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Uncontrolled Occupational Exposure to 1,1-Dichloro-1-Fluoroethane (HCFC-141b) Is Associated With Acute Pulmonary Toxicity*

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Background: **The toxicity of 1,1-dichloro-1-fluoroethane (HCFC-141b), a hydrochlorofluorocarbon (HCFC), is low according to animal studies. However, pulmonary manifestations associated with acute HCFC exposure by inhalation have not been reported as yet in man. We evaluated the pulmonary effects of HCFC-141b inhalation, caused by an accident, in previously healthy individuals.**
Methods: **The subjects in this study were 15 workers in whom unpleasant symptoms developed after inhaling HCFC-141b at work. Clinical manifestations, radiologic findings, and changes in pulmonary function and airway hyperresponsiveness (AHR) over time were assessed, and BAL fluid analyses findings for four subjects were compared with those of four healthy volunteers (control subjects).**
Results: **(1) Cough, shortness of breath, and malaise developed in most patients, but only two patients complained of a sore throat. (2) A high-resolution CT scan of the chest revealed bilateral diffuse ground-glass opacities that were predominant in upper lung zones. (3) The mean (± SD) FVC was 71.4 ± 18.86% predicted, and the mean FEV_1/FVC ratio was 92.9 ± 4.25%. Eleven patients (73%) showed restrictive ventilatory impairments during the initial tests. FVC gradually improved, and the FEV_1/FVC ratio gradually decreased with time. (4) AHR was observed in four subjects during the initial tests. (5) BAL fluid samples revealed significantly higher neutrophil counts than those in control subjects.**
Conclusions: **Overexposure to HCFC-141b was associated with parenchymal lung injury that was characterized by ground-glass opacities, elevated BAL neutrophil counts, and restrictive ventilatory impairment. Restrictive impairments improved with time after exposure.**
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Key words: 1,1-dichloro-1-fluoroethane; pulmonary intoxication

Abbreviations: AHR = airway hyperresponsiveness; CFC = chlorofluorocarbon; HCFC = hydrochlorofluorocarbon; HCFC-141b = 1,1-dichloro-1-fluoroethane; HRCT = high-resolution CT; PC_{20} = provocative concentration of methacholine causing a 20% fall in FEV_1; PFT = pulmonary function test

Hydrochlorofluorocarbons (HCFCs) were developed to replace chlorofluorocarbons (CFCs), which cause ozone depletion and adversely affect human health.[1,2] 1,1-dichloro-1-fluoroethane (HCFC-141b), an HCFC, is a volatile, colorless liquid with little water solubility and a relatively high vapor pressure.[3] HCFC-141b is currently commonly used as an alternative to CFCs as a solvent and blowing agent, and thus, extensive toxicologic studies[1,3–8] have been conducted in animals. These studies have determined that HCFC-141b has low acute and subchronic toxicity, although there was one case report[9] of fatal intoxication in humans. However, pulmonary manifestations in humans attributable to direct HCFC-141b inhalation have not been previously reported.

We evaluated the pulmonary effects of HCFC-141b inhalation resulting from an industrial accident, in which acute respiratory distress developed in 15 previously healthy workers after exposure to HCFC-141b. We describe the clinical symptoms, laboratory findings, radiologic features, pulmonary function test (PFT) results, and airway hyperresponsiveness (AHR) findings, and the results of BAL fluid analyses in these patients.

Materials and Methods

Subjects and the Incident

The 15 subjects in this study were assembling parts for electronic appliances in a factory on August 7, 2006. They started

