Acknowledgments. We are grateful to Dr. Rosalie Crouch and to Mary Simpson for their assistance in purifying the rat Cu-Zn SOD used in this project. The authors thank Ana Maria Zaragoza for her technical assistance.

From Estelle Doheny Eye Foundation and Departments of Ophthalmology and Pathology, University of Southern California, Los Angeles, and from the Medical University of South Carolina.* Supported by Estelle Doheny Eye Foundation research funds, in part by Research to Prevent Blindness and by the National Institute of Health grant EYO5662. Submitted for publication: July 25, 1984. Reprint requests: N. A. Rao, MD, Estelle Doheny Eye Foundation, 1355 San Pablo Street, Los Angeles, California 90033.

References

Effect of Oxygen on Aqueous Humor Dynamics in Rabbits

Michael E. Yablonski,* Pamela Galia† and Douglas Shapio†

A study was made in albino rabbits of the effect on aqueous humor dynamics of 100% oxygen, administered by face mask. A mean decrease in intraocular pressure of 4.9 mm Hg was found. This was accompanied by a decrease in episcleral venous pressure of 4.5 mm Hg. Anterior chamber aqueous humor flow decreased transiently after oxygen administration but returned to pre-oxygen levels after about 60 min. It was concluded that the sustained decrease in intraocular pressure which was caused by oxygen was secondary to the decrease in episcleral venous pressure and not to a decrease in the production of aqueous humor. Invest Ophthalmol Vis Sci 26:1781-1784, 1985

Administration of 100% oxygen by face mask was shown by Gallin and coworkers1 in humans and albino rabbits to lower intraocular pressure. The mechanism of this action of oxygen was unclear; therefore, the present study was undertaken in rabbits to elucidate the effect of oxygen administration on aqueous humor dynamics. Fluorophotometry was used to measure anterior chamber aqueous humor flow. Tonography was used to measure outflow facility. In addition, episcleral venous pressure was measured.

Materials and Methods. In albino rabbits weighing 2.0-2.5 kg, 100% oxygen was administered by face mask as described previously.1 The effect of oxygen on intraocular pressure, anterior chamber aqueous humor flow, episcleral venous pressure, and total outflow facility in unanesthetized rabbits wrapped in cloth restraint was determined. In the case of all measurements the values of the two eyes of the rabbit were averaged and considered representative of one "cycloptic" eye of each rabbit.

Fluorophotometry was done on 20 rabbits using the method of Yablonski and coworkers.2 Each eye was given 0.25% fluorescein and 0.4% HCl benoxinate (Fluress, Barnes-Hind; Sunnyvale, CA), 2 drops every 15 min for a total of 4 administrations (8 drops). Four and one half hours after the last fluorescein administration, fluorophotometry measurements were begun. Baseline fluorophotometry measurements were made at 45-min intervals for a total of 4 sets of measurements. One hundred per cent oxygen administration was then begun, during which time fluorophotometry measurements were continued at 20-min intervals.

The effect of oxygen administration on episcleral venous pressure was determined by the chamber method.3 The end point was the complete collapse of the vessel. Baseline episcleral venous pressure measurements were made in both eyes of 20 unanesthe-
CHANGE IN I.O.P. WITH OXYGEN ADMINISTRATION

Fig. 1. The effect of 100% oxygen administration on the mean ± S.E.M. intraocular pressure in 20 unanesthetized albino rabbits. Asterisks signify statistically significantly different from baseline IOP (P < 0.05, paired t-test).

Fig. 2. Effect of 100% oxygen inhalation on the time course of anterior chamber aqueous humor flow in 20 unanesthetized albino rabbits. Oxygen administration began at time 0 and continued throughout the 180 min shown. The asterisks signify statistically significantly different from baseline aqueous humor flow (P < 0.05, paired t-test).

