Retinal Tissue Oxygen Tension in Normoxic Cats Under Enflurane Anesthesia

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Purpose. General anesthesia reduces systemic blood pressure and, thus, ocular perfusion pressure (at constant intraocular pressure). Whether this reduction in ocular perfusion pressure produces retinal hypoxia is unknown. To answer this question, the authors measured inner retinal oxygen tension in cats under general enflurane anesthesia at three clinically relevant levels of anesthesia under normoxic conditions.

Methods. Polarographic oxygen microelectrodes were used to measure inner retinal oxygen tension in cats under enflurane anesthesia at 21% inspired oxygen tension. Measurements were made in the preretinal vitreous body within 100 to 200 μm of the internal limiting membrane of the retina. Three levels of enflurane anesthesia were used: 1.2%, 2.4%, and 3.6%, corresponding to 0.5, 1.0, and 1.5 minimal alveolar concentration. Intraocular pressure of the cats was maintained at a constant normal level throughout the experiments.

Results. Under normoxic conditions, inner retinal oxygen tension remained unchanged or increased slightly as ocular perfusion pressure decreased with deeper levels of enflurane anesthesia.

Conclusion. Commonly used surgical levels of enflurane general anesthesia do not cause hypoxia of the inner retina in cats breathing 21% inspired oxygen. This may be the result of preservation of retinal vascular autoregulation under enflurane anesthesia, retinal vasodilation secondary to a direct smooth muscle relaxing effect of enflurane, or decreased retinal oxygen use under enflurane anesthesia. Invest Ophthalmol Vis Sci. 1995;36:1943–1946.

Enflurane is a commonly used general inhalational anesthetic for ocular surgery. During enflurane anesthesia, systemic blood pressure decreases with increasing depth of anesthesia. At constant intraocular pressure, ocular perfusion pressure will decrease as systemic blood pressure decreases. How the decrease in ocular perfusion pressure with enflurane anesthesia affects inner retinal tissue oxygen tension (PrO₂) is unknown.

In these experiments, the behavior of inner retina oxygen tension during enflurane anesthesia is assessed by measuring preretinal oxygen tension in the vitreous body at three levels of anesthesia.

METHODS. Eight adult cats of either sex weighing 2.5 to 4 kg were used in these experiments. Our procedures conformed to the National Institutes of Health Guidelines and to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

After receiving 1% tropicamide and 1% cyclopentolate eye drops to produce mydriasis, the cats underwent induction of anesthesia in a closed plexiglass box through which flowed a mixture of enflurane (Ethrane; Anaquest, Madison, WI), oxygen, and nitrous oxide delivered by an anesthesia machine. Anesthesia was continued by face mask as a tracheostomy tube and bilateral femoral arterial and venous lines were placed. The cats were then paralyzed with pancuronium bromide (Pavulon; Organon, West Orange, NJ) 0.15 mg/kg per hour intravenously, and the anesthetic was changed to 1.2% enflurane in 21% oxygen, with the balance nitrogen. A maintenance intravenous infusion of normal saline at 4 ml/kg per hour was begun. Each animal was in the supine position with the head stabilized in a stereotactic frame for the entire experiment.

Femoral cannulas connected to transducers referenced to the level of the right atrium were used to follow mean arterial pressure and central venous pressure. Inspired oxygen concentration, electrocardiogram, and arterial blood gases were monitored. Intraocular pressure was held constant at 20 mm Hg using an anterior chamber cannula connected to a saline reservoir through a pressure transducer. Mydriasis was maintained for the duration of the experiment (up to 12.5 hours) with 1:1,000,000 epinephrine in the anterior chamber perfusion fluid. Arterial blood was sampled approximately hourly to determine arterial blood gases and hematocrits. Arterial pH was maintained at 7.40 ± 0.15 (mean ± SD).

Preretinal oxygen tension reflects the behavior of inner retina tissue oxygen tension.1–6 The PrO₂ measurements were made with our previously reported technique using an oxygen microelectrode (723 O₂ Electrode; Diamond Electro-tech, Ann Arbor, MI).4

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†Proprietary interest category: N.

