Sodium Fluoroacetate Poisoning

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• We observed a case of poisoning with sodium fluoroacetate, an extremely lethal rodenticide that has had relatively strict controls placed on its use. The case was unusual in the very long time the rodenticide had been present in the home, the mild nature of the poisoning, and the remarkably delayed onset of serious central nervous system symptoms. It demonstrates the need for even stronger controls on the use of sodium fluoroacetate.

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Sodium fluoroacetate, a potent rodenticide developed during World War II, is highly effective because it is stable for long periods, tasteless, and uniformly lethal. Unfortunately, the high toxicity extends to other species including man. Its lethal dose for man, extrapolated from animal studies, is about 5 mg/kg and is comparable to that of strychnine. For this reason, sodium fluoroacetate has been restricted to licensed pest control operators and public health officials for use under limited conditions. As judged by the following case, this restriction seems inadequate.

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REPORT OF A CASE

The patient, an 8-month-old girl, was referred to the Medical University of South Carolina for treatment following the ingestion of a poison thought to be sodium fluoroacetate. About noon on the day of admission, she was found chewing on a black-dyed bait cup placed ten months previously (prior to her birth) behind the refrigerator by a licensed pest control operator. Her family immediately gave her large quantities of milk and induced emesis by manual gagging. She was seen by her family physician within 30 minutes after the ingestion. Emesis was again induced by syrup of ipecac. She was sent home, but was noted to be anxious and agitated for the next few hours. The family again contacted the family physician who thought that treatment should be provided by a large medical center and who arranged immediate airplane transportation. While she was en route to the Medical University of South Carolina, the pediatric admitting resident consulted the Poison Information Service and the Charleston Community Pesticide Program for information about sodium fluoroacetate.

The patient had been followed up at the Medical University of South Carolina since birth for a ventricular septal defect that appeared to be closing. She had been treated with erythromycin in the week prior to admission for otitis media.

On admission, the patient was slightly irritable, but alert, active, and in no apparent distress. She appeared slightly dehydrated. Her pulse rate was rapid (160 beats per minute), but no arrhythmia was noted. Results of her neurological examination and the rest of her physical examination were within normal limits.

Laboratory evaluation on admission showed that results of a complete blood count, lumbar puncture, and serum chemical analyses were normal, with the exception of a mild elevation of the blood urea nitrogen level to 22 mg/100 ml. An electrocardiogram showed a sinus tachycardia at 160 beats per minute, with slight peaking of T waves. There were no ST changes or ectopic beats.

Toxicological evaluation showed a normal red blood cell count and a normal plasma cholinesterase level by the pH stat method.[1] Plasma chlorinated hydrocarbon pesticide levels were not elevated as determined by gas-liquid chromatography. No arsenic was detected in the blood by atomic absorption spectroscopy.

On admission, the patient received constant cardiac monitoring in the intensive care unit. Except for two episodes of vomiting, she remained asymptomatic until 20 hours after ingestion when she had a generalized seizure of one minute's duration for which phenobarbital was administered. Subsequently, in a 12-hour period, she had three further episodes of relatively brief seizures. During the interictal period, she was quite drowsy but easily arousable, and she displayed no localizing neurological signs. The seizures ceased approximately 12 hours later and did not recur. She subsequently had an entirely uneventful course and was discharged four days after admission on phenobarbital therapy. All laboratory values and the ECG were normal at that time. When seen in follow-up two weeks later, the electroencephalogram was normal and results of the physical and neurological examination were within normal limits. The family could note no change in her behavior or intellectual or motor performance.

Subsequent investigation confirmed that the material in the cup was sodium fluoroacetate, when analyzed by the laboratory of the South Carolina State Board of Health. The pest control operator confirmed that he knew that the material in the bait cup was, indeed, sodium fluoroacetate, that he had placed it there ten months prior to the ingestion, and that he had used this same material in several homes. He was not licensed in this state, but had crossed the border from an adjacent state where he was licensed. He did not have a permit to use sodium fluoroacetate and had obtained the material illegally. This resulted in a revocation of his license.

COMMENT

Sodium fluoroacetate and some closely related compounds appear to have a unique mode of action. The toxicity is apparently not due to its fluoride content, as the clinical toxicity and pathological findings are quite distinct from those in fluoride poisoning. Several investigators have tried to determine the biochemical action of this material, and the best present evidence is that it appears to act by formation of a fluorocitrate compound that inhibits the reactions of the Krebs cycle.[2,3] For this reason, there is a delay in the onset of its action that is related to the need to metabolize the fluoroacetate. However, most writers have emphasized that this delay is usually only one or two hours, and may be as short as 30 minutes.[3,4] Remarkably, in this case, definitive symptoms first occurred about 20 hours after ingestion.

The symptoms of poisoning in man appear primarily related to the central nervous system (CNS) and the cardiovascular system. The CNS effects are usually agitation, depressed consciousness, seizures, and eventually coma. The cardiovascular effects, which often result in death, appear to take the following course: First, there is tachycardia and increase in amplitude of T waves followed by ST elevation and irregular rhythm with premature ventricular contractions that may progress to a bigeminal pattern. Finally, in adults, there may be ventricular tachycardia and fibrillation leading to death. In children, the final stage is usually heart failure and cardiac standstill.[2]

Because the onset of toxicity is usually abrupt and severe, therapy has usually been unsuccessful despite the availability of several antidotes that are at least theoretically useful. Among these are ethanol, propylene glycol, glyceryl triacetate, glyceryl diacetate, and glyceryl monoacetate (monacetin). Considering the three acetate compounds, Chenoweth et al[5] chose monacetin as the least toxic in animals. Their extensive animal studies have indicated that this compound would probably be useful in acute poisoning although the effective dose appears to be quite close to the toxic dose. They have also demonstrated that ethanol and propylene glycol are probably not effective antidotes and are certainly less efficacious than monacetin. Further, they have shown that sodium acetate, digoxin (or other cardiac glycosides), sodium chloride, potassium chloride, and calcium chloride all seem to enhance the toxicity of sodium fluoroacetate, making infusion or administration of any of these materials quite hazardous.

