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Isopropanol and Isopropanol Deaths—Ten Years' Experience

REFERENCE: Alexander, C. B., McBay, A. J., and Hudson, R. P., **"Isopropanol and Isopropanol Deaths—Ten Years' Experience,"** *Journal of Forensic Sciences,* JFSCA, Vol. 27, No. 3, July 1982, pp. 541-548.

ABSTRACT: A population of persons who were found, at death, to have significant levels of isopropyl alcohol (isopropanol) in their blood is described. The role of isopropanol in causing death is reviewed in 57 fatal cases. The contribution of acetone, the major metabolite of isopropanol, to death is assessed. Results indicate that mixed alcohol poisoning with ethanol and isopropanol suggests decreased production of acetone. Modalities for antemortem and postmortem detection of isopropanol are presented.

KEYWORDS: isopropanol, acetone, toxicology

Isopropyl alcohol is ubiquitous: it is found in most homes as isopropyl rubbing alcohol. Taken in small doses, isopropyl alcohol probably causes little or no residual damage. In large doses, however, respiratory depression, shock, and coma occur [*1*]. Although metabolized and excreted much more slowly than ethanol, isopropyl alcohol is at least twice as potent a central nervous system (CNS) depressant. As little as 240 mL (8 oz) of isopropyl alcohol can be fatal [*2*]. Despite the fact that poisoning with this substance occurs most frequently in chronic alcoholics, such individuals are reported to be relatively tolerant to isopropyl alcohol. Survivals have occurred after ingestion of more than 500 mL (1 pt).

Isopropyl alcohol is absorbed rapidly from the gastrointestinal tract: 82% in 30 min and 99% by 2 h. Once absorbed, it takes approximately 2 h for maximal tissue distribution. Metabolism occurs slowly in the liver. Only 30 to 50% of the isopropyl alcohol ingested is oxidized to acetone; the rest is excreted unchanged in the urine or through the lungs [*3*]. Since acetone is not only toxic but also a more potent anesthetic than ethanol, the potency of isopropanol as a CNS depressant may be related to the generation of acetone.

The finding of significant ketosis without acidosis is almost pathognomonic of isopropyl alcohol poisoning [*2*]. For unknown reasons, the acetone does not appear to be shunted into the formation of acetoacetic and β-hydroxybutyric acids. Blood and urine glucose is either normal or slightly elevated following isopropyl alcohol poisoning, further differentiating this

Received for publication 22 Sept. 1981; revised manuscript received 11 Dec. 1981; accepted for publication 14 Dec. 1981.

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condition from diabetic ketoacidosis. Normoglycemic ketoacidosis is rare but does occur [4-6]. Nonspecific elevations of the blood urea nitrogen and serum glutamic oxalacetic transaminase may occur. Associated hemorrhagic gastritis may result in a decreased hematocrit. Blood isopropanol levels of 150 mg/dL are usually associated with deep coma, and concentrations greater than 200 mg/dL are rarely compatible with survival [2]. Fatalities may, however, occur at much lower levels.

Treatment for isopropyl alcohol poisoning is usually symptomatic; however, in life-threatening situations, hemodialysis may be useful. It has been reported that a 28-year-old man who ingested 1 L of rubbing alcohol in 10 min survived with a blood isopropyl alcohol of level of 440 mg/dL after receiving this treatment [7]. Since isopropyl alcohol is secreted by the salivary glands and stomach, continued gastric lavage with water is recommended. Oxygen, artificial respiration, and pressor agents should be used as required.

In an attempt to document the potential toxicity of this drug, a retrospective study was conducted of medical examiner cases over a 10-year period in North Carolina involving isopropyl alcohol poisoning. This report is the result of that study.

Materials and Methods

For the period between 1970 and 1980, 57 medical examiner cases were discovered in which toxicologic assays had indicated the presence of isopropanol. The jurisdictional population from which these cases arose is a relatively stable population of 5.7 million people. The background jurisdictional population is representative of approximately 1/40th of the nation's population and is an urban and rural mixture. During the 10-year period, approximately 25% of the total deaths per year (10 000/44 500) were investigated as medical examiner cases. Approximately 40% of these cases were autopsied. Toxicologic material was obtained in 60% of the total cases, or 6000 per year.

