Some cardiovascular effects of ketamine in man

J. G. BOVILL*, R. S. J. CLARKE, E. A. DAVIS and J. W. DUNDEE, *Department of Anaesthetics, The Queen's University of Belfast, Northern Ireland*

Ketamine is chemically related to phencyclidine and has recently been introduced into anaesthetic practice as an agent which can be given by intravenous or intramuscular injection. In contrast to barbiturates which frequently cause cardiovascular depression, the usual adult intravenous induction dose of ketamine (2 mg/kg) is almost invariably followed by a rise in blood pressure and heart rate (Dundee, Bovill, Knox, Clarke, Black, Love, Moore, Elliott, Pandit & Coppel, 1970). Studies carried out in five groups, each of twenty-five fit female subjects premedicated with 0·6 mg atropine only, receiving 1·0, 1·5, 2·0, 2·5 and 3·0 mg/kg (injected over 40–60 s) failed to show any relationship between the dose and degree of induced hypertension. All observations were made before surgery. The maximum rise in pressure occurred between 3 and 5 min after injection. The mean peak rise in systolic pressure in these patients was $29{\cdot}1 \pm 1{\cdot}53$ mmHg, and on occasions was as great as 90 mmHg. Analysis of our data fails to confirm the findings of Gjessing (1968) that the increase is less when the initial pressure is high. A factor in this difference may be the absence of hypotensive patients in our series.

Injecting the induction dose at the rate of 20 mg/min produced a degree of hypertension comparable with that following the standard injection rate. This applied to atropinized and non-atropinized patients and was not affected by the simultaneous administration of nitrous oxide-oxygen. Pulse rate changes were very variable in all series and may have been influenced by unpleasant sensations during a slow induction.

In similar patients blood pressure rises after intramuscular ketamine (8–10 mg/kg) were comparable to those following intravenous injection. Changes were more variable when this route was used and the maximum rise occurred between 7–10 min after injection. The mean peak rise in ten patients was $32{\cdot}5 \pm 6{\cdot}03$ mmHg.

Plasma catecholamines, determined by the semi-automated trihydroxyindole method described by McCullough (1968) and incorporating the improvements described by Davis & Sheridan (1970) showed the following findings (Table I) in seventeen patients and in a similar series anaesthetized with a barbiturate.

In view of the rise in plasma catecholamine after ketamine one was not surprised to find that the earlier intravenous administration of 5 mg droperidol reduced, but did not completely abolish, ketamine induced hypertension. When ketamine (2 mg/kg) was injected intravenously 4 min after droperidol the average peak rise in systolic pressure was $22 \pm 3{\cdot}67$ mmHg. This protective effect was not as marked when droperidol was given intramuscularly as premedication.

TABLE 1. *Changes in plasma catecholamines attributable to ketamine or methohexitone anaesthesia*

	No. of patients	Total mean±S.E. μg/l.		Noradrenaline mean±S.E. μg/l.		% of patients showing rise>0·2 μg/l.	
		Control	anaesthesia	Control	anaesthesia	Total	noradrenaline
Ketamine 2·0 mg/kg	17	1·76* ±0·183	2·72* ±0·290	1·62† ±0·171	2·43† ±0·254	82	70
Methohexitone 1·6 mg/kg	11	1·36‡ ±0·336	1·01‡ ±0·204	1·28§ ±0·306	0·95§ ±0·186	20	20

* = $P<0{\cdot}01$ † = $P<0{\cdot}02$
‡ = $P>0{\cdot}30$ § = $P>0{\cdot}30$

REFERENCES

DAVIS, E. A. & SHERIDAN, B. (1970). Plasma catecholamine estimations. *Lancet*, **2**, 364–365.

DUNDEE, J. W., BOVILL, J., KNOX, J. W. D., CLARKE, R. S. J., BLACK, G. W., LOVE, S. H. S., MOORE, J., ELLIOTT, J., PANDIT, S. K. & COPPEL, D. L. (1970). Ketamine: a preliminary report on its use as an induction agent. *Lancet*, **1**, 1370–1371.

GJESSING, J. (1968). Ketamine (Cl-581) in clinical anaesthesia. *Acta anaesth. scand.*, **12**, 15–21.

McCULLOUGH, H. (1968). A semi-automated method for the differential determination of plasma catecholamines. *J. clin. Path.*, **21**, 759–763.

Hangover effects of hypnotics in man

M. H. LADER* and A. J. WALTERS, *Department of Psychiatry, Institute of Psychiatry, University of London*

Using a battery of psychological tests, Kornetsky, Vates & Kessler (1959) found significant impairment of performance 15 h after a hypnotic dose (200 mg) of chlorpromazine or quinalbarbitone. Similarly Malpas, Rowan, Joyce & Scott (1970) reported behavioural impairment and electroencephalographic changes 12 h or more after nitrazepam or amylobarbitone sodium. Such effects detectible the morning after taking a sleeping tablet, can be termed residual or 'hangover'.

The study to be reported investigated the hangover effects of two commonly prescribed hypnotics: butobarbitone sodium (100 and 200 mg doses) and nitrazepam (5 and 10 mg doses) as compared with placebo. Ten normal subjects each received all five treatments at weekly intervals as part of a balanced design, using double-blind procedures. The drug was taken at 23·00 h and the battery of physiological and psychological tests was carried out between 11·5 and 12·5 h later. The physiological tests included recording the electroencephalograph (E.E.G.) both at rest and during an auditory reaction time task, and palmar sweat gland activity. Psychological tests included tapping rate (a measure of simple motor speed), the digit symbol substitution test (a measure of coding and associative skills) and linear scales on which the subjects rated themselves for such features as quality of sleey the previous night and their feeling of alertness at the time of testing.

In general, on the mornings following drug induced sleep, tapping was slower, auditory reaction time was prolonged and fewer items of the digit symbol substitution test were completed than on placebo occasions. Impairment of performance was marked after the higher doses of each drug and was mainly due to a slowing down process as performance times were increased much more than were errors. Subjectively, quality of sleep was improved after the drugs but alertness at the time of testing was diminished only after the higher doses.

The E.E.G. also showed significant changes: the slow wave-bands were decreased and the fast bands increased. For example, the proportion of fast wave activity (13·5–26·0 Hz) was increased by both drugs and this variable was very sensitive to drug effects.

Thus, definite hangover effects are demonstrable 12 h after hypnotic doses of a barbiturate and a new, widely used, non-barbiturate hypnotic. Although these hypnotics lessen the distress of the insomniac patient, attention is drawn to the psychological impairment and electrophysiological changes which are inevitably left the next morning.