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Case Report

Exposure Assessment for Toxic Hepatitis Caused by HCFC-123

Ki-Woong Kim [1,*], Hae Dong Park [2], Konghwa Jang [2], Jiwon Ro [2]

[1] Chemical Research Bureau, Occupational Safety and Health Research Institute, Korea Occupational Safety and Health Agency, Republic of Korea
[2] Work Environment Research Bureau, Occupational Safety and Health Research Institute, Korea Occupational Safety and Health Agency, Republic of Korea

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This case report attempts to present a case of acute toxic hepatitis in fire extinguisher manufacturing workers exposed to 2,2-dichloro-1,1,1-trifluoro-ethane (HCFC-123) in August 2017 in Korea. Twenty-two-year-old male workers were exposed to HCFC-123 for 1.5 hours one day and for 2.5 hours the other day, after which one worker died, and the other recovered after treatment. The workers were diagnosed with acute toxicity of hepatitis. However, exposure levels of HCFC-123 were not known with no work environment measurement done. Therefore, this study was conducted to estimate the exposure concentration of HCFC-123 via a job simulation experiment. In the simulation, the HCFC-123 exposure concentration was measured with the same working practice and working time as with the workers aforementioned. As a result, the workers who infused HCFC-123 into storage tanks were estimated to be exposed to HCFC-123 at a concentration of 20.65 ± 10.81 ppm, and a mean concentration of area samples within a working radius were estimated as 70.30 ± 18.10 ppm. Valve assembly workers working on valves of a fire extinguisher filled with HCFC-123 were exposed to HCFC-123 at concentrations of 91.65 ± 4.03 ppm and 115.55 ± 7.28 ppm, respectively, in the simulation, and area samples simulated within the working radius were also found to be high with concentrations of 122.75 ± 91.15 ppm and 126.80 ± 60.25 ppm, respectively. Nitrogen gas packing workers, who did not handle HCFC-123 directly, were exposed to the agent at a concentration of 71.80 ± 8.49 ppm. These results suggest that exposure to HCFC-123 at high concentrations for 1.5–2.5 hours caused acute toxic hepatitis in two workers.

1. Introduction

The chlorofluorocarbons (CFCs), which were developed and used more than 60 years ago, have been shown to destroy stratospheric ozone; therefore, HCFC-123 (2,2-dichloro-1,1,1-trifluoroethane: CAS No. 306-83-2), which has a relatively low potential for ozone depletion than CFCs, is widely used [1]. HCFC-123 is a hydrochlorofluorocarbon (HCFC). CFCs and HCFC-123 contain chlorine; however, unlike CFCs, HCFC-123 contains hydrogen, which decomposes in the lower atmosphere before reaching the ozone layer, resulting in short atmospheric lifetimes and low ozone depletion potentials [2]. HCFC-123 is widely used as an air-conditioning refrigerant, foam blowing agent, detergent, and other refrigerant, but it has been reported to be toxic in humans and animals [3–6]. Therefore, the production and consumption of CFCs and HCFCs are gradually being reduced in accordance with the protocol adopted in June 1990 in Montreal, Canada. Therefore, there are recommendations for handling and storage precautions of HCFC-123 and prevention of exposure to HCFC-123, and its use is restricted for preventing health hazard caused by exposure to this agent. In particular, the use of HCFC-123–filled extinguishers is prohibited globally to protect the health of producers and users. However, Korea has been manufacturing HCFC-123–filled fire extinguishers from 2006 to 2017. According to the report by the Korea Fire and Disaster Management Institute, commercial fire extinguishers in Korea are classified into powder and gas fire extinguishers. Further, 2.18% of all fire extinguishers are gas fire extinguishers, and about 90% of them are HCFC-123–filled fire extinguishers. Therefore, HCFC-123–filled extinguisher manufacturing workers in Korea were likely to have health impairment due to HCFC-123 exposure, and there was a concern in August 2017 as two workers in the fire extinguisher manufacturing factory suffered from acute toxic hepatitis due to HCFC-123 exposure, resulting in one case of death and one case of recovery after

* Corresponding author. Chemical Research Bureau, Occupational Safety and Health Research Institute, Korea Occupational Safety and Health Agency, 30, Expo-ro 339 beon-gil, Yuseong-gu, Daejeon 34122, Republic of Korea.
E-mail address: k0810@kosha.or.kr (K.-W. Kim).

