

## KETAMINE PHARMACOKINETICS; A COMPARISON IN CHILDREN AND ADULTS

J.A.Clements, W.S.Nimmo & I.S.Grant, Department of Pharmacy, Heriot-Watt University, Edinburgh, EH1 2HJ and Department of Anaesthesia, Western Infirmary, Glasgow, G11 6NT.

Although ketamine is widely used to induce and maintain anaesthesia in children, there are very few reports of pharmacokinetic studies of this group of patients. Anaesthesia is induced by i.v. injection of 2 mg ketamine/kg body weight or by i.m. injection of 6 to 10 mg/kg but the dose required varies greatly with age (Lockhart & Nelson, 1974). Also, children and young adults appear to be resistant to some of the effects of ketamine (Sussman, 1974).

The pharmacokinetics of ketamine were investigated in children and adults given ketamine either by i.v. injection (2 mg/kg) or i.m. injection (6 mg/kg) (Table 1). Anaesthesia was maintained in all patients using halothane and nitrous oxide in oxygen. Five venous blood samples were taken from children at intervals up to 5 h and 12 to 17 samples from adults for up to 9 h. Plasma ketamine and norketamine concentrations were measured by gas-liquid chromatography (Clements & Nimmo, 1981).

Table 1. Characteristic of patients. Mean  $\pm$  s.d.

Group	i.v. injection			i.m. injection		
	Number	Age (yr)	Weight (kg)	Number	Age (yr)	Weight (kg)
Children	4 (3♂)	6.6 $\pm$ 2.0	21.5 $\pm$ 2.5	5 (5♂)	6.9 $\pm$ 1.7	19.9 $\pm$ 3.7
Adults	5 (3♂)	52 $\pm$ 15	69 $\pm$ 13	3 (1♂)	41 $\pm$ 24	64 $\pm$ 10

After i.v. injection in adults, distribution was very rapid with  $t_{1/2}(\alpha)$  of 15  $\pm$  3 min (s.e.); plasma clearance was 890  $\pm$  100 ml/min and  $t_{1/2}(\beta)$  was 168  $\pm$  18 min. Plasma ketamine concentrations in children did not differ significantly from those in adults over the first 3 h (Table 2) but were lower at 5 h (children 79 ng/ml; adults 159 ng/ml), suggesting that the terminal half-life is shorter in children. Areas under the curve from 0 to 5 h were similar (138  $\pm$  45 min  $\mu$ g/ml in children; 135  $\pm$  18 min  $\mu$ g/ml in adults). In contrast, plasma norketamine concentrations were initially much higher in children. Differences were significant up to 60 min but not at 3 h or 5 h. Thus, oxidative demethylation of ketamine appears to occur more rapidly in children than in adults. Although ketamine is a highly cleared drug, distribution initially accounted for 70% (range 56 to 80%) of the decrease in plasma concentration in adults. An increase in metabolism would have a relatively small effect on the concentration decline in the  $\alpha$ -phase. After i.m. injection absorption was rapid in both groups with mean peak plasma concentrations of 2570 ng/ml at 17 min in children and 2920 ng/ml at 22 min in adults. There were no significant differences in plasma concentrations between groups but absorption did appear to be faster in children (Table 2). Norketamine concentrations were significantly higher in children only at 60 min.

Table 2. Mean plasma ketamine and norketamine concentrations.

Route	Group	Ketamine, ng/ml				Norketamine ng ml			
		5	15	60	180 min	5	15	60	180 min
i.v.	Children	2000	970	630	250	242*	463*	415*	285
	Adults	1800	1070	516	290	52	283	202	209
i.m.	Children	2090	2150	1270	500	37	279	695*	658
	Adults	440	1710	1440	700	0	83	422	472

\*Significantly different from adults ( $p < 0.05$ , t-test).

Supported by Scottish Hospital Endowments Trust.

Clements, J.A. & Nimmo, W.S. (1981) Br.J.Anaesth. 53: 27-31

Lockhart, C.H. & Nelson, W.L. (1974) Anesthesiology 40: 507-508

Sussman, D.R. (1974) Anesthesiology 40: 459-464