revealed similar trends which were significant only in the first 2 h. No significant differences were present 2 h following various doses of methohexitone. These results suggest that the CFM is a sensitive indicator of persistent effects of anaesthesia.

REFERENCES

HIGH PRESSURE AND I.V. ANAESTHESIA
B. Wardley-Smith, C. P. Bailey, C. J. Green* and M. J. Halsey
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High pressure “reverses” general anaesthesia produced by every gaseous anaesthetic agent studied so far. However, it is not clear if this phenomenon applies also to the i.v. anaesthetic agents. Phenobarbitone anaesthesia in mice is antagonized by pressure (Winter et al., 1976), although the long duration of action of this drug makes it difficult to exclude changes in metabolism in response to pressure. Roth, Smith and Paton (1976) found no pressure reversal with pentobarbitone on frog peripheral nerve, in contrast with tadpoles showed pressure reversal with all the gaseous and i.v. agents tested (Halsey and Wardley-Smith, 1975).

We have devised a technique to study in intact mammals the effects of pressure on the short-acting i.v. agents. The left lateral tail vein of male Sprague-Dawley rats was cannulated with a small nylon cannula which was connected to an infusion pump. The rate of perfusion could be controlled remotely, and the anaesthetic dose varied as required. Anaesthesia was assessed by means of an electrical stimulus applied to the tail, and temperature, heart rate and respiration were monitored continuously. Experiments were carried out at normal and increased pressures for comparable times.

Althesin, methohexitone, thiopentone or propanidid anaesthesia were antagonized by pressure (Table I) although there were differences in side-effects. Work in progress with ketamine, a “dissociative” anaesthetic agent, demonstrates a much smaller change in anaesthetic requirement at pressures up to 10.1 MPa. However, the convincing demonstration of pressure reversal of the four common intravenous induction agents lends further support to the hypothesis of an underlying common mode of action for all anaesthetic agents.

REFERENCES

INTERACTION OF ISOFLURANE ANAESTHESIA, BETA-RECEPTOR BLOCKADE AND BLOOD LOSS IN THE DOG
B. F. Horan, C. Peys-Roberts, P. Foex and J. G. Roberts
Nuffield Department of Anaesthetics, The Radcliffe Infirmary, Oxford

To complete our studies of the cardiovascular interactions of beta-receptor blockade and inhalation anaesthetic agents, we have compared haemodynamic dose–response curves and the response to blood loss during isoflurane anaesthesia before and after beta-receptor blockade, in six dogs. Ten days before the study a left ventricular intracavity pressure transducer, electromagnetic aortic flow transducer and pulmonary artery and left atrial catheters were implanted in each dog. An aortic catheter was inserted on the day of study.

During artificial ventilation set to maintain $P_{CO_2}$ at 5.3 kPa, equipotent steady-state inspired concentrations of halothane and isoflurane were determined sequentially in each dog using response or no-response to paw clamping.

Multiples of this minimum inspired concentration of isoflurane 1.2% (SD 0.2%) were administered to each dog to obtain dose–response relationships, before and after the administration of propranolol 0.3 mg/kg. The responses to withdrawal and subsequent reinfusion of 20% of the estimated blood volume were observed at the minimum inspired concentration of isoflurane, before and after propranolol.

At equipotent minimum inspired concentrations, isoflurane 1.2% caused less impairment of myocardial contractility than halothane 1.0% (SD 0.1%), LV dP/df (+40%), peak aortic acceleration (+32%) and peak LV power (+21%) being significantly higher ($P < 0.05$) during isoflurane anaesthesia.

Increasing inspired concentrations of isoflurane to 3.0% caused a dose-dependent impairment of all indices of myocardial contractility and progressive but slight arterial hypotension which became significant only at higher concentrations. Although stroke volume was reduced at

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**Table I. Percentage increase in dosage at pressure relative to control anaesthetic dose ($AD_{10}$) (mean ± SD)**

<table>
<thead>
<tr>
<th>Agent</th>
<th>2.1–2.4</th>
<th>3.8–4.4</th>
<th>5.3</th>
<th>7.0</th>
<th>10.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Althesin</td>
<td>122.0</td>
<td>146.0</td>
<td>174.0</td>
<td>147.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 4.3</td>
<td>± 5.0</td>
<td>± 20.9</td>
<td>± 13.0</td>
<td></td>
</tr>
<tr>
<td>Methohexitone</td>
<td>120.4</td>
<td>150.0</td>
<td>212.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 0.1</td>
<td>± 16.4</td>
<td>± 46.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propanidid</td>
<td>112.8</td>
<td>128.8</td>
<td>148.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 0.3</td>
<td>± 2.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiopentone</td>
<td>117.0</td>
<td>136.3</td>
<td>255.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>± 10.7</td>
<td>± 13.1</td>
<td>± 51.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 10.1 MPa = 100 ATA.
† In the rats at these pressures, the high pressure nervous syndrome was too severe to permit further readings.
higher concentrations, cardiac output was well maintained since heart rate increased in a dose-dependent manner.

