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MEPROBAMATE INTOXICATION TREATED BY PERITONEAL DIALYSIS:

Report of a case

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MEPROBAMATE (2 methyl-2-n-propyl 3-propanediol dicarbamate) has been used extensively since 1955 in the treatment primarily of anxiety and tension states. The mode of action is felt to be its ability to block selectively interneuronal circuits, reduce exaggerated reflexes and muscle tension.

Not long after its initial use reports of untoward reactions and idiosyncrasy to the drug appeared in the literature. The list has grown over the years.5-7 After as little as 200-400 mgm. of meprobamate, sensitive patients have experienced hypotension, syncope, fever, urticaria, angioneurotic edema, erythematous rashes and non-thrombocytopenic purpura. Diarrhea, nausea, epigastric discomfort, excitement, nervousness, arthralgias, diplopia, and temporary extra-ocular muscular paralysis have also been reported. One death due to aplastic anemia followed the use of 400 mgm. of meprobamate three times a day for 8 days.8 In general, side-reactions have been variously reported to occur in 2-17 per cent of patients treated.

As might be excepted, cases of overdosage and attempted suicide have occurred. The case presented below demonstrates many of the findings typical of severe meprobamate intoxication with an unexpected and rapid recovery following the use of peritoneal dialysis.

CASE REPORT

G. F., a 49 year old married tailor was brought to the Emergency Room at approximately 10 a.m., June 9, 1962, in a comatose state. History obtained from the patient's wife revealed that he had ingested eighty 400 mgm. meprobamate tablets and seven 200 mgm. amobarbital and secobarbital capsules between 8 and 9 a.m. of the same morning. The patient was known to the hospital having been followed since 1958 for post-gastrectomy weight loss and depression. He had recently been re-evaluated for his gastrointestinal complaints.

Physical examination revealed a thin elderly appearing white male in deep coma. Blood pressure was 70/50, pulse 100 and regular, respiration 24, regular and shallow. The patient did not respond to painful stimuli, the pupils were dilated and reacted sluggishly to light. Deep tendon reflexes were hypoactive and the plantar responses were flexor in character.

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Emergency Room treatment consisted of gastric lavage and the institution of intravenous fluids. With maximal intravenous levartenerol, the blood pressure which subsequently fell to 50/40 was maintained at 80-100 systolic levels. Respirations, however, became agonal in character and required endotracheal intubation with the use of a positive pressure respirator. Intravenous bemegride in 100 mgm. and 50 mgm. dosages had no appreciable affect.

At 5:30 p.m. on the day of admission peritoneal dialysis was instituted; introduction of the catheter was performed without anesthesia and was bloodless. Over the next 24 hours the patient was dialysed regularly in two hour cycles with a total of some 24,000 cc. of Impersol 1½ (Abbott). Potassium chloride, tetracycline and heparin were added to the dialysing fluid. During the same period the patient received 6,500 cc. of intravenous fluids (5 per cent glucose in water and 5 per cent glucose in normal saline).

During the first five hours following institution of the peritoneal dialysis, the patient's condition remained essentially unchanged. At 11 p.m. a slight cough reflex was noted with endotracheal suction and at approximately 3:30 a.m. the following morning the patient's reaction was such that the endotracheal tube had to be removed. At this time there was also noted to be a return of the deep tendon reflexes which were now hypoactive and equal. The pupils became reactive and the patient responded to painful stimuli. By 4:30 a.m. of the same morning, the patient was responding to questions and though still lethargic was able to recognize his family. Blood pressure at this time was 100/80, pulse 110, respirations 26 and shallow. At 6:30 a.m. the levophed was discontinued and the blood pressure remained stable. By 9:00 a.m. the patient was completely responsive and taking fluids by mouth.

Peritoneal dialysis was discontinued at 6:00 p.m. on June 10th at which time the patient was able to sit in a chair and complained principally of weakness and numbness of the left foot. Examination at that time revealed paresis of the dorsiflexors of the left foot with decreased sensitivity to pinprick over the lower 1/3 of the left leg. This weakness gradually improved during the patient's hospitalization but was still demonstrable at the time of discharge ten days later. No further sequelae were noted.

DISCUSSION

Previous reports of the effects of meprobamate overdosage have all stressed the degree of hypotension which is out of proportion to the respiratory depression, the reverse of the situation seen with barbiturate intoxication. Both hypotension and respiratory depression were marked in our case.

As has been noted, hypotension has been reported with therapeutic doses of meprobamate. Ingestion of 2.4 grams to 44 grams has resulted in profound and prolonged shock lasting up to 72 hours.\(^9\),\(^10\),\(^11\) It has been suggested that the marked hypotension may be related to the effect on muscular tension; with complete loss of muscle tone, there is a lack of support to the vascular structures with pooling of blood and resulting hypotensive shock.

Five suicidal deaths due to meprobamate intoxication have been reported, with ingested amounts of 12-47.6 grams of the drug. These patients died from cardiovascular collapse in periods ranging up to five days post-ingestion. Autopsies revealed pulmonary congestion, bloody bronchial secretions and small pulmonary hemorrhages.\(^15\),\(^16\),\(^17\)

The majority of meprobamate intoxications have been treated symptomatically with support of blood pressure and respiration when needed. Methylphenidate* and pentamethylene tetraol** have been used with survival of the patient.\(^13\)

* Ritalin (Ciba)
** Metrazol (Knoll)
MEPROBAMATE INTOXICATION

With severe intoxication and resulting profound hypotension which may prove refractory to antihypotensive agents over a prolonged period, more aggressive treatment would seem to be in order. To our knowledge, the present case of meprobamate intoxication is the only reported one which has been treated by peritoneal dialysis. Barbiturate, aspirin and methyldialcohol intoxication have been treated successfully by this technique. It is generally conceded that hemodialysis is the treatment of choice for severe intoxications with dialyzable poisons. However, this method is cumbersome and not always available. Peritoneal dialysis represents a simple and effective alternate choice.

Unfortunately, laboratory data to support the severity of the meprobamate intoxication of the present case is lacking. Blood levels drawn on admission revealed barbiturate level of 0.54 mgm per cent which is considerably below the level considered clinically significant. Meprobamate levels could not be determined due to technical difficulties.

Distribution and excretion studies of meprobamate indicate that it is freely diffusible and thus amenable to dialysis. Intraperitoneal injections of meprobamate in laboratory animals have resulted in excellent absorption.35

It is difficult to prove our contention that peritoneal dialysis was lifesaving in the present case. However, the rapidity of change following its institution in a patient as singularly and profoundly depressed as was our case, was most impressive and would lead us to feel that peritoneal dialysis did have a decisive effect.

Of interest was the development of unilateral foot drop in our patient. This complication of meprobamate poisoning has been previously reported, adding to the list of unusual side effects of meprobamate that of neurologic involvement.

SUMMARY

A case of attempted suicidal poisoning with meprobamate is presented. Hypotension, respiratory and central nervous system depression with transient foot drop characterized the clinical course. Initial treatment consisted of gastric lavage, support of blood pressure and respiration. Peritoneal dialysis was instituted with the patient in an agonal state, following which there was dramatic improvement over the succeeding 12 hours to subsequent complete recovery.

The mode of action, side effects and toxicology of meprobamate is briefly reviewed.
REFERENCES


