J Forensic Sci, May 2004, Vol. 49, No. 3
Paper ID JFS2003250
Available online at: www.astm.org

CASE REPORT

Zhenggang Xiong,[1] *M.D.; Joseph Avella,*[2] *M.S.; and Charles V. Wetli,*[1,2] *M.D.*

Sudden Death Caused by 1,1-difluoroethane Inhalation

ABSTRACT: A 20-year-old man was found dead on the floor next to a computer, with a nearly full can of "CRC Duster" dust remover located next to the deceased on the floor, and an empty can of the same product on the computer desk. Toxicologic evaluation using either gas chromatography/mass spectrometry (GC/MS) or gas chromatography/flame ionization detector (GC/FID) method identified the active ingredient 1,1-difluoroethane (Freon 152a) in all tissues analyzed. Tissue distribution studies revealed highest concentration in central blood, lung, and liver. It is believed that the 1,1-difluoroethane inhalation was the cause of death.

KEYWORDS: forensic science, sudden death, forensic toxicology, volatile substance inhalation, difluoroethane, Freon

1,1-difluoroethane (Freon 152a) is a newly introduced propellant and refrigerant found in a variety of commercial products including aerosols. Because of its euphoric effect and easy accessibility, this substance has become a substance of abuse (1,2). A recent fatality provided the opportunity for a quantitative assessment of 1,1-difluoroethane in blood and various tissues.

Case History

A 20-year-old man was found dead on the floor next to a computer. A nearly full can of "CRC Duster" dust remover (commercially used to clean computer keyboards) was found next to the deceased on the floor, and an empty can of the same product was found on the computer desk. The items were both purchased earlier in the day. The decedent had a pituitary tumor irradiated 5 years earlier and had a history of testicular torsion with loss of one testicle. He was followed by an endocrinologist for hypothyroidism and was receiving thyroid hormone and testosterone injections. He was known to abuse cocaine for the past several months. There was no cardiac disease diagnosed in the past.

Postmortem Examination

Autopsy was performed approximately 24 h later (the body was stored at 4°C). No external injuries or abnormalities were noted. The decedent was 66 in. tall and 201 lbs. His 350-g heart had a 2.5 cm hypertrophied free wall and interventricular septum. The left ventricular chamber appeared small. Histologically, the myocardium appeared normal with no areas of interstitial fibrosis, contraction band necrosis or myofibrillar degeneration. The lungs were 930 g combined and congested. The remainder of the autopsy was unremarkable.

Biological specimens submitted for toxicologic analysis included blood, urine, vitreous fluid, gastric content, brain, lung, liver, kidney, muscle, and fat tissue, and stored at either 4°C or −20°C.

Toxicological Analysis

A general unknown toxicological analysis was carried out. Toxicological analyses performed on urine using EMIT® did not reveal any drugs of abuse. The liver was prepared using liquid/liquid extraction and submitted to chromatography/mass spectrometry (GC/MS) for basic drugs, and aortic blood was extracted and analyzed by GC/MS for weak acids and neutrals. In addition, femoral blood was analyzed by capillary gas chromatography/flame ionization detector (GC/FID) equipped with a headspace autosampler for common volatiles. The results of these analyses were negative.

1,1-difluoroethane (DFE) Analysis

During autopsy a selection of tissues were collected in 10 mL headspace vials and sealed with Teflon caps. The vials were stored at −20°C until analysis. Specimens are analyzed with either GC/MS or GC/FID method.

GC/MS

GC/MS was initially used to exclude other interfering volatiles. A sample of 5.7 g of brain was heated to 60°C. Using a gas tight syringe, a 5 uL aliquot was delivered to a sorbent tube. That sample was then submitted to a Varian CP 3800 GC equipped with a 75 m RTX-VMS® capillary column and Saturn 2000 Ion Trap MSD. The initial oven temperature was −30°C and was ramped to 240°C.

