**Effect of Carbogen Breathing and Acetazolamide on Optic Disc Po2**

Joannis K. Petropoulos, Jean-Antoine C. Pournaras, Jean-Luc Munoz, and Constantin J. Pournaras

**PURPOSE.** Acetazolamide was previously shown to increase optic disc partial pressure of oxygen (Po2). The study was conducted to evaluate optic disc Po2 variations during normoxia, hyperoxia (100% O2), and carbogen breathing (95% O2, 5% CO2), before and after intravenous administration of acetazolamide.

**METHODS.** Po2 measurements were obtained at intervascular areas of the optic disc in nine anesthetized minipigs using oxygen-sensitive microelectrodes (10-μm tip diameter) placed at 50 μm from the optic disc. Po2 was measured continuously during 10 minutes under normoxia, hyperoxia, or carbogen breathing. Oxygen measurements were repeated under these conditions after intravenous injection of acetazolamide (500-mg bolus).

**RESULTS.** In hyperoxia, optic disc Po2 increased moderately (ΔPo2 = 4.81 ± 1.16 mm Hg (mean ± SD; 24%; P < 0.001) after a much larger increase in systemic PaO2. Carbogen breathing induced a significant increase in both systemic PaO2 and PaCO2, which resulted in a large increase in optic disc Po2 (ΔPo2 = 13.17 ± 2.18 mm Hg; 67%; P < 0.001). Acetazolamide induced a slow and progressive increase in both systemic PaCO2 and optic disc Po2 (30 minutes ΔPo2 = 4.24 ± 2.45 mm Hg; 24%; P < 0.04). However, it was when carbogen was simultaneously administered that optic disc Po2 increased most substantially (ΔPo2 = 18.91 ± 5.23 mm Hg; 90%; P < 0.002).

**CONCLUSIONS.** Carbogen breathing increases optic disc Po2 significantly in minipigs, more than hyperoxia. The association of acetazolamide injection with carbogen breathing could induce an additional increase in optic disc Po2 through the effect of higher systemic PaCO2. (Invest Ophthalmol Vis Sci. 2005;46: 4139 - 4146) DOI:10.1167/iovs.05-0258

Blood flow modifications and perturbations of the autoregulatory mechanisms of the optic nerve head (ONH) circulation have been incriminated in several ocular disorders, including glaucomatous and ischemic optic neuropathy. Knowledge of the parameters that can influence the autoregulatory responses of the ONH might improve our understanding of the pathogenesis of those diseases and might lead to new therapeutic modalities.

Retinal and ONH blood flow is closely dependent on systemic partial pressure of oxygen (Pao2) and systemic partial pressure of carbon dioxide (Paco2). High Paco2 (hyperoxia) causes vasoconstriction of cerebral arteries and retinal arterioles and a decrease in retinal blood flow. However, hyperoxia does not affect the tissue oxygen supply, as tissue partial pressure of oxygen (Po2) remains relatively stable in the inner retinal or at intervascular areas of the ONH.

In contrast, carbon dioxide is a well-known dilator of arterial circulation, and high Paco2 has been shown to dilate retinal arterioles and to increase retinal blood flow in monkeys and in humans. Furthermore, carbogen breathing (95% O2, 5% CO2), which has been shown to increase brain tumor oxygenation, has also been reported to increase preretinal Po2 in cats and rats and in minipigs. Carbogen may also be effective in increasing oxygen delivery in the ONH, though it has not yet been shown to increase optic disc Po2 in an experimental setting.

Blood flow can be influenced by several other chemical substances or drugs. Intravenous administration of acetazolamide has been shown to increase cerebral blood flow and has been used as a provocation test to assess cerebrovascular reserve capacity. It has also been reported to increase retinal and choroidal blood flow, as well as optic disc Po2. High Paco2 leading to arterial vasodilation is thought to be the mechanism of increased tissue blood flow by acetazolamide. CO2-associated vasodilation is apparently mediated in the extravascular tissue through acidification of the interstitial space of the inner retina, a mechanism similar to that occurring at the cerebral cortex.

