Isocapnia Blocks Exercise-Induced Reductions in Ocular Tension

Alon Harris,* Victor E. Malinovsky,† Louis B. Cantor,‡ Patricia A. Henderson,† and Bruce J. Martin*

Previous reports suggest that isometric exercise (2-min handgrip at 50% maximal voluntary contraction [MVC]) substantially lowers intraocular pressure (IOP). The authors questioned whether the mechanism for lowered IOP in exercise is secondary to hyperventilation. Accordingly, in this study 11 subjects, with elevated IOP (>18 mm Hg) and otherwise healthy, did 2 min of handgrip exercise at 50% MVC with and without carbon dioxide supplementation to maintain isocapnic conditions. Compared with a control experiment that involved neither exercise nor CO2 addition, exercise induced a fall in IOP from 18.3 to 15.6 mm Hg (P < 0.001). This statistically significant decline in IOP persisted for 15 min after the exercise session. At the point of minimum IOP (1 min after the end of exercise), the minute ventilation was elevated from 6.5-8.1 l/min (P < 0.05), and the end-tidal partial pressure of CO2 (Pco 2) was reduced from 37.0 to 33.7 mm Hg (P < 0.05) with respect to control values. By contrast, adding CO2 sufficient to maintain isocapnic conditions (experimental end-tidal Pco 2 = 38.9 versus 38.5 mm Hg in the control study; P = not significant) abolished the exercise-induced ocular hypotension (experimental IOP = 17.8 versus 18.1 mm Hg in the control study; P = not significant). It was concluded that prevention of hypocapnia during isometric handgrip exercise blocks the subsequent fall in IOP, suggesting both that isometric exercise per se has no direct influence on IOP and that therapy for ocular hypertension could involve manipulation of blood gases. Invest Ophthalmol Vis Sci 33:2229-2232, 1992

Exercise provokes a profusion of physiologic responses, some still poorly understood. One of these is the fall in intraocular pressure (IOP) that occurs after physical activity.1-9 Some studies show dramatic lowering of IOP, suggesting that exercise might be therapeutic for elevated intraocular tension.1,2,6 At the same time, some studies show modest IOP changes,9 and in no study, is there a mechanistic link between IOP and exercise.

We attempted to determine whether ocular hypotension after static exercise results from hyperventilation. Previous studies report lower IOP during and after controlled hyperventilation.10-13 Because isometric handgrip contractions elicit hyperventilation,14-16 it is possible that the IOP reduction observed during isometric handgripping is caused by alterations in blood gas tension and pH. Our objective was to determine whether maintenance of isocapnic conditions after exercise would block exercise-induced ocular hypotension.

Materials and Methods

Subjects

Eleven volunteers (mean age, 23 yr) with a pre-screening IOP averaging 18 mm Hg or more participated in the study. All subjects signed informed consent, and all experimental procedures were reviewed and approved by an institutional human subject protection committee. Before testing, each subject was examined at the Indiana University School of Optometry Clinic. The screening test included: visual acuities with best spectacle correction, anterior segment biomicroscopy, fundus examination, and repeated applanation IOP determinations. None of the subjects were receiving medication, and all had good ocular and systemic health.

Experimental Design

After a familiarization experiment, each subject was studied under each of three different conditions: (1) rest, (2) exercise with no CO2 addition, and (3) exercise with addition of CO2 sufficient to maintain isocapnic conditions. All experiments were done at the same time in the afternoon and conducted in a counterbalanced fashion. Isometric handgripping was done for 2 min at 50% of maximal voluntary contraction (MVC). This was determined before each experi-
ment as the highest value recorded in three trials. Baseline IOP, minute ventilation, and end-tidal Pco2 measurements were taken 20 and 10 min before the handgrip exercise. The same measurements were taken 1, 3, 5, 15, 30, and 60 min after exercise.

**IOP Measurement**

A slit-lamp mounted Goldmann applanation tonometer was used to measure IOP. Before each measurement, one drop of a combination of benoxinate hydrochloride 0.4% and fluorescin sodium 0.25% was instilled in the eye. A single drop of this drug was used to measure IOP during minutes 1, 3, and 5 of recovery after exercise. The IOP was measured by either of two optometrists from the Indiana University School of Optometry who were experienced with this technique. Measurements during all three experiments on a given subject were made by a single optometrist, who was unaware of the experimental condition, to avoid the introduction of systematic observer bias.

**Minute Ventilation and End-Tidal Partial Pressure of CO2 (Pco2) Measurements**

At each point of measurement, during all three experiments, subjects breathed on a low-resistance valve into a Tissot spirometer for at least 2 min to determine the minute ventilation. End-tidal CO2 was determined from the mouthpiece using a Beckman LB-2 CO2 analyzer. The CO2 analyzer had a 90% response time to a step change in Pco2 of 100 msec; this was adequate for accurate measurement of end-tidal Pco2 at rest. During the isocapnic experiment, CO2 was added manually from a 100% CO2 tank to a 5-l mixing chamber in amounts sufficient to prevent hypocapnia in end-tidal CO2 during hyperpnea. The subjects breathed continuously on the apparatus for 15, 30, and 60 min postexercise. The apparatus used for ventilation and Pco2 measurement is shown schematically in Figure 1.

**Isometric Handgrip Exercise**

Isometric handgripping exercise was done using a handgrip dynamometer with the subjects in the seated position. They were instructed to rest their forearm on a table in front of them with the elbow angle kept at 90° during the sustained muscular contractions. This posture was maintained during measurement of MVC and during sustained efforts at 50% MVC.