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treatment. Although HCFC-123 exposure was judged to cause acute toxic hepatitis, the exposure dose of HCFC-123 was not evaluated, and the exact exposure level was not known. Therefore, this study aimed to evaluate the HCFC-123 exposure level through job simulation experiments after setting the same work conditions (work method, working time, etc.) as those of workers with acute toxic hepatitis.

2. History of acute toxic hepatitis in workers

In August 2017, acute toxic hepatitis occurred in two workers at the HCFC-123 fire extinguisher manufacturing factory located in Gyeonggi-do, Korea.

Worker 1, aged 22 years, joined the company on July 26, 2017 and filled HCFC-123 into a fire extinguisher for 1.5 hours on August 2, 2017 and for 2.5 hours on August 9, 2017 and assembled the valve. On the afternoon of August 12, 2017, he had fever, muscle pain, abdominal pain, dizziness, and fatigue. He was admitted to the hospital on August 13, 2017 and was diagnosed with acute toxic hepatitis (August 17, 2017). Worker 2 was also 22 years old. He joined the company on July 27, 2017 and worked with employee 1 at the same time in the same work process. He had fever symptoms on August 11, 2017. He was hospitalized, but he died on August 24, 2017. The autopsy results showed acute toxic hepatitis. In this workplace, workers were provided with only silicone-treated gloves, and no cartridge respirator was provided, and local and total ventilations were not installed.

3. Exposure assessment by a job simulation experiment

3.1. Design of the job simulation experiment

Two workers developed acute toxic hepatitis due to HCFC-123 exposure, and the Korean Ministry of Employment and Labor temporarily suspended all operations in the workplace. We attempted to evaluate the exposure levels of HCFC-123 through job simulation experiments by reproducing the same work condition as that of workers who developed acute toxic hepatitis.

First, the record of work status, production volume, work method, and time for workers with acute toxic hepatitis were identified and confirmed by interviews with other workers and job managers. Two workers were selected, and the exposure level of HCFC-123 was evaluated by setting the same conditions as those of workers who developed acute toxic hepatitis. Five workers were included in the survey, and detailed explanations on the research purpose, method, health risks were provided, personal information protection methods were followed, and consent was obtained from workers who voluntarily wished to participate in the survey. Job simulation experiments were carried out with workers wearing cartridge respirators. Institutional Review Board of the Occupational Safety and Health Research Institute, Korea Occupational Safety and Health Agency, reviewed the protocol.

3.2. HCFC-123 levels in workplace

Sampling and analysis for evaluating HCFC-123 exposure levels were performed according to the method described by Shin et al. [7]. HCFC-123 in the air was collected by a sample collection pump (GSA 350, Germany) with an activated carbon tube (Lot no. 226-09, SKC Inc., PA, USA), and the sample collection flow rate was set at 0.1 L/min for personal and stationary samples, and it was measured for 63–130 min the working time. To assess short-term exposure levels, the sample collection flow rate was set at 0.2 L/min, and it was measured at intervals of 15 minutes to prevent breakage of the sample during the actual working time. The collected HCFC-123 samples were transferred to the laboratory in a refrigerated state and analyzed. Analysis was performed using the gas-chromatograph equipped with a flame ionization detector (7890B, Agilent, California, USA) according to the conditions shown in Table 1 and instrumental detection limit value was 5.8 μg/mL.

Extractive Fourier transform infrared (FTIR) gas analyzer (FACE-3000, Mastek Technologies Inc., Taiwan) was used for real-time monitoring. It was composed with He–Ne laser, 10m gas cell, and mercury cadmium telluride (MCT) detector. The resolution was 1 cm^{-1}, and the minimum detection limit by the manufacturer was 22 ppb for HCFC-123. Approximately 250 L of air per hour was drawn into the FTIR using a pump, and the analysis of HCFC-123 was performed at 1166–1202 cm^{-1}.

4. Results

4.1. Working process and environment

The work process in the fire extinguisher manufacturing factory is shown in Fig. 1.