[1] Department of Pathology, State University of New York at Stony Brook, Stony Brook, NY.
[2] Suffolk County Office of the Medical Examiner, Hauppauge, NY.
Received 4 Aug. 2003; and in revised form 12 Oct. 2003; accepted 21 Nov. 2003; published 7 April 2004.

TABLE 1—*Quantitation of 1,1-difluoroethane.*

Tissue	Concentration
Liver	92.7 mg/kg
Kidney	24.3 mg/kg
Lung	91.1 mg/kg
Muscle	80.5 mg/kg
Adipose	29.8 mg/kg
Brain	43.8 mg/kg
Femoral Blood*	83.5 mg/L
Pulmonary Blood*	141.1 mg/L
Aortic Blood*	122.7 mg/L

*Samples not sealed in headspace vials at autopsy.

These parameters allowed for the separation of DFE from other volatiles that may have been present in the CRC Duster canister. The use of the MSD allowed for the positive identification of DFE and no other volatiles compounds were detected by this method. Following identification of DFE, a standard curve was generated using DFE obtained from Aldrich chemical and the amount of DFE in brain tissue was calculated. Using 66.1 g/mole (mole/24.45 L at 25°C), volumes of DFE are converted to weight. The instrument was calibrated using a standard curve from 0.0 to 127.5 nL/on column (nL/OC). The AUC of the sample was then plotted against the calibration. The tissue concentration was then determined after correcting for sample volume and weight. The brain tissue was found to contain 43.8 mg/kg of DFE.

GC/FID

Upon positive identification of DFE in brain tissue and having found no other interfering volatiles, a more rapid method of GC headspace analysis similar to that used by Broussard et al. (2) was employed. A sealed vial containing 10 mL of methanol was prepared and weighed, and then DFE (Aldrich Chemical) was added until the amount of DFE was equal to 6.24 mg/mL. Blood calibrators and controls were prepared by sealing 2 mL of negative blood in 10 mL headspace vials. Amounts of the methanolic standard were added to create a standard curve from 0.0 to 312.0 mg/L. All specimens were analyzed using a Hewlett Packard 5890 GC/FID with 7694 autosampler. The samples were allowed to equilibrate at 40°C for 15 min prior to the injection using a 1 mL sample loop. The vial parameters in minutes were as follows: pressurization 0.15, loop fill 0.15, and sample inject 0.25. The GC column was a 30 m, 0.53 mm ID Restek RTX-BAC1®. The GC oven temperature was 40°C (isothermal) with injector temperature set at 200°C and detector at 225°C.

The quantitative analyses of 1,1-difluoroethane were performed on blood, lung, liver, kidney, muscle, fat, and brain. The results are showed in Table 1.

Discussion

1,1-difluoroethane is a halogenated hydrocarbon used as a propellant or refrigerant, and exists in many commercial products such as adhesive removers, correction fluid, and aerosols. Human exposure can occur by inhalation, ingestion, and cutaneous contact. Inhalation is the most common route due to their high volatility. Exposures may occur from recreational abuse or from industrial exposure (3,4). However, fatal industrial exposure has not been reported (5,6), probably because of imposed industrial exposure limits and close monitoring. Since halogenated hydrocarbons are easily available and capable of producing euphoria, they have been intentionally inhaled by substance abusers as a legal and inexpensive substitute for other drugs, particularly among adolescent males (1,5).

As a halogenated hydrocarbon, 1,1-difluoroethane is well absorbed via the lung, and rapidly distributed to organs with high fat content such as brain (7). Due to its high blood gas partition coefficient, the onset of effects with inhalation of this substance can be as rapid as an intravenous injection (8,9) although the peak effects may be delayed because of slower tissue diffusion (10). Since pulmonary absorption circumvents the hepatic extraction and metabolism (6), the toxic dosage may be reduced.

