Evaluation of Exposure to 2,2-Dichloro-1,1,1-Trifluoroethane (HCFC-123) in Air-conditioner Manufacturing Workers and their Health Effects in South Korea

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Abstract: Evaluation of exposure to 2,2-Dichloro-1,1,1-trifluoroethane (HCFC-123) in air-conditioner manufacturing workers and their health effects in South Korea: Yong Chul Shin, et al. Department of Occupational Health and Safety, Inje University—Hepatic dysfunction in workers exposed to HCFC-123 has recently been reported, but information on the level of exposure to the material and the related hepatotoxicity in workers handling the material is very limited. This study evaluated the exposure status in some Korean workers handling the chemical and whether they have liver dysfunction. We investigated all four factories manufacturing large-sized industrial air-conditioners operating in South Korea in 1998. The range and geometric mean of the estimated 8-hour TWA concentrations at two factories were 2.2 ppm (0.89–4.2 ppm) and 32.5 ppm (4.9–113.9 ppm), respectively. It was estimated that the HCFC-123 concentrations at the other two factories were lower than those at the former two. Liver function was within the normal range in all the exposed workers. The present study did not show any health effect of HCFC-123 on workers. Worker exposure in this study was intermittent and lower than in studies which reported cases of liver dysfunction, so that the level and pattern of exposure to HCFC-123 would be very important as a cause of liver dysfunction. Our study showed that liver dysfunction did not occur at an exposure concentration less than 32.5 ppm as an 8-hour TWA of HCFC-123. (J Occup Health 2002; 44: 108–111)

Key words: 2,2-Dichloro-1,1,1-trifluoroethane, HCFC-123, Air-conditioner, South Korea, Intermittent exposure, Liver toxicity

Hydrochlorofluorocarbons (HCFCs) are used in refrigerator and air-conditioning applications, in the manufacture of insulating foams, and in fire protection applications. HCFCs, including 2,2-dichloro-1,1,1-trifluoroethane (HCFC-123), are increasingly being used in industries as a substitute for ozone-depleting chlorofluorocarbons (CFCs)

Several studies have recently reported hepatic dysfunction in workers exposed to HCFC-123, but information on exposure to the material and hepatotoxicity in workers handling the material is very limited. The aim of this study was to evaluate the exposure status in some Korean workers handling the chemical and whether they have liver dysfunction.

Materials and Methods

Materials

We investigated all four factories manufacturing large-sized industrial air-conditioners operating in South Korea in 1998. Large-sized industrial air-conditioners called "Turbo air-conditioners" used HCFC-123 as a refrigerant that easily becomes volatile in at low pressure. HCFC-123 was injected into the industrial air-conditioners, performance of the air-conditioners was tested, and finally HCFC-123 was degassed and recovered in the testing process, the last process in air-conditioner manufacturing. Injection time ranged from 20 minutes to two hours depending on the size of the air-conditioners, and degassing and recovery time was approximately one hour. The frequency of testing processes varied greatly depending on the number orderd, and the size of the air-conditioners in each factory. Workers may be exposed to HCFC-123 in the testing process. There were 2–5 workers exposed to
HCFC-123 in each factory, for a total of 12 exposed workers in the four factories. Venous blood samples and spot urine samples were collected from exposed workers.

Table 1 shows the characteristics of the twelve exposed workers, including age, exposure duration and alcohol consumption.

**Table 1.** Demographic and laboratory features of male workers studied

<table>
<thead>
<tr>
<th>Factory</th>
<th>Worker</th>
<th>Age (yr)</th>
<th>Duration of exposure (yr)</th>
<th>Alcohol consumption</th>
<th>Liver function (IU/l)</th>
<th>AST</th>
<th>ALT</th>
<th>GTP</th>
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<tr>
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<td>1.7</td>
<td>No</td>
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<td></td>
<td>2</td>
<td>27</td>
<td>2.9</td>
<td>No</td>
<td>20 16 22</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>B</td>
<td>3</td>
<td>38</td>
<td>11.1</td>
<td>Yes*</td>
<td>22 18 16</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>4</td>
<td>35</td>
<td>6.0</td>
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<tr>
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<td>5</td>
<td>47</td>
<td>17.5</td>
<td>Yes</td>
<td>23 21 36</td>
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<tr>
<td></td>
<td>6</td>
<td>40</td>
<td>5.4</td>
<td>No</td>
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<tr>
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<td>1.5</td>
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<td>10</td>
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<td>1.2</td>
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<tr>
<td>D</td>
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<td>39</td>
<td>11.2</td>
<td>No</td>
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<td></td>
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<td>12</td>
<td>37</td>
<td>10.5</td>
<td>Yes</td>
<td>27 29 46</td>
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<tr>
<td>Mean (SD)</td>
<td></td>
<td>37.3</td>
<td>6.8</td>
<td></td>
<td>22.7 20.4 27.8</td>
<td>(5.4)</td>
<td>(5.3)</td>
<td>(3.6)</td>
</tr>
</tbody>
</table>

AST: aspartate aminotransferase, ALT: alanine aminotransferase, GTP: γ-glutamyltransferase.
Reference range (IU/l): AST (10–34), ALT (9–43), GTP (11–50). *: one drink or more a week.

