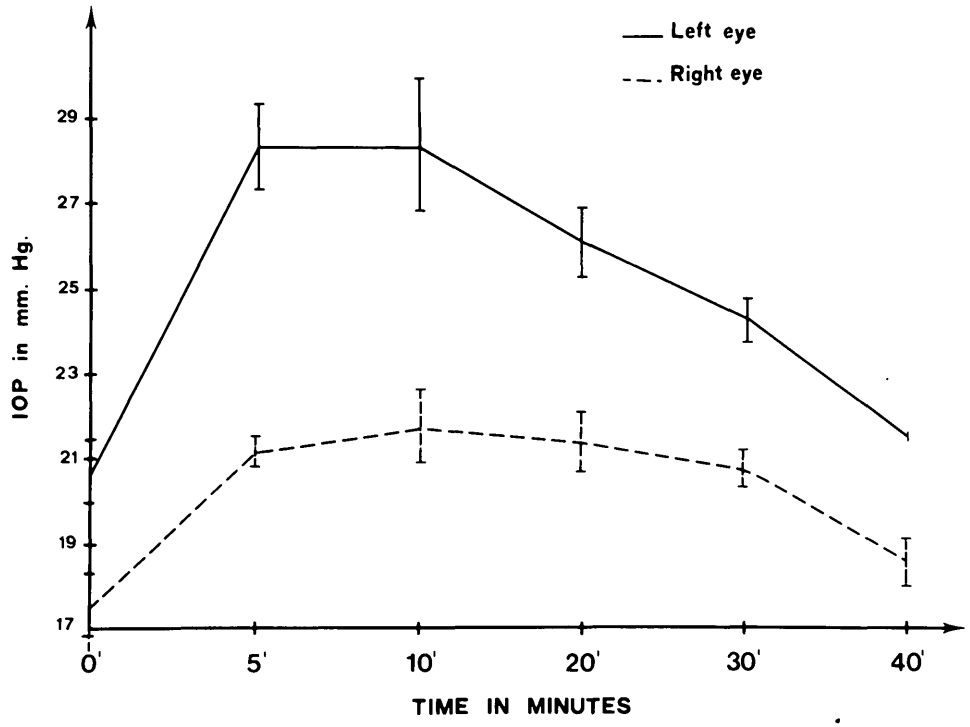

Fig. 4. Mean intraocular pressure in six rabbits after intravenous infusion of 15 ml. per kilogram of 5 per cent glucose solution. The right eye was treated with 10 per cent guanethidine; the left eye was untreated.

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Effect of pilocarpine drops on the diurnal intraocular pressure variation in patients with glaucoma. DAVID M. WORTHEN.

The diurnal intraocular pressure was measured in 14 eyes of patients with glaucoma while they were using no medication and compared to the diurnal pressures while they were using pilocarpine drops. During the 48 hour control period, the pressures measured every 3 hours by the noncontact tonometer had a mean value of 26 mm. Hg and a mean maximum diurnal variation of 18.5 mm. Hg. During the pilocarpine treatment period, the mean pressure and maximum diurnal variation dropped to 17 and 8.5 mm. Hg, respectively. The greatest pressure-lowering effect occurred between 9 A.M. and 6 P.M.

This study was conducted to measure the effect of pilocarpine drops on the diurnal pressure variation in a group of patients with glaucoma. Kitazawa and Horie[1] recently reported on the diurnal pressure variation in a group of 27 eyes with glaucoma. They found the peak pressure to occur between 8 and 14 hours (on a 24 hour clock) when the pressure was 37.6 ± 4.78 mm. Hg and the lowest pressure to occur around 1 hour when the pressure was 21.8 ± 2.43 mm. Hg. They measured the pressure every hour with a Goldmann applanation tonometer.

Henkind, Leitman, and Weitzman[2] studied the diurnal curve in 11 subjects, six of whom had glaucoma. Pressures were measured hourly for 24 hours with a MacKay-Marg tonometer. The lowest pressures were measured between 2 and 4 A.M. in all subjects and the highest pressures between 10 and 16 hours for the 10 eyes with glaucoma.

Pratt-Johnson, Drance, and Innes[3] compared the effect of pilocarpine and echothiophate on the diurnal curve in 20 eyes of patients with either ocular hypertension or glaucoma. Pressures were measured every 4 hours for 44 hours with a Schiøtz tonometer. The lowest pressures occurred between midnight and 4 A.M. and the highest pressures at noon. The untreated eyes had mean pressure values of 16 mm. Hg at the minimum and 27 mm. Hg at the maximum. On 4 per cent pilocarpine those values fell to 13 and 23 mm. Hg, respectively; and on 0.06 per cent echothiophate iodide the values dropped further to 9 and 16 mm. Hg, respectively.

In the present study a noncontact tonometer (American Optical Corp., Buffalo, N. Y.) was used to avoid topical anesthesia and corneal abrasion which could affect the absorption and pressure-lowering effect of the pilocarpine.

