

Health Effects of Exposure to Ethylene Glycol Monoethyl Ether in Female Workers

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Received August 13, 2004 and accepted September 15, 2004

Abstract: Ethylene glycol monoethyl ether (EGEE) is a solvent commonly used in industry. To find the health effect of the solvent exposure in women, we did an investigation on 32 female workers exposed to EGEE in factories manufacturing photopolymer sensitization plate, and 20 subjects working in the same companies without potential exposure to the solvent. The mean age was 35.0 and 33.9 yr in the two groups, respectively. The mean concentration of the urinary metabolite (ethoxyacetic acid) was 120.87 mg/g creatinine (geometric mean) in the exposed group, and 2.71 mg/g creatinine in the control group. Average RBC count and hemoglobin levels were normal in both groups. However, there were 2 subjects in the exposed group with an RBC count and hemoglobin concentration slightly lower than the standard. Out of 20 controls, 5 subjects reported irregular menstruation, and in comparison, 4 out of 32 exposed females had the same complaint. The most common health complaints were dizziness and swelling of the legs, with the same frequencies seen in both groups. Overall, our study suggests that although female workers were exposed to high concentrations of EGEE, subsequent health problems possibly due to such exposure were not significant.

Key words: Ethylene glycol monoethyl ether, Occupational exposure, Health effect, Women

Ethylene glycol monoethyl ether (EGEE) is one of a family of glycol ethers widely used as an organic solvent for resins, paints and dyes, and as a thinner in industry. It is miscible with both water and other organic solvents, and can be easily absorbed through the skin as well as via inhalation^{1,2}. The compound possesses a low order of acute toxicity as shown in animal experiments^{3,4}. However, repeated exposure to EGEE can induce disorders in the haematopoietic system and pathological changes in the testes^{5–7}. Studies with laboratory animals also showed that in utero exposure to EGEE induces malformation among offspring, suggesting that the solvent is a developmental toxin⁸. However, despite extensive exposure to the solvent, investigations regarding

its effect on humans are very limited. In males exposed occupationally to EGEE, reproductive effects and anemia have previously been reported^{9–11}. However, little is known about its health effects among women. In the present study, we report the effects of EGEE exposure on the health of female workers in China.

A total of 32 female workers exposed to EGEE in two factories in suburban Beijing were included in the study. The factories were manufacturing photopolymer sensitization plates and EGEE was used as a paint thinner on the plates. Twenty female subjects in the same workplaces who did not use the solvent were enrolled as controls. Control subjects were matched to the exposed group in terms of age range, mean age, percentages of drinking and smoking habits. All subjects were interviewed by qualified occupational

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Table 1. General characteristics of study subjects

	Control (n=20)	EGEE Exposure (n=32)
Mean age \pm S.D. (Min–Max) (yr)	33.85 \pm 8.54 (20–49)	35.00 \pm 8.86 (18–50)
Age group (No. and %)		
–24	4 (20)	6 (19)
25–34	6 (30)	9 (28)
35–44	7 (35)	12 (38)
45–	3 (15)	5 (16)
Mean work duration \pm S.D. (Min–Max) (yr)	2.13 \pm 1.62 (0.5–8.0)	2.23 \pm 1.55 (0.5–7.0)
Work duration		
< 1 yr	3 (15)	5 (16)
1–2 yr	12 (60)	16 (50)
3–4 yr	4 (20)	9 (28)
5 yr–	1 (5)	2 (6)

physicians on a one-to-one basis, to ascertain basic demographic items, work history, health complaints and history of childbirth. A total of 32 items relating to health complaints were included, such as symptoms of the central nervous system, mucous membrane irritation, digestive system, urinary and reproductive system, perception organs (eye, nose, ear and fingers), general symptoms (fatigue, change in body weight, etc) and menstruation conditions. Blood samples were taken for examination of blood cells, sex-related hormones and plasma aminotransferases. To monitor total exposure through the skin and via inhalation, spot urinary samples were collected at the end of 8 h work-shifts. Quantification of the solvent and its metabolite ethoxyacetic acid (EAA) was achieved using gas chromatography with a mass detector, and the metabolite was corrected for concentrations of urinary creatinine. Organic gas sampling badges (3M) were fixed on the chest pocket position of some workers (4 and 23 in control and exposure group, respectively) to monitor exposure to ambient EGEE and any other solvents during work hours. The sampling time was 6 to 8 h.

