The Effect of Hyperbaric Oxygen on Experimental Cerebral Infarction in the Dog

With Preliminary Correlations of Cerebral Blood Flow at 2 Atmospheres of Oxygen

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Recent reports indicate the possible value of hyperbaric-oxygen therapy in any condition in which anoxia, either during surgery or caused by disease, is present. A significant difference in survival has been demonstrated in experimental occlusion of the coronary artery. Furthermore it has been shown that an enhanced survival time followed cardiac arrest. The value of such therapy in carbon-monoxide poisoning has been proven clearly. The maintenance of electrical activity in dogs with occluded carotid and vertebral arteries under high pressure has indicated a possible role of hyperbaric oxygen in cerebrovascular disease and in surgery on intracranial aneurysms. The present investigation has been designed to further assess these possibilities.

Method

Unselected mongrel dogs were used. Anaesthesia was induced with thiopentone and the animals were intubated with a cuffed Magill tube. Anaesthesia was maintained thereafter either with small increments of Pentothal and suxamethonium chloride or with halothane as indicated below. Respiration was either assisted manually or controlled on a positive-pressure Palmer Pump, the stroke volume of which was adjusted to maintain an arterial pCO₂ between 30–40 mm. Hg.

The right middle cerebral artery was occluded just distal to the bifurcation of the internal carotid artery with a silver clip. An infratemporal approach was used, the zygomatic arch was resected and the pyriform lobe was retracted to expose the circle of Willis. A short segment of artery was cleared of arachnoid mater, great care being taken not to damage either any adjacent vessels or the small perforators in or around the chiasm. Intravenous urea (1½ gm./kg.) was used to gain easier access. The dura mater was left open and the defect was covered with a thin layer of foam gelatin. Methylmethacrylate was used to repair the skull defect.

The dogs were observed postoperatively for 8–14 days, and any neurological deficit was noted. At the end of this period the brains were removed and the vessels were examined both by naked eye and microscopically for evidence of patency. The brains were fixed in formal saline, sectioned coronally, and examined for macroscopic and microscopic evidence of infarction.

Six groups were studied:

Group 1. Five normothermic, normobaric controls—blank operations, vessel exposed, but not occluded. Thiopentone, suxamethonium chloride, halothane anaesthesia, inspired oxygen 760 mm. Hg. Manual respiration.


Group 3. Four hypothermic, normobaric blanks, vessels exposed not occluded. Anaesthesia thiopentone, suxamethonium, halothane, respiration controlled with a positive-pressure pump, inspired oxygen 760 mm. Hypothermia was induced by surface cooling in water bath to ~6–27.5°C. Oesophageal temperatures only were monitored. Aortic blood pressure was measured via a femoral-artery cannula on a damped mercury manometer. Arterial pH, pCO₂ and standard bicarbonate were measured on a micro-Astrup apparatus and the pH temperature corrections of Rosenthal were applied. Base deficit was corrected with 8.4 per cent bicarbonate intravenously. The pCO₂ was not altered either by changing pump, the setting or the inspired gas tension.

Group 4. Five animals hypothermic, normobaric, vessel fully occluded. Anaesthesia etc., as in Group 3.

Group 5. Eight animals normothermic, hyperbaric. Anaesthesia thiopentone etc. with manual assistance. After induction and intubation both experimental team and the animal were pressur-
ised to 2 atmospheres. The procedure was then carried out with the dog breathing oxygen at 1500 mm. Hg. partial pressure. The clip was applied after 1/2–2 h. of exposure to this high oxygen tension. Four dogs were exposed after occlusion to a further short period of 1½–2½ h. and then decompressed and returned to the kennels. Four other dogs were allowed to recover from anaesthesia while breathing pure oxygen within the chamber. Thereafter, as the pressure within the chamber was maintained with an air compressor, the dogs were placed in a large Perspex box in the pressure chamber with oxygen blown through at 10 litres per min. We considered that at this high flow the PO2 within the box would be very close to 100 per cent. Estimations of this value were between 1400 and 1450 mm. Hg. The oxygen was humidified. Temperature of the box was kept down to 20°C and pCO2 did not rise above 8 mm. Hg.

**Group 6.** Four dogs (nonsurvivors). Cerebral cortical blood flow was measured by the method of Krypton clearance. A normothermic, normobaric/normothermic, hyperbaric comparison on thiopentone anaesthesia was carried out. The pCO2 was adjusted to 34–38 mm. Hg. with a positive-pressure pump. Electroencephalographic control of anaesthesia was performed with an Offner 8 channel type T amplifier. Stainless-steel extradural electrodes were employed with bi-frontal, right frontotemporal and temporo-occipital positions. Arterial samples were obtained from a femoral catheter and venous samples from a cannula mounted in the sagittal sinus. Arteriovenous-oxygen saturations were measured with a Kipp haemoreflector and PO2 values with a Clark electrode and a Bishop cuvette.* Arterial pH, pCO2 and standard bicarbonate were measured with a micro-Astrup apparatus.

These measurements were all carried out within the pressure chamber; the pCO2 tensions for the micro-Astrup apparatus were adjusted accordingly. The PO2 electrode was calibrated against gas, saline and blood, tonometered in air and pure oxygen both in and out of the chamber, and recalibrated with each sample. Haemoglobins were measured with each flow on a Unicam S.P. 600 Spectro-photometer at ambient room conditions.

**Results**

Table 1 shows the results of Groups 1 and 2. None of the blank controls had either any clinically overt neurological deficit or any evidence of infarction post mortem.

The normothermic, normobaric animals with occluded vessels evidenced a fairly standardised syndrome of ipsilateral circling, and a varying degree of contralateral hemiparesis with a tendency to steady improvement over the recovery period. We are unable to assess any homonymous hemianopia as the facial nerve had been divided in the operative approach. Two animals remained drowsy, densely hemiparetic and died 3 days postoperatively. One animal showed no neurological deficit.

At postmortem examination ischaemic infarcts were found in the capsular-basal ganglion region. These infarcts were moderate in size and in keeping with the observed neurological deficits (Fig. 1).

In Table 2 are given the results of the hypothermic, normobaric groups. It will be noted that only 2 animals were affected clinically—one minimally and the other moderately. The first recovered in 3 days. The paresis in the second disappeared after 4 days, but circling remained.

Four brains in Group 4 showed minimal damage and 1 was normal. The infarcts were small and circumscribed, localised to capsule and thalamus (Fig. 2).

Table 3 shows the results of the hyperbaric group. All animals surprisingly were affected severely neurologically. Two dogs were exposed for 7½ and 20 h. to hyperbaric oxygen and evidenced oxygen toxicity with extreme dyspnoea, coughing and frothy sputum, and eventual asphyxia. No animals had epilepsy or any other signs suggestive of cerebral toxicity. Examination of the brains revealed somewhat larger infarcts than the normobaric-normothermic controls and also a trend to oedema of the pyriform lobe. Compared with the hypothermic group the difference was very marked (Figs. 3 and 4). The lungs on the last 2 confirmed the clinical features of toxicity—a haemorrhagic atelectatic picture.

Preliminary results of cerebral blood flow and other parameters are impressed in Table 4. As indicated each animal was studied under room conditions, breathing either air or pure oxygen and in the pressure chamber breathing again air and pure oxygen. The initial measurements of flow were always