Provided there is no change in tissue oxygen consumption, tissue oxygen tension reflects corresponding blood flow variations and enables an accurate estimation of tissue oxygen supply in the physiological state or ischemic disease. Optic disc Po2 was first measured in vivo with microelectrodes in cats and in monkeys. Thereafter, Po2 measurements were obtained within the ONH tissue at various depths in minipigs and in cats. A dose-dependent significant increase in optic disc Po2 in pigs after intravenous administration of acetazolamide or dorzolamide using polarographic oxygen electrodes placed in front of the optic disc was recently described. However, the effect of carbogen inhalation on the optic disc oxygenation has not been tested. It would therefore be reasonable to see whether carbogen is sufficient to increase optic disc Po2, as well as to test the effect of the combined use of acetazolamide and carbogen on optic disc Po2. This may be useful in defining new therapeutic modalities for ischemic diseases of the optic nerve.

Based on these considerations, we sought in the present study to evaluate the variations of optic disc Po2 during normoxia, systemic hyperoxia (breathing of 100% O2), and carbogen breathing (95% O2, 5% CO2), before and after intravenous administration of acetazolamide.

Copyright © Association for Research in Vision and Ophthalmology

I. K. Petropoulos, None; J.-A. C. Pournaras, None; J.-L. Munoz, None; C. J. Pournaras, None

The publication costs of this article were defrayed in part by page charge payment. This article must therefore be marked ‘advertisement’ in accordance with 18 U.S.C. §1734 solely to indicate this fact.

Corresponding author: Constantin J. Pournaras, Department of Ophthalmology, University Hospitals of Geneva, 22 Alcide-Jentzer Street, CH-1211 Geneva 14, Switzerland; constantin.pournaras@hcuge.ch.
MATERIALS AND METHODS

Experiments were conducted in one eye of 9 minipigs (Arare Animal Facility, Geneva, Switzerland) weighing 10 to 12 kg. The advantage of using the minipig is the anatomic similarity of its optic nerve to the optic nerve of the primates, except that the retinal arteries arise from the ciliary circulation. All the experiments were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Animal Preparation

Minipigs were prepared for the experiments, as previously described. In brief, after the minipigs received intramuscular injection of 2 mL (10 mg) of the tranquilizer midazolam maleate (Dormicum; Roche Pharma, Reinach, Switzerland), 3 mL (120 mg) of the tranquilizer azaperon (Stresnil; Janssen Pharmaceutica, Beerse, Belgium), and 1 mL (0.5 mg) of atropine, anesthesia was induced with 2 to 3 mg thiopental sodium (Pentothal; Abbott AG, Baar, Switzerland) injected into the ear vein. Curarization was performed with 2 mL (4 mg) of pancuronium bromide (Pavulon; Organon SA, Pfäffikon, Switzerland). The animals were intubated and artificially ventilated. After arterial, venous, and bladder catheterization, anesthesia and myorelaxation were maintained throughout the experiment by continuous perfusion of thiopental and pancuronium, respectively.

Each animal was ventilated at approximately 18 strokes/min, with a continuous flow of 20% O2 and 80% N2O, through a variable-volume respirator. Systolic, diastolic, and mean arterial pressures were monitored through the femoral artery with a transducer. Temperature was maintained between 36°C and 37°C with a thermostubinet. PaO2, PaCO2, and pH were measured intermittently from the same artery with a blood gas analyzer (Labor-system; Flukiger AG, Menziken, Switzerland) and kept under control by adjusting ventilatory rate, stroke volume, and composition of the inhaled gas.

A head-holder was used to avoid movements due to respiration. Upper and lower eyelids were removed, as well as a rectangular area of skin surrounding the eye; the bulbar conjunctiva was detached; the sclera was carefully cleaned to 5 mm from the limbus; the superficial scleral vessels were thermocauterized; the globe was fixed with a metal ring sutured around the limbus; and a sclerotomy at the pars plana was performed. The pupil was dilated with 1% atropine eye drops and the fundus was observed using an operating microscope (Carl Zeiss Surgical GmbH, Oberkochen, Germany).

PO2 Measurements

Optic disc PO2 measurements were obtained using double-barreled, recessed oxygen-sensitive microelectrodes with a 10-μm tip diameter, as previously described. The microelectrodes were prepared in our laboratory according to a technique described in detail in previous papers. They were calibrated before insertion into the eye and again after withdrawal in a buffered saline solution at 35°C, which was equilibrated with air. The microelectrodes were inserted into the vitreous cavity through a sclerotomy placed 2 to 3 mm posterior to the limbus, aided by an electronic micromanipulator. The microelectrode tip was positioned at a distance of less than 50 μm from the optic disc, over intervascular areas, as follows: When the microelectrode tip touched the optic disc surface, the reference barrel recorded a sudden negative DC potential shift of several millivolts. At the moment of contact, the position display was zeroed, and the microelectrode was then withdrawn less than 50 μm from the optic disc surface.