The work process proceeded in the following order: infusing HCFC-123 into the storage tank, filling the fire extinguisher with HCFC-123, assembling the fire extinguisher valve, measuring the charge amount of HCFC-123, nitrogen gas filling, and pressure testing and inspection. All work was carried out continuously in a unit workspace, and all workers were very likely to be exposed to HCFC-123 except for the workers who performed pressure testing and inspection. In addition, exposure levels of HCFC-123 in the workplace were closely related to the work skills of the HCFC-123 filling workers and fire extinguisher valve assembly workers.

The reason for this is that after HCFC-123 is filled in the extinguisher, the valves must be assembled quickly during the valve assembly process to minimize the evaporation of HCFC-123 and to prevent diffusion to other work processes.

Table 1
Analytical conditions

GC	Agilent 7890B
Injection volume	1 μL
Inlet	Temp. 150°C Split 20:1
Column	DB-WAX (30m × 0.25mm × 0.5μm) Flow 1 mL/min
Oven	40°C (4 min)-30°C/min-100°C (1 min)
Detector	Type: FID Temp. 160°C H2 35mL/min Air 350mL/min Makeup (N2) 29mL/min

FID, flame ionization detector; GC, gas chromatograph.

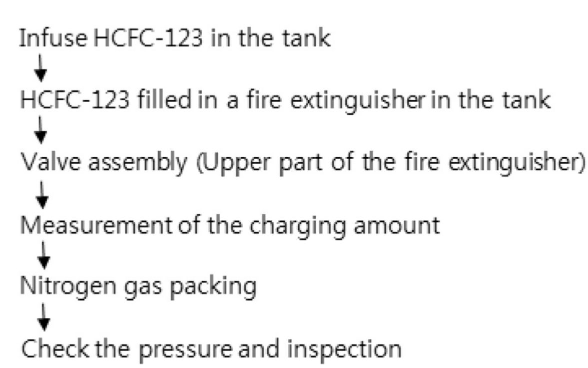

Fig. 1. Work process.
HCFC-123, 2,2-dichloro-1,1,1-trifluoro-ethane.

4.2. HCFC-123 levels in workplace

HCFC-123 concentrations in workplace measured in the job simulation experiments are shown in Table 2. As a result, workers who infused HCFC-123 into the storage tanks were exposed to mean concentration of 20.65 ± 10.81 ppm, and concentrations in the area samples within the working radius was 70.30 ± 18.10 ppm. Workers who were involved in HCFC-123 filling in a fire extinguisher that led to acute toxic hepatitis were exposed to mean concentration of 91.65 ± 4.03 ppm, and the concentration of HCFC-123 measured in the area sample was 122.75 ± 91.15 ppm. In addition, the fire extinguisher valve assembly workers were exposed to HCFC-123 at mean concentration of 115.55 ± 7.28 ppm, and area samples mean concentration around these workers was 126.80 ± 60.25 ppm. Workers who filled nitrogen gas and did not directly handle HCFC-123 were exposed to the agent at mean concentration of 71.80 ± 8.49 ppm and 93.90 ± 26.02 ppm in area samples within their working radius. In particular, short-term exposure level values for HCFC-123 at a fire extinguisher-filling line and a valve assembly line were measured at 171.35 ± 31.18 ppm and 114.74 ± 21.20 ppm, respectively (Table 2). Additionally in the real-time monitoring results during and after working shifts using FTIR Spectroscopy (Fig. 2), the concentration was above 200 ppm during work, and HCFC-123 remained in the workplace for more than 1 hour. These results suggest that after the end of work, workers are likely to be exposed to HCFC-123 remaining in the workplace as they clean up their workplace. To perform biological monitoring of HCFC-123 exposure, trifluoroacetic acid, a metabolite of HCFC-123 in the urine, was measured by collecting urine three times (before work, after work, and the next day before work). The measurement results were not found in all workers. This result seems to be due to the fact that the workers used respirators before work.

