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Fatal Methadone Poisoning in Children: Report of Four Cases

During the past two years, the Brooklyn office of the Office of the Chief Medical Examiner of New York City has encountered four deaths in children due to methadone poisoning. In all cases, prepared methadone drinks or methadone hydrochloride tablets were carelessly left around the house within the reach of children by either parents or friends of the family who were on a methadone maintenance program. The increasing use of this oral methadone maintenance technique in the management of heroin addicts has made this drug more accessible, thereby increasing the danger of accidental ingestion by children. It is to be expected that with even wider adoption of this program, that accidental methadone poisoning in children will become more common. Four deaths in children due to methadone poisoning are presented in this communication.

Case Histories

Case 1—A 5½-year-old white male was seen in the emergency room of a hospital, 2½ h after ingesting 80 mg of liquid methadone. On admission, the child was apneic and cyanotic with constricted fixed pupils and a heart rate of 60 beats per minute. Endotracheal intubation was performed, with mouth to mouth breathing. Spontaneous respirations occurred in 15 s and the heart rate increased to 96 beats per min. Four mg of intravenous nalorphine hydrochloride were administered within a three min period. The endotracheal tube was removed and the child transferred to the intensive care unit with a blood pressure of 110/60 mm of Hg, a heart rate of 120 beats per min, a respiratory rate of 20 per min, and a temperature of 99°F. The sensorium remained depressed with muscle tone and deep tendon reflexes diminished. Initial laboratory values were within normal limits.

Approximately three h after admission, there was a marked depression of the sensorium and the respiration. Two mg of nalorphine hydrochloride were given intravenously. This produced a marked clinical improvement and the child began to talk coherently to his family and the nurses. Thirteen h after hospitalization, the patient was found unresponsive with respiratory depression and nonreactive pupils. His blood pressure was 130/70 mm Hg, with a heart rate of 88 beats per min. Twenty mg of methylphenidate hydrochloride (Ritalin) were given intravenously, resulting in respiratory improvement and increased responsiveness.

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Over the next few hours diastolic hypertension developed with values as high as 140 mm Hg. The patient remained semiconscious. Six h after his last dose of methylphenidate, he again developed respiratory depression. Intravenous methylphenidate hydrochloride was administered intravenously but with no response. After 1 h he was noted to have a blood pressure of 190/150 mm Hg. Soon after, he suffered a respiratory arrest requiring intubation with ventilation by intermittent positive pressure. Physical examination revealed fixed and dilated pupils with fresh flamed shaped hemorrhages of both fundi. Manitol and dexamethasone sodium phosphate (Decadron) were administered for cerebral edema. A lumbar puncture revealed clear cerebrospinal fluid with a pressure of 50 mm H_2O. The child remained flaccid, apneic, and unresponsive to all stimuli and expired on the 4th hospital day.

At postmortem examination there was bilateral hydrothorax, left fibrinous pleuritis, pulmonary edema, and bilateral aspiration pneumonia. The brain weighed 1150 g and on microscopic examination showed extensive encephalomalacia.

Case 2—A 4-year-old negro male was admitted to the hospital after ingesting two 40 mg tablets of methadone. There was a delay before the child, an epileptic, was brought to the hospital; and it was reported that he suffered two convulsive seizures prior to admission.

Physical examination revealed a drowsy but responsive child with shallow respiratory movements. The pupils were constricted and nonreactive to light. There was absence of the gag reflex, depressed deep tendon reflexes, and decreased motor power. No Babinski reflexes were elicted. Emergency procedures included gastric lavage, oxygen, and intravenous infusion of 5 per cent dextrose and water. After approximately 15 min, the child's condition became critical. He became completely unresponsive and cyanotic with decreased and shallow respirations. Nalorphine hydrochloride, 0.1 mg/kg of body weight, was administered intravenously and repeated in 20 min. This produced a slight, but temporary, clinical improvement. The child developed a tachycardia of 136 beats per min, a tense, distended abdomen with no audible bowel sounds, and became oblivious to painful stimuli. Three h after admission, he vomited a large amount of undigested food, went into respiratory arrest, and developed bradycardia of 30 to 40 beats per min. Resuscitative measures were instituted which consisted of endotracheal intubation, intravenous sodium bicarbonate, furosemide (Lasix), hydrocortisone, and intracardiac epinephrine. Blood gases revealed a pH of 7.25 and a pCO_2 of 50. Respiration was maintained by a Bird respirator. The child never regained consciousness and expired 15 h after admission.