The timeline of PO2 measurements was as follows: Baseline measurements under normoxia and a stable continuous recording for at least 10 minutes preceded inhalation of 100% O2 (hyperoxia) for 10 minutes. Then normoxia was again induced, with the purpose of obtaining a stable recording for at least 10 minutes. This recording was considered the baseline before inhalation of carbogen for 10 minutes. Each condition was confirmed by corresponding PaO2, PaCO2, and pH measurements. PaO2 had to be high in hyperoxia, whereas both PaO2 and PaCO2 had to be high during carbogen breathing. The timeline of measurements was performed before and after intravenous injection of acetazolamide (500 mg bolus; Diamox; Vifor SA, Fribourg, Switzerland). Though higher than that used in clinical practice, the dose of 500 mg was chosen in accordance with previous results, of studies in which various doses had been tested and the dose of 500 mg had been the lowest one to produce maximum effects on optic disc PO2.

Nitrous oxide (N2O) was present in the breathing gas during normoxia, whereas it was absent during hyperoxia or carbogen breathing. However, this was not considered to affect the results, as we have previously tested the effect of the presence or absence of N2O in the breathing gas during normoxia and we have not found any differences in pH, PaO2, PaCO2, or optic disc PO2 (data not shown).

Under normoxia (PaO2 = 104.09 ± 6.06 mm Hg; PaCO2 = 35.45 ± 2.41 mm Hg; pH = 7.45 ± 0.06; n = 28), mean optic disc PO2 recorded in intervascular areas of nine eyes was 20.11 ± 2.47 mm Hg (n = 28), a level similar to those previously described.

The inhalation of 100% O2 induced a mean increase in optic disc PO2 of ΔPO2 = 4.81 ± 1.16 mm Hg or 24% (nine eyes; n = 15; Fig. 1) after 7 minutes. Under systemic hyperoxia, mean optic disc PO2 increased from 20.36 ± 2.88 to 25.18 ± 3.75 mm Hg and that difference, although moderate, was statistically significant (P < 0.001), yet disproportional to a substantial increase in PaO2 (ΔPaO2 = 334.40 ± 39.36 mm Hg; ΔPaCO2 = −4.66 ± 2.27 mm Hg; ΔpH = 0.03 ± 0.01; n = 13). The effect was fully reversible after return to normoxia.

The inhalation of carbogen induced a mean increase in optic disc PO2 of ΔPO2 = 13.17 ± 2.18 mm Hg or 67% (nine eyes; n = 15; Fig. 1) after 7 minutes. Mean optic disc PO2 increased significantly from 19.89 ± 2.13 to 33.05 ± 3.45 mm Hg (P < 0.001). Under the effect of carbogen, both PaO2 and PaCO2 increased significantly (ΔPaO2 = 371.72 ± 95.19 mm Hg; ΔPaCO2 = 10.31 ± 3.71 mm Hg; n = 15). The CO2 increase induced a respiratory acidosis from a mean pH of 7.45 ± 0.06 to 7.38 ± 0.07 (ΔpH = −0.07 ± 0.02; n = 15). The effect was also fully reversible after return to normoxia.

Considering 12 optic disc territories of nine minipigs submitted to the same conditions at four different time points (2, 5, 7, and 10 minutes), the Friedman test revealed a statistically more significant effect of carbogen inhalation on the optic disc PO2 variations with time (P < 0.0001) than of hyperoxia (P < 0.05).
0.02; Fig. 2). Furthermore, at each of the four analyzed times, the Wilcoxon signed-rank test showed a significantly greater effect of carbogen inhalation on the optic disc PO2 variations than that of hyperoxia (P < 0.02 at 2 minutes; P < 0.003 at 5, 7, and 10 minutes; Fig. 2).