Following propranolol administration, some indices of myocardial contractility were significantly reduced at all isoflurane concentrations, but in other respects the dose-response curves were similar to those obtained before betareceptor blockade. At higher isoflurane concentrations, cardiac output was significantly lower following propranolol, resulting partly from the absence of a marked increase in heart rate as observed in unblocked dogs.

The haemodynamic responses to withdrawal of 20% of the estimated blood volume (17 ml/kg) were similar before and after beta-receptor blockade. Although heart rate did not increase in response to blood loss, and indices of myocardial contractility were impaired by propranolol, the changes of aortic pressure, cardiac output and systemic vascular resistance in response to bleeding were not significantly altered by beta-receptor blockade.

We conclude that, in the dog, isoflurane causes much less myocardial depression and impairment of cardiac function than either its isomer enflurane (Horan et al., 1976) or halothane. Beta-receptor blockade induced with propranolol does not appear to cause any serious interaction with isoflurane.

REFERENCE

ACCUARATE MEASUREMENT OF TIDAL AND MINUTE VOLUMES BY PNEUMOTACHOGRAPHY

C. J. HULL AND A. SIBBOLD
Royal Victoria Infirmary, Newcastle

A previous paper (Hull, 1976) has described an improved iso-carbon dioxide technique in which a pneumotachograph was used to measure minute volumes (V) over a wide range of values (4-40 litre/min) for the measurement of the respiratory effects of fentanyl. The present paper discusses the errors inherent in integrated pneumotachography, and describes how they may be obviated to produce an accurate system.

(1) "To-and-fro" breathing through a pneumotachograph produces intractable errors, as a result of temperature changes and condensation. If the transducer is heated, condensation is eliminated, but the temperature effects are increased. Measurement of expired gas alone presents a lesser problem, but saturation with water vapour demands a heated transducer, which is difficult to calibrate (Smith, 1963).

(2) Gas approaching a pneumotachograph may become turbulent at surprisingly low flow rates (well within the operating range of the pneumotachograph itself). This effect introduces a marked non-linearity in flow calibration.

(3) Integration of the pneumotachograph flow signal provides a further source of error, because of input zero drift, changes in input offset current and voltage, capacitor leakage and re-setting errors.

(4) As a breath-by-breath value for ventilation is required, each volume signal must be divided by the inter-breath interval. Analog timers and dividers are subject to error, which, combined with multiplication of volume error, may result in major inaccuracies.

(5) Recording and reading errors must be added to the final signal error.

The present system has the following features:

(a) A wide-bore Fleisch pneumotachograph, with a profiled input port, is placed in the inspiratory limb of a very low resistance, non-return breathing circuit (the pneumotachograph is therefore at ambient temperature, measuring gas flow at ambient temperature and humidity).

(b) The inspiratory flow signal is generated conventionally by means of an H.P. type 270 pressure transducer and 350-1000 carrier pre-amplifier.

(c) The flow signal zero is corrected continuously so that the integrator "sees" a drift-free input signal. The integrator resets during each expiration, so that input offset errors and capacitor leakage do not produce significant drift.

(d) Inter-breath interval measurement, and analog dividers are performed to 0.5% error limits.

(e) Recorder output is from an updating "sample and hold" circuit, so that a continuous value for ventilation is displayed, at ATPH or BTPS.  

(f) For calibration purposes, a digital voltmeter is used, so that recorder and reading errors are eliminated.

(g) Calibration is performed by a reciprocating pump, which delivers a near-sine-wave over wide ranges of volume and cycling speed. Calibration accuracy is ensured by electronic timing and water-displacement measurement of stroke volume.

Performance data: Calibration by reciprocating pump, over a range of tidal volumes 0.5-2 litre, and ventilation 4-40 litre/minute: 

\[ V_T \text{ measurement error range: } \pm 1.2\% \text{ of measured volume} \]

\[ \dot{V} \text{ measurement error range: } \pm 1.5\% \text{ of measured volume} \] 

(mean absolute error 3.4 ml/min).

REFERENCES


METABOLISM OF ENFLURANE IN MAN

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Enflurane (Ethrane) is a new volatile anaesthetic agent, with properties similar to those of halothane. However, it is metabolized to inorganic fluoride in man (Cousins et al., 1976) and in this respect enflurane resembles methoxyflurane. Inorganic fluoride produced during methoxyflurane anaesthesia is thought to cause dose-related renal damage (Cousins and Mazze, 1973). Cousins and his colleagues (1976) showed that, during anaesthesia with enflurane conducted under North American conditions, a peak mean serum concentration of 22.2 μmol/litre inorganic fluoride occurred about 4 h after anaesthesia. Serum inorganic fluoride concentrations in excess of 50 μmol/litre are thought to cause renal dysfunction. The present study was undertaken to evaluate inorganic fluoride production during anaesthesia with enflurane in the U.K.