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The retina and electrode were viewed through a contact lens and a Zeiss (Oberkochen, Germany) operating microscope. All measurements were made away from visible blood vessels under photopic conditions as provided by the illuminating system of the microscope.

Once in the vitreous cavity, each electrode was checked for its response to changes of inspired oxygen concentration. In the measuring position, the electrode current output (corresponding to oxygen tension at the electrode tip) demonstrated regular fluctuations with the same frequency as breaths from the ventilator. This occurred because of choroidal engorgement secondary to increased venous pressure in the head with each positive pressure breath from the ventilator. As the choroidal blood volume fluctuated, the retina moved closer to or further from the electrode. The average of the peak and trough values was taken as the preretinal oxygen tension.

Oxygen tension measurements were made in the vitreous immediately adjacent to the retina in the superonasal quadrant 2 mm to 4 mm from the optic disk. Held by a micromanipulator, the electrode was advanced until it produced dimpling of the internal limiting membrane and then was withdrawn 100 μm to 200 μm. At each level of enflurane anesthesia, five measurements of preretinal oxygen tension were made over a 30-minute period in a localized area of retina (no measurement more than 1 mm distant from the initial site) away from visible large blood vessels. Between each of the five measurements, the electrode was pulled back into the vitreous cavity and readvanced to the same retinal location as judged by the operator. Oxygen electrodes were calibrated in 100% nitrogen and 10% oxygen in nitrogen before and after the experiment.

Enflurane at concentrations up to 3.6% had no effect on oxygen currents in the calibration cell. This agrees with published reports that enflurane is not reduced at the voltage used for oxygen tension measurements.5,6,

Ocular perfusion pressure (PP) in a supine animal may be approximated by mean systemic blood pressure minus intraocular pressure.7 To reduce ocular PP sequentially, enflurane end-tidal concentration was first increased from 1.2% to 2.4%, and then to 3.6%. For cats, these concentrations correspond to 0.5, 1.0, and 1.5 minimal alveolar concentration, or MAC, which are levels used commonly in clinical practice.8 In going from lighter to deeper anesthesia, a 30-minute equilibration was allowed before measurements were resumed. The terms “baseline PP” and “baseline Pro2” refer to measurements made on 1.2% end-tidal enflurane. At the conclusion of the experiment, the cats were killed with intravenous potassium chloride while they were still under anesthesia.

**RESULTS.** Eight cats were studied under general enflurane anesthesia at 21% inspired oxygen concentration (normoxic conditions). In seven cats, Pro2 was measured at three levels of anesthesia. Because of technical difficulties with one cat, Pro2 was measured at only two levels of anesthesia.

Arterial blood parameters for each cat remained relatively constant throughout each experiment, but arterial PO2, Pco2, and hematocrit did vary between cats. For the eight cats, average baseline arterial PO2, arterial Pco2, and hematocrit were, respectively: 92 ± 18 mm Hg, 31 ± 4 mm Hg, and 34% ± 6%.

As expected, systemic blood pressure and ocular PP declined progressively as general anesthesia deepened. At the lowest level of enflurane anesthesia (1.2%), the mean baseline arterial PP of the eight cats was 97 ± 13 mm Hg. Mean ocular PP of the cats declined to 62 ± 12 mm Hg (n = 8) and 54 ± 10 mm Hg (n = 7) at 2.4% enflurane and 3.6% enflurane, respectively. This corresponds to an average percent decrease in ocular PP compared to baseline of 36% ± 11% (n = 8) at 2.4% enflurane and 45% ± 8% (n = 7) at 3.6% enflurane. Comparing cats at 2.4% end-tidal enflurane to cats at 3.6% end-tidal enflurane, the decrease in mean ocular perfusion pressure was 11% ± 10% (n = 7, P = 0.035). Although this decrease in perfusion pressure between 2.4% and 3.6% enflurane was statistically significant, the decrease was actually so small in some cats that for all practical purposes, Pro2 was tested at only two values of ocular PP.