The effect of oxygen administration on total outflow facility was determined in both eyes of eight unanesthetized albino rabbits wrapped in cloth restraints using the alcon tonography unit and topical proparacaine anesthesia. On another day, face mask oxygen was administered, during which time, beginning 15 min after the onset of oxygen administration, tonography measurements were repeated. On another day, tonography was carried out similarly on the contralateral eye during oxygen administration.

All methods used in this study involving animals conform to the ARVO Resolution on the use of animals in research.

**Results.** The effect of oxygen administration on intraocular pressure is shown in Figure 1. Intraocular pressure fell from a mean ± S.E.M. value of 21.9 ± 0.6 mm Hg to 17.0 ± 0.5 mm Hg within 30 min after the onset of oxygen administration and was maintained at this level during the entire time of oxygen administration. After cessation of oxygen, the intraocular pressure promptly returned to its preoxygen level.
The effect of oxygen administration on anterior chamber aqueous humor flow determined fluorophotometrically is shown in Figure 2. Although a marked initial decrease in anterior chamber aqueous humor flow was found, the effect was not sustained, and aqueous humor flow returned to baseline levels after 60 min, despite continued oxygen administration.

Figure 3 shows the effect of oxygen administration on episcleral venous pressure. A drop in episcleral venous pressure was found from a baseline value of 14.3 ± 0.4 mm Hg to 9.8 ± 0.3 mm Hg 30 min after the onset of oxygen administration. This effect on episcleral venous pressure was maintained for the duration of oxygen administration.

In the masked studies there was no statistically significant difference between the two observers with respect to either the baseline or the post oxygen episcleral venous pressure determination (P > 0.05, paired t-test). The value of the mean difference in measurements between the two observers was 0.32 ± 0.72 mm Hg for the baseline measurements and 0.35 ± 0.85 mm Hg for the post oxygen measurements. In these experiments combining the results of the 2 observers, the mean baseline episcleral venous pressure was 14.1 ± .5 mm Hg and the mean post oxygen value was 9.6 ± .5 mm Hg. The difference between these two values was statistically significant (P < 0.05, paired t-test).

Tonography showed a slight decrease in total outflow facility at mean time of 15 min after the onset of oxygen administration. Baseline total outflow facility was 0.31 ± .02 µl/min/mm Hg falling to 0.25 ± 0.03 µl/min/mm Hg after oxygen. This difference was statistically significant (P < 0.05, paired t-test).

Discussion. As found previously, 100% oxygen administration did lower the intraocular pressure in rabbits. In the present study, the mean decrease in intraocular pressure was 4.9 mm Hg within the first 30 min of oxygen administration and was maintained at this level for the duration of oxygen administration.

This decrease in intraocular pressure was shown by fluorophotometry not to be due to a decrease in aqueous humor production, since the initial decrease in anterior chamber aqueous humor flow was not sustained, despite continuous oxygen administration. The most likely explanation for this finding is that the oxygen caused a contraction of choroidal volume during which time anterior chamber aqueous humor flow would be expected to decrease; however, once choroidal contraction was complete, if no change had occurred in the rate of aqueous humor production by the ciliary body, one would expect anterior chamber aqueous humor flow to resume its pre-oxygen value.

In contrast to the effect on anterior chamber aqueous humor flow, the effect of oxygen administration on episcleral venous pressure was maintained for the duration of oxygen administration. Also the magnitude of the decrease in episcleral venous pressure (Fig. 3), was similar to the magnitude of the decrease in intraocular pressure (Fig. 1). The 120-min value of episcleral venous pressure in Figure 3, which was 30 min post oxygen administration, was statistically significantly greater than baseline, evidently representing a slight rebound phenomenon. Thus the decrease in intraocular pressure caused by oxygen administration can be explained entirely on the basis of the effect of oxygen to decrease episcleral venous pressure. The reason episcleral venous pressure decreases with oxygen is uncertain; however, the most likely explanation is a decrease in blood flow due to arterial constriction.

The double masked studies showed that the decrease in the episcleral venous pressure measurement was not dependent on the observers’ knowledge of oxygen administration. In addition, the small value of the interobserver measurement difference demonstrated that the measurements were reproducible.

