Promising biological monitoring for occupational 1,2-Dichloropropane exposure by urinalysis for unmetabolized solvent

Toshio KAWAI1, Koji MITSUYOSHI1 and Masayuki IKEDA2

1Osaka Occupational Health Service Center, Japan and 2Kyoto Industrial Health Association, Japan

Abstract: Promising biological monitoring for occupational 1,2-Dichloropropane exposure by urinalysis for unmetabolized solvent: Toshio KAWAI, et al. Osaka Occupational Health Service Center—Objectives: The aim of this study was to examine the applicability of urinalysis for unmetabolized solvent to biomonitor 1,2-dichloropropane (1,2-DCP) exposure. Methods: Thirty three male printers exposed to 1,2-DCP and 5 nonexposed male controls participated in the study. The 8-hr average levels of exposure to 1,2-DCP in air and 1,2-DCP in the end-of-shift urine samples were measured with capillary FID-GC. Results: The geometric mean (the maximum) concentrations was 7.1 ppm (23.1 ppm) for 1,2-DCP in air, and the level in urine (without correction for urine density) was 77 μg/l (247 μg/l). A regression analysis showed a correlation coefficient of 0.909 (p<0.01). No 1,2-DCP was detected in the urine samples from nonexposed subjects. Conclusions: The high correlation and low background (essentially zero) showed that urinalysis for unmetabolized 1,2-DCP is a promising tool for biomonitoring of occupational exposure to this carcinogenic solvent at lower levels (e.g. <1 ppm).

Key words: 1,2-Dichloropropane, Biomonitoring, Occupational exposure, Unmetabolized solvent, Urinalysis

1,2-Dichloropropane (1,2-DCP) has been used in printing industries for removal of ink from printing rolls after printing work1,2). The International Agency for Research on Cancer recently evaluated its potential to induce cholangiocarcinoma and classified it in Group 13 (i.e., human carcinogen). It is the purpose of this communication to report a promising experience in biomonitoring of occupational exposure to this solvent by means of urinalysis for unmetabolized 1,2-dichloropropane. It should be added that the use of unmetabolized chemical (such as organic solvents) in urine has become popular in occupational health practice4.

Materials and Methods

The workers participating in the study were 33 male printers and 5 nonexposed male controls (19–60 years of age). About 61% of the workers were smokers. About 34% were drinkers and consumed <25 g ethanol/day; they were asked to refrain from drinking on the day before the survey. All of the exposed and nonexposed workers provided informed consents. The printers worked with a solvent mixture containing 1,2-DCP (by ca. 30%) for cleaning of the printing rolls. The workers used protective gloves but no masks. The 8-hour average intensity of exposure to 1,2-DCP was monitored by use of diffusive samplers with KF-1500 as the adsorbent5, 6). Immediately after the end of the shift, the workers collected urine samples in paper sampling cups, from which 5 ml portions were transferred to vials designed for HS-GC (see below for details of the vials). The carbon cloth in each diffusive sampler was removed in a solvent-free room and wrapped in a piece of n aluminum foil. Creatinine concentration and urine specific gravity were measured by colorimetry and refractometry, respectively.

Routine assays for 1,2-DCP were conducted with a flame ionization detector-equipped gaschromatograph (FID-GC; Model 6890; Hewlett Packard, Palo Alto, USA) connected with a liquid auto-injector (Hewlett Packard Model 6890) or a headspace (HS) air-autosampler (Model 7694; Hewlett Packard, Palo Alto,
A 60 m-long J&W capillary DB-WAX column (Agilent Technologies, Santa Clara, CA, USA) was employed for separation. For identification of 1,2-DCP in samples, a mass spectrometer (Model 5973; Agilent Technologies, Santa Clara, USA) connected with the GC was employed.

1,2-DCP (purity: >98%) and carbon disulfide (purity: >99% with no benzene contamination) were purchased from Kanto Pure Chemical (Tokyo, Japan) and Wako Pure Chemical Ind. (Osaka, Japan), respectively. Carbon cloth, KF-1500, was obtained from Toyobo Spinning Co. (Osaka, Japan).