As subjects in the two factories were engaged in similar work and exposed to the same materials, combined data from the two factories was analyzed. Age and work duration are shown in Table 1. Most of the workers had worked for less than 5 yr. There were no subjects who smoked tobacco and only a few who drank alcoholic beverages occasionally. The average work (exposure) period was little over 2 yr in both groups, with the shortest exposure being 6 months. The results of monitoring badges showed that control subjects were exposed to very low concentrations of EGEE (0.56 ppm), whereas EGEE exposure was 6.44 ppm in the exposed group. Traces of acetone and ethylene glycol monomethyl ether were still detected in a few badges, although concentrations of these latter chemicals were very low (lower

Table 2. EAA level in urine of study subjects by work duration*

	Control (n=20)	EGEE Exposure (n=32)
Overall	2.71 (0.32–9.46)	120.87 (10.66–3670.99)
<1 yr	3.12 (1.26–6.49)	109.63 (28.19–635.62)
1–2 yr	3.85 (1.02–9.46)**	173.02 (10.66–3670.99)
3–4 yr	1.10 (0.33–2.00)	91.19 (13.59–1271.30)
5 yr–	n.d.	63.75 (31.44–129.27)

*: Geometric mean and range. **: EAA was only detected in 9 of 12 subjects. n.d.: not detected.

than 0.1 ppm), indicating that EGEE was virtually the only organic gas in the workplace. Although these subjects were clearly exposed to EGEE (due to ambient EGEE and contact of their hands with materials containing the solvent), protective masks or gloves were not being used at the time of our survey.

Solvent exposure as represented by urinary EAA concentration and related to work duration, is shown in Table 2. Urinary EAA content in the exposed group was over 40 times higher than in the control subjects (although with a wide range), suggesting that female workers were exposed to high concentrations of EGEE. There was no EGEE detected in any urinary samples from the controls. However, out of 32 samples from exposed subjects, 10 samples were positive for the solvent (geometric mean: 1.96 mg/g creatinine). Average RBC and WBC counts and hemoglobin levels were normal in both groups, as shown in Fig. 1. However, there were 2 subjects in the exposed group with RBC counts and hemoglobin concentrations slightly lower than the standard range. Out of 20 controls, 5 subjects reported irregular menstruation, and in comparison, 4 out of 28 exposed workers had the same complaint (Table 3). The mean concentrations of blood prolactin were within the normal range for both groups (9.11 and 10.83 ng/ml, in the

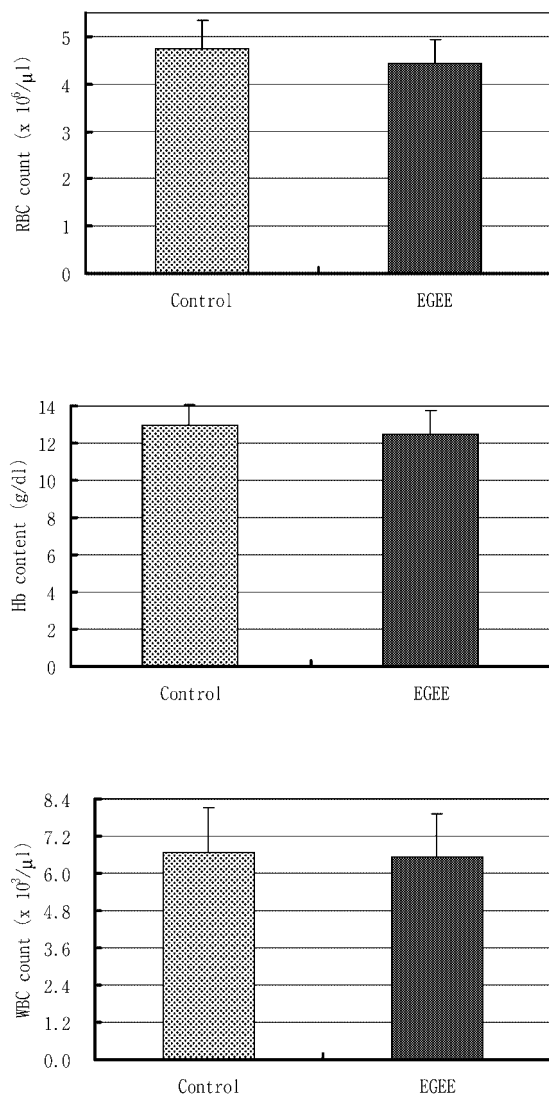


Fig. 1. Hematological results in female workers.

Each bar represents the mean + SD for 20 and 32 subjects in control and EGEE groups, respectively.

control and exposed groups, respectively), but there were respectively 3 and 5 women who exhibited higher levels of this hormone in the two groups.

Most of the female workers in this study had been married and given birth before they were engaged in EGEE work. No more than two children were reported from each woman due to China's stringent family planning policy (Table 4). Therefore, it is not known if exposure to this solvent affects childbirth. The most common health complaints were dizziness, headache or swelling of the legs, with similar frequencies seen in both groups (Table 3). Other complaints included fatigue, reduced appetite, eye irritation, low back pain and so on, but they were only from one or two subjects.

