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Reports

Effect of Cold Air on Aqueous Humor Dynamics in Humans

Gerald J. Ortiz, David J. Cook, Michael E. Yablonski, Harvey Masonson, and Gregory Harmon

Several parameters of aqueous humor dynamics were measured in 11 human subjects before and after exposure of one eye to a continuous stream of cold air. In the treated eye, I.O.P. was found to decrease significantly from a mean ± SD pre-treatment value of 14.1 ± 2.3 mmHg to a post-treatment value of 12.6 ± 2.6 mmHg. Episcleral venous pressure was found to decrease significantly from a pre-treatment value of 8.4 ± 1.5 mmHg to a post-treatment value of 6.2 ± 1.3 mm Hg. No significant changes were found in aqueous flow or total outflow facility, indicating that cold air exposure decreased I.O.P. by causing a decrease in episcleral venous pressure. Invest Ophthalmol Vis Sci 29:138–140, 1988

Aqueous humor production has been shown to be decreased by decreasing body temperature in rabbits.[1,2] To our knowledge, no quantitative data exist concerning the effects of local application of cold to the rabbit or human eye. Wilensky reported that he minimized elevations of intraocular pressure (I.O.P.) immediately after anterior segment laser surgery by applying ice packs to the treated eye.[3] The present study was designed to specifically measure the effect on aqueous humor dynamics of the application of cold to the human eye.

Materials and Methods. Eleven healthy volunteer subjects were studied. Informed consent was obtained after the nature of each of the procedures had been explained fully.

One eye of each of the 11 subjects was randomly chosen as the experimental eye and the subject placed this closed eye directly in front of a stream of cold air for 40 continuous minutes. The other eye, which also remained closed throughout the 40 min, was not subjected to the cold air and served as the control eye. The stream of cold air originated from a tank of compressed dry air and then passed through a standard styrofoam ice chest containing a mixture of ordinary ice and dry ice in a ratio of three to one by volume. The stream of cold air exited the ice chest at the opposite end via a 2-inch diameter hole and was directed at the experimental eye via a styrofoam eye cup. The temperature of the cold air reaching the eye was constantly monitored with the probe of a digital thermocouple (United Systems Corporation, Dayton, OH, Digitec Digital Thermometer) which was positioned in the eyecup, in the direct path of the oncoming stream of cold air, 1 inch from the subject's eye. The flow rate was adjusted so that the temperature of the air was −19°C.

In the initial measurement session, using topical proparacaine (0.5%) anesthesia, baseline I.O.P. and episcleral venous pressure (E.V.P.) values were determined in each eye by averaging five readings taken during the hour prior to treatment with cold air. I.O.P. was measured with an Alcon Applanation Pneumatonograph. E.V.P. was measured with the Zeimer Venomanometer.[4] The end point was defined as complete collapse of the episcleral veins.[4] After 40 min of exposure to the cold air, treatment was stopped and the measurements of I.O.P. and E.V.P. were again taken. The subject then resumed cold air treatment for an additional 10 min in order to compensate for any warming of the eye during the E.V.P. and I.O.P. measurement. Then, tonography (using a Sonometrics TTS-400 Tonography System; Coopervision, Irvine, CA) was immediately done, first on the experimental, then on the control eye. Baseline or pre-cold tonography was measured on a separate day.

On another day, seven subjects underwent a second measurement session using fluorophotometry to determine the effect of cold air on aqueous humor flow. In the morning, the subject instilled one drop in each eye of 0.25% sodium fluorescein and 0.4% benoxinate hydrochloride (Barnes-Hind Fluress; Sunnyvale, CA). This was repeated every 5 min for a total of ten administrations to each eye. Four and one half hours later, fluorescein concentration readings were begun using the Coherent Fluorotron Master (Palo Alto, CA). Readings were made at 30 min intervals for a total of four readings to determine the baseline aqueous flow. The cold air treatment was then begun on the same eye as used in measurement session one. The cold air treatment was continued for 40 min after which the final fluorescein scans were immediately taken to detect any changes in aqueous flow. Anterior chamber depths and corneal thickness measurements necessary for the aqueous flow calculations were made with a Haag Streit pachymeter (Bern, Switzer-

land). The method used to calculate aqueous flow was previously described by Yablonski, Cook and Grey.[5]

In order to determine the time course of the decrease in I.O.P., six subjects underwent a third measurement session in which the I.O.P. was measured every 10 min throughout a 40 min period of cold air treatment.

