Experience with cellulose acetate-coated activated charcoal haemoperfusion in the treatment of severe hypnotic drug intoxication

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Summary

A haemoperfusion column containing activated charcoal coated with cellulose acetate was used to treat 7 patients with barbiturate or ethchlorvynol poisoning. Six of the patients showed marked lightening of coma and all showed a significant fall in plasma drug concentration. Plasma drug clearance and platelet loss were similar to those reported for other coated charcoal columns. Cellulose acetate-coated charcoal haemoperfusion may reduce the period of coma in severe poisoning with barbiturates and other hypnotic drugs and thus the morbidity and mortality.

Introduction

In England and Wales, the mortality from drug poisoning amongst those patients admitted alive to hospital is less than 1%. However, if only severely intoxicated patients are considered a different pattern emerges, with mortality rates of 14% (Volans *et al.*, 1977) and 21% (Hampel and Widdop, 1978) being reported in 2 recent studies. For such patients, extra-corporeal haemoperfusion may reduce the period of coma and hence morbidity and mortality.

The original haemoperfusion devices contained uncoated activated charcoal. Although effective in removing the drug from the circulation, unacceptable side effects of thrombocytopenia, fibrinogen loss and pyrogen reactions were observed (Yatzidis *et al.*, 1965). Various protective coatings have therefore been applied to the charcoal particles in order to make the systems more bio-compatible. The authors have used one such device with an acrylic-hydrogel as the coating system and another in which the uncoated charcoal particles have been attached to a fixed-bed (Vale *et al.*, 1975a; Volans *et al.*, 1977; Hampel and Widdop, 1978). This paper

describes an experience in treating patients with a third type of charcoal haemoperfusion column in which the particles are coated with cellulose acetate.

Patients and methods

Patient selection

As in the other series (Vale *et al.*, 1975a, 1975b; Volans *et al.*, 1977; Hampel *et al.*, 1980) patients were selected for treatment on the basis of clinical features of severe intoxication in the presence of high plasma drug concentrations. These clinical criteria can be subdivided into (a) severe poisoning (Grade IV coma, respiratory depression, hypotension); (b) prolonged coma with complications such as pneumonia; and (c) suspected brain death following a cardiac or respiratory arrest.

In all cases a full toxicological screen was performed before haemoperfusion, and quantitative plasma assays by specific gas-chromatographic methods were carried out for those drugs which were detected.

Haemoperfusion techniques

An arterio-venous shunt was fashioned between the radial artery and a suitable forearm vein. Skin incisions were kept small in order to minimize bleeding. The patient then received an i.v. injection of 10 000 units of heparin followed by a continuous infusion adjusted to produce a plasma heparin concentration of 2 u./ml. The patient's blood was pumped through a 300-g cellulose acetate-coated charcoal column (Adsorba 300C, Gambro Ltd, Hechingen, West Germany) which had been flushed with one litre of saline containing 1000 units of heparin. At the end of haemoperfusion, heparinization was reversed by an i.v. injection of protamine sulphate. Blood flows of 150-300 ml/min were

TABLE 1. Clinical features in seven patients treated with cellulose acetate-coated activated charcoal column haemoperfusion for severe hypnotic drug poisoning

Patient	Age	Sex	Drug ingested	Clinical features				Length of haemoperfusion	Time taken to respond to painful stimuli
				Before haemoperfusion	At the start of haemoperfusion	At the end of haemoperfusion	Subsequent to haemoperfusion		
1.	37	F	Amylobarbitone Quinalbarbitone	Grade IV coma Required ventilation Hypotensive Hypothermic	Grade IV coma Ventilated Hypotensive	Drowsy Breathing spontaneously	Temperature rose to 42°C	13 hr	12 hr
2.	37	M	Butobarbitone	Grade IV coma Required ventilation Hypotension	Grade IV coma Ventilated Hypotensive	Drowsy Breathing spontaneously	Uneventful Recovery	4 hr 30 min	3 hr 30 min
3.	42	F	Butobarbitone	Grade III-IV coma Required ventilation Hypotensive	Grade IV coma Ventilated Hypotensive	Grade II coma Breathing spontaneously	Small right sided pleural effusion	10 hr 40 min	10 hr
4.	19	M	Amylobarbitone	Grade IV coma Required ventilation Hypotensive Hypothermic	Grade IV coma Ventilated Hypotensive	Grade II coma Breathing spontaneously	Chest infection (T = 40°C)	18 hr	23 hr
5.	31	F	Ethchlorvynol	Grade IV coma for 5 days Required ventilation Hypotensive Hypothermic (T = 24°C)	Grade IV coma Ventilated Pneumonia Hypotensive	Drowsy Breathing spontaneously	Pneumonia responded to antibiotics	9 hr	2 hr 10 min
6.	64	M	Amylobarbitone Quinalbarbitone Butobarbitone	Cardiac-respiratory arrest on admission	Grade IV coma Ventilated Hypotensive	Grade IV coma Hypotension Breathing spontaneously	Left ventricular failure. Neck haematoma. Subsequently ventilated (see text)	17 hr 20 min	—
7.	60	F	Phenobarbitone Phenytoin	Grade III-IV coma Intubated Forced alkaline diuresis for four days	Grade IV coma Pneumonia	Drowsy Breathing spontaneously	Uneventful recovery	10 hr 40 min	4 hr 40 min

Grades of coma: IV No response to painful stimuli; III Responds to painful stimuli only; II Responds to minimal stimuli.

maintained except when this was prevented by hypotension. Haemoperfusion was continued until the patient's level of coma had lightened significantly, or until plasma drug concentrations had fallen to low levels. Blood samples were taken before, during and after haemoperfusion for haematological, biochemical and toxicological investigations. All patients were treated in an intensive care unit and received full supportive treatment.