**Determination of airborne HCFC-123 concentrations**

Workplace air monitoring was conducted at two factories manufacturing industrial air-conditioners. At the other two factories, air-conditioners were not being manufactured because the manufacturers did not get orders. These two factories had done much less testing than the other two manufacturers on a yearly basis, and so workers’ exposure levels at these factories were estimated to be lower than those at the others. HCFC-123 was used to test the refrigerating performance of air-conditioners. One factory (A) has used HCFC-123 once in 1 to 3 months for four years. The two workers have been potentially exposed to the chemical. Because there was no operation handling the refrigerant on that day, air monitoring was conducted in working conditions which simulated actual work. Duration of injection of the refrigerant was approximately 20 to 30 minutes. The amount of refrigerant injected into air-conditioners was 250 kg. The other factory (B) has used HCFC-123 every day for five years. Five workers have been potentially exposed to the chemical. Duration of injection of the refrigerant was approximately 2 hours. The amount of refrigerant injected into air-conditioners ranged approximately from 200 to 1000 kg depending on the size of the air-conditioners. Refrigerant tanks in air-conditioners were vacuumed and connected to the outlet of containers containing HCFC-123 with hoses, and then the refrigerant was injected into the tanks. No local ventilation or personal respiratory protective device was used when handling HCFC-123 in these factories.

An activated coconut-shell charcoal tube (commercially available, Anasorb CSC, SKC Corp.) was selected for the collection of airborne HCFC-123 vapor. The charcoal tube consists of two sections, i.e., front and back sections containing 400 mg and 200 mg, respectively. The HCFC-123 air samples were collected in workers’ breathing zones and areas near workers. The time-weighted average concentration and short-term concentration of HCFC-123 were measured. Airborne HCFC-123 was sampled for 16–69 minutes in the breathing zones during refrigerant charging and degassing to determine the short-term exposure level. All air samples were collected at less than 0.05 l/min. The short-term concentrations were used to estimate the 8-hour-TWA concentrations.

The front and the back sections of the sampling tube were separately analyzed. Analyte on the sorbent was desorbed with 2 ml of dichloromethane (Reagent Grade, Aldrich Chemical Co.) containing 0.5% n-hexane as an internal standard for one hour and analyzed by means of a gas chromatograph/flame ionization detector (GC/FID; HP 5890 II, Hewlett Packard Co.) installed with a column (Supelcowax 10™, 15 m × 0.5-mm ID, 0.53-µm film thick, Supelco Co.). Both injector and detector were set at 150°C. Oven temperature was programmed as follows: 40°C (5-minute holding) to 100°C (0.2 minute holding) at 30°C/min, recycled to 40°C at - 30°C/min. The flow
rate of the carrier gas, helium, was set at 1.9 ml/min. A 1 µl sample was injected. Desorption efficiency was determined for every experimental set, and the mass of analyte found in the sample was corrected for desorption efficiency. The average of desorption efficiencies of the sampling and analytical procedures was 99.0%, and the bias was 4.6%. The overall precision was 0.060. A similar method for determining HCFC-123 concentration in the environment has been reported7).

Questionnaires and laboratory testing
Each participant was seen at the factory clinic. We administered a questionnaire and collected samples of blood and urine. The questionnaire elicited basic demographic information and information about smoking, alcohol consumption, medications and recent medical history. Each participant was asked about his work history.

A sample of blood was obtained for complete blood count, and liver function testing such as aspartate aminotransferase, alanine aminotransferase, and γ-glutamyltranspeptidase to determine liver dysfunction. Urinalysis was also done.

