

Treatment of Methaqualone Overdose with Resin Hemoperfusion

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We recently utilized the technique of resin hemoperfusion (employing an Amberlite XAD-4 resin cartridge) to remove drug from a patient in deep coma after an estimated ingestion of greater than 4.5 grams of methaqualone. At plasma flow rates of 204 ml/min, the mean value for plasma clearance of methaqualone was 179 ml/min. The amount of methaqualone recovered from the cartridge at the end of the 10-hour procedure was 1,565 mg measured by gas chromatography. The patient became responsive to deep pain by the end of the procedure. The only complication encountered was a transient decrease in the formed blood elements. The present study verifies that a large, pharmacologically significant quantity of methaqualone can be removed in a short time using resin hemoperfusion.

The value of hemoperfusion in the treatment of acute drug poisoning has recently been stressed [1-3], but caution has been advised against widespread use of this form of therapy until its worth has been established [3,4]. It has been suggested that data concerning clearance rates and total drug removal should be established for each toxin and the results of hemoperfusion compared with conservative management before this technique is assigned a major role in the therapy of drug overdose [3,4]. We recently had the opportunity to study a patient with a massive overdose of methaqualone (Quaalude, Lemmon Pharmaceutical Company, Sellersville, PA). To our knowledge, clinical data reporting both clearance values and amount of methaqualone removed with resin hemoperfusion have not yet been published. We present this case to provide data on the use of resin hemoperfusion in methaqualone overdose.

CASE REPORT

A 35-year-old man with a history of previous suicide attempts was admitted 48 hours after ingesting approximately 30-40 150 mg tablets of methaqualone. Although breathing spontaneously, he showed no response to deep pain. BP = 180/90, P = 110, T = 100.8°F. His pupils were midplane and reactive, and corneal reflexes were present. Except for this Stage III coma, the physical exam was otherwise unremarkable. A methaqualone level drawn on admission was 9.8 µg/ml, 3-5 times the concentration of 2-3 µg/ml seen with therapeutic doses [5,6].

Initially, an attempt was made to minimize absorption of the drug by gastric lavage followed by instillation of activated charcoal. Respiratory function was

controlled with endotracheal intubation and mechanical ventilation and urinary output was maintained at 200 ml/hour with intravenous fluids. Despite this conservative therapy, he remained in deep coma. Spontaneous respirations became intermittent and then ceased during the first few hours of hospitalization. In an attempt to minimize the prolonged coma known to occur after ingestion of this quantity of methaqualone [8], hemoperfusion was started six hours after admission, using an Amberlite resin XAD-4 cartridge (Extracorporeal Medical Specialties, Inc., King of Prussia, PA) and was continued for 10 hours. Blood samples for methaqualone levels were obtained at three-hour intervals, spun immediately, and stored frozen until analyzed. The patient became responsive to pain and developed spontaneous movements by the end of the procedure and was fully awake by the following day.

MEASUREMENT OF METHAQUALONE

Analyses of Plasma

Assays were performed on a Perkin Elmer 3920 gas chromatograph equipped with a nitrogen detector, and 6 ft 3 percent OV-17 column. One ml of plasma (patient or standard) was adjusted to pH 12 and extracted three times with 4 ml of hexane containing 3 percent isoamyl alcohol. The pooled solvent extracts were evaporated to dryness under N₂, reconstituted in hexane: ethyl acetate (2:1), and chromatographed isothermally at 240°C. The internal standard (methadone) was added to the plasma prior to extraction. Concentrations were determined using relative peak heights.

Analysis of Cartridge

A homogeneous slurry of the cartridge was prepared, and an exactly weighed aliquot was removed, adjusted to pH 12 and successively extracted twelve times with methanol:ethyl acetate (1:1). Each aliquot of solvent was supplemented with internal standard and submitted to gas chromatography. The last three extractions were free of methaqualone. Completeness of recovery was validated by extraction of XAD-4 resin to which a known quantity of methaqualone had been added.

RESULTS

During the ten hours of hemoperfusion, blood flow through the Amberlite column averaged 300 ml/min, equivalent to a plasma flow rate of 204 ml/min (Hct = 32). The mean extraction rate for methaqualone,

$$\left(\frac{\text{arterial level} - \text{venous level}}{\text{arterial level}} \times 100 \right)$$

was 85 percent, and never fell below 75 percent. These two values yielded a mean plasma clearance rate of 179 ml/min. Specifically, plasma clearance values fell slightly, from 186 ml/min during hour 3 to 153 ml/min during hour 10. There was a transient fall of white blood cell count, from 10,700 to 5,300, and of platelet count, from 170,000 to 90,000. These returned to normal after the procedure. The hematocrit also dropped, from 37 to 31 vol percent, but this was not associated with microangiopathic changes on peripheral smear. Serum calcium concentration did not decrease. The amount of methaqualone recovered from the cartridge after 10 hours was 1,565 mg.

DISCUSSION

Methaqualone is a drug commonly ingested during street drug abuse and one occasionally encountered in suicide attempts. Since the half life in the body is quite long (36–74 hr) [7], prolonged coma is common with doses of greater than 4.5 grams [8]. Although mortality is usually low, death can result [8]. The drug is highly protein-bound, very lipid-soluble, and metabolized mainly by the microsomal enzymes in the liver [9]. Since only a small amount of the parent compound is excreted unchanged in the urine [9], forced diuresis is an ineffective means of increasing drug removal. Conventional dialysis techniques add little to the management of these patients since clearance rates by both hemodialysis (29 ml/min) and peritoneal dialyses (7.5 ml/hr) are low [10]. In contrast, data from one patient report [11] and from studies in dogs [12] demonstrate that plasma clearance rates using charcoal hemoperfusion are quite high (120–200 ml/min). In the present patient study using an XAD-4 resin cartridge, a mean plasma clearance of 179 ml/min was achieved. The amount of the drug removed from the Amberlite resin cartridge, 1,565 mg, was in excess of that which would be predicted from the plasma flow rates alone. This suggests that methaqualone may be present in the red blood cell compartment and that drug removal from whole blood may be greater than from plasma. As whole blood levels of methaqualone were not measured in the present study, whole blood clearances could not be calculated.

The procedure was well tolerated by the patient. As in previous studies, a transient fall in formed blood elements was observed but most of these changes reverted to normal after the procedure.

Hemoperfusion appears to be an effective method for the removal of methaqualone. The decision to utilize this technique in a patient with methaqualone overdose must be individualized, based on the approximate ingested dose, blood level, and clinical condition. In this case, hemoperfusion was used because the patient was in deep coma with a toxic blood level of methaqualone after the ingestion of an amount of drug known to produce prolonged coma. Although the correlation between blood concentration of methaqualone and either level of consciousness or mortality is not exact, concentrations above 8 $\mu\text{g/ml}$ are usually associated with coma [13] and death has been reported with concentrations of 10–30 $\mu\text{g/ml}$ [14]. We could not establish that the patient's outcome was significantly influenced by the use of hemoperfusion. The present study does, however, verify that a large, pharmacologically significant quantity of methaqualone can be removed in a short time using resin hemoperfusion. Additional data are needed to document the amount of drug removed, the risks of the procedure, and the clinical course of patients treated with hemoperfusion following methaqualone overdose before this therapy can be widely recommended.

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