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Cocaine-Related Death

Cocaine (benzoylmethylecgonine), a local anesthetic and intoxicant in use for hundreds of years, currently is enjoying widespread popularity in the United States. This frequent use probably is due to the profound stimulatory effect of cocaine on the central nervous system and is occurring despite aggressive law enforcement activity because cocaine is a Schedule II substance [1].

Adverse effects of cocaine are highly controversial, and frank cocaine poisoning appears to be rare. We have been able to find only five reasonably documented cases of death associated with cocaine use in the English language literature [2-4]. This paper reports three cases of death believed to be secondary to cocaine effects and six others in which cocaine was associated with death.

Methods

In all cases, blood was analyzed for ethanol and related volatiles by gas chromatography. Multiple tissues were analyzed for acidic, neutral, and amphoteric compounds as well as for basic compounds. A variety of methods, including gas chromatography, was employed for these screens.

Cocaine, along with other bases, was extracted from tissue slurries either at physiological or alkaline pH with organic solvents. The first, fifth, sixth, and ninth cases were extracted with chloroform, the second, third, fourth, and seventh cases with *n*-butyl chloride [5], and the eighth case with a mixture composed of *n*-butyl chloride, hexane, and amyl alcohol.

In all cases, the organic solvent layer was removed and extracted with acid. The acid layer was then transferred, made alkaline, and re-extracted with solvent. The solvent layer containing the cocaine was then removed, taken to near dryness, and chromatographed after the addition of an internal standard. Lidocaine, methaqualone, and mepivacaine were found to be satisfactory as internal standards for the procedure.

Several glass columns were used, including a 6-ft (1.8-m) by 1/8-in. (3.175-mm) inside diameter column with 3% OV-1 on 100-120 mesh Gas Chrom Q; a 6-ft (1.8-m) by 1/8-in. (3.175-mm) inside diameter column with 3% OV-17 on 100-120 mesh Gas Chrom Q; and a 6-ft (1.8-m) by 2-mm inside diameter column with 3% OV-1 on 80-100 mesh Chromosorb W. No attempt was made to identify and quantitate the major metabolites

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benzoylecgonine and ecgonine, and the data given in Table 1 reflect the tissue recovery of the parent drug cocaine.

Case Reports

Cocaine Alone

Case 1—According to a witness, the decedent, a 16-year-old white female in Orange County, California, in 1974, injected intravenously what was purchased as 0.5 g of cocaine. She became comatose and was hospitalized. Despite emergency treatment, she died shortly thereafter, at least 8 h after injection. Field investigation was incomplete and previous drug use is not known. Toxicologic analysis of blood, brain, liver, lung, bile, stomach, and nasal swabs revealed the presence of cocaine in three locations, but no other drugs (see Table 1). Pathologic findings included bilateral pulmonary edema, tracheobronchial aspiration, numerous fresh needle marks in many locations, foreign body material in pulmonary capillaries, and chronic inflammation of hepatic portal triads.

Case 2—Upon hearing a loud thud in an upstairs apartment in Alameda County, California, in 1975, the tenants below investigated and found the door locked. Police were summoned and gained entry by force to find the decedent, a 33-year-old white male, dead on the bathroom floor. A syringe and needle were in his right hand and a glass with liquid was found on the lavatory. A belt was found near the body. Analysis of the syringe and glass revealed the presence of cocaine. Cocaine was detected in the blood, liver, and kidney (see Table 1). Examination of the blood, gastric contents, bile, and liver for other common drugs was negative. At autopsy, old and recent needle puncture sites were seen. The pupils were widely dilated and symmetrical. Marked congestion and edema of the lungs were present. Liver congestion and fatty change and gastritis were noted.