In order to determine the extent of extraocular hypothermia caused by the cold air treatment, three subjects underwent a measurement session in which a temperature probe was placed under the closed lid of the treated eye. The extraocular temperature was continuously monitored using a Brooks (Minneapolis, MN) digital thermocouple and recorded at 1 min intervals until the temperature stabilized for five consecutive readings.

Changes from baseline for all parameters of aqueous humor dynamics were analyzed using a paired t-test. A P value less than 0.05 was considered significant.

Results. As seen in Figure 1, the I.O.P. time course study showed a sustained decrease in I.O.P. in the experimental eyes throughout the 40 min of cold air treatment.

As shown in Table 1, treatment with cold air caused a statistically significant decrease in I.O.P. of 1.5 ± 1.7 mm Hg in the treated eyes. The control eyes did *not* show a significant change after treatment. The cold air treatment also caused a statistically significant decrease in E.V.P. of 2.2 ± 1.4 mm Hg in the treated eyes. The control eyes did *not* show a significant change. In only five cases were both the pre-cold and post-cold tonography values considered of good enough quality to be analyzed. Cold air treatment was found to cause no statistically significant change in total outflow facility, Ctotal. Also no statistically significant change was found in the rate of aqueous flow determined by fluorophotometry.

The extraocular temperature studies showed a statistically significant decrease in temperature from a mean baseline value of 33.3 ± 0.7°C to a mean value of 11.76 ± 2.9°C. The maximum decrease in temperature occurred at a mean time of 9.6 ± 1.5 min after the onset of cold air treatment, after which it stabilized.

A correlation coefficient was determined between the magnitude of change in I.O.P. and change in E.V.P. yielding a value of 0.79 ($P < 0.02$) for treated eyes. No correlation was found for the untreated control eyes.

Discussion. These data suggest that changes in I.O.P. after exposure of the eye to cold were a result of a decrease in E.V.P. The only two parameters of aqueous humor dynamics which were altered by exposure to the cold air were I.O.P. and E.V.P. The changes in I.O.P. showed a high, statistically significant correlation with changes in E.V.P. Also, the changes in I.O.P. and E.V.P. were similar in magnitude.

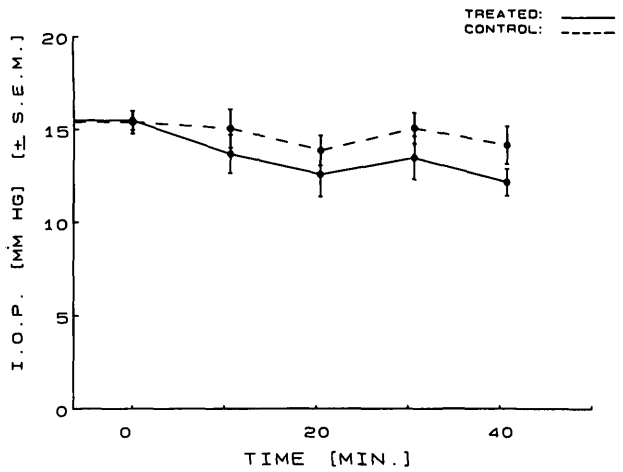

Fig. 1. I.O.P. (mm Hg) time course study. Unilateral cold air application, −19°C, began at time 0 and continued for 40 min in six subjects. A paired t-test was performed comparing values for the treated versus control eye at each 10 min period. A statistically significant decrease in I.O.P. was found for all points except at 30 min where a P value of 0.207 was obtained.

The decreased E.V.P. found after the stream of cold air was directed against the closed eyelids appeared to be a response to episcleral hypothermia. Hypothermia is, in general, known to cause arteriolar vasoconstriction and decreased blood flow in many tissues.[6,7] This response to episcleral hypothermia would be expected to cause a concomitant decrease in pressure within the veins of the area. The I.O.P. would thus be expected to fall, establishing a new steady state in which the difference between I.O.P. and E.V.P. would have returned to baseline. Similar

Table 1. Effect of cold air on aqueous humor dynamics

Component of aqueous humor dynamics	*N*	*Mean ± SD*	
		Pre-cold	*Post-cold*
I.O.P. (mm Hg)			
Treated	11	14.1 ± 2.3	12.6 ± 2.6*
Control	11	14.7 ± 2.1	14.5 ± 1.8
E.V.P. (mm Hg)			
Treated	11	8.4 ± 1.5	6.2 ± 1.3*
Control	11	8.3 ± 1.5	8.3 ± 1.6
Ctotal (μl/min/mm Hg)			
Treated	5	0.25 ± 0.09	0.19 ± 0.05
Control	5	0.21 ± 0.11	0.23 ± 0.08
Aqueous flow (μl/min)			
Treated	7	2.0 ± 0.5	2.3 ± 1.3
Control	7	2.2 ± 0.6	2.1 ± 0.9