**Measurements after Intravenous Administration of Acetazolamide**

After inducing a transient decrease in optic disc PO2 due to a transient systemic hypotension (confirmed by our arterial pressure monitoring) related to the injection, intravenous administration of 500 mg of acetazolamide led to a slow and progressive increase in optic disc PO2 (Fig. 3A) in parallel with a slow and progressive increase in PaCO2 (Fig. 3B), as previously described.10,24 In six intervascular optic disc territories of six eyes, after the injection of acetazolamide and during normoxia, the optic disc PO2 measured 30 minutes later revealed an increase (ΔPO2 = 4.24 ± 2.45 mm Hg, or 24%). More specifically, acetazolamide had increased optic disc PO2 from a mean of 18.00 ± 3.08 to 22.13 ± 4.04 mm Hg and that difference, though moderate, was statistically significant (P < 0.04). PaCO2 had simultaneously increased by 31% in average (ΔPaCO2 = 10.11 ± 4.42 mm Hg; ΔPaO2 = 1.27 ± 6.51 mm Hg; n = 6).

The CO2 increase induced a metabolic acidosis from a mean pH of 7.47 ± 0.05 to 7.39 ± 0.04 (ΔpH = -0.08 ± 0.03; n = 6).

The inhalation of 100% O2 under the effect of acetazolamide led to a significant increase in optic disc PO2 (ΔPO2 = 12.86 ± 4.08 mm Hg, or 58%; six eyes; n = 10; Fig. 4) after 7 minutes, from a mean level of 22.97 ± 4.23 to 35.83 ± 5.52 mm Hg (P < 0.002). In hyperoxic conditions, PaO2 increased significantly (ΔPaO2 = 374.42 ± 43.77 mm Hg), whereas PaCO2 and pH remained practically stable (ΔPaCO2 = -1.42 ± 3.27 mm Hg; ΔpH = -0.001 ± 0.05; n = 10).

During carbogen inhalation under the effect of acetazolamide, the greatest increase in optic disc PO2 was recorded (ΔPO2 = 18.91 ± 5.23 mm Hg, or 90%; six eyes; n = 10; Fig. 4) after 7 minutes, from a mean of 21.90 ± 5.03 to 40.81 ± 7.70 mm Hg (P < 0.002). Carbogen breathing induced a significant increase in both PaO2 and PaCO2 (ΔPaO2 = 404.14 ±
36.82 mm Hg; \( \Delta P_{\text{PaCO}_2} = 10.42 \pm 4.05 \text{ mm Hg}; n = 10 \), leading to a deeper systemic acidosis from \( pH = 7.37 \pm 0.06 \) to 7.30 \( \pm 0.06 \) (\( \Delta pH = -0.07 \pm 0.02 \); \( n = 10 \)).

With the Friedman test, the effect of hyperoxia and carbogen breathing was analyzed at four different time points (2, 5, 7, and 10 minutes) and in nine optic disc territories of six minipigs placed in the same conditions after acetazolamide injection (Fig. 5). This test revealed the statistically significant effect of both hyperoxia or carbogen inhalation on the optic disc \( P_{\text{O}_2} \) variations with time at all four analyzed time points (\( P < 0.0002 \)). Furthermore, the Wilcoxon signed-rank test demonstrated a significantly greater effect of carbogen inhalation on the optic disc \( P_{\text{O}_2} \) variations compared with hyperoxia (Fig. 5), at all time points (\( P < 0.02 \)) except 2 minutes (\( P < 0.07 \)).

In addition, with the Friedman test, the effect of hyperoxia was analyzed at four different time points (2, 5, 7, and 10 minutes) and in the same eight optic disc territories of six minipigs tested before and after acetazolamide injection (Fig. 6). This test revealed a significantly greater effect of hyperoxia after acetazolamide injection on optic disc \( P_{\text{O}_2} \) variation with time (\( P < 0.0005 \)), compared with hyperoxia before acetazolamide injection (\( P < 0.04 \)). That effect of hyperoxia after acetazolamide injection was confirmed by the Wilcoxon signed-rank test, at all four time points (\( P < 0.02 \)).

Finally, with the Friedman test, the effect of carbogen inhalation was analyzed at four different time points (2, 5, 7, and 10 minutes) and in the same seven optic disc territories of six minipigs tested before and after acetazolamide injection (Fig. 7). This test revealed a statistically significant effect of carbogen before and after acetazolamide injection on optic disc \( P_{\text{O}_2} \) variation with time (\( P < 0.002 \)). Furthermore, the Wilcoxon signed-rank test demonstrated a significantly greater effect on optic disc \( P_{\text{O}_2} \) variation with time of carbogen breathing after acetazolamide injection than of carbogen breathing before acetazolamide injection, at all four time points (\( P < 0.03 \)).