In addition to toxicological data, information concerning the past history of the deceased, circumstances surrounding the death, autopsy findings, and the final certified disposition of the case were collected. The cases included were generally subject to complete postmortem investigations and a majority (58%) had complete autopsies.

The location at which death occurred was most commonly a private residence, often the deceased's own house or apartment. Slightly more than 90% of the total deaths occurred at home. Hospitals were the least common location. In no case was there documented vigorous medical therapy prior to death. In 29 of the 57 deaths, investigation prior to the autopsy and toxicological examination revealed that isopropanol had been available to the deceased and that the individual had stated he or she intended to drink isopropyl alcohol. In other cases, it was found in the house.

Results

Characteristics of Deceased

The ages of the deceased ranged from 24 to 72 years. Most were 50 to 60 years old, and individuals between 35 to 50 years old constituted the next largest group. Whites accounted for more than 90% of the cases, as did males.

Of the 57 cases, 46 (81%) had a prior medical history of alcoholism. The manner of death listed in the 57 cases included accident (34), suicide (4), natural (2), homicide (1), and undetermined (12).

Terminal Events and Postmortem Pathological Findings

In 33 of the 57 deaths in the survey, a postmortem medical examination was conducted. The majority of cases were autopsied within 24 h of death; approximately 70% of the deaths

were known to have occurred within 10 h preceding autopsy. Most of the fatalities were believed, based on reports from investigators at the scene, to be associated with some type of overdose.

As noted by Adelson [*8*], no pathognomonic postmortem features are seen in isopropanol abuse. The 33 autopsied cases in this study support this contention. The most common observation at autopsy was pulmonary congestion. This is typical of deaths involving drug-induced CNS depression but cannot be considered diagnostic or specific. In only one case was there evidence of prior intravenous drug abuse substantiated by medical history. Also, for these 33 cases, four or five potentially lethal conditions were detected. A prior history of alcoholism was the most frequently encountered condition, representing 70% of all cases. Other significant and potentially lethal disease processes encountered were myocardial infarction (two), gunshot wound (three), subdural hematoma (one), and Wernicke's encephalopathy (one). None of the deceased were known to be diabetic.

In four instances, the deceased had a documented binge episode, and the isopropanol was consumed following a 14- to 40-day binge. Symptoms consistent with withdrawal or delirium tremors or both were reported to the investigators by witnesses in four other cases. The ability of isopropanol to delay, retard, or otherwise affect alcohol withdrawal syndrome is unclear. These cases tend to indicate no effect. Chronic isopropanol ingestion for longer than four months was documented historically in one case. In this case, economics rather than true preference seemed to dictate chronic use.

Toxicological Findings

The one feature common to the cases was the presence of isopropanol and its major metabolite, acetone, in the blood or body fluids of the deceased. The initial specimen was blood; however, in some instances, urine was also tested. The method of isopropyl alcohol analysis in the laboratory was consistent throughout the study period. The screening procedure used a dichromate reduction method [*9*]. If this proved positive, isopropanol was identified and quantitated by gas liquid chromatography [*10*]. Methanol, acetone, and ethanol were determined at the same time, since the production of acetone may be affected by ethanol [*11*]. The blood isopropanol levels ranged from a low of 10 mg/dL to a high of 470 mg/dL, with a mean of 240 mg/dL. The published values for lethal blood levels cover a broad range from 100 to 400 mg/dL. More than 54% of the cases shown in Table 1 had blood concentrations of 150 mg/dL or less, or fewer than 33% had levels greater than 200 mg/dL.