Case 3—The deceased, a 28-year-old white female, was found dead in the bathroom of her boyfriend's apartment in Dallas County, Texas, in 1973. A scarf, apparently used as a tourniquet, was in her left hand, and a syringe (containing cocaine) was approximately 25 cm from the body. White powder, later found to be 74% cocaine, was nearby in a bottle. At autopsy, eight needle puncture sites were seen near the left antecubital fossa, and most appeared old. A recent needle puncture site with fresh hemorrhage was present in the right antecubital fossa. The lungs had marked congestion and edema with froth in the trachea and bronchi. Enlarged lymph nodes were present near the liver and pancreas. Some polarizable foreign particles were present in the vessels of the lungs on microscopic examination. Cocaine was identified in blood, liver, kidney, stomach contents, and vitreous humor (see Table 1). Analysis for drugs other than cocaine proved negative.

Cocaine and Other Drugs

Case 4—A 32-year-old white female arrived home in Marin County, California, in 1975 at about 2:00 a.m., sniffed a substance believed to be cocaine, and may have smoked some marihuana. Later that night her husband heard her making strange sounds in the bathroom. He found her in a state of semicollapse and moved her to a bed. At noon the next day he awakened and found her dead. On arrival of the coroner's deputy, the body was found in bed with a slight degree of rigor mortis. Postmortem examination revealed mild cerebral edema, mild to moderate enlargement of the liver with congestion and fatty metamorphosis, a laceration of the lower lip, and multiple resolving cutaneous ecchymoses. Cocaine was identified in blood, liver, urine, gastric content, and nasal swab as well as in a liquid found in a glass at the scene (see Table 1). Morphine was identified

TABLE 1—*Toxicologic findings.*

Case	Age	Sex	Weight, kg	Route of Administration	Cocaine, mg/100 ml or 100 g							
					Blood	Urine	Liver	Kidney	Brain	Lung	Vitreous	Other Drugs
1	16	f	54	injection	N/D	N/A	0.01	N/P	0.04	0.01	N/A	...
2	33	m	...	injection	0.82	N/A	0.15	2.70	N/A	N/A	N/A	...
3	28	f	56	injection	0.75	N/A	0.13	1.68	N/P	N/P	0.38	...
4	32	f	47	inhalation	2.1	21.5	2.0	N/P	N/P	N/P	N/P	morphine in bile and urine
5	21	f	59	inhalation	0.4	N/A	0.1	N/P	1.5	0.6	N/A	lidocaine in blood, liver, brain, and lung; blood ethanol 0.05% blood ethanol 0.12%
6	24	m	68	injection	0.1	N/A	0.2	N/P	N/P	N/P	N/A	phenmetrazine, phendimetrazine, amitriptyline, and nortriptyline in urine
7	28	m	90	rectal	<0.01 ^a	0.98 ^a	N/D	N/P	N/P	N/P	N/D	ruptured berry aneurysm with subarachnoid hemorrhage
8	28	m	85	uncertain	0.02	0.56	N/D	0.02	0.03	0.09	N/P	shotgun suicide; blood ethanol 0.22%
9	33	m	70	injection	0.02	0.15	0.03	N/P	N/P	0.09	N/A	

N/D = not detected.
 N/P = not performed.
 N/A = not available.
^a Antemortem specimen.

in bile and urine. Examination of the blood, gastric content, bile, and urine for other drugs was negative.

Case 5—A 21-year-old white female in Orange County, California, in the company of friends in 1975, after several ethanol cocktails, snorted a white powder believed to be cocaine and soon experienced convulsions. She was immediately hospitalized but failed to respond to emergency measures and was pronounced dead about 40 min after admission. Several other people at the party admitted inhaling the same substance but denied any untoward symptoms. Autopsy revealed pleural petechiae and moderate pulmonary edema. Slight hemorrhagic gastritis and generalized visceral congestion were present. No needle marks were found. Toxicologic analysis of blood, liver, brain, lung, and gastric contents revealed cocaine and lidocaine, and the blood ethanol was 0.05% (see Table 1). No other drugs were identified.

Case 6—A 24-year-old white male was found dead in a truck in Orange County, California, in 1972. There was evidence that the body had been moved after death. A spoon, syringe, powder, and a tablet (amphetamine) were found in the truck. The syringe and powder contained cocaine. Injection sites were present on the arm. The state of decomposition suggested that the decedent had been dead about 5 days. A blood ethanol concentration of 0.12% was found. Cocaine was present in blood, liver, and gastric contents, and tests for other drugs were negative (see Table 1). The body was extensively decomposed with gaseous distension and greenish-black discoloration most prominent around the face. The lungs weighed approximately 500 to 600 g each and showed edema and congestion.

