Case Report:
MANAGEMENT OF SEVERE THEOPHYLLINE OVERDOSAGE
BY CHARCOAL HAEMOPERFUSION
by
A. C. UPRICHARD,¹ R. BAILIE² and E. McATEER³
Royal Victoria Hospital, Belfast

XANTHINE derivatives are widely used in the treatment of asthma and related conditions and are increasingly implicated in cases of attempted suicide by overdose. We report the case of a potentially lethal overdose of a long-acting theophylline preparation successfully treated by charcoal haemoperfusion.

A 28-year-old unemployed bar manager presented to the Casualty Department at 4.00 am having consumed fifty 400 mg tablets of a slow-release preparation of theophylline ("Uniphylline" — Napp Laboratories) three hours previously. An asthmatic since childhood, he had been taking 400 mg of this preparation daily for the previous year. There was no past psychiatric history and the taking of the overdose of tablets appeared to be a reactionary gesture following a disagreement with a close friend.

He was fully alert and orientated although nauseated and retching. His pulse was regular (160 per minute), blood pressure 120/70 mmHg. He was not dehydrated and showed no cerebral irritability. ECG showed sinus tachycardia with no other disturbance of rhythm. The stomach was washed out. He was transferred to the Coronary Care Unit for cardiac monitoring. The initial serum theophylline level was greater than 80 mg/L (60 mg/L is accepted as representing severe poisoning¹). Two hours later this had fallen slightly and it was decided to continue conservative management, but later that morning he developed signs of increasing toxicity with a tachycardia of 200 per minute, and his blood pressure fell to 90/60 mmHg. Five hours after admission, serum theophylline was greater than 120 mg/L and the patient was transferred to the Intensive Care Unit for charcoal haemoperfusion.

Femoral arterial and venous cannulae were inserted and he was started on haemoperfusion through a standard adult haemoperfusion column. He was intubated and ventilated for the duration of the procedure. Constant haemoperfusion was continued for nine hours. During haemoperfusion his platelet count fell to 65,000/uml and he required a transfusion of platelets from six donors. Two short runs of self-terminating ventricular tachycardia occurred early on in the procedure, but otherwise he remained in sinus rhythm throughout. Acid-base and electrolyte status remained normal during this time.

The following morning (24 hours after admission) his theophylline level was within the therapeutic range and he was transferred to a general medical ward and discharged (after psychiatric assessment) three days later.

¹ Neurology Registrar, Ward 21. ² Senior House Officer, Department of Anaesthetics. ³ Consultant Anaesthetist, Respiratory and Intensive Care Unit.
Theophylline

Theophylline is a xanthine derivative (1, 3 dimethylxanthine) from which a number of long-acting preparations have been derived. Its prime use is in the treatment of asthma and chronic obstructive airways disease, but its pharmacological effects involve a number of other systems of which the cardiac and cerebral are the most important. Even in therapeutic dosage, theophylline toxicity is a relatively common problem although a well-defined plasma level (10-20 mg/L) has been established.2 The most prominent symptoms of early toxicity are anorexia, nausea, vomiting, insomnia, restlessness and irritability. Signs of severe toxicity include delirium, tachycardia, dehydration, convulsions and coma. Hypotension is a grave prognostic sign.

The treatment of theophylline overdose has classically been with stomach washout up to four hours after the overdose and with symptomatic management of arrhythmias and convulsions. Haemodialysis or peritoneal dialysis have little to offer, but the introduction of charcoal column haemoperfusion represents a significant advance, and with its use there have been reports of patients surviving with initial levels as high as 190 mg/L.3

Charcoal Haemoperfusion

Although haemoperfusion was described as a measure of dealing with theophylline overdose as early as 1979,4 our patient was the first treated by this method in Northern Ireland. Two previous patients referred to this hospital with serum levels of greater than 60 mg/L died from extreme hypotension. We currently use an arterio-venous pump system. After cannulation of the femoral artery and vein, systemic arterial pressure is used to drive blood through the charcoal column, where theophylline adsorption takes place, and the blood is then returned to the patient. Local heparinisation of the column is used to prevent clotting, and is monitored by frequent measurement of activated clotting time. For successful haemoperfusion, a systolic blood pressure of 100 mmHg is required, and this may need to be maintained with volume loading and inotropes. We hope in the near future to change to a synchronised venous pump system which will avoid the need for arterial cannulation and allow haemoperfusion of more hypotensive patients.

A recognised complication of the technique is a fall in the circulating platelet count, which we measure two-hourly during perfusion. A number of explanations have been offered for the thrombo-cytopenia, the most likely being that platelets adhere to the column. This is often a transitory phenomenon, but it is not unusual for platelet transfusion to be required.

COMMENTS

The purpose of presenting this case is to make two points. Firstly, we wish to emphasise the importance of repeated serum theophylline levels during the management of theophylline overdose. Clinical features do not correlate well with the plasma levels and early signs of toxicity may not always be present.5 The graph shows a biphasic pattern in that the initial fall in theophylline levels was followed by a sudden and potentially lethal rise. This may be due in part to the sustained release of the theophylline preparation, although a delayed secondary rise in theophylline concentration with recurrence of the features of toxicity has been ascribed to compartmental distribution of the drug.6
Secondly, the Royal Victoria Hospital Intensive Care Unit would wish physicians throughout the province to be aware of the service now offered for serious overdosages with theophylline levels greater than 60 mg/L. As charcoal haemoperfusion is, at present, technically impossible in the hypotensive patient, we would advocate early referral in all such cases.

Our thanks go to the Biochemistry Department, Royal Victoria Hospital, for their help in supplying quick and accurate theophylline levels throughout the night while our patient was being haemoperfused. Our thanks also to Dr. J. A. Weaver for his assistance and to Miss M. Hazlett and Mrs. M. Loughran for typing the manuscript.

REFERENCES
1 Vale JA, Meredith TJ. Poisoning: diagnosis and treatment. London: Update Books, 1981; 67-68.
2 Mitenko PA, Ogilvie RI. Rational intravenous doses of theophylline. *N Engl J Med* 1973; 289: 600-603.
3 Ehlers SM, Zaske DE, Sanchuk RJ. Massive theophylline overdose. *JAMA* 1978; 240: 474-475.
4 Muir KT, Pond SM. Removal of theophylline from the body by haemoperfusion. *Clin Pharmacokinet* 1979; 4: 320-321.
5 Stirt JA, Sullivan SF. Aminophylline — a review article. *Anesth Analg* (Cleve) 1981; 60: 587-602.
6 Connell JMC, McGeachie JF, Kneple J, Thomson A, Junor B. Self-poisoning with sustained release aminophylline: secondary rise in serum theophylline concentration after charcoal haemoperfusion. *Br Med J* 1982; 284: 943.