1,1-difluoroethane concentrations of 35 mg/L and 78 mg/L in blood have been reported to interfere with physiologic functions (2). The fatal case presented here had much higher concentrations (Table 1). The acute fatal effects of halogenated hydrocarbons are due to central nervous system depression and/or cardiac arrhythmia from direct damage to the neural cell membrane, which in turns alters neurotransmission (11–13). Exposure to halogenated hydrocarbon stabilizes myocardial cell membranes and, therefore, blocks electrical impulse transmission (14). Under this circumstance, the ectopic impulses dominate the cardiac activities, and life-threatening arrhythmias may occur. Animal studies have also showed that halogenated hydrocarbons sensitize the myocardium to catecholamine which may also lead to an arrhythmia (15), and halogenated hydrocarbon induced cardiac arrhythmia has been associated with release of endogenous catecholamine as well (16). In this case, the heart appeared hypertrophied despite the normal weight. Whether this hypertrophy made this victim more susceptible to an arrhythmia is conjectural. The cause of death was attributed to toxicity from 1,1-difluoroethane inhalation and the manner of death was accidental.

Although it is reasonable to assume that some loss of DFE will occur after some period of storage, it is noteworthy that the blood samples that had not been stored in Teflon sealed headspace vials still contained substantial amounts of DFE six months later.

References

1. Litovitz TL, Felberg MA, White S, Klein-Schwartz W. 1995 annual report to the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emergency Medicine 1996;14(5): 487–537.
2. Broussard LA, Brustowicz T, Pittman T, Atkins KD, Presley L. Two traffic fatalities related to the use of difluoroethane. J Forensic Sci 1997;42(6):1186–7. [PubMed]
3. Anderson HR, MacNair RS, Ramsey JD. Deaths from abuse of volatile substances: A national epidemiological study. Br Med J 1985;290–304.
4. Garriott J, Petty CS. Death from inhalant abuse: toxicological and pathological evaluation of 34 cases. Clin Toxicol 1980;16(3):305–15. [PubMed]
5. Maxwell JC. Deaths related to the inhalation of volatile substances in Texas: 1988–1998. Am J Drug Alcohol Abuse 2001;27(4):689–97. [PubMed]
6. Ford MD, Delaney KA, Ling LJ, Erickson T. Halogenated hydrocarbons. Clinical toxicology. Philadelphia: W.B. Saunders Publishing Company, 2001:795–801.
7. Hormes JT, Filley CM, Rosenberg NL. Neurological sequelae of chronic solvent vapor abuse. Neurology 1986;36(5):698–702. [PubMed]
8. Pihlainen K, Ojanpera I. Analytical toxicology of fluorinated inhalation anesthetics. Forensic Sci Int 1998;97(2–3):117–33. [PubMed]
9. Watson JM. Solvent abuse: presentation of clinical diagnosis. Hum Toxicol 1982;1(3):249–56. [PubMed]
10. Linden CH. Volatile substances of abuse. Emerg Med Clin North Am 1990; 8(3):559–78. [PubMed]
11. Bass M. Sudden sniffing death. JAMA 1970;212(12):2075–9. [PubMed]

12. England A, Jones RM. Inhaled anesthetic agents: from halothane to the present day. Br J Hosp Med 1992;48(5):254–7. [PubMed]
13. Onofrj M, Thomas A, Paci C, D'Andreamatteo G, Toma L, Rotilio D. Optic neuritis with residual tunnel vision in perchloroethylene toxicity. Euro Neurol 1999;41(1):51–3.
14. Henry J, Cassidy. Membrane stabilizing activity: A major cause of fatal poisoning. Lancet 1986;1:1414. [PubMed]
15. Shepherd RT. Mechanism of sudden death associated with volatile substance abuse. Hum Toxicol 1989;8(4):287–97. [PubMed]
16. Mullin LS, Azar A, Reinhardt CF, Smith PE Jr, Fabryka EF. Halogenated hydrocarbon–induced cardiac arrhythmias associated with release of endogenous epinephrine. Am Ind Hyg Assoc J 1972;33(6);389–96.

Additional information and reprint requests:
Zhenggang Xiong, M.D.
Department of Pathology
State University of New York at Stony Brook
Stony Brook, NY 11794
E-mail: zhxiong@notes.cc.sunysb.edu