**Statistical Analysis**

Data was analyzed from the 11 subjects (left eye only) using a paired student t-test adjusted for multiple comparisons to a single control value. The control experiment was used as the baseline in these experiments because of a possible drift in IOP induced by either time or repeated measurements.

**Results**

**IOP**

The IOP decreased during the 1st minute after the isometric handgrip to 15.6 ± 0.6 mm Hg compared with 18.3 ± 0.7 mm Hg at an equivalent time during the rest experiment ($P < 0.01$, Fig. 2). Individual initial values of IOP during the experiment ranged from 14–20.5 mm Hg; the extent of IOP depression caused by the handgrip exercise was not correlated with the initial IOP. The mean IOP remained significantly lower during the exercise experiment compared with
control for 15 min after the completion of exercise. By contrast with exercise without CO2 addition, the IOP was equal to the control condition when subjects were maintained under isocapnic conditions (Fig. 2). The IOP fell slightly but significantly during the control experiment from the first measurement to those occurring 45 and 75 min later (P < 0.05).

**Minute Ventilation**

Minute ventilation increased during the 1st minute after the isometric handgripping to 7.9 ± 0.6 l/min compared with 6.5 ± 0.3 l/min in the control experiment (P < 0.05, Fig. 3). This significantly higher value was maintained for 3 min after the completion of the exercise. The minute ventilation also was higher during the exercise isocapnic experiment compared with control (P < 0.05). This elevated level persisted for 5 min after the completion of exercise and was higher than the control experiment also at 60 min after exercise (P < 0.05, Fig. 3).

The end-tidal Pco2 was significantly lower than control during the 1st minute after the completion of exercise without CO2 addition (P < 0.05, Fig. 4). This difference in Pco2, unlike the fall in IOP, was lost at 3, 5, and 15 min after exercise (Fig. 4). The addition of CO2 predictably eliminated the CO2 difference between exercise and control (Fig. 4).

**Discussion**

It has been reported previously that static exercise can lower IOP.1 We found that hypocapnia induced by exercise was associated with a fall in IOP.

Our data revealed a significant reduction in IOP after 2 min of handgrip contraction at 50% MVC, which remained significantly lower than control values for 15 min after the completion of exercise and slowly returned to normal within 1 hr. Similar results were reported by others.1 These authors found handgrip contractions at tensions of 20% and 55% of MVC, done to the point of fatigue, significantly reduced IOP immediately after exercise.

Our data supports the hypothesis that the exercise-IOP link is through hypocapnia, brought about by hyperventilation. The small and transient, albeit statistically significant, elevation in minute ventilation and depression of end-tidal Pco2 that we detected after isometric handgripping agreed with the results of other workers.14-16 In addition, other studies report a significant lowering of IOP after voluntary hyperventilation.10-13 For example, a sudden cessation of CO2 administration or sudden initiation of hyperventilation leads to a rapid simultaneous fall in IOP during general anesthesia.12 Central to our results, of course, is the finding that CO2 addition, sufficient to maintain the subjects' in an isocapnic condition after handgripping while ventilation remained elevated, was adequate to eliminate the ocular hypotension. From this, it appears that hyperventilation per se is not responsible for the drop in IOP after isometric exercise, but rather that decreased carbon dioxide tension is the associated factor.

Our study, however, does not define the link between hypocapnia and reduced IOP. Some authors suggest that CO2-conditioned IOP changes primarily are mediated through changes in central venous pressure, leading to changes in choroidal venous blood volume.12 To support this hypothesis, it has been shown that alterations in central venous pressure,
brought about by postural changes, induce similar IOP changes (in magnitude and configuration) to those seen after hypocapnia and hypercapnia. Because hypocapnia is accompanied by peripheral vasconstriction, it is conceivable that the fall in IOP resulted from vasconstriction in the choroidal vessels leading to decreased choroidal blood volume. It is also plausible that the reduction in IOP was precipitated by a decrease in aqueous formation. Previous reports have shown that elevated PCO₂ in anesthetized cats resulted in elevated IOP, probably from vasodilation of the ciliary processes and increased aqueous formation. In addition, changes in central venous pressure (seen during hypercapnia or hypocapnia) may alter IOP by affecting aqueous drainage into the lymphatics. Some authors, however, assume that such a rapid fall in IOP (as observed during general anesthesia or immediately after exercise in our study) cannot be caused by the relatively slow changes in aqueous humor turnover.

Our results also may relate to the mechanism by which acetazolamide lowers IOP. This drug produces a systemic acidosis and a subsequent fall in arterial PCO₂. Although its action occurs through carbonic anhydrase inhibition or induction of systemic acidosis, our results suggest an additional potential input from systemic hypocapnia.

In summary, the fall in IOP after isometric hand-gripping is associated with hypocapnia, rather than with either hyperventilation or exercise per se. This result implies that control of elevated IOP could be achieved by systemic hypocapnia, if such could be maintained in the face of compensatory mechanisms. In addition, understanding the role of hypocapnia in IOP may help target other topical or local therapeutic agents to specific biochemical processes that would produce the ocular effects of systemic hypocapnia without systemic effects. The mechanisms linking CO₂ to IOP, however, are unclear and warrant additional investigation.

**Key words:** Intraocular pressure, isometric exercise, hyperventilation, hypocapnia, isocapnia

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**References**