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Cardiovascular effects of pancuronium in anaesthetized man

G. R. KELMAN* and B. R. KENNEDY (introduced by J. L. MALCOLM), *Departments of Physiology, University of Aberdeen, and Anaesthetics, Aberdeen Royal Infirmary, Aberdeen*

Pancuronium (2β,16β-dipiperidino-5α-androstane-3α,17β-diol diacetate dimethobromide) is a non-depolarizing neuromuscular blocking agent which clinically does not appear to cause the arterial hypotension which may accompany the administration of tubocurarine (McDowell & Clarke, 1969). This communication describes an investigation into the cardiovascular effects of pancuronium bromide given intravenously (0·07 mg/kg body weight) to anaesthetized humans. The subjects were in-patients undergoing routine surgery under general anaesthesia. All had consented to the investigation. Premedication was with hyoscine (0·4 mg) and papaveretum (15–20 mg) given intramuscularly 30 min before induction of anaesthesia with thiopentone (250–400 mg). After tracheal intubation under succinylcholine relaxation, anaesthesia was maintained with 60% nitrous oxide in oxygen, supplemented with phenoperidine (0·065 mg/kg body weight). Artificial ventilation was performed with a Manley ventilator to maintain the end-tidal P_{CO_2} at 30±2 mmHg.

At 18 and 20 min after induction of anaesthesia, control measurements were made of heart rate and rhythm, systolic and diastolic blood pressures, and end-tidal P_{CO_2}; cardiac output was estimated by dye dilution using indocyanine green and a photoelectric earpiece. This technique accurately records changes of output (Gabe, Tuckman & Shillingford, 1962) but does not give absolute values; therefore all results are expressed as a percentage of the control values. The subjects were then given either pancuronium (ten patients) or no drug (five patients), and the measurements repeated 2, 5 and 10 min later. There was a marked increase of heart rate, with lesser increases of mean arterial pressure and cardiac output; total peripheral resistance was unchanged (Table 1).

TABLE 1. *Changes in cardiovascular parameters at various intervals after intravenous injection of pancuronium*

	No drug (n=5)			Pancuronium (n=10)		
	2 min	5 min	10 min	2 min	5 min	10 min
Heart rate	98·8±1·1	97·9±0·6*	97·3±0·9*	122·2±4·6**	125·3±3·0**	125·9±3·4**
Cardiac output	96·0±3·9	98·5±3·1	100·0±4·1	108·6±3·5*	106·7±3·0	105·8±3·1
Stroke volume	97·9±4·7	100·6±3·1	102·8±4·2	89·7±4·2*	85·6±3·6**	84·6±3·6**
Mean arterial pressure	99·2±1·0	99·4±2·8	98·6±1·1	109·3±2·1**	108·6±2·1**	108·3±2·0**
Total peripheral resistance	103·9±3·5	101·3±3·8	99·1±3·3	103·2±4·3	102·9±4·6	102·9±4·5

All results (mean±S.E.M.) are expressed as percentages of values obtained before injection of pancuronium (0·07 mg/kg body weight) or no drug.
* $0·01<P<0·05$. ** $P<0·01$.

The precise explanation of these findings is uncertain. Bonta, Goorissen & Derkx (1968), however, showed in the cat that pancuronium blocked the fall of arterial pressure induced by vagal stimulation. This suggests that our results may perhaps be due to depression of inhibitory vagal influences, although clearly other interpretations are possible.

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The use of post-operative vomiting as a means of evaluating anti-emetics

R. S. J. CLARKE, J. W. DUNDEE* and W. B. LOAN, *Department of Anaesthetics, Queen's University, Northern Ireland*

The multiplicity of factors which predispose to nausea and vomiting make the reliable evaluation of anti-emetic drugs difficult. One can give them to patients with established emesis, or use them prophylactically in a situation where vomiting is expected in a known proportion of cases. Post-operative vomiting falls into this latter group. Sufficiently large numbers of patients have operations of comparable severity and duration to form a standard population on which studies can be carried out.

Our experience has shown that patients scheduled for minor gynaecological surgery form a suitable group for such studies. Anaesthesia can be kept constant with methohexitone–nitrous oxide–oxygen, but emetic sequelae are uncommon in the absence of opiate premedication. Other factors influencing the incidence of sickness are the duration of anaesthesia, necessity for dilatation of the cervix, the degree of ambulation and fluid restrictions and ward surroundings.

It is feasible to visit patients at 1 and 6 h after operation and record the occurrence of any emetic effects during this time. Prolonging the study after 6 h causes problems because of visitors, eating, ambulation and also the tendency to sleep. With half the subjects on each series having cervical dilatation, groups of 100 patients give reproducible results. These numbers are required to minimize differing individual tendency to motion sickness, etc. (Morrison, Hill & Dundee, 1968).

TABLE 1

Pre-anaesthetic medication	% Vomiting	% Nausea	% Nil
Saline	11	7	82
Pethidine 100 mg	40	24	36
with cyclizine 50 mg	16	19	65
trimethobenzamide 100 mg	17	23	60
promazine 25 mg	22	30	48
trifluprom azine 10 mg	21	10	69
propromazine 20 mg	16	15	69
promethazine 25 mg	10	22	68
thiethylperazine 10 mg	12	13	75
perphenazine 5 mg	7	9	84
,, 2·5 mg	8	11	81
hyoscine 0·4 mg	20	20	60
metoclopramide 10 mg	10	21	69
diazepam 10 mg	32	16	52