Case 7—A 28-year-old male with schizophrenia had recently moved into his father's house in Dallas County, Texas, in 1975 after a separation from his wife. The father was awakened one night and found his son yelling, kicking, and screaming. He told his father that he had put some cocaine that he had obtained on the street into his rectum and that it had not been diluted as he had expected. After an enema, administered by the father, he remained wild and incoherent, and was transported to the hospital by ambulance. Shortly after arrival at the emergency room he had a respiratory arrest, followed by a seizure and cardiac arrest. After resuscitation the patient was restored to a rapid tachycardia, then gradually returned to a sinus tachycardia with normal blood pressure. The next morning, neurological examination revealed evidence of irreversible central nervous system damage. He died 3½ days later. At autopsy, marked congestion of the viscera was present, with lungs weighing 1200 and 1400 g. Cerebral edema was marked. Sutured lacerations of the tongue and lower lip were present as a result of injuries suffered during the seizures. Toxicologic analysis of urine obtained on admission to the hospital revealed cocaine, phenmetrazine, phendimetrazine, amitriptyline, and nortriptyline (see Table 1). Examination of postmortem blood, liver, bile, vitreous, and kidney was negative for cocaine and phendimetrazine. Postmortem tissue was positive, however, for phenmetrazine, amitriptyline, and nortriptyline.

Cocaine and Other Causes of Death

Case 8—According to a witness, the decedent, a 28-year-old white male, in San Diego, California, in 1975 had used multiple drugs on the day of death. Some alcoholic beverages had been consumed early in the evening, followed by two pipes of hashish. Shortly after midnight, the subject began sniffing cocaine and continued to do so at intervals until about 2:00 a.m. when he clutched his forehead and collapsed. The friend called the fire department, and he was rushed to the nearest hospital where he was pronounced dead on arrival less than 30 min after collapse. A small vial present at the scene was found to contain cocaine. Autopsy findings included cardiac hypertrophy, bilateral pulmonary edema, and a spleen enlarged to 380 g. A ruptured, "berry"

aneurysm of the right superior cerebellar artery was associated with diffuse basilar subarachnoid hemorrhage. Toxicologic analysis identified cocaine in blood, gastric contents, kidney, brain, lung, urine, and nasal swabs. Analysis for other drugs was negative.

Case 9—A 33-year-old white male in Orange County, California, in 1974 was observed to act drunkenly on a yacht. After speaking to a girlfriend on the telephone and threatening suicide, he went below and shot himself fatally in the neck and head with a shotgun. A spoon, syringes, and needles were found in his possessions. Recent needle punctures were on both forearms. A disruptive shotgun wound of neck and head had produced death by avulsion of the brain. Toxicologic analysis of blood, urine, lung, and liver were positive for cocaine. Blood ethanol was positive (see Table 1). Analysis of these specimens failed to show the presence of any other drugs.

Discussion

Although cocaine legally has been regarded as a narcotic for many years, its pharmacologic actions consist of potent local anesthesia and central nervous system stimulation. The central stimulant effect is of short duration because of rapid body metabolism into inactive products. While serious adverse effects of pure cocaine use probably are uncommon, they do occur. Most cocaine use in the United States is by sniffing or snorting of powder via the nostrils. The principally recognized adverse effect of this use is epistaxis, probably secondary to local vasospasm. As with most other drugs, the effect the drug has on a user is highly related to the manner in which it is administered. In five of the cases reported here, including all three pure cocaine fatalities, needle injection, probably into a vein, was the route of administration. With almost all drugs, this route, while the most effective, is also the most dangerous.