Table 2
Levels of HCFC-123 at workplace

Work process	Sampling type	Sampling time	Levels of HCFC-123 mean ± SD, ppm
Infusion of HCFC-123 in the tank	Personal ($n = 2$) Area ($n = 2$)	73 min. 73 min.	20.65 ± 10.81 70.30 ± 18.10
Filling of HCFC-123 in a fire extinguisher in the tan	Personal ($n = 2$) Area ($n = 2$)	88 min. 88 min.	91.65 ± 4.03 122.75 ± 91.15
Valve assembly	Personal ($n = 2$) Area ($n = 2$) STEL ($n = 2$)	88 min. 88 min. 15 min.	115.55 ± 7.28 126.80 ± 60.25 171.35 ± 31.18
Nitrogen gas packing	Personal ($n = 2$) Area ($n = 2$) STEL ($n = 2$)	130 min. 130 min. 15 min.	71.80 ± 8.49 93.90 ± 26.02 114.75 ± 21.20

HCFC-123, 2,2-dichloro-1,1,1-trifluoro-ethane; SD, standard deviation; STEL; short-term exposure level.
Two air monitoring samplers were attached to one worker (personal), and two additional samplers were set within a working radius of the worker (area) to conduct the job simulation experiments. The collected samples were analyzed and the results were presented as mean and standard deviation.

5. Discussion

The toxicity of HCFC-123 has already been demonstrated in animal and human studies.

Therefore, there is always a risk of health hazards among people handling HCFC-123, and thus, handling of HCFC-123 should be limited. However, if it is absolutely necessary to handle HCFC-123, in order to protect the health of handling workers, it is important to minimize the amount of handling and to regularly perform exposure assessment and work management. If this is not done, it is likely that such cases of acute toxic hepatitis in workers at the fire extinguisher manufacturing factory will continue to occur.

This study was conducted to investigate the occupational relevance of acute toxic hepatitis in fire extinguisher manufacturing factory workers. As a result of the investigation through interviews and documents, it was found that there was no other cause than HCFC-123 that resulted in acute toxic hepatitis.

Exposure concentrations of HCFC-123 obtained from job simulation experiments were found to exceed Japan's Recommendation of Occupational Exposure Limit of 10 ppm [8], as well as the limit of 50 ppm recommended by the American Industrial Hygiene Association [9]. In addition, workers who infused HCFC-123 into the storage tank (13.0–28.3 ppm), workers who filled HCFC-123 in a fire extinguisher (88.8–94.5 ppm), and workers who assembled valves (110.4–120.7 ppm), as well as workers involved in the nitrogen gas filling process (65.8–77.8 ppm) who did not directly handle HCFC-123 were also exposed to high concentrations.

Exposure levels of hazardous substances in the workplace partially depend on how much they are removed by local exhaust ventilation before harmful substances reach the respiratory areas of workers from the source. However, local exhaust is not installed in this workplace, and HCFC-123 generated is blown away by using a fan, so it spreads to the entire workplace, and workers are exposed to HCFC-123 at a high concentration.

Therefore, based on the HCFC-123 exposure assessment results obtained through job simulation experiments, it was confirmed