Isopropanol, like ethanol, is widely distributed and easily available. The abuse of isopropanol is apparently specific to a particular group of individuals. In only two cases were other drugs found. In one case, phenothiazines were found in the urine, and, in the other, pentazocine was found. The latter was the only historically confirmed drug addict. The 57 cases represented a small percentage of drug-caused fatalities in the study population. Our study population indicates that isopropanol is popular among chronically alcoholic white males in greater than the fourth decade of life who are in a binge phase of drinking.

Comment

Of the 57 cases in which isopropanol or acetone or both were determined to be present in the body, 31 deaths can be substantiated as resulting from isopropanol poisoning alone (54% of the total). The best measure of the role played by any drug in overdose fatalities is the frequency with which death can be associated with the presence of that drug. The blood isopropanol concentrations in these 31 cases ranged from 10 to 250 mg/dL, with a mean of 140 mg/dL. The acetone concentrations ranged from 40 to 300 mg/dL, with a mean of 170 mg/dL. Isopropanol and acetone levels in these individuals are listed in Table 2. Acetone is known to be a CNS depressant. As suggested in a clinical study of two cases by Daniel et al

TABLE 1—*Characteristics of deceased.*

Individual			Concentration, mg/dL					Prior Medical History of		
Age	Race	Sex	Isopropanol	Acetone	Ethanol	Place of Death	Autopsy	Ethanol Abuse	Cause of Death	Manner
						1970				
46	w	m	230	10	170	city, Charlotte	yes	yes	acute isopropanol intoxication	accident
53	w	m	10	110	ND[a]	city, High Point	no	yes	acute isopropanol intoxication	accident
54	w	m	70	130	ND	rural	no	yes	gunshot wound to head	suicide
61	w	m	220	80	30	rural	yes	...	acute isopropanol intoxication	accident
34	w	m	20	180	ND	city, Charlotte	yes	yes	acute isopropanol poisoning	accident
55	w	m	120	170	ND	city, Greensboro	no	yes	acute isopropanol poisoning	accident
68	b	m	60	40	120	rural	no	yes	exposure and isopropanol	accident (found in ditch)
						1971				
37	b	m	90	20	ND	city, Durham	yes	yes	sickling, splenic infarcts, myocardial scars, and fatty metamorphosis of liver	accident
33	w	m	40	60	220	rural	yes	yes	acute ethanol and isopropanol poisoning	accident
25	w	m	210	160	ND	rural	yes	yes	acute isopropanol poisoning	accident
37	w	m	200	230	ND	rural	no	...	acute isopropanol poisoning	accident
57	b	m	80	90	110	city, Wilmington	yes	...	acute myocardial infarction	natural

35	w	f	160	140	ND	city, Charlotte	yes	yes	generalized edema	apparent suicide
62	b	f	100	40	300	city	yes	yes	acute ethanol and isopropanol poisoning	accident
39	w	m	250	trace	ND	rural	no	...	exsanguination	accident
						1972				
31	b	m	110	30	110	rural	yes	yes	exsanguination and shock	homicide
38	w	m	150	320	ND	...	yes	yes	cerebral infarction	natural
24	b	m	190	90	ND	rural	no	...	pedestrian-vehicle	accident
53	w	m	20	90	30	city, Charlotte	yes	yes	withdrawal (?)	
31	w	m	50	60	300	city	yes	yes	acute alcohol poisoning	accident
						1973				
54	w	f	180	150	ND	city	no	yes	isopropanol poisoning	accident
59	b	m	trace	80	70	city	yes	...	no other cause of death identified	undetermined
...	b	m	110	240	ND	rural	yes	...	isopropanol poisoning	undetermined
						1974				
32	b	m	140	ND	290	city, Raleigh	yes	yes	mixed ethanol-isopropanol poisoning	accident
49	w	m	90	230	ND	...	no	yes	isopropanol poisoning	suicide
47	w	m	160	0	100	city	no	yes	mixed ethanol-isopropanol poisoning	accident
51	w	m	30	200	ND	...	yes	yes	isopropanol poisoning	accident
47	w	m	220	170	ND	city	no	yes	isopropanol poisoning	accident
28	b	f	280	trace	250	city	yes	...	mixed isopropanol-ethanol poisoning	accident
						1975				
39	b	m	230	180	ND	rural	yes	...	isopropanol poisoning	accident
50	w	m	220	40	ND	rural	...	...	isopropanol poisoning	undetermined
58	w	m	250	140	ND	rural	no	yes	isopropanol poisoning	undetermined
58	w	m	130	180	ND	city	yes	...	isopropanol poisoning	accident
24	w	m	125	100	ND	...	yes	...	isopropanol poisoning	undetermined
						1976				
54	w	m	230	30	50	city	no	yes	acute isopropanol poisoning	apparent suicide
61	w	m	190	170	ND	rural	yes	yes	acute isopropanol poisoning	accident