**DISCUSSION**

Nutrition and oxygenation of the ONH depends on its blood flow, which is proportional to the perfusion pressure in the ONH and inversely proportional to the resistance to flow. Resistance is closely dependent on \( P_{\text{O}_2} \) and \( P_{\text{CO}_2} \). As a result, elevated \( P_{\text{O}_2} \) decreases ONH blood flow, whereas elevated \( P_{\text{CO}_2} \) increases ONH blood flow, to ensure a constant supply of the ONH in oxygen.

Previous findings in minipigs indicate regulation of retinal blood flow during systemic hyperoxia, maintaining preretinal nutrition and oxygenation of the ONH. Therefore, this study aimed to investigate the effect of hyperoxia on optic disc \( P_{\text{O}_2} \) and \( P_{\text{CO}_2} \) in minipigs.
PO$_2$ at a constant level despite the elevation of PaO$_2$.\textsuperscript{6,7} In addition, previously published data demonstrated that, although juxta-arteriolar tissue PO$_2$ of the ONH increases (due to direct O$_2$ diffusion from the arteriolar wall), intervascular tissue PO$_2$ within the ONH and in front of the optic disc remains practically unchanged.\textsuperscript{8,9} In our experiments, systemic hyperoxia significantly increased PaO$_2$. This high PaO$_2$ induced a slight increase in optic disc PO$_2$, probably due to O$_2$ diffusion from the arterioles (Fig. 1).

The slight increase in optic disc PO$_2$ recorded in our experiments during systemic hyperoxia may be related in part to the tip diameter of the microelectrode used. Juxta-arteriolar and intervascular PO$_2$ in the vitreous are significantly different at 50 μm from the vitreoretinal interface.\textsuperscript{30-39} Given the microelectrode’s properties,\textsuperscript{33} a small tip diameter ensures an intervascular PO$_2$ measurement at that distance. Investigations involving a tip diameter of 3 to 6 μm\textsuperscript{8,9} found no increase in optic disc PO$_2$ over intervascular areas during systemic hyperoxia. Because our electrode had a 10-μm tip diameter, it is likely that we also recorded a small part of the O$_2$ diffusing directly from the ONH arterioles; however, after the initial PO$_2$ increase, the PO$_2$ remained constant throughout measurements under hyperoxia.

Carbogen breathing induces a simultaneous increase in PaO$_2$ and PaCO$_2$, affecting the retinal and ONH arteriolar reactivity. Elevated PaO$_2$ induces arteriolar vasoconstriction, whereas elevated PaCO$_2$ induces a vasodilation\textsuperscript{11} similar to that observed in cerebral arterioles.\textsuperscript{40} In retinal circulation, due to the vasodilatory effect of elevated PaCO$_2$, carbogen breathing leads to less reduction of retinal blood flow compared with systemic hyperoxia.\textsuperscript{41}

Assuming similar reactivity of the ONH arterioles, carbogen breathing should lead to a less important arteriolar vasoconstriction at the level of the ONH compared with hyperoxia.\textsuperscript{41} Indeed, in our experiments, optic disc PO$_2$ increased significantly during carbogen breathing (Fig. 1), more than after systemic hyperoxia (67% vs. 24%), as also confirmed by statistical comparison. Our results are in agree-
ment with those observed in normal retinas of newborn and adult rats and in normal and ischemic intervascular retinal territories of minipigs.

In addition to blood flow changes induced by carbogen, the blood CO₂ increase and the resultant pH decrease should affect the ability of hemoglobin to bind oxygen. Elevated PaCO₂ induces a rightward shift of the oxyhemoglobin dissociation curve, which reflects decreased affinity of hemoglobin for oxygen, meaning that oxygen is released from hemoglobin more readily, increasing oxygen availability in the tissue. Thus, the optic disc Po₂ increase measured in our experiments during carbogen breathing reflects both the effect of carbogen on the ONH circulation and the increased oxygen delivery to the ONH tissue due to a rightward shift of the oxyhemoglobin dissociation curve.

Intravenous administration of acetazolamide increases cerebral, retinal, and choroidal blood flow, with simultaneous increase in PaCO₂. This PaCO₂ increase is due to significant bicarbonate losses in the renal tubules, resulting in hyperchloremic metabolic acidosis. The CO₂ produced by cells cannot be eliminated by carbonic anhydrase and so increases PaCO₂ by diffusing in the blood through the basement membrane.