Table 3. Frequency of health complaints among study subjects

Group	Control	EGEE
Abnormal menstruation	5/20 (25.0%)	4/28 (14.3%)*
Dropsy in legs	2/20 (10.0%)	3/32 (9.4%)
Dizziness/Headache	5/20 (25.0%)	5/32 (15.6%)

*: Except for the abnormal menstruation, four women with their ages over 46 yr in EGEE group had menopause.

Table 4. Children birth history of the married female workers

Group	Control (n=18)	EGEE (n=28)
Women with kids		
No. (%)	14 (77.8)	27 (96.4)
Marriage year	14.1 ± 5.5	14.3 ± 6.0
Work year	2.2 ± 1.9	2.4 ± 1.6
Women without kids		
No. (%)	4 (22.2)	1 (3.6)
Marriage year	2.0 ± 1.4	2.0
Work year	1.9 ± 0.9	3.0

Blood AST, ALT and LDH activities were not significantly altered by solvent exposure (data not shown).

In the workplaces we investigated, EGEE by itself, rather than a mixture of solvents, was the only solvent to which the workers were exposed. This made it possible to more clearly distinguish the effects due to EGEE on women's health. Female workers in the exposed group were exposed to EGEE concentrations over 5 ppm, which is the TLV for EGEE in China. A high urinary EAA content in the exposed group also indicates that workers were exposed to high concentrations of EGEE via inhalation and through the skin. On the other hand, low levels of air EGEE and urinary EAA were detected among some control subjects. All control subjects were working in offices separated from, but in reasonable proximity to, the high EGEE concentration workplaces. Although this appears to have included a small EGEE exposure for the control subjects, their overall burden was clearly much lower than in the exposure group. Regarding effects of the solvent on the haematopoietic system, only 2 females out of 32 showed slightly lower RBC counts and Hg content than the lower limit of the standard range. Average values for subjects were almost the same as those in controls. It is important to note that lifestyle factors, such as weight loss, diet and nutrition can affect the results of blood counts in women^{12, 13}. It appears therefore, that the effect of EGEE exposure on the haematopoietic system was equivocal among females within this study.

Although EGEE may cause a reduction of sperm count in males¹⁴, we did not find any obvious effects of EGEE on the menstrual cycle of exposed females, suggesting that it may not influence the process of ovulation. Age was also taken into consideration with regard to abnormal menstruation, but no clear relationships were found. Possibly, this was due to the small number of subjects in our study. Some sex-related hormones, such as estradiol, luteinizing hormone and follicle-stimulating hormone, cannot be used for the evaluation of reproductive function in females due to wide fluctuations in blood levels during the ovarian cycle. Therefore, we determined the blood prolactin concentration, a hormone with some relationship to reproductive function, among other physiological effects¹⁵. No significant changes in this hormone were found when compared to controls. On the other hand, most female workers had been married and given birth before they were exposed to EGEE. Therefore it was difficult to ascertain whether the solvent affects pregnancy or child birth during this study. Further research will be needed to test such a hypothesis.

Aside from common complaints such as headache, dizziness, fatigue and so on, a unique symptom (dropsy in lower legs) was reported by individuals in both the exposed and control groups. EGEE has previously been reported to cause kidney damage¹⁶ and butoxyethanol caused acidosis¹⁷ during acute intoxication. Whether the dropsy witnessed in our study was related to such effects is not known.

EGEE is metabolized *in vivo* to ethoxyacetaldehyde by alcohol dehydrogenase and cytochrome P450 2E1 and further to EAA by aldehyde dehydrogenase^{18, 19}. In this study we found that a small proportion is also excreted as a transformation-free form in urine, suggesting the possibility of urinary EGEE as an alternative of exposure biomarker. It is generally believed that the metabolite EAA plays a significant role in the solvent's toxicity²⁰. On the other hand, enzymes involved in the metabolism of EGEE are known to be polymorphic²¹, and whether such polymorphisms exert any effect on the metabolism and/or toxicity of EGEE in female individuals, will need to be clarified.

Overall, this study suggests that although female workers were clearly exposed to high concentrations of EGEE, subsequent health problems possibly due to this exposure were difficult to identify. More detailed research is currently underway to help clarify this result.

Acknowledgements

We are grateful to Dr Derek R Smith from the National Institute of Industrial Health, Japan for his kind assistance

with this manuscript. Our study was supported by a Grant-in-Aid for Scientific Research (C) from Japan Society for the Promotion of Science.

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