Methaqualone Poisoning with Muscular Hyperactivity Necessitating the Use of Curare*

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Methaqualone, a relatively new sedative hypnotic drug in the United States, has unique properties which make the handling of overdosage somewhat different from the standard procedures. We report the case of a 20-year-old woman who ingested a large quantity of the drug and required curarization and artificial ventilation during the course of her recovery. The paper recounts the details of this treatment and reviews available literature on principles of therapy for methaqualone overdose.

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CASE REPORT

A 20-year-old woman was admitted to the Hospital of the University of Pennsylvania at 6:00 p.m. on Dec. 3, 1971 because she could not be aroused for the previous four hours. Her friends admitted that she frequently abused the following drugs: methaqualone, diazepam, barbiturates and heroin. On examination she was unresponsive to deep pain, her blood pressure was 140/90 mm Hg, with a pulse rate of 132/min and a respiration rate of 24/min. She was afibrile. The pupils were moderately dilated and did not react to light; corneal reflexes were present. Excessive salivation was present and the gag reflex was depressed. Generalized muscle twitchings and shivering movements were noted; the deep tendon reflexes were exaggerated and bilateral ankle clonus was present. Babinski responses were flexor. The result of the physical examination was within normal limits.

A nasotracheal tube was introduced, gastric lavage was performed and fluids were administered intravenously. There was no depression of minute ventilation as measured with a Wright respirometer, and arterial blood gas values were normal. Complete blood count, electrolyte and blood urea nitrogen levels were within normal limits, and a lumbar puncture showed no abnormalities. Prothrombin time and platelet count were normal; the partial thromboplastin time was 50 seconds (control 32-45 sec). She received supportive treatment in the respiratory intensive care unit, with maintenance of intravenously administered fluids and an adequate urine output; endotracheal intubation was instituted to ensure a patent airway. Because of excessive muscular hyperactivity, repeated dosages of diazepam (total 40 mg) was given intravenously over the next 15 hours, with some decrease in muscle movement but no respiratory depression. By the 18th hour after admission, the hyperactivity became increasingly marked, flailing movements developed in her extremities, which could not be controlled with an additional 35 mg of diazepam given over an hour. Because of the fear that the marked muscular activity could lead to exhaustion or trauma to the patient, muscular paralysis was induced with 12 mg of d-tubocurarine given intravenously 20 hours after admission, and the endotracheal tube was connected to a volume-controlled respirator (Bennett MA-1). Paralysis lasted for one hour, and d-tubocurarine was given again in two more doses of 12 mg at one-hour intervals. Twenty-six hours after admission, the patient started responding to pain. Three hours later, she had an episode of agitation, which was controlled by 10 mg of methadone given intramuscularly; otherwise, her recovery was uneventful and no further sedatives were required. Forty hours after admission, the patient recovered consciousness and the endotracheal tube was removed. She was observed for 24 hours, then referred for psychiatric evaluation and management. The patient admitted to the ingestion of 30 tablets of methaqualone (300 mg).

Serum levels of methaqualone determined by a fluorometric assay (Metabolic Chemistry Department, Wm. H. Rorer, Inc) were 1.85 mg/100 ml on admission, 1.37 mg/100 ml the next morning, and by December 6 had decreased to 0.42 mg/100 ml. Serum chromatographic analysis was negative for barbiturates, opiates and phenothiazines.