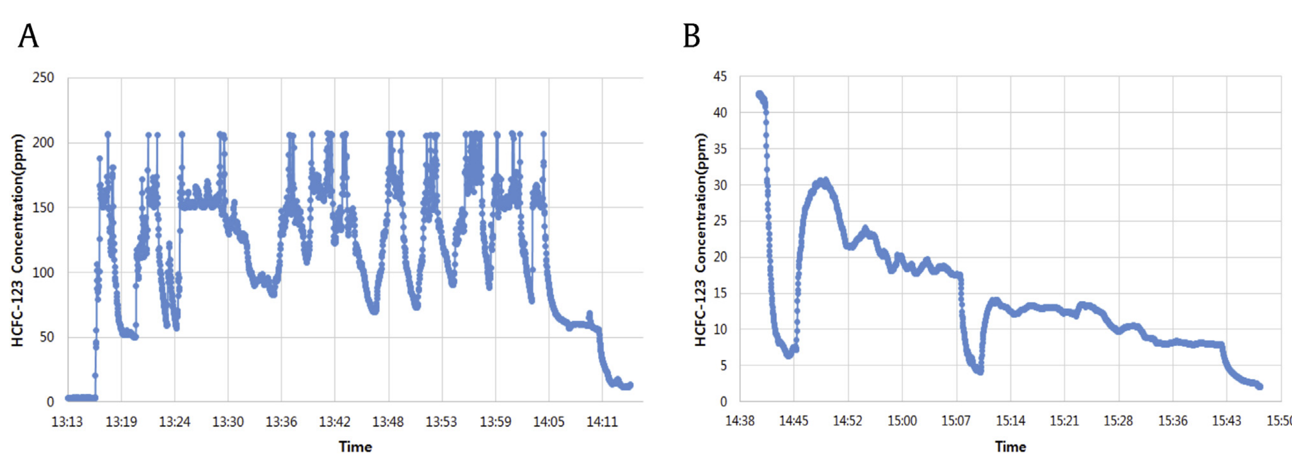

Fig. 2. Real-time monitoring results using Fourier Transform Infrared Spectroscopy. (A) Filling of HCFC-123 in a fire extinguisher in the tank. (B) End-of-work. HCFC-123, 2,2-dichloro-1,1,1-trifluoro-ethane.

that HCFC-123 was the cause of acute toxic hepatitis in workers in August 2017.

In a study in which hepatotoxicity-inducing concentrations of HCFC-123 were determined, concentrations of 10,000 ppm in dogs, 5,000 ppm in guinea pigs, and 1,000 ppm in monkeys were reported, and there was a difference in hepatotoxicity-inducing concentrations depending on the species. Based on the results of these studies, 50 ppm was the recommended concentration for humans, and no health problems were reported below this concentration [10]. Takebayashi et al. reported [4] that in cases of hepatic injury caused by HCFC-123 exposure, the refrigerant operation started on September 22nd, and the cases showed symptoms in early October. In other cases, the refrigerant operation started on September 18th, and the cases showed symptoms in early October. The results of this study did not present the exact exposure level, but the symptoms appeared 10–15 days after exposure. Omae et al. reported [11] a case of toxic hepatitis in a female worker who worked in the bridal section of a hotel. The female worker performed cleaning work for 8 years, and during busy working hours, she was exposed to more than 1,000 ppm of HCFC-123. Shin et al. [7] evaluated HCFC-123 exposure concentrations and liver function in air-conditioner manufacturing workers, and they found that the workers were exposed to HCFC-123 at concentrations of 14.3–222.2 ppm (estimated 8-hour time-weighted average (TWA) concentration, 32.5 ppm) for 1.7–17.5 years and showed that liver dysfunction did not occur. Although few cases of HCFC-123–induced toxic hepatitis have been reported in humans, it is difficult to be certain. However, some researchers have found that toxic hepatitis caused by HCFC-123 does not depend on the exposure concentration and duration. These results suggest that the dose–response relationship in toxic hepatitis caused by HCFC-123 exposure is also important, but the susceptibility of individuals is closely related.

In this study, we have demonstrated acute toxic hepatitis caused by exposure to HCFC-123, but there are some questions that need to be addressed as this finding is due to a slightly different result from that reported by other researchers mentioned above.

It is a question of exposure time and duration.

As presented in the “Study subjects and methods” section, the exposure period was too short compared to that in other studies because workers were exposed to HCFC-123 for 1.5 hours on August 2, 2017 and again for 2.5 hours on August 9, 2017, and then, acute toxic hepatitis occurred.

In this study, there was no specific problem in liver function of workers with acute toxic hepatitis, the result of hepatitis virus test was negative, autoimmune disease test was normal, and there was no other cause than HCFC-123 that resulted in acute toxic hepatitis. In addition, the results of the job simulation experiments showed that workers were exposed to high concentrations of HCFC-123. However, trifluoroacetic acid, a metabolite of HCFC-123, in the urine was not detected. These results are attributed to the fact that the workers were wearing cartridge respirator during the later job simulation experiments. However, workers with acute toxic hepatitis confirmed (from the supervisor and the coworkers) that they had worked without a cartridge respirator or any kind of respirator. Therefore, it is presumed that a large amount of HCFC-123 was absorbed into the workers' body via their respiratory system.

Therefore, acute toxic hepatitis in workers at the HCFC-123 fire extinguisher manufacturing factory was confirmed as an occupation-related acute toxic hepatitis cause due to HCFC-123 exposure. This study showed little, if any, HCFC-123 absorption via the respiratory system when the cartridge respirator was worn. Therefore, it is recommended to wear a cartridge respirator for the health protection of HCFC-123 handling workers.

Conflict of interest

The authors declare that they have no competing interest that might be perceived to influence this research paper.

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