The urine and carbon cloth samples after collection were stored in a refrigerator till analyses. The headspace air (1 m³) in each vial was subjected to the HS-GC analysis. 1,2-DCP in the exposed cloth was extracted with carbon disulfide (5 ml) by shaking, and a 1 µl portion was introduced to the FID-GC system. All analyses were terminated within 24 hours after sample collection.

Quantification limits (QL) were determined following the definition of a spike/noise ratio>10¹⁰, and were 0.1 ppm for 1,2-DCP in air, and 10 µg/l for 1,2-DCP in urine.

The study protocol was retrospectively reviewed by the Ethics Committee, Occupational Health Service Center, Japan Occupational Safety and Health Association. The Committee considered that the study met with the exemption criteria.

### Results

The 8-hour average intensity of exposure to 1,2-DCP vapor was such that the geometric mean (GM) for the 33 printers was 7.1 ppm [geometric standard deviation (GSD)=2.44] and the highest intensity of exposure was 23.1 ppm. The GM and GSD for 1,2-DCP in the end-of-shift urine samples (uncorrected for urine density) were 77 µg/l and 1.90, and the maximum was 247 µg/l.

The results of the correlation analysis between the 1,2-DCP in air and that in urine are summarized in Table 1. There was a significant correlation (p<0.01) between the 1,2-DCP in air and the 1,2-DCP in urine; the correlation was significant when the observed (i.e., uncorrected) values for 1,2-DCP in urine were employed, and also after correction for the creatinine concentrations or specific gravities of urine samples. The cases with observed 1,2-DCP in urine showed the largest correlation coefficient (0.909). The correlation was depicted in Fig. 1 for visual understanding of the closeness. It should be noted that the intercept was minimal with a sharp exposure-related increase (with a slope of 9.02 µg/l/ppm) in the levels of 1,2-DCP in urine. In fact, no 1,2-DCP was detected in urine from the nonexposed subjects. In other words, the background level was zero.

### Discussion

It is thus possible to conclude from the present study that biomonitoring of occupational 1,2-DCP exposure can be performed taking advantage of analysis of end-of-shift urine samples for unmetabolized 1,2-DCP.

A possible limitation of the present study is the
fact that the 1,2-CDP exposure studied was relatively high in reflection of the fact that no occupational exposure limit was proposed at the time; the Japan Society for Occupational Health(1) later proposed 1 ppm as the limit for 1,2-DCP, taking the carcinogenicity into consideration. It was not possible in the present survey to examine the applicability of the present method to the cases with, for example, <1 ppm 1,2-DCP exposure. Nevertheless, the present findings indicating that the correlation is very close (Fig. 1 and Table 1), that the QL for urinalysis is sufficiently low (i.e., 10 µg/l) and that the background level is zero are as a whole quite promising and encouraging. The recent development of a technique for rapid transfer of a urine sample into a confined space(2) will facilitate the application of the present urinalysis method. Use of electron capture detectors rather than FID may further increase the sensitivity of GC analysis. Thus, additional survey of individuals working in improved working environments (e.g., with 1,2-DCP at <1 ppm) is quite desirable.

In the present survey, the correlation coefficient was largest for uncorrected values of 1,2-DCP in urine. It is conceivable that this was due to the mechanism of transfer of unmetabolized 1,2-DCP into urine. The mechanism is simple diffusion with no relation to creatinine metabolism or metabolism of specific gravity-affecting substances in urine.

It was previously shown that 1,2-DCP is biotransformed into three metabolites in experimental animals(3, 4). No reports are however available on the accounts for unmetabolized 1,2-DCP in urine and in exhaled breath, or the accounts for urinary metabolites. Urinalyses for unmetabolized solvents are popularly employed in occupational health practice(5, 6, 7, 8) possibly because the method is simple and semi-automatized, whereas urinalysis procedures for 1,2-DCP metabolites(9) are rather complex and time-consuming. Nevertheless, it is too early to perform critical evaluation of the two types of biomonitoring for workers exposed to 1,2-DCP at low concentrations such as <1 ppm.

Conflicts of interests: The authors declare that they have no conflicts of interest.

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References