Postmortem examination revealed cerebral edema with a brain weight of 1450 g, pulmonary edema, and bilateral bronchopneumonia. Toxicological examination demonstrated the presence of a small amount of methadone in the liver.

Case 3—A 15 month old negro female was admitted to the hospital after taking half of a 40 mg methadone tablet. On admission, the child was unconscious with subcostal retractions, rales and rhonchi in all lung fields, faint heart sounds, and an irregular heart rate of 100 beats per min. The extremities were flaccid. Emergency measures were instituted, consisting of endotracheal intubation, levallorphan tartrate (Lorfan) 0.2 mg intravenously, epinephrine, gastric lavage, and intravenous infusion of 5 per cent dextrose and water. There was no improvement in her condition and two h after admission she died.

Postmortem examination revealed cerebral edema with a brain weight of 1300 g, pulmonary edema, and early bronchopneumonia. Toxicologic examination revealed a small amount of methadone present in the liver.

The past history of this child is intriguing in that there was a previous hospital admission at the age of 8 months after ingestion of an unidentified pill. At the time of that admission,

her pupils were constricted and sluggishly reactive to light with all reflexes diminished in intensity. The hospital course was complicated by pulmonary problems. It is tempting to speculate that this may have been a prior episode of methadone intoxication.

Case 4—A 3-year-old negro girl was found dead in bed after drinking orange juice containing methadone. The girl and her cousin had been given the orange juice by an aunt who had found it in a soft drink bottle in the refrigerator. She was completely unaware that methadone had been dissolved in the juice. It was the cousin's respiratory distress which made a parent investigate the deceased's room and discover her.

Postmortem examination revealed cerebral edema with a brain weight of 1450 g and marked pulmonary edema. Toxicologic examination of the stomach contents demonstrated a small amount of methadone.

On admission to the hospital, the cousin of the deceased child was apneic with constricted pupils. Endotracheal intubation was not successful in this case and a tracheostomy was performed. The patient responded to repeated doses of nalorphine hydrochloride. His hospital course was complicated by pulmonary edema, pulmonary atelectasis and bilateral aspiration pneumonia. He gradually improved and was discharged after one month. Toxicologic examination of his urine revealed the presence of methadone.

Discussion

The use of methadone as a maintenance drug in heroin addicts began only in 1964, when Dole and Nyswander [*1*] launched an experimental program at Beth Israel Medical Center in New York City. At the present time, there are approximately 450 licensed methadone programs in the United States which treat 50,000 addicts [*2*]. The methadone maintenance therapy of addicts is based on the premise that methadone is effective in blocking both the euphoria and craving for heroin in individuals addicted to the latter drug [*1,3*]. While methadone is a narcotic and potentially addicting, it is less so than either heroin or morphine [*3*]. In the therapy of heroin addicts with methadone, one is basically substituting a cheap legal narcotic for an expensive illegal one with the full knowledge that the legal addiction is probably a lifelong affair [*3,4*].

When properly administered and supervised, methadone is supposed to permit an addict to function normally in society with no sedative effects and little or no impairment of intellectual capacity and somatic or psychological reaction [*3*]. Under medical supervision, the addict is given small amounts of methadone which are gradually increased until the amount given will end his craving for and block the effects of heroin. The majority of patients will reach a maintenance level of 80 to 120 mg per day. Some patients, however, have been maintained on doses as high as 300 mg per day and others as low as 30 to 50 mg [*5*]. For comparison, the oral or subcutaneous dose for analgesia varies from 2.5 to 10 mg every 6 to 8 h [*6*].

In methadone maintenance programs, the methadone is dissolved in water, orange juice, or artificial fruit juices and taken by mouth. The drug is readily absorbed from the G.I. tract and becomes effective 20 to 30 min after ingestion. Methadone is rapidly removed from the blood, and it localizes in the lung, liver, kidney, and spleen [*6*]. Peak levels in the brain are reached in one to two h after parenteral administration [*6*]. Methadone is detoxified in the liver, and the major fraction of the detoxified products appear in the urine and feces. Less than 10 per cent is excreted unchanged [*6*]. While a single dose of methadone produces analgesia for four to six h, the respiratory depression action of this drug may last 36 to 48 h [*3,5,7,8*].