* Signifies a statistically significant change from the pre-cold value (paired t-test, $P < 0.05$).

findings were found in rabbits who experienced concomitant decreases of I.O.P. and E.V.P. after exposure to 100% oxygen administration.[8]

Other investigators have measured changes in aqueous humor dynamics after subjecting entire animals to hypothermia.[1,2] A decrease in aqueous humor production was found, presumably caused by an effect on the energy-requiring active transport of aqueous across the ciliary epithelium. Since the rate of aqueous humor production was unaltered in this study, it seems likely that the application of cold air to the eye did not affect the temperature of the intraocular structures, despite a documented decrease in extraocular temperature.

Key words: aqueous humor dynamics, hypothermia, episcleral venous pressure, intraocular pressure, vasoconstriction

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References

1. Becker B: Hypothermia and aqueous humor dynamics in the rabbit eye. Trans Am Ophthalmol Soc 58:337, 1960.
2. Pollack IP, Becker B, and Constant MA: The effect of hypothermia on aqueous humor dynamics: I. Intraocular pressure and outflow facility of the rabbit eye. Am J Ophthalmol 49:1126, 1960.
3. Winter Glaucoma Symposium, 1985, Palmas Del Mar, Puerto Rico (Transcript). Sponsor: Coopervision Inc. Robin AL, editor. Baltimore, The Wilmer Ophthalmology Institute, The Johns Hopkins Hospital.
4. Zeimer RC, Gieser DK, Wilenski JT, Noth JM, Mor MM, and Odunuke EE: A practical venomanometer. Arch Ophthalmol 101:1447, 1983.
5. Yablonski ME, Cook DJ, and Grey J: A fluorophotometric study of the effect of argon laser trabeculoplasty on aqueous humor dynamics. Am J Ophthalmol 99:579, 1985.
6. Guyton AC: Textbook of Medical Physiology. Philadelphia, W.B. Saunders Co., 1986, p. 344
7. Kwon HJ, Rhee JG, Song CW, and Waite DE: Effects of temperature on blood flow in facial tissue. J Oral Maxillofac Surg 44:10, 1986.
8. Yablonski ME, Gallin P, and Shapiro D: Effect of oxygen on aqueous humor dynamics in rabbits. Invest Ophthalmol Vis Sci 26:1781, 1985.

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Corneal Changes in Nine-Banded Armadillos With Leprosy

Raga Malaty* and Birgitta Togni

Leprosy is the third leading cause of blindness worldwide; however, little is known about the ocular changes that occur during the disease process. We have studied the eyes of two nine-banded armadillos with experimental *Mycobacterium leprae* infection by light and electron microscopy. Both animals had been inoculated intracutaneously, one 5 years and the other 2 years previously. Light microscopy revealed invasion by acid-fast bacilli which were seen in keratocytes and mononuclear phagocytes in all layers of the corneal stroma. In both animals, large macrophage granulomas were observed in the deep stroma, which was vascularized. Acid-fast bacilli were also were found in macrophages and vascular endothelial cells. By electron microscopy, numerous bacilli were found in the keratocytes, macrophages, and Schwann cells of myelinated and unmyelinated axons, and in the endothelial cells of blood vessels. The localization of *M. leprae* and the presence of inflammatory cells in the ocular tissue of both animals suggest that the bacilli reach the eye by the neural and/or vascular route. One animal showed much more extensive disease and bacillary yield than the other, indicating that ocular involvement may be independent of the generalized infection. Further studies of early ocular involvement in the armadillo and other animals could help to clarify the pathogenesis of this potentially blinding infection. Invest Ophthalmol Vis Sci 29:140–145, 1988

Leprosy is a chronic systemic infection that involves the skin, peripheral nerves, and eyes. Of the 15 to 16 million leprosy patients in the world, as many as 90% suffer from the ocular complications of the disease, which may ultimately lead to blindness,[1-3] and up to 1 million leprosy patients may be blind as a result of this infection.[4]

Leprosy is manifested clinically in a pattern depending upon the host's immune response to infection with *M. leprae.* Lepromatous (multibacillary) and tuberculoid (paucibacillary) leprosy represent the two opposite poles of the spectrum. Borderline leprosy is an intermediate form.

Ocular leprosy is primarily an anterior segment disease. Corneal involvement, particularly transitory opacification of corneal nerves, may be the earliest ocular manifestation and a specific finding in leprosy.