TABLE 1—*Continued.*

Individual			Concentration, mg/dL					Prior Medical History of		
Age	Race	Sex	Isopropanol	Acetone	Ethanol	Place of Death	Autopsy	Ethanol Abuse	Cause of Death	Manner
50+	w	m	250	200	50	rural	yes	yes	acute isopropanol poisoning	accident
62	b	m	20	140	ND	city	no	yes	alcoholism	natural
50	w	f	300	30	80	city, Durham	yes	yes	isopropanol overdose	accident
51	b	m	110	100	ND	rural	yes	...	exposure	accident
72	b	f	70	120	ND	city, Raleigh	yes	yes	isopropanol poisoning	accident
						1977				
25	b	m	200	50	30	rural	no	yes	apparent drowning	accident
38	b	m	110	170	ND	rural	no	...	isopropanol poisoning	undetermined
41	w	m	170	250	ND	rural	no	yes	isopropanol poisoning	undetermined
45	w	m	60	60	30	rural	no	yes	acute alcohol poisoning	undetermined
66	w	m	280	20	30	rural	no	yes	isopropanol poisoning	undetermined
65	w	m	110	290	ND	rural	no	yes	isopropanol poisoning	accident
65	w	m	180	140	ND	city, Raleigh	yes	yes	isopropanol poisoning	accident
50	b	m	220	50	ND	city, Durham	yes	yes	isopropanol poisoning and exposure	accident
						1978				
41	b	m	250	90	ND	rural	no	yes	acute isopropanol poisoning	undetermined
63	w	m	470	70	20	rural	yes	yes	isopropanol poisoning	undetermined
40+	b	m	90	190	ND	rural	yes	yes	acute isopropanol poisoning	accident
51	b	f	60	300	ND	city	yes	yes	acute isopropanol poisoning	accident
						1979				
51	w	m	210	130	ND	rural	yes	...	acute isopropanol poisoning	undetermined
41	w	m	140	260	ND	rural	no	yes	acute isopropanol poisoning	undetermined
48	b	m	70	190	ND	...	yes	yes	isopropanol poisoning	accident
45	w	m	150	280	ND	...	no	yes	acute and chronic isopropanol poisoning	accident

[a]Not detectable.

TABLE 2—*Combined isopropanol/acetone lethal cases.*[a]

Concentration, mg/dL		
Isopropanol	Acetone	Isopropanol and Acetone
	1970	
10	110	120
20	180	200
120	170	290
	1971	
210	160	370
200	230	430
	1973	
180	150	330
110	240	350
	1974	
90	230	320
30	200	230
220	170	390
	1975	
230	180	410
220	40	260
250	140	390
130	180	310
125	100	225
	1976	
190	170	360
20	140	160
110	100	210
70	120	190
	1977	
110	170	280
170	250	420
110	290	400
180	140	320
220	50	270
	1978	
250	90	340
90	190	280
60	300	360
	1979	
210	130	340
140	260	400
70	190	260
150	280	430

[a]Excluded from this group are all with other identified cause of death and those with ethanol.

[*12*], the prolonged presence of acetone may explain the long-term toxic effects of isopropanol. The data support this contention.