DISCUSSION

A striking feature of methaqualone poisoning is the high incidence of muscular hypertonicity, the increased tendon reflexes and the myoclonia; such signs are characteristic enough to provide a diagnostic clue to this type of poisoning. The series of 116 cases reported by Matthew et al pyramidal signs were often observed, but the authors did not comment on whether the muscular hyperactivity posed any management problem necessitating the use of sedatives. Toxic convulsions were observed by Ibe in some of his cases and he advocated the use of sedatives in order to avoid exhaustion as a result of the convulsions; in case of inadequate sedation with drugs, the use of succinyl choline and simultaneous artificial respiration was advised. Other authors reporting isolated cases have used paraldehyde, barbiturates
and paraldehyde, and diazepam to control the muscular hyperactivity or convulsions. In the case reported by Sanderson et al., a generalized convulsion lasting for ten minutes was accompanied by central cyanosis and unresponsiveness to stimuli and terminated fatally. These authors pointed out that there were five other fatal cases in the literature in which tonic-clonic spasms and convulsions were predominant features. In the case reported by Doughty, the intravenous administration of 10 mg of diazepam was followed by apnea; after endotracheal intubation and mechanical ventilation, spontaneous respiration resumed in two hours and was not followed by any further difficulty in management. In our patient, measurement of minute ventilation did not reveal any respiratory depression despite the use of large doses of diazepam. Although initially some sedation was obtained with diazepam, it was later ineffective and we had to use curare. We consider it dangerous to use sedatives to control the convulsions of muscular hyperactivity accompanying methaqualone poisoning, without the use of endotracheal intubation to assure a patent airway and without provisions for the immediate institution of artificial ventilation in case of need.

In the cases reported initially from Edinburgh, a methaqualone level of 2.5 mg/100 ml was considered indicative of dangerous poisoning. However, experience with the larger series reported by Matthew et al. revealed that the level of consciousness was poorly correlated with plasma methaqualone level. These authors concluded that the assessment of severity of poisoning should be made on clinical grounds independent of the results of methaqualone determinations.

Unlike other hypnotics, dangerous depression of respiration was not encountered with methaqualone poisoning, even in patients with severe depression of consciousness. Reversible and inconstant electrocardiographic abnormalities and abnormal serum enzyme levels (glutamic and pyruvic oxaloacetic transaminase) were found in a small number of patients in the Edinburgh series. Also, unlike symptoms resulting from ingestion of other hypnotic drugs, severe hypotension did not occur in the 116 cases of methaqualone poisoning described from Edinburgh; the mild hypotension noted in a few patients responded favorably to simple elevation of the foot of the bed. In more severe poisoning hypotension may occur. Previous authors had noted the development of pulmonary edema; although increased vascular permeability induced by methaqualone was postulated as a cause, one wonders if the forced diuresis used in the treatment of these patients did not contribute to the development of pulmonary edema.

According to Proudfoot et al. at least 14 fatal cases of methaqualone poisoning had been reported in the literature. However, Matthew et al. did not encounter a single fatality among their 116 patients who received intensive supportive therapy alone, and they strongly advised against the use of forced diuresis. An additional patient from Edinburgh who was severely poisoned with a very high level of methaqualone (23 mg/100 ml) was treated with peritoneal dialysis and hemodialysis but died from respiratory and circulatory complications. Measurement of methaqualone in the dialysate indicated that the drug could be removed by both peritoneal and hemodialysis; however, the use of dialysis in less severely poisoned patients did not seem warranted. Severely poisoned patients in whom dialysis was successful have been reported by others. A bleeding tendency has been noted in some patients. In the Edinburgh series, the platelet count was below 150,000/cu mm in 13 of 65 patients, and the prothrombin time was prolonged in 9 of 72 patients. Pulmonary edema and diazepam coma may also be treated with peritoneal dialysis and hemodialysis.

In summary, methaqualone poisoning is often accompanied by characteristic pyramidal signs such as hypertonicity, increased tendon reflexes and myoclonia; unlike barbiturates, dangerous depression of respiration and hypotension are not encountered. Management should follow the general principles of intensive supportive therapy. Gastric lavage should be performed only if there is an adequate cough or gag reflex or after endotracheal intubation to protect the lungs from aspiration. Forced diuresis is highly ill advised. When it is necessary to control the muscular hyperactivity, sedatives or curare may be used, but a patent airway must be assured by prior endotracheal intubation, with provisions for the immediate application of artificial ventilation if respiratory depression occurs.

REFERENCES

1 New Drugs. Chicago, American Medical Association, 1967, p 163
2 Ibe K: Acute methaqualone intoxication II. Arch Toxicol 21:289-309, 1966
5 Brown SS, Smart GA: Fluorometric assay of methaqualone in plasma by reduction to 1,2,3,4-tetrahydro-2-methyl-4-oxo-3-0-tolylquinazoline. J Pharm Pharmacol 21:466-468, 1969

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