The use of acetate (sodium or potassium) to antagonize sodium fluoroacetate would tend to result in hypernatremia and hyperkalemia as well as creating a more severe metabolic alkalosis. The use of potassium or calcium chloride or cardiac glycosides tends to enhance the cardiovascular manifestations of toxicity.

Monacetin provides acetate and a nontoxic cation. It is available commercially as 95% active ingredient, with no assay of the remaining 5%. No pharmaceutical dosage form of monacetin is available commercially, and to our knowledge, none is available for investigation. The material is quite hygroscopic[6] and must be used quickly after opening the shipping container.

The practical grade is viscous, and so is difficult to sterilize by filtration with 0.22μ or 0.45μ filters. Sterilization by autoclaving may result in hydrolysis, thereby increasing the free acetic acid content. Therefore, prior to injection of this chemical, it would appear desirable to send an aseptically collected sample from the sealed commercial container to the microbiology laboratory for culture. Doses for injection should be withdrawn from a freshly opened container and administered immediately. In the event a secondary infection occurs, the laboratory report indicates the pathogen that may have been introduced. Unfortunately, time does not usually allow for the completion of a culture prior to administering the compound to the patient. The compound is administered parenterally since absorption after oral administration is erratic and since orally administered monacetin produces emesis in dogs and monkeys,[5] suggesting that it would do the same in humans. In light of all known information, Chenoweth et al have recommended the following therapy and management[5]:

1. Intramuscular administration of monacetin in repeated, hourly doses of 0.1 to 0.5 ml/kg as soon after ingestion as possible, to be continued until a clinical response is noted
2. Continuous cardiac monitoring
3. Seizure control with administration of usual anticonvulsant medications
4. Avoidance of infusion of calcium or potassium salts as well as sodium chloride, bicarbonate, or acetate
5. Fluid replacement with plasma in a cautious manner
6. Avoidance of cardiac glycosides.

Since a gastroenterohematic circulation of fluoroacetate compounds has been suggested,[7] repeated gastric lavages and catharsis may be useful in such cases. However, there is no convincing evidence to support these modes of therapy, and they should be applied with care and monitored to avoid disruption of the electrolyte or acid-base status of the patient.

In our case, monacetin was not administered because the compound was not available until 36 hours after ingestion and there was no evidence of cardiotoxicity at that time. The patient's condition appeared to be improving. Furthermore, fluid replacement was not made with plasma but with a more conventional pediatric replacement solution that consisted of solutions believed to be of no risk to the patient as they were relatively low in sodium and potassium salts (primarily 0.2% sodium chloride in 5%

dextrose in water with careful addition of potassium chloride for replacement and maintenance). Note that this was an exceptionally mild instance of poisoning with sodium fluoroacetate, as compared to other reported cases,[8-10] and the onset was so delayed as to cast some doubt on the diagnosis in the early stages.

The successful treatment of this unusual case of poisoning seems to hinge on several factors: The referring physician immediately gave appropriate first aid and arranged rapid transfer to a hospital whose staff had an interest in acute poisoning, and a team of professionals including a physician, research pharmacist, and toxicologist was available for consultation and backed by the facilities of the poison control center. This team was able to provide information beyond the scanty information available in the usual toxicology handbooks[4,11] and provided management of maximal benefit to the patient without introducing harmful or unnecessary therapy. Fortunately, it was not necessary in this case to attempt therapy with monacetin.

It appears clear that limitations on the use of this rodenticide are inadequate to prevent misuse and accidental poisoning, particularly in light of the long life and treacherous nature of this compound. It would appear logical at this time to completely ban its use, as there are several reasonable alternatives that are much safer and easier to control.

Conclusion

An active, aggressive, well-informed team of poison control persons should be available regionally for guidance in all unusual or especially toxic poisonings in order to provide optimum therapy. Early consultation with such a team clearly provides the best opportunity for a successful outcome in such cases.

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60 Years Ago in AJDC

The Atropin Treatment for the Exudative Diathesis in Infancy

Czerny gave the name of "Exudative Diathesis" to a group of symptoms characterized by an exudation into the skin and mucous membranes. The skin of infants suffering from exudative diathesis shows some form of eczema . . . with excoriation. Catarrhal affections of the respiratory tract—coryza, pharyngitis, recurrent bronchitis, and asthma—make their appearance. A catarrh of the gastrointestinal tract is often present. General glandular enlargement with an enlarged spleen may be combined with . . . other manifestations. An eosinophilia is found in . . . some . . . cases. The exudative diathesis is generally encountered either in very obese or in very thin infants; some of the cases, however, are normal in weight and development.

Although the cause of the exudative diathesis is unknown,[1] Eppinger and Hess believe that it is an infantile form of vagotonia, and various manifestations are thus due to increased tone in the vagus system. . . .

During the past year I have administered the atropin treatment to ten infants suffering from symptoms of the exudative diathesis. . . . The results of the atropin treatment . . . were excellent; and this despite the fact that no changes in diet were made, and no other drugs administered.

It is fair to conclude that atropin sulphate in increasing doses given over long periods of time is of great value in the treatment of those severe and obstinate manifestations . . . of the exudative diathesis which do not respond to the ordinary dietary and local treatment.—"The Atropin Treatment for the Exudative Diathesis in Infancy," J. S. Leopold, MD, New York.