Drug clearance was calculated from the formula:

$$\text{Clearance} = \frac{C_A - C_V}{C_A} \times \text{flow (ml/min)},$$

where C_A and C_V are the drug concentration in the inlet and outlet plasma samples respectively. Flow was measured by a bubble-transit time technique.

The total amount of drug removed was calculated from the following formula derived by Winchester *et al.*, (1975).

Amount removed,

$$\frac{1}{2} \times (t_y - t_x) \times [(C_1 - C_2) + (C_3 - C_4)] \times F,$$

where $t_y - t_x$ is the time interval; C_1 and C_2 are the inlet and outlet drug concentrations at time t_x ; C_3 and C_4 are the corresponding values at time t_y ; F is the blood flow rate through the column.

Results

Seven patients were treated, 6 for barbiturate poisoning and one for the ethchlorvynol poisoning. Table 1 summarizes their clinical features.

The plasma drug concentrations at initial screening, at the start and end of haemoperfusion, together with the plasma clearance and the calculated

total amount of drug removed are shown in Table 2. Six of the patients received a single haemoperfusion, whilst one received 2 treatments separated by 5 hr, the first using a cellulose acetate-coated column and the second an acrylic hydrogel-coated column. The cellulose acetate-coated column failed to lower the plasma drug concentration in this patient. This was probably a reflection of continued absorption of drug from the intestine or redistribution of drug from the tissues into the blood since the clearance data indicated that the drug was being removed at a somewhat faster rate than that achieved with the second column.

Platelet counts were performed in 5 of the 7 patients. The fall at 30 min after starting haemoperfusion ranged from 6.7 to 64.3% with a mean of 34.6%. By the end of the procedure no platelet count was more than 30% below the pre-perfusion values.

Six of the 7 patients showed marked lightening of coma during this active treatment, the mean time taken to respond to painful stimuli being 9.2 hr (range 2 hr 10 min to 12 hr). Two of these patients recovered uneventfully, one had a small right-sided pleural effusion caused by a misplaced supraclavicular catheter inserted before haemoperfusion, and 2 other patients developed high temperatures. In one case this was associated with a severe chest infection, whilst in the other case there was no obvious cause of fever.

The 7th patient, who suffered a cardio-respiratory arrest on admission to hospital and before haemoperfusion had started, failed to regain consciousness despite a fall in total plasma barbiturate concentration from 51.6 mg/l to 19.5 mg/l after 17.5 hr of treatment. The following day he began to respond to

TABLE 2. Plasma drug concentrations, drug clearances and total amount of drug removed

Patient	Drug	Plasma drug concentrations (mg/l)			Blood flow (ml/min)	Drug clearance (ml/min)		Amount of drug removed (g)	Length of perfusion
		At initial screening	At the start of perfusion	At the end of perfusion		Max.	Min.		
1.	Quinalbarbitone	20	24	3.3	100-200	161	22	0.5	13 hr
	Amylobarbitone	26	32.5	4.4		166	35	0.7	
2.	Butobarbitone	56	86	34	175-260	155	71	1.6	4 hr 30 min
3.	Butobarbitone	75	75	19	200	18.9	67	2.9	10 hr 50 min
4.*	Amylobarbitone	59	57.6	59	200	131	64	1.4	5 hr
			59	25.5		100	40	2.7	13 hr
5.	Ethchlorvynol	78	50	36	200	180	100	2.4	9 hr
6.	Amylobarbitone	12	13.5	7.4	300	144	81	0.7	17 hr 20 min
	Quinalbarbitone	25	19.9	8.1		147	110	0.8	
	Butobarbitone	20	18.2	3.9		213	95	1.2	
7.	Phenobarbitone	108	90	36	150	137	34	2.2	10 hr 40 min
	Phenytoin	24	40	27		105	10	0.6	

* This patient received 2 haemoperfusions, the second using an acrylic hydrogel-coated charcoal column.

painful stimuli and his subsequent course was uneventful. None of the other patients had clinical complications attributable to haemoperfusion, or to anti-coagulation. Haemoperfusion was interrupted in the patient who received 2 treatments because of a defect in the extra-corporeal blood lines.

Discussion

Several charcoal haemoperfusion devices are now available commercially. These differ with regard to column design, the type and quantity of charcoal and the nature of the protective coating material. The performance of these devices must be judged on their ability to clear drugs from the circulation, their effects on the blood elements and their overall clinical safety. In all these respects, the cellulose acetate column was comparable to the devices which the authors have used previously.

Although there were no deaths in this series it would not be justified to compare these results directly with other series of similarly poisoned patients in whom there was a high mortality (Volans *et al.*, 1977; Hampel and Widdop, 1978). The numbers in the present series were small and they were not matched for dosage of drug ingested and quality of supportive care. Nevertheless, the rapid lightening of coma seen in some patients strongly suggests that this technique might reduce morbidity.

The authors would advocate the use of haemoperfusion for severely poisoned patients who are either not responding or who are deteriorating despite receiving adequate intensive supportive care. The treatment is recommended for patients with prolonged coma and cardio-respiratory complica-

tions provided that accurate toxicological analyses have revealed the presence of high plasma concentrations of an adsorbable drug. Although this technique is relatively simple it is always attended by the risk of haemorrhage and it is suggested that haemoperfusion should be carried out only in units equipped with the necessary toxicological and clinical facilities.

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