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The Effect of Halothane on Renal Cortical Blood Flow in Normotensive and Haemorrhagic Hypotensive Dogs

Alan G. MacDonald

University Department of Anaesthesia, Western Infirmary, Glasgow

Investigations into the effect of halothane on renal blood flow (RBF) in man and in dog have shown conflicting results in the normotensive state. This paper reports the effects of 0.5% halothane on RBF in 7 normotensive and 8 hypotensive dogs, using the Krypton 85 clearance technique to measure renal cortical blood flow (RCBF) (Bell and Harper, 1965). The dogs were anaesthetized with thiopentone, intubated and ventilated to produce normocapnia. In the normotensive group several blood flow measurements were made under unsupplemented nitrous oxide-oxygen anaesthesia and then during halothane anaesthesia and finally following discontinuance of halothane.

The results of these normotensive experiments were variable. There was a slight fall in RCBF in 4 animals, a slight rise in 2, and in 1 there was no change. There was an insignificant mean fall in RCBF during halothane administration, an insignificant mean fall in mean BP, and an insignificant rise in renal vascular resistance (RVR).

In the hypotensive experiments, after the control period, the animals were gradually bled to a mean BP of 100 mm Hg, and after further flow measurements under N2O-O2 in this shocked state, halothane was administered, and blood was retransfused to maintain the mean BP at 100 mm Hg. Flows were measured during and after halothane administration. There was a significant fall in RCBF when mean BP was maintained from 143 to 100 mm Hg by haemorrhage, under N2O and O2, and there was a rise in RVR. During halothane administration, there was an increase in RCBF when mean BP was maintained at 100 mm Hg by retransfusion and there was a fall in RVR, all these changes being significant at the <1% level. On discontinuing halothane, RCBF fell and RVR rose.

Many workers have shown that haemorrhage results in renal vasoconstriction, due mainly to increased sympathetic tone. These present results suggest that halothane reduces this increased sympathetic tone, thereby reducing RVR, and thus allowing renal blood flow to improve towards pre-haemorrhage values.

Reference


The Shift of Blood Buffer Line (Δ pH) Due to Reduction of Haemoglobin at Constant Pco2

G. R. Kelman

Department of Physiology, University of Aberdeen

Oxyhaemoglobin is a stronger acid than reduced haemoglobin. The buffer line of reduced blood therefore lies to the right of that for oxygenated blood on the Siggaard-Andersen nomogram. The influence of pH and Pco2 on this shift has been investigated.

Blood was equilibrated in two Radiometer micrometers with either 3% and 8% CO2 in O2, or 3% and 8% CO2 in N2, and the final pH measured in each case. The horizontal position of the buffer line was calculated as the pH at Pco2=20, 40 and 60 mm Hg, a linear relationship being assumed between pH and log Pco2. The shift (Δ pH) was determined on blood with Hb concentration=16 g/100 ml and normal non-respiratory acid-base state (mean standard bicarbonate=22.8 m.equiv./l.), and on blood diluted to twice its original volume with 3 isotonic solutions containing various proportions of NaCl and NaHCO3. These samples had 8 g Hb/100 ml and mean standard bicarbonates of 14.8, 22.8 and 37.0 m.equiv/l.

For blood with normal non-respiratory acid-base state, the mean Δ pH at Pco2=40 mm Hg was 0.051 (SE±0.002) pH unit (Hb=16 g/100 ml), and 0.027 (SE±0.002) pH unit (Hb=8 g/100 ml). There was a linear correlation between Δ pH and actual (oxygenated) pH at Pco2 of 60 and 20 mm Hg (r=−0.634 and −0.915, respectively), i.e. Δ pH decreased with increasing metabolic alkalosis. The slopes of the regression lines were −0.083±0.007 (Pco2=20 mm Hg) and −0.046±0.011 (Pco2=60 mm Hg). The slope was therefore markedly steeper at the lower tension. A similar linear relationship was found when Δ pH was plotted against standard bicarbonate, but not when Δ standard bicarbonate was plotted against standard bicarbonate concentration.

The Astrup technique for determination of bicarbonate concentration and of Pco2 by interpolation is based on the oxygenated buffer line. Inaccuracies can therefore arise if the blood is initially desaturated. A nomogram has been constructed for the calculation of the position of the true line.