In our experiments, acetazolamide injection induced a slow and progressive increase in optic disc Po₂ in association with a slowly and progressively increasing PaCO₂, as previously described. This probably reflects, as in the case of carbogen, a vasodilatory effect of acetazolamide on the ONH arterioles and an increased dissociation of oxygen from hemoglobin, both due to the elevated PaCO₂. Rightward shift of the oxyhemoglobin dissociation curve with increased oxygen availability under the effect of acetazolamide has also been described in the treatment of myocardial ischemia. Moreover, our results indicated that concomitant administration of acetazolamide and carbogen can increase optic disc Po₂ more significantly than the association of the former with hyperoxia (90% vs. 58%). This effect is apparently due to the additive action of acetazolamide and carbogen on the elevation of PaCO₂. Indeed, PaCO₂ was higher when acetazolamide was associated with carbogen than with hyperoxia.

To our knowledge, this is the first time that concomitant administration of acetazolamide and carbogen has been tested for the ONH. This is important, as one can extrapolate that carbogen inhalation, especially in association with intravenous injection of acetazolamide, may improve oxygen delivery to a hypoxic ONH. In disturbed perfusion through the ONH capillaries, this association improves the oxygenation of the ONH by increasing O₂ diffusion from the ONH arterioles. In that case, the association would be beneficial as a treatment modality for disorders related to ONH ischemia or dysregulation of the ONH blood flow, such as glaucoma and nonarteritic anterior ischemic optic neuropathy (NAION).

Regarding glaucoma, acetazolamide is being used for its intraocular pressure (IOP)-lowering action, which increases the perfusion pressure in the ONH, but the double effect of elevated PaCO₂, described herein is also possible. Flammer and Drance gave oral acetazolamide in patients with glaucoma and observed visual field improvement without correlation with the IOP reduction and without change in perfusion pressure, suspecting improved ONH blood flow from decreased vascular resistance. In addition, the presence of relative vasconstriction has been shown in patients with glaucoma, at least partially reversed by hypercapnia. Finally, carbogen breathing was reported to improve visual fields of patients with normal-tension glaucoma, postulated to reverse an initial vasoconstriction.

Regarding NAION, no established treatment exists. Intraocular acetazolamide was administered by Hayreh in patients with NAION and progressive loss of vision or visual fields, pretreatment IOP < 20 mm Hg, and (in some of them) angiographic evidence of poor perfusion in posterior ciliary artery system; further deterioration was prevented. Hayreh actually wanted to lower IOP to improve the perfusion pressure in the ONH, whereas, retrospectively, a beneficial effect through elevated PaCO₂ also seems possible.

In clinical practice, if acetazolamide alone, or associated with carbogen breathing, can exert a beneficial functional effect through increased oxygenation, this should also be reflected in the results of functional tests. However, acetazolamide attenuates the amplitudes of ERG responses. Moreover, under hypercapnic conditions, the b-wave of ERG is depressed, as a result of reduction in extracellular K⁺. In addition, recent studies have shown either no effect or decreased contrast sensitivity by CO₂. Thus, a blood flow increase by acetazolamide and/or carbogen breathing does not necessarily mean a functional benefit resulting from increased

![Box plots displaying the optic disc ΔPO₂ levels obtained in the same seven optic disc territories of six eyes at four different time points (2, 5, 7, and 10 minutes) under carbogen breathing before and after intravenous injection of acetazolamide. Error bars: 5th and 95th percentiles of the ΔPO₂ levels. A Wilcoxon signed-rank test revealed a statistically more significant effect on optic disc ΔPO₂ of carbogen breathing after acetazolamide injection than of carbogen breathing before acetazolamide injection, with time and at all time points (P < 0.03; n = 9).](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933437/)
Clinical studies are needed, however, to confirm these speculative dysregulation. This would be of particular interest, as acetazolamide could be a good therapeutic modality in cases of ischemia or intravenous injection of acetazolamide with carbogen breathing increases dissociation of O2 from hemoglobin. The association of most probably inducing ONH arteriolar vasodilation and increased dissociation of O2 from hemoglobin. The association of intravenous injection of acetazolamide with carbogen breathing can improve the oxygenation of the ONH substantially and could be a good therapeutic modality in cases of ischemia or dysregulation. This would be of particular interest, as acetazolamide is already being used in the treatment of glaucoma. Clinical studies are needed, however, to confirm these speculations.

Acknowledgments

The authors thank Andrew R. Whatham, DPhil, for a critical reading of the manuscript and useful suggestions.

References