At baseline, the mean Pro2 was 28 ± 9 mm Hg for the eight cats. The Pro2 under normoxic conditions tended to remain the same or to increase with ocular PP for all eight cats when comparing 1.2% enflurane anesthesia (baseline) to 2.4% enflurane anesthesia (Fig. 1). When comparing 2.4% to 1.2% enflurane anesthesia, the average percent change in Pro2 was 10% ± 18% (n = 8; range, -7.2% to +45.3%). Comparing Pro2 at the deepest level of anesthesia (3.6% enflurane) to baseline revealed an average percent increase of 35% ± 32% (n = 7; range, -0.2% to +95.3%). Data for each of the cats were plotted as the linear regression line in Figure 1. The average of the eight linear regression equations is as follows: Pro2 = 43 − 0.166 PP, where the units are mm Hg for both Pro2 and PP. This average linear regression line is drawn as a darker, dashed line in Figure 1. Both the mean slope and the mean intercept are significantly different from zero (P < 0.05).

The duration of the experiments ranged from 4.25 to 12.5 hours, with an average of 7.7 ± 2.7 hours. Simple linear regression of Pro2 on duration of anesthesia revealed that Pro2 did not depend on the duration of anesthetic delivered until the time the oxygen tension measurement was made.
FIGURE 1. Inner retinal tissue oxygen tension (Pro2) versus ocular perfusion pressure (mean systemic blood pressure minus intraocular pressure) in eight normoxic cats. Lines join the individual experimental points. The average of the slopes and the intercepts of the eight individual linear regression lines was used to give the average line, which was drawn darker and dashed.

DISCUSSION. At clinically relevant levels of general enflurane anesthesia, systemic blood pressure is reduced below normal levels because of peripheral vasodilatation\(^9\) and decreased cardiac output\(^{10,11}\) (secondary to depressed myocardial contractility and decreased heart rate). Therefore, ocular perfusion pressure is reduced (assuming relatively constant intraocular pressure). It is conceivable that the anesthesia-related reduction in ocular perfusion pressure could produce retinal hypoxia. These experiments indicate that, at least in cats breathing 21% oxygen, inner retinal tissue oxygen tension (as indicated by preretinal vitreal oxygen tension) remains relatively unchanged or increases under general enflurane anesthesia despite the reduction in ocular perfusion pressure. The enflurane levels used in these experiments (1.2%, 2.4%, and 3.6%, corresponding to 0.5, 1.0, and 1.5 MAC) correspond to levels used in routine clinical practice, including ophthalmic surgery.

The resistance of the inner retina to hypoxia under general anesthesia may result from the maintenance of relatively normal retinal blood flow in the face of declining ocular perfusion pressure. For comparison, cerebral blood flow in dogs is maintained under general enflurane anesthesia despite declining cerebral perfusion pressure. Because the retina is derived from the forebrain embryologically, it is reasonable to expect retinal blood flow to show similar behavior in response to enflurane. Retinal blood flow could be maintained by retinal vasodilatation resulting either from intact retinal autoregulation or from direct enflurane-induced retinal vascular smooth muscle relaxation. The question of whether retinal vascular autoregulation remains intact under enflurane anesthesia could possibly be answered by further experiments in which Pro2 is measured as ocular perfusion pressure is varied by changing intraocular pressure. In such an experiment, the systemic blood pressure would be held constant at a given level of enflurane anesthesia.

An alternative explanation for the rise of inner retinal tissue oxygen tension as ocular perfusion pressure declines under enflurane anesthesia is a decrease in oxygen use by the retina under the influence of enflurane. Although no data on retinal oxygen use under enflurane anesthesia are available, there are such data for the brain. Cerebral oxygen metabolism measured in dogs decreased by approximately 34% at 2.2% to 2.4% enflurane anesthesia.\(^{12}\) In these dogs, however, cerebral blood flow simultaneously increased by approximately 33% at 4.2% enflurane, indicating an “uncoupling” of metabolic autoregulation. Again, it is of interest to speculate that the retina may exhibit behavior analogous to that of the brain. In our experiments, the mean ocular perfusion pressure declined 44% from baseline, whereas mean preretinal oxygen tension increased 35% over baseline for the seven cats studied at the deepest level of anesthesia (3.6% enflurane). The observed behavior of preretinal oxygen tension in these experiments could be explained if, as in the brain, retinal oxygen use decreases or retinal blood flow increases under enflurane anesthesia administered under normoxic conditions.

Key Words

autoregulation, cat, enflurane, oxygen tension, retina

References

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