Results
Workers’ levels of exposure to airborne HCFC-123
The workers’ time-weighted average (TWA) exposure concentrations at two factories are shown in Table 2. Airborne HCFC-123 concentrations (n=6) measured at workers’ breathing zones during the refrigerant injection in factory A ranged from 14.3 to 67.6 ppm (geometric mean <GM>: 35.4 ppm). The workers’ 8-hour TWA concentrations at this factory were estimated to be 0.89–4.2 ppm. In factory B, air samples at four workers’ breathing zones were collected from starting the task, i.e. air-conditioner performance testing. The GM of HCFC-123 TWA concentrations for sampling or work duration was 83.9 ppm. The range and GM of the estimated 8-hour TWA concentrations for these workers’ were 4.9 to 113.9 ppm, and 32.5 ppm, respectively. The highest 8-hour TWA value, 113.9 ppm, was higher than the American Industrial Hygiene Association (AIHA) Workplace Environmental Exposure Level (WEEL) GUIDE of 50 ppm as an 8-hour TWA concentration for HCFC-1238).

Liver function in exposed workers
Liver functions were within the normal range in all the exposed workers (Table 1).

Discussion
HCFC-123 is a colorless light-ether-odor liquid with a boiling point of 27.6 ( at 1 Torr), and is used as a refrigerant mainly in large-sized industrial air-conditioners5. In guinea pigs, a single exposure to 1,000 ppm of HCFC-123 for 4 hours caused increases in aspartate aminotransferase and alanine aminotransferase compatible with hepatocellular
necrosis\(^9\)). In subchronic studies done in rats and dogs, increased liver weight, slight focal liver necrosis, induction of peroxisomal activity, and hepatocellular adenomas have been found. Hoet \textit{et al.}\(^2\) recently reported an outbreak of toxic hepatitis caused by a mixture of HCFC-123 and 124. Takebayashi \textit{et al.}\(^3\) also recently reported a cluster of severe liver dysfunction among workers who had been exposed to HCFC-123. The mechanism of hepatotoxicity of HCFC-123 was suggested to be probably similar to that of halothane (1-bromo-1-chloro-2,2,2-trifluoroethane)\(^9\), whose structure is very similar to that of HCFC-123, but information on exposure to the material and hepatotoxicity in workers handling the material is very limited.

Hoet \textit{et al.}\(^2\) reported an epidemic of liver diseases without exposure data. Takebayashi \textit{et al.}\(^4\) reported that hepatodysfunction was caused by exposure to HCFC-123 at more than 200 ppm with a peak concentration of 1,000 ppm for 5 weeks. The workers showing signs of severe liver damage had been working in the refrigerant enclosure operation 50 hours a week or more for about a month. The exposure concentrations were estimated from job simulation during a 6-hour experiment, but the 8-hour TWA concentrations in workers’ breathing zones were not presented in that study\(^4\). We could roughly estimate the TWA concentration to be more than 50 ppm despite the rather limited information. Omae \textit{et al.}\(^5\) reported a case of acute hepatitis induced by repeated exposure to HCFC-123 in a dry-cleaning solvent. The patient used the chemicals for 1 hour a day during the busiest work period. Average exposure concentration of HCFC-123 was more than 1,300 ppm in subjects during the job simulation. We estimated that the subject had been exposed to more than 170 ppm of HCFC-123 as an 8-hour TWA concentration which was much higher than the AIHA WEEL GUIDE (50 ppm)\(^8\).

The present study is the first one investigating workers exposed to HCFC-123 in the air-conditioner manufacturing process. Liver function parameters of all the exposed workers were in the range of reference values. The present study has the clear limitation that it observed an exposure group without a comparison group. Nevertheless, it is estimated, though not guaranteed, that the effects of HCFC-123 on liver function were not seen in the exposed workers considering the rather high prevalence of liver diseases in the general population in South Korea\(^9\). The present study showed that the average HCFC-123 exposure level was equal to or less than 32.5 ppm as the 8-hour TWA and 192.4 ppm as the short-term concentration in the air-conditioner factories in South Korea. This study also showed that the exposure pattern in the factories was very intermittent. The process and exposure levels were different from those in the workplace reported by Takebayashi \textit{et al.}\(^4\) and Omae \textit{et al.}\(^6\), so that an intermittent low exposure pattern as in air-conditioner factories which is estimated to be much lower than those reported in previous studies might hardly cause liver dysfunction. The exposure level and pattern of HCFC-123 would be very important in causing liver dysfunction. Our study showed that liver dysfunction did not occur at an exposure concentration lower than 32.5 ppm as the 8-hour TWA of HCFC-123, which concentration was below those reported by Takebayashi \textit{et al.}\(^3\) and Omae \textit{et al.}\(^6\).

It is necessary that workers’ exposure levels should be determined and well-designed epidemiological studies, including control workers as well as exposed workers, be performed rather precisely to evaluate the dose-response relationship between HCFC-123 and its effects on health. The present study was limited because it did not cover these points.

References