The mean lethal dose (LD_{50}) and minimal lethal dose of cocaine have been reported for different routes (intravenous, subcutaneous, intraperitoneal) in laboratory animals (mouse, rat, guinea pig, rabbit, cat) and range between 15 and 250 mg/kg body weight [6]. Comparable data in humans are not available. The average amount of cocaine present per "hit" in Los Angeles street samples is 12 mg (range, 2 to 20 mg), producing a strong effect from snorting. Doses as high as 100 mg orally in humans have resulted in little or no effect, whereas doses as low as 2 to 16 mg intravenously have produced consistent psychological and physiological effects [7]. The doses taken in the cases reported here are uncertain.

Overdose of cocaine results in excitement, apprehension, headache, nausea, and vomiting, progressing to tonic and clonic seizures. If the overdose is fatal, death is said to result from ensuing circulatory and respiratory failure [8]. The exact pathophysiologic mechanism of death from cocaine alone is obscure. As with many drugs, anaphylaxis must be considered. No specific pathologic findings were present in these cases to support that diagnosis. The pathologic changes here were those seen in association with deaths in acute and chronic intravenous drug abuse cases: multiple needle puncture sites, intracapillary foreign material, and passive congestion and edema of viscera, none drug-specific.

In assessing any drug-related death, presence of concomitant or predisposing types of disease must be considered. All of these patients were young adults with no clinical or autopsy evidence of any other serious disease, except in Case 8. Since most psychoactive drug users use multiple drugs, drug interaction or synergistic/additive effects must be considered in drug overdoses. Careful, complete analytical toxicologic analyses for all usual toxic drugs and chemicals from several body fluids and tissues were performed in all of these cases and were negative in the first, second, third, and eighth cases. Of course, some other rare or undetected substance could have been present, but there were

no other clinical, autopsy, laboratory, or scene evidences to suggest that other drugs were present.

In the fourth case, it seems likely that cocaine overdose was of major importance in the causation of death. Yet, the presence of morphine in bile and urine indicates probable mixed toxicity.

In the fifth case, the combination of cocaine, lidocaine, and ethanol proved to be lethal. Although lidocaine and other local anesthetics commonly are used as additives or substitutes for cocaine, we have not seen another example in which there was a lethal result. In an overdose situation, the toxic effects of lidocaine include dizziness, agitation, seizures, hypotension, and respiratory arrest [9]. The toxic effects of cocaine and lidocaine may be additive. The role of cocaine in the death in the sixth case is not certain but seems probable. The blood ethanol is significant but may have been produced in part by the state of decomposition of the body. The action of multiple drugs together probably resulted in seizures, producing anoxia and irreversible brain damage in the seventh case.

The only previously reported fatal case attributed to the use of cocaine that we have found in which body distribution studies were performed is that of Price [2]. His case involved the ingestion of probably 2 to 3 g of cocaine hydrochloride. Death occurred in less than 5 h and followed collapse and convulsions. In two of four cases of the present series in which witnesses were present, seizures were reported.

The finding of a ruptured berry aneurysm in the eighth case raises the question of whether the stimulant effect of cocaine may have produced enough hypertension acutely or chronically to have resulted in the development or rupture, or both, of the aneurysm. Without supportive evidence, this remains speculative. In regard to the ninth case, a strong relationship between cocaine and violence has not been reported. It seems likely that the high blood ethanol concentration was the more important finding since ethanol and violence, including suicide, are so commonly associated [10].

It is obvious from the authors' experience that death from cocaine use is extremely rare, compared to that from many other drugs. For example, during the 3-year period surveyed in Dallas County, two deaths involving cocaine were found. During that same period, at least 226 deaths were recognized as resulting from other drug use in some form.

From the data presented here, it seems reasonable to state that cocaine may be a legitimate suspect as a cause of death in overdose cases; that "mainlining" of cocaine may be particularly hazardous; and that the mixture of cocaine and other drugs may produce unexpected toxic effects.

Summary

Cocaine use and abuse, an ancient custom, is once again commonplace. While severe toxicity appears to be rare, overt poisoning including death can occur. This report documents nine cases of death associated with cocaine use; in three of these cocaine appears to be causative. Toxicologic analysis of body fluids and tissues was affirmative and levels are reported. Cocaine should be considered in serious drug overdose-reactions, especially after illicit injection.

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