Exhibit 2

Near Fatal Reaction to Ingestion of the Hallucinogenic Drug MDA

SEVERE

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3,4-Methylenedioxyamphetamine (MDA) is a hallucinogenic drug for which, thus far, there have been no reported serious adverse effects. Three cases reported here document a near fatal, a severe, and a mild adverse reaction to ingestion of a single 500 mg capsule of pure MDA. Graded doses of pure MDA were administered to a series of mice, a cat, and a dog. Similar effects were observed, but the dosage was approximately ten times greater.

Methylenedioxyamphetamine (MDA) has been known to the drug subculture for a few years as a potent psychotomimetic agent, somewhat resembling lysergic acid diethylamide-25 (LSD-25) in its effects. Structurally, it resembles mescaline and 2,5-dimethoxy-4-methylamphetamine (DOM or STP). MDA is generally taken orally, occasionally intravenously. Thus far, it has been felt to be a relatively "safe" hallucinogen (*Rolling Stone*, May 17, 1969, p 3). No serious adverse effects have been reported.

The following case reports detail our experience with one near fatal, one severe, and one mild reaction to the ingestion of single capsules of MDA.

Report of Cases

NEAR FATAL

Case 1.—A 22-year-old white man had been using amphetamines, barbiturates, and various hallucinogens for one year prior to admission. Six weeks prior to admission he developed mild jaundice, presumably secondary to viral hepatitis. For the five days before admission he had been taking amphetamine and secobarbital orally, and had not slept or eaten. On the night of hospitalization, he and five others each ingested a single capsule containing approximately 500 mg of MDA. This was his first experience with the drug. Within 15 minutes he had a tonic seizure and lost consciousness. He was brought to the emergency department by ambulance.

Upon admission, the patient did not respond to verbal stimuli. His pulse rate was 140 beats per minute. Respirations were 30 per minute and labored. Blood pressure was 140/90 mm Hg. Rectal temperature was 104.6 F (40.3 C). He was profusely diaphoretic, and showed marked generalized pilo-erection. His pupils were fixed and maximally dilated. Both eyes were deeply sunken into the orbits. There was pronounced trismus. His neck and extremities were rigidly extended, and it was impossible to flex his hips or knees. The deep tendon reflexes were symmetrically hyperactive, with clonus, and he reacted to loud noises and shaking with short clonic movements of his arms and legs. The remainder of the examination was unremarkable. Results of laboratory studies revealed respiratory acidosis with arterial blood pH 7.158, carbon dioxide pressure 59 mm Hg, and carbon dioxide content, 20 millimol/liter. Chest roentgenogram was normal. Serum glutamic oxalacetic transaminase was 70 Karmen units, icterus index was 16 Meulengracht units, and prothrombin time was normal.

Intubation was done blindly with a nasotracheal tube, and gastric lavage and forced diuresis were begun. During the subsequent two hours, respiratory insufficiency secondary to muscle spasm progressed so that ventilation could no longer be adequately maintained with a mechanical pressure respirator. When diazepam administered intravenously, failed to produce muscular relaxation, he was treated with tubocurarine chloride. Muscular paralysis was achieved and ventilation was controlled. Adequate spontaneous respiration was allowed to resume after six hours, and he gradually awoke. The nasotracheal tube was removed 15 hours after the ingestion of MDA. Examination 24 hours after the ingestion revealed normal mental status, with no evidence of psychosis, and with normal neurological findings. He was discharged on the fourth hospital day.

Case 2.—A 21-year-old white man had been using various drugs, and had taken amphetamine and secobarbital orally during the five-day period prior to hospitalization. He had no prior experience with MDA. On the night of admission he ingested one capsule of the drug.

Upon arrival in the emergency department about one hour after the ingestion, the patient was diaphoretic and tremulous. His pulse rate was 140 beats per minute and his respiratory rate was 30 per minute. Blood pressure was 150/80 mm Hg. His pupils were widely dilated and nonreactive. There were constant lateral roving eye movements, occasionally-rotatory eye movements, coarse tremors of the lips, and a facial expression suggestive of risus sardonicus. His neck became rigid in extension. Initially he responsed to simple commands, but soon developed such extreme reflex hyperexcitability that minimal auditory, visual, or tactile stimuli precipitated repetitive clonic convulsions. Arterial blood gases and results of his liver-function tests were unremarkable.

It was not possible to place a nasotracheal tube, or a tube for gastric lavage because all attempts precipitated repeated severe convulsions. Diazepam, administered intravenously, did not noticeably reduce seizure activity. The patient was then placed in a quiet, dimly lit room, and treated with fluids given intravenously to produce a forced diuresis. The seizure activity ended after 3 to 4 hours, and it was possible to discharge the patient 12 hours after the ingestion of MDA. At that time, results of the neurologic examination were normal, except for sluggish pupillary reaction to light.

MILD

Case 3.—A 25-year-old white man had a long history of oral and intravenous drug abuse. He had taken MDA several times previously, but apparently in doses only one-third the amount of the one capsule he ingested on the night of admission. He had also been taking amphetamine and secobarbital for the five days prior to admission, but had arranged his intake so that he was able to eat and sleep intermittently during this period.

