that methanol toxicity is lower in inhalational exposure than in case of ingestion [19], since pharmacokinetic theory

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indicates that the peak level of methanol after inhalation does not reflect the same body burden of formate as an equivalent level after oral exposure [17]. In this study, it is interesting that there was a gap between urinary and air concentration of methanol, which is supposed to be resulted from the considerable amount of dermal exposure. According to work thorough and interviews by an occupational physician, dermal exposure in these CNC cutting factories was possible when working without proper protective clothes and gloves, especially during the task of dividing coolant usually performed by turns. Two workers of sub-chronic poisoning did not wear any protective gloves, clothes as well as respirators since those were not provided [8]. Exposure of one hand to liquid methanol for only 2 minutes would lead to the absorption of as much methanol as would be taken up by the lungs from an 8 hour exposure to an air concentration of 50 mg/m3 [20]. Therefore, the primary route of exposure to methanol seems to be inhalational, but dermal exposure may also play an important role in increasing the body methanol exposure level.

Limitations of this study are as follows. First, it is possible that this study population did not include all workers who were exposed to methanol at the five factories. Although this health examination was conducted by the order based on the occupational health and safety law, some employer and workers would not comply. Second, the cases with abnormal clinical findings could be underreported since workers only who complained eye symptom were referred to the ophthalmologist and some workers could not receive neurobehavioral test. These are not a limitation that authors can overcome.

5. Conclusions

In short, this study showed that about ten-fold high level of methanol by inhalational and dermal exposure for several days to months can produce toxic effects on the eye and central nervous system. Methanol itself would not be severely toxic if the work environment were properly controlled. 'Outsourcing risk' is toxic because that subcontractor manufacturing and dispatched labor have to be faced with hazardous task without any protective measure. Regulations such as the prohibition of dispatched labor and subcontractor manufacturing for the hazardous work should be kept to prevent from such occupational poisonings occurring again.

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