Reference

THE OXYGEN UPTAKE OF ISOLATED PERFUSED RAT HEART AT ONE AND TWO ATMOSPHERES ABSOLUTE
D. C. WHITE AND C. R. DUNDA
Department of Anaesthetics, Royal Infirmary, Aberdeen

An apparatus was constructed in which the isolated rat heart could be perfused on the Langendorff principle, a cannula being tied into the aorta through which perfusate was passed under pressure thus perfusing the coronary vessels.

The rate of flow of perfusate to the heart was measured by a Rotameter and the perfusion pressure was controlled by a variable pressure regulator and measured by a mercury manometer. The Po of the perfusate before and after passage through the heart was measured polarographically and the oxygen consumption of the heart was calculated from these figures together with the perfusate flow rate. All experiments were conducted at 27°C.

The perfusate used was a modified Krebs-bicarbonate medium which was gassed with 5% CO2 in O2 for experiments at 1 atmosphere and with 2.5% CO2 in O2 for experiments at 2 atmospheres absolute.

It was found that if the perfusion pressure was kept constant the perfusate flow rate rapidly decreased during the course of an experiment and the oxygen consumption fell in a parallel manner. If, however, the perfusion pressure was continuously increased to maintain a constant flow rate then the oxygen consumption showed considerably less variation during the course of an experiment. For this reason the results quoted are from experiments in which a constant perfusate flow rate was maintained.

In 11 experiments the mean oxygen uptake during a 30-minute period at 1 atmosphere absolute was found to be 0.1186 ml (SE ±0.0044) O2 at NTP/min/g of wet heart weight. The corresponding figure for 6 experiments at 2 atmospheres absolute was found to be 0.2006 (SE ±0.0126) showing the mean oxygen uptake at 2 atmospheres to be 69% greater than that at 1 atmosphere, the difference being statistically significant (P<0.001).

These figures suggest that a degree of anoxia is present in this preparation when perfused at an oxygen tension of 1 atmosphere.

CRITIQUE OF A METHOD OF STUDYING DRUGS GIVEN BEFORE ANAESTHESIA:
SUMMARY
JOHN W. DUNDEE, JAMES D. MORRISON AND GERRY B. HILL
Department of Anaesthetics, The Queen's University of Belfast, Northern Ireland

A standard method for assessing the properties of drugs when used as premedicants, which was originally evolved from a pilot study in 400 patients has now been used in over 10,000 subjects. This method has been described elsewhere (Dundee, Moore and Clarke, 1964). It is based on giving the experimental drug, in a standard dose, to groups of 100 female patients before minor gynaecological surgery, each group consisting of 50 patients having dilatation and curettage, and 50 having curettage alone.

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The following facets were examined:
(a) Homogeneity of series with respect to age and body weight. The results of analysis revealed a wide distribution of individual weights, but with 95% falling within the mean ±2 SD. There was homogeneity of ages and weights between groups of 100 patients. The mean age of patients having dilatation and curettage was greater than that of those having curettage alone.

(b) The significance of this weight scatter with respect to the outcome of a trial where dosage is unrelated to weight was tested by comparing dose/response curves for pethidine obtained by using a standard dose in groups of 100 patients with those obtained by using a weight-related dosage. The responses investigated in this way included both subjective and objective parameters. There were no differences between these dose/response curves and it would seem that in groups of not less than 100 patients individual variation in body weight does not affect the outcome of the trial.

(c) Observation differences. 50% of the patients were seen four times pre-operatively, the remainder being seen once. Patients having the multiple pre-operative visits showed a greater incidence of sedation and a lesser incidence of apprehension, and at the same time more side effects, than did the other group.

(d) The nature and duration of the operation were investigated in respect to their influence of the incidence of emetic sequelae. The results indicated a persistently greater incidence of emetic sequelae in those patients who had had dilatation of the cervix compared to those in whom the cervix did not require dilatation. This effect was independent of the duration of the operation, but in all patients, of either operation group, increasing duration of operation was associated with increasing incidence of nausea and vomiting.

