CASE REPORTS

Severe meprobamate poisoning: successful treatment with haemoperfusion

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Summary

Charcoal haemoperfusion used to treat a 56-year-old woman who had taken a very large overdose of meprobamate was followed by full recovery. The plasma clearance of meprobamate was 153 ml/min and this compares favourably with values obtained for haemodialysis. The indications for haemoperfusion are reviewed.

Introduction

Severe meprobamate poisoning is uncommon in this country, only nine deaths being attributed to this drug in 1974 (Office of Population, Censuses and Surveys, 1976). The clinical features resemble those seen after an overdose of barbiturates but as meprobamate is rapidly metabolized coma rarely lasts for more than 24 hr. Plasma meprobamate concentrations above 100 mg/l are associated with deep coma (Maddox and Bloomer, 1967) and in a series of fatal meprobamate poisonings the mean plasma meprobamate concentration was found to be 239 mg/l (Felby, 1970). The case history is reported of a severely poisoned patient with an initial plasma meprobamate level of 260 mg/l who recovered completely after charcoal haemoperfusion, a technique which has previously been reported by the authors for severe barbiturate, glutethimide, salicylate and paraquat poisoning (Vale *et al.*, 1977; Volans *et al.*, 1977).

Case history

The patient, a 56-year-old woman, was admitted to St James' Hospital, Balham, having been found unconscious at home. She had a long history of depression, including treatment with electro-convulsive therapy and she had previously been prescribed meprobamate and tricyclic antidepressants.

On arrival at hospital she was drowsy, but responded to oral commands, and her blood pressure and respiratory rate were normal. In view of the history and physical findings a diagnosis of self-poisoning was made. After approximately 9 hr her degree of coma deepened such that she was unresponsive to maximal painful stimuli. Her blood pressure fell to 80/50 mmHg (10.6/6.7 kPa) but her respiratory rate did not change. In the following 24 hr there was no improvement in her clinical condition. At this stage the results of analyses of blood and urine samples taken that morning were available, and these revealed a plasma meprobamate level of 260 mg/l (Flanagan and Berry, 1977) and the presence of tricyclic antidepressants. In view of this extremely high level and the failure of her condition to improve with supportive care she was transferred to Guy's Hospital for haemoperfusion therapy.

After arrival she was found to be in Grade IV coma (Matthew and Lawson, 1975) with bilaterally reduced tendon reflexes. Both her pupils responded to light, she exhibited a divergent gaze and oculocephalic and caloric reflexes were absent, these signs suggested a severe metabolic cause for her coma (Plum and Posner, 1972). She was maintaining spontaneous respiration, but this was considered clinically to be of small tidal volume and reduced rate. The chest radiograph showed bilateral linear atelectasis and her arterial blood gases, while breathing 40% oxygen, were pH 7.38, P_{aO_2} 58 mmHg (7.7 kPa), P_{aCO_2} 41 mmHg (5.5 kPa) and a bicarbonate of 22 mmol/l. These clinical findings were considered to indicate a severe state of respiratory depression which had resulted in secondary changes in her lungs. Assisted ventilation was therefore started.

An arterio-venous shunt was inserted in the arm and 33 hr from her initial hospital admission

haemoperfusion was started. This was continued for 4 hr using a commercially available acrylic hydrogel coated activated charcoal column.* Within 30 min of starting haemoperfusion she was responding to oral commands and when it was discontinued after 4 hr she was awake and breathing spontaneously with a P_{aO_2} of 156 mmHg (20.8 kPa) and a P_{aCO_2} of 44 mmHg (5.9 kPa) on 60% oxygen. Her chest radiograph was now clear and she was transferred back to St James' Hospital the next day.

Subsequent toxicological analyses revealed amitriptyline and nortriptyline concentrations of 88.5 µg/l and 14 µg/l respectively. These were within the therapeutic range. The immediate pre-perfusion plasma meprobamate concentration however was 97 mg/l and after perfusion this figure had fallen to 62 mg/l. The calculated mean clearance of meprobamate by the column was 153 ml/min at a flow rate of 300 ml/min.

Discussion

This case has been reported because it is the first severe meprobamate poisoning which has been managed using charcoal haemoperfusion.

The authors considered haemoperfusion was necessary because of the high initial plasma level and the severity of the patient's coma, as judged by the absence of response to noxious stimuli and the loss of brain stem reflexes, together with the signs of depressed respiration.

It might be argued that after this patient had survived for 33 hr and the plasma level had by then fallen to 97 mg/l that she could have recovered without ancillary aid. But clinically the response to haemoperfusion was very rapid, a finding Rosenbaum, Kramer and Raja (1976) have reported with overdoses treated with resin haemoperfusion. During the 4-hr spell of haemoperfusion it was estimated, on the basis of plasma concentrations, that over 4 g

of meprobamate were removed from the blood compared with only 2 g recovered in the urine over a 36-hr period starting 12 hr before the commencement of haemoperfusion.

There is a small group of severely poisoned patients who, having taken sedative drugs, present in a profound state of coma. This may be associated with loss of brain stem reflexes, depression of respiration and loss of autonomic vascular control. In these patients active removal of the drug is indicated when supportive measures are not successful, or if respiratory complications develop.

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