The minimum lethal dose of methadone in adults is believed to be in the range of 60 to 120 mg in nontolerant individuals [9]. In children, ingestion of a 10 mg tablet of methadone caused the death of a 20 month old negro girl [8] while 10 mg administered rectally produced death in a 14 month old child [10]. In Case 3 above, ingestion of 20 mg resulted in the death of a 15 month old child.

Deaths of children due to methadone poisoning are uncommon in the literature. Perusal of the European literature revealed only 6 cases [10–12]. In the American literature, Aronow et al [8] reported one death in their series of 18 cases of childhood poisoning. This was the 20 month old negro girl who ingested 10 mg of methadone. Baden briefly describes one case of a child dying after ingestion of methadone (Case 1 above) and alludes to, but does not describe, three others [13].

Treatment

Children admitted with methadone poisoning are usually in severe respiratory distress. In such cases, it is imperative that an adequate airway be established for proper ventilation. This can be accomplished by insertion of an endotracheal tube with an inflatable cuff. The cuff is important because it acts to prevent aspiration of gastric contents. In cases of severe respiratory distress, artificial ventilation should be accomplished by the best means available with no delay.

The next step is the administration of a narcotic antagonist. Three principle drugs are used: naloxone hydrochloride, nalorphene hydrochloride, and levallorphan tartrate. Dosage of the drugs is determined by the body weight of a child: naloxone - 0.01 mg/kg; nalorphene - 0.1 mg/kg; levallorphran - 0.02 mg/kg [7,14]. While all three drugs will effectively relieve the respiratory depression caused by a narcotic, naloxone is the drug of choice [15]. If the respiratory depression is due to a barbiturate or a disease process, nalorphene and levallorphran will further increase it [7,14,15]; but naloxone will cause no further respiratory deterioration [7,14,15].

Initial administration of these drugs should be by the intravenous route. An improvement in the child's respiratory function should be observed within two min. If, in five min after injection, respiration has improved, but is not yet sufficient, the injection should be repeated. Failure of any response within five min suggests an error in diagnosis. In such cases, a repeat injection of naloxone is safe [7,14]. However, further injections of nalorphene or levallorphran should be deferred for 30 min while the patient is reevaluated. This is due to the potential of these drugs to augment respiratory depression in certain disease processes [7,14,15].

Once the child's respiratory depression has been alleviated, he must be monitored closely for at least 48 h [7,8,14]. This is because narcotic antagonists reverse methadone induced respiratory depression for only two to three h, while the depressant action of methadone may persist for 24 to 48 h [3,7,8,14]. This prolonged respiratory depressive action of methadone is illustrated in Case 1 above. If at any time the child shows any recurrence of respiratory distress, the narcotic antagonists should be readministered. Narcotic antagonists should not, however, be used in an attempt to arouse a comatose patient if the patient's respiratory function is adequate [7].

Other measures for treating methadone poisoning include gastric lavage and intravenous infusions. A patient admitted immediately after methadone ingestion should have gastric lavage. Some physicians, however, will lavage even after longer periods. They feel that methadone can induce gastrointestinal spasms which delay absorption thus making the drug susceptible to removal by lavage [16]. The intravenous infusions serve to hydrate the patient and maintain an open vein for intravenous therapy.

In treating methadone poisoning, dialysis is not indicated as the amount of methadone in the blood is negligible even after a fatal ingestion [*7,14*]. The central nervous system stimulants are likewise ineffective against the depressant action of methadone, and these may augment the deleterious stimulant effects of the latter drug [*7,14*].

Conclusion

The emergency room physician must be aware of methadone poisonings as a clinical entity. If he suspects this diagnosis, then he can intelligently question the family concerning any members or friends who are drug addicts on the maintenance program. Once methadone ingestion is established as a fact, he can immediately institute the proper therapy.

Preventing methadone poisoning means keeping the drug out of the reach of children. The responsibility of preventing methadone fatalities is equally shared by the doctor and drug addict. Drug addicts on the methadone maintenance program must be impressed with the fact that methadone can be fatal to children. They must be instructed to keep the tablets in a container and put in a place which is inaccessible to children. They must be warned not to be careless with their orange juice methadone drinks. Once they prepare their methadone solution, they should be told to drink it immediately.

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