REFERENCE

SOME FACTORS INFLUENCING THE BINDING OF BROMOSULPHAPHTHALEIN BY SERUM ALBUMIN
J. SELWYN CRAWFORD AND HELEN W. Y. HOOI
Research Department of Anaesthetics, Royal College of Surgeons, London

The binding of bromosulphaphthalein (BSP) to serum albumin was investigated by equilibration dialysis at 37°C and pH 7.4 using Visking bags. A high negative linear correlation was observed between the number of molecules BSP bound per molecule albumin and the concentration of albumin. This relationship was obtained from experiments with pooled human serum albumin, and also from collected data derived from individual investigations of serum from 100 subjects. The latter were divisible equally into five groups: male controls, female controls, normal pregnant women at term, neonates (cord blood samples), and healthy females who had been taking an oral contraceptive for at least 6 months. Serum from the latter three categories of subjects (the "pregnancy hormone groups") had a notably different characteristic, vis-à-vis the molecules per molecule binding of BSP by albumin, from serum from the male and female controls.
The implications of these findings with respect to the interpretation of the BSP test of hepatic function, were discussed, as were, briefly, their importance to the general study of pharmacokinetics.

HYPOXIC PULMONARY VASCULAR RESPONSE DURING INTERMITTENT POSITIVE PRESSURE VENTILATION IN THE RABBIT

J. B. OWEN-THOMAS and J. T. REEVES
Nuffield Institute for Medical Research, University of Oxford, and the Nuffield Department of Anaesthetics, Radcliffe Infirmary, Oxford

The response to hypoxia as a rise in pulmonary artery pressure (p.a.p.) has hitherto not been established in the rabbit.

Forty-six rabbits (0.4–4.4 kg) were studied under pentobarbitone anaesthesia. Nine were studied during spontaneous breathing and, of these, 8 showed a mean rise of 33% in p.a.p. during hypoxia at a mean arterial oxygen tension (Pao₂) of 41 mm Hg (29–53 mm Hg) with 10–12% oxygen in the inspired gas (FiO₂). The p.a.p. returned to its control level at a Pao₂ = 77.1 mm Hg (60–103 mm Hg) on breathing air.

Twelve further rabbits were studied during assisted ventilation,* 6 with the chest wall intact and 6 with both pleural spaces open to the atmosphere. The rabbits studied with chest wall intact showed a mean rise in p.a.p. of 19% during hypoxia at a mean Pao₂ = 52.2 mm Hg (37–65 mm Hg) with 12% FiO₂, returning to a mean Pao₂ = 102.5 mm Hg (74–143 mm Hg) when breathing air. The p.a.p. returned to its control level. Of the 6 animals studied with the chest open to atmosphere, 5 showed no rise in p.a.p. with 12% FiO₂, and this was associated with a greater tendency to develop pulmonary oedema. In 25 rabbits, the lungs were perfused in situ. In only 1 animal was a rise in p.a.p. seen during hypoxia, although in each the pulmonary vasculature responded to a small dose of acetylcholine by a large rise in p.a.p.

In anaesthetized rabbits the rise in p.a.p. in response to hypoxia was diminished by IPPV, was further diminished by opening the chest to atmosphere, and was abolished in the isolated lung preparation.

* Ventilator lent by Bourns Inc., Iowa, U.S.A.

EFFECT OF HYPOTENSIVE ANAESTHESIA ON MENTAL FUNCTION IN THE ELDERLY

W. N. ROLLASON, G. S. ROBERTSON and C. M. CORDINER
Departments of Anaesthetics and Mental Health, University of Aberdeen

Previous work (Eckenhoff et al., 1964) indicated that hypotensive anaesthesia did not lead to changes in mental function in the younger age groups but in this investigation the eldest patient was only 39 years of age. This study is being undertaken to confirm that mental function in the older age groups is also unaffected by hypotensive anaesthesia as was suggested by a previous investigation (Rollason and Hough, 1960). The work at present is based on a series of 27 male patients undergoing retropubic prostatectomy under spinal and light general anaesthesia.

Two days before operation psychometric tests are carried out and these are repeated 5 days and 6 weeks postoperatively. At interview the subjects' general behaviour is assessed and the following group of tests are applied:

1. Wechsler adult intelligence scale;
2. Inglis Isaacs paired associates test;
3. Bender visual motor Gestalt test;
4. Benton visual retention test;
5. Letter marking test;
6. Wechsler memory scales.

Patients are categorized into hypotensive or non-hypotensive groups according to random numbers. In the non-hypotensive group the systolic pressure is maintained by the use of a vasopressor drug. Other parameters measured are the e.e.g., e.c.g., blood loss and the blood pH and blood-gases.

The statistical analysis of this study so far indicates that in elderly males lowering of blood pressure by some 50–60% below pre-induction level does not induce a greater incidence of mental or e.e.g. changes than does a technique involving maintenance of normal blood pressure by the use of vasopressor drugs. No significant respiratory or metabolic acidosis has been produced in any of the patients.

REFERENCES