In our opinion, assessment of an individual case for potential lethality should include quantitation of isopropanol and acetone. Using combined levels may allow greater accuracy in predicting the clinical course of the condition in a specific patient. These data tend to corroborate potentially lethal effects in individuals with blood concentrations of isopropanol and acetone greater than 110 mg/dL. The possibility exists of even greater sensitivity to isopropanol and acetone in children, who are known to be extremely sensitive to ethanol. Since no children were included in the study group, definite conclusions cannot be made.

In those clinical chemistry and forensic science laboratories conducting multiple forensic toxicology determinations, it is recommended that gas liquid chromatography be used to identify and quantitate this agent. Limitations to enzymatic methods have been described [*13*]. The use of delta osmolality has also been suggested as a rapid procedure to detect isopropanol [*14*]. The nature of this study precludes assessment of this technique in our population.

References

[*1*] Wills, J. H., Jameson, E. M., and Coalston, F., "Effects on Man of Daily Ingestion of Small Doses of Isopropyl Alcohol," *Toxicology and Applied Pharmacology,* Vol. 15, 1969, pp. 560-565.

[*2*] Gleason, M. N., Gosselin, R. E., Hodge, H. C., and Smith, R. P., *Clinical Toxicology of Commercial Products,* The Williams and Wilkins Co., Baltimore, 1969, p. 131.

[*3*] Stolman, S., Ed., *Toxicology: Mechanisms and Analytical Methods,* Vol. 1, Academic Press, New York, 1960.

[*4*] Spencer, S. E., "Causes of Hyperketonemia," *Journal of the American Medical Association,* Vol. 242, No. 18, Nov. 1979, p. 1968.

[*5*] June, C. H., "Alcoholic Ketoacidosis and Isopropyl Alcohol Intoxication," *Archives of Internal Medicine,* Vol. 138, No. 4, April 1978, p. 660.

[*6*] Agarwal, S. K., "Non-acidotic Acetonemia: A Syndrome Due to Isopropyl Alcohol Intoxication," *Journal of the Medical Society of New Jersey,* Vol. 76, No. 13, Dec. 1979, pp. 914-916.

[*7*] King, L. H., Jr., "Hemodialysis for Isopropyl Alcohol Poisoning," *Journal of the American Medical Association,* Vol. 211, March 1970, p. 1855.

[*8*] Adelson, L., "Fatal Intoxication with Isopropyl Alcohol," *American Journal of Clinical Pathology,* Vol. 38, Aug. 1962, pp. 144-151.

[*9*] McBay, A. J., "Ethanol Type A Procedure," in *Methodology for Analytical Toxicology,* I. Sunshine, Ed., CRC Press Inc., West Palm Beach, FL, 1975, pp. 145-146.

[*10*] Parker, K. D., Fontan, C. R., Yee, J. L., and Kirk, P. L., "Gas Chromatographic Determination of Ethyl Alcohol in Blood for Medicolegal Purposes," *Analytical Chemistry,* Vol. 34, July 1962, p. 1234.

[*11*] Kemal, H., "Beitrag zur Kenntnis der Schicksale des Isopropyl-alkohols im menshlichen Organismus," *Biochemische Zeitschrift,* Vol. 187, June 1927, pp. 461-466.

[*12*] Daniel, D. R., McAnalley, B. H., and Garriott, J. C., "Isopropyl Alcohol Metabolism After Acute Intoxication in Humans," *Journal of Analytical Toxicology,* Vol. 5, Feb. 1981, pp. 110-112.

[*13*] Vasiliades, J., Pollock, J., and Robinson, C. A., "Pitfalls of the Alcohol Dehydrogenase Procedure for the Emergency Assay of Alcohol: A Case Study of Isopropanol Overdose," *Clinical Chemistry,* Vol. 24, No. 2, Feb. 1978, pp. 383-385.

[*14*] Glasser, L., Sternglanz, P. D., Combie, J., and Robinson, A., "Serum Osmolality and Its Applicability to Drug Overdose," *American Journal of Clinical Pathology,* Vol. 60, Nov. 1973, p. 695.

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