work at 8:30 AM, and one of them cleaned printed circuit boards with HCFC-141b (Preventer; Koki Korea Co. Ltd; Pyungtaik, Korea) from 11:00 AM to 5:00 PM. This was the first time that HCFC-141b had been handled in a confined space in the factory, because the cleaning process was usually conducted in a dedicated area that was well equipped with ventilation facilities. The workers wore no protective clothes or masks. Furthermore, ventilation facilities and the air conditioner in the working area did not work. The room temperature was about 32 to 33°C. Some of the workers started to feel shortness of breath, chest discomfort, and malaise at about 2:00 PM after being exposed to HCFC-141b for 3 h. All of the workers experienced similar symptoms at about 2:30 PM. However, though they felt progressively worse during the working day, they continued working and did not complain, because most believed that their symptoms were caused by the hot weather. One of the workers left work early at about 4:00 PM because of progressive discomfort, whereas the others kept working regardless and finished work at 7:00 PM. The individual who left work early was taken to hospital at that evening, and the others experienced vague chest discomfort, malaise, and dyspnea overnight. However, the following morning all were rushed to the hospital with similar discomfort. An immediate and thorough investigation was initiated by the Korean National Center for Occupational Health and Safety Resources to determine why acute respiratory symptoms had simultaneously developed in the 15 workers. Finally, acute respiratory morbidities evoked by exposure to HCFC-141b in the workplace were deemed to have developed in all 15 workers.

The study protocol was approved by the new Institutional Review Board of Pochon CHA University, and written informed consent was obtained from each patient. However, only four patients consented to a bronchoscopic examination.

High-Resolution CT Scanning

All subjects underwent high-resolution CT (HRCT) scanning of the chest on the first day of hospital admission. HRCT scans were performed using 1.5-mm sections obtained at 10-mm intervals throughout the entire thorax.

PFTs

All 15 study subjects underwent PFTs at 3 days, 1 week, and 1 month after injury, and 13 subjects underwent PFTs at 3 months after injury. Spirometry was performed (Elite series spirometer; MedGraphics; St. Paul, MN), and findings obtained using a reference spirometry equation[10] were assessed using the American Thoracic Society criteria.[11] Each subject performed the test at least three times, and the best performances were used for the analysis.

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AHR

Bronchial responsiveness to methacholine was determined, according to American Thoracic Society guidelines,[12] in subjects who had undergone a PFT on hospital admission day 2, and at 1 month and 3 months after injury. Increasing methacholine concentrations were administered until FEV_1 declined by 20% of baseline (*ie*, the provocative concentration of methacholine causing a 20% fall in FEV_1 [PC_{20}]) or the maximum concentration was administered. The results are expressed as the PC_{20} as determined by linear interpolation using log dose-response curves. Subjects with a PC_{20} of < 8 mg/mL were considered to show AHR.

Analysis of Cellular Constituents in BAL Fluid

Bronchoscopic BAL examinations were performed in only four patients on hospital admission day 2. After inducing local anesthesia of the throat, larynx, and bronchi with a 4% lidocaine solution, a flexible bronchoscope (model 1200; Olympus; Tokyo, Japan) was introduced into the bronchial tree and gently wedged into the medial segmental bronchus of the right middle lobe.[13] Three 40-mL aliquots of warm sterile saline solution were then instilled and aspirated using a syringe via the bronchoscope channel. The first aliquot was discarded, and the others were pooled for analysis. The total numbers of cells were determined, and the remaining samples were spun down in a cytometer. May-Grünwald-Giemsa staining was used to identify the differential profiles of cellular constituents after cytospin preparation.

Healthy Control Subjects

The control group consisted of four normal, healthy, nonsmoking volunteers with no relevant medical history of illness. All subjects signed an informed consent form before undergoing the examination. The findings of clinical examinations, chest radiographs, spirometry, and bronchial methacholine challenge test results were normal. All four subjects underwent bronchoscopy with BAL, as described above.

Statistical Analysis

The data are presented as the mean ± SD, unless otherwise stated. Comparisons were made using the Mann-Whitney test and the Wilcoxon signed rank test for continuous data, and using χ^2 analysis for discontinuous data. A p value of < 0.05 was considered to be statistically significant.

RESULTS

Characteristics and Clinical Features

The characteristics and clinical features of the subjects are summarized in Table 1. Of the 15 victims, there were 8 women. The mean subject age was 31.5 years (age range, 18 to 45 years). None of the subjects had a preexisting lung disease or allergic disorder before the incident. Three were current smokers.

In terms of presented clinical features, most of the exposed workers had a cough, dyspnea, and malaise. About half of them complained of dizziness and headache, about 30% had chest pain, and about 10% had sore throats. These symptoms were most severe