He accompanied the first two patients to the hospital and initially did not appear to be ill. Shortly after arrival he developed coarse, predominantly horizontal, bilateral nystagmus and twitching of the lips. His pupils became widely dilated and nonreactive. For several hours he was hyperalert and very talkative. He did not develop seizures or respiratory difficulties and did not lose consciousness, but his deep tendon reflexes became extremely hyperactive with clonus.

Within six to eight hours the effects had subsided and the neurologic findings were

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again normal. There was no evidence of psychosis. He was discharged, but returned the next night complaining of visual hallucinations occurring spontaneously, without subsequent drug ingestion. These hallucinations disappeared over the next 24 hours.

Laboratory Investigation

We were unable to find any reports detailing laboratory investigation of toxic effects of MDA in animals or man. Therefore we attempted to determine whether the effects observed could be reproduced in laboratory animals.

Materials and Methods.—Graded doses of chemically pure MDA were administered intraperitoneally to mice. Purity was determined by gas chromatography. Doses ranged from 1,0 mg/kg of body weight to 1,000 mg/kg. Each dose was given to two to six mice. A dose of 100 mg/kg was administered intraperitoneally to a cat. A dose of 50 mg/kg was administered intravenously to a dog.

Results.—In the mice, doses up to 10 mg/kg had no apparent effect. Doses of 40 mg/kg produced hyperactivity, salivation, and pilo-erection. Doses of 70 to 90 mg/kg produced clonic convulsions and profuse salivation. None of the mice died suddenly, but several were found dead in their cages the next morning.

Doses of 100 to 1,000 mg/kg generally produced tonic convulsions with respiratory paralysis and death. One mouse receiving 100 mg/kg, however, did not convulse and only became hyperexcitable.

The cat developed extreme mydriasis, pilo-erection, and salivation. It lost its visual tracking ability and no longer made purposeful motor responses to stimuli. It remained oblivious to a mouse placed in front of it, and made no response when the mouse climbed up its forelegs. No seizures were observed. The cat, however, was found dead in its cage the next morning.

The dog receiving MDA intravenously became tremulous and developed mydriasis and salivation. Within 15 minutes it began to have clonic convulsions which progressed to tonic convulsions with opisthotonos, respiratory paralysis, and death. 50 mg/kg I.V.

Comment

There is little published information on MDA. Fairchild et al[1] and Shulgin et al[2] reported that MDA is three to five times as potent as mescaline as a hallucinogen in man. Naranjo et al[3] gave doses of 150 mg orally to experienced volunteers and found that they reported intensification of feelings, facilitation of insight, and heightened empathy and aesthetic enjoyment. They did not experience hallucinations, perceptual distortions, or closed-eye-imagery, but suggested a marked similarity to the intoxication produced by LSD-25. The only physical effect noted was moderate mydriasis.

Thus far the only reported possible adverse effect associated with MDA is increased rigidity after ingestion of an unspecified dose of MDA in one patient with Parkinson's disease.[4]

When our patients came to the emergency department, we initially thought we were dealing with strychnine ingestion. Strychnine has reportedly been used to adulterate heroin and LSD, and it seemed reasonable to believe that our patients had received an unfortunately large dose of it. Analysis by gas chromatography, and then infrared and ultraviolet spectroscopy of the contents of the remaining capsules in the patients' possession, revealed chemically pure MDA with no strychnine or other adulterants. Gas chromatography of the first patient's serum and urine also failed to reveal any traces of strychnine. The urine did contain MDA.

The animal studies, although preliminary, appear to support the impression that MDA can produce the effects seen in these three patients. The approximate intraperitoneal 50% lethal dose (LD_{50}) for mice was 75 mg/kg. The 500 mg ingested by each of our patients represents approximately 7.5 mg/kg. The convulsion threshold to amphetamines is known to be higher in mice than in man, however, so the precipitation of seizures in man by 7.5 mg/kg seems compatible with the animal pharmacology.

The variability in response to similar doses of MDA is considerable, especially since three other persons ingested similar capsules with no adverse effects at all. It is also alarming that the severe responses seen by us could occur at a dose level only slightly greater than three times the dose administered in the one reported clinical trial of MDA.[3]

The clear capsules were hand-packed from a bulk source of MDA, but the patients claim all appeared full. Significant variation in dosage therefore seems somewhat unlikely. Differences in individual responsiveness would seem to be a more likely explanation. These differences could be inherent, or they could have been caused by a number of variables, none of which have been studied. These variables include the effects of starvation and pretreatment with other drugs, such as barbiturates and amphetamines, on the metabolism of MDA.

Since MDA appears to be readily available to the drug subculture, and is apparently becoming more so all the time, and since it can be synthesized fairly easily, the observation of serious adverse effects points to a need for more detailed studies of MDA, and a general warning about the hazards of its use.

B. C. Raino, toxicologist, Rochester (NY) General Hospital, performed the gas chromatographic analysis of MDA and strychnine. John Temmerman, Monroe County (NY) Public Safety Laboratory, initially identified the ingested substance as MDA.

References

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