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Effect of Oxygen on Aqueous Humor Dynamics in Rabbits

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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 percent 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 unaneste-
In both eyes of 20 unanesthetized albino rabbits wrapped in cloth restraints, using topical proparacaine, 0.5%. The rabbits were then given face mask oxygen, during which time episcleral venous pressure measurements were repeated at 10-min intervals.

To test the reliability and interobserver variability of the measurements of episcleral venous pressure, measurements in 12 rabbits were made successively by 2 observers. Observers were masked as to whether the animals were receiving 30 min of oxygen administration or air administration by face mask. When air was used, no oxygen had been administered for at least 3 hr. The measurements of the two observers were always within 3 min of each other.

In both eyes of 20 unanesthetized albino rabbits wrapped in cloth restraint, the effect of oxygen administration on intraocular pressure was determined. Intraocular pressure measurements were made using the alcon pneumotonometer with topical proparacaine anesthesia. Baseline measurements of intraocular pressure were made every 15 min until 3 successive measurements in each eye stabilized within 4 mm Hg. Oxygen administration was then begun, during which time intraocular pressure measurements were repeated at 10-min intervals.

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 inter-observer 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, Ctot, as shown in equation 1, is
the sum of true outflow facility, Ctr, and pseudofacility,
Cps, it should be noted that a decrease in Ctot may be
due to a decrease in Cps as well as a decrease in Ctr.

Equation (1): Ctot = Ctr + Cps

Since the fluorophotometry data indicated that the ox-
ygen caused a contraction in choroidal volume, it seems
likely that the observed decrease in Ctot was due to a
decrease in Cps. Part of Cps 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 Ctot due
to oxygen was found in humans. 1 This was accompa-
nied by an increase in ocular rigidity which was ex-
plained by a contraction of choroidal volume. Finally,
seems unlikely that the decrease in Ctot was due to a
decrease in Ctr 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

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

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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 incu-
bation mixture produced a marked decrease in this incorpo-
ration. Dexamethasone was active at 10^-8 M and higher con-
centrations. The specificity of the hormone effect was dem-
onstrated by its inability to alter 3H-leucine incorporation in
these cells. These results indicate that dexamethasone de-
creases the synthesis of collagen, a major component of the
extracellular matrix, in the trabecular meshwork. Invest
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Glucocorticoids have been shown to increase intra-
ocular 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 glycosaminogly-
cans in the outflow pathway region. 7 Whether these
changes are due predominantly to alteration in synthesis
or degradation is not known. Previously we have dem-
onstrated that dexamethasone causes a decreased incor-
poration of 3H-glucosamine and increased incor-
poration 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 hu-
man 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-