The effect of oxygen on outflow facility was somewhat complicated. Tonography showed a statistically
significant decrease in total outflow facility from a pre-oxygen value of 0.31 μl/min/mm Hg to a post-oxygen value of 0.26 μl/min/mm/Hg. Keeping in mind that total outflow facility, C rot, as shown in equation 1, is the sum of true outflow facility, C tr, and pseudofacility, C ps, it should be noted that a decrease in C rot may be due to a decrease in C ps as well as a decrease in C tr.

Equation (1): C rot = C tr + C ps

Since the fluorophotometry data indicated that the oxygen caused a contraction in choroidal volume, it seems likely that the observed decrease in C rot was due to a decrease in C ps. Part of C ps is due to the occurrence of an expulsion of choroidal fluid during tonography. 4 This would be expected to be a less important factor if the choroidal volume were already diminished by oxygen administration. A similar decrease in C rot due to oxygen was found in humans. 1 This was accompanied by an increase in ocular rigidity which was explained by a contraction of choroidal volume. Finally, it seems unlikely that the decrease in C rot was due to a decrease in C tr since this would be expected to cause an increase in IOP instead of the decrease which was observed.

Key words: oxygen, intraocular pressure, fluorophotometry, episcleral venous pressure, aqueous humor flow

From Cornell University Medical Center* and Mt. Sinai Hospital,† New York; Dr. Yablonski is formerly from the Department of Ophthalmology, Mt. Sinai Medical School, New York, New York. Supported in part by a research grant from Fight for Sight, Inc., New York City, In Tribute to the memory of Herman M. Burian, M.D., and by USPH Grant EY 04796-03. Submitted for publication: January 9, 1985. Reprint requests: Michael E. Yablonski, M.D., Ph.D., Department of Ophthalmology, Cornell University Medical Center, 515 East 71st Street, New York, New York 10021.

References


The Effect of Dexamethasone on the Synthesis of Collagen in Normal Human Trabecular Meshwork Explants

M. Rosario Hernandez, Bernard I. Weinstein, Michael W. Dunn, Gary G. Gordon, and A. Louis Southren

This study demonstrates that the trabecular meshwork cells of the human eye incorporate 3H-Proline into collagen during in vitro incubation. Addition of dexamethasone to the incubation mixture produced a marked decrease in this incorporation. Dexamethasone was active at 10^{-8} M and higher concentrations. The specificity of the hormone effect was demonstrated by its inability to alter 3H-leucine incorporation in these cells. These results indicate that dexamethasone decreases the synthesis of collagen, a major component of the extracellular matrix, in the trabecular meshwork. Invest Ophthalmol Vis Sci 26:1784–1788, 1985

Glucocorticoids have been shown to increase intraocular pressure (IOP) in sensitive humans 1,2 and in young rabbits. 3 The mechanism of this effect appears to be related to a decrease in facility of aqueous humor outflow, 4,5 which has been postulated to be due to an alteration in extracellular matrix components such as glycosaminoglycans 6 and collagens. Chronic topical application of dexamethasone in rabbits results in changes in the relative distribution of glycosaminoglycans in the outflow pathway region. 7 Whether these changes are due predominately to alteration in synthesis or degradation is not known. Previously we have demonstrated that dexamethasone causes a decreased incorporation of 3H-glucosamine and increased incorporation of 3H-proline in the outflow pathway cells of the rabbit. 7

The present study was designed to determine the effect of dexamethasone on the synthesis of collagen, a major component of the extracellular matrix, in human trabecular meshwork tissue. This initial study in the human involves explants of outflow tissue from nonglaucomatous patients.

Materials and Methods. Human eyes obtained at autopsy were enucleated within 12 hr of death, stored at 4°C for 2 or 4 hr, and transported to the laboratory on ice. Before dissection the eyes were cleaned with 10% Betadine solution and washed several times in sterile Hanks’ balanced salt solution or PBS. The an-