Materials and methods. Patients in the Glaucoma Clinic at the Veterans Administration Hospital in San Diego were asked to take part in the study. All were considered responsive to pilocarpine and all had field defects typical of glaucoma. The study protocol was reviewed by the University Committee on Investigations and Activities Involving Human Subjects and each patient signed an informed Consent Form. The patients were hospitalized for the duration of the study but sent out on pass between the control and pilocarpine treatment phases of the study to avoid pressure lowering due to hospitalization per se. Each patient stopped epinephrine 2 weeks before hospitalization, pilocarpine 48 hours before hospitalization, and acetazolamide 24 hours before hospitalization. Each patient arrived at 7:00 to 8:00 A.M. of the first day and the first pressure measurement was made at 9:00 A.M. that day. Pressures were then measured around the clock at 3 hour intervals for 48 hours. Afterward the patients were started back on the concentration (2 or 4 per cent) of pilocarpine drops which had previously been shown to control their intraocular pressure. The patients then went on pass for 34 to 36 hours. The next day members of the study staff instilled one drop of pilocarpine in each eye at 7, 12, 17, 21 hours (24 hour clock). Pressures were again measured every 3 hours for 48 hours starting at 9. On completion of the study, the patients were discharged on their previous medication.

Pressures were measured in the sitting position at the patient's bedside. If supine, they sat for 5 minutes to equilibrate before pressures were measured. The American Optical noncontact tonometer[4] (NCT) was used and a minimum of five readings taken on each eye. The lowest readings were used and usually consisted of at least three readings of the same pressure. Goldmann applanation tonometry was done at 9 hours each day in each patient and correlated ± 2 mm. Hg with the NCT readings. Previous unpublished studies by the author in 72 glaucoma eyes with pressures from 2 to 53 mm. Hg showed correlation coefficients of 0.97 between the NCT and Goldmann tonometers. Analysis of the present data consisted of calculated means, standard deviations, standard errors, and the paired t test for statistical significance.

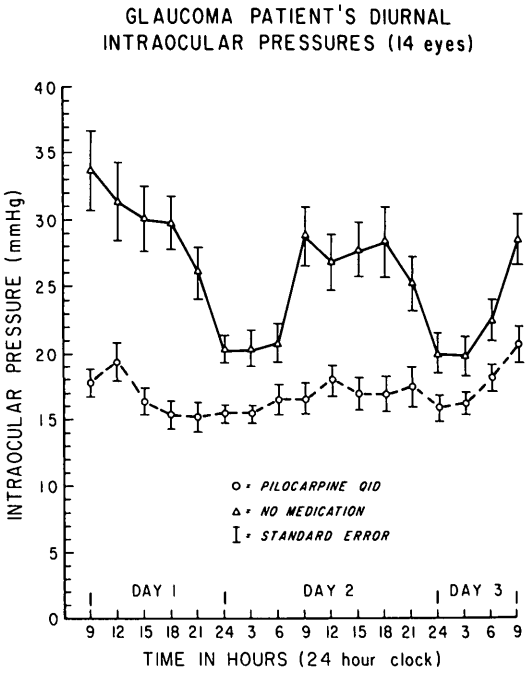

Fig. 1. A plot of intraocular pressure vs. time of day over a 48 hour period. The triangles represent pressures with no medication and the circles, pressures while receiving pilocarpine treatment.

Results. A total of seven patients completed the study. Many patients were excluded since they did not meet the study criteria or could not safely be taken off their medication. Three who started the study failed to be present for all pressure measurements or had pressures rise to dangerous levels and were discontinued for fear of further optic nerve damage.

Analysis of all pressure readings showed the lowest pressure recorded was 9 mm. Hg in Patient 7 at 21 hours on pilocarpine treatment. The highest pressure was 55 mm. Hg in Patient 2 at 9 hours on the first control day. Most patients had higher pressures at the first recording (by both applanation and NCT models), possibly related to their apprehension and the novelty of the testing situation. There was also a slight upward trend in pressures on the last pressure recording during pilocarpine treatment. During the control period, most patients recorded their

Table I. Single highest and lowest pressures for each eye during the 48 hour period

Patient	*Eye*	*Control*			*Pilocarpine*		
		High	*Low*	*Difference*	*High*	*Low*	*Difference*
1	OD	27	14	13	25	16	9
	OS	28	14	14	20	13	7
2	OD	35	18	17	22	14	8
	OS	57	27	30	35	20	15
3	OD	30	17	13	18	12	6
	OS	54	26	28	19	13	6
4	OD	41	14	27	18	12	6
	OS	51	15	36	24	16	8
5	OD	23	13	10	20	12	8
	OS	24	16	8	19	12	7
6	OD	28	15	13	20	12	8
	OS	32	18	14	27	14	13
7	OD	35	18	17	19	10	9
	OS	32	15	17	19	9	10
Mean		35.5	17.1	18.4	21.8	13.2	8.6
Standard deviation		±11.1	± 4.3	± 8.4	± 4.7	± 2.8	± 2.6

Table II. Mean pressures for each eye during the control and pilocarpine treatment periods

Patient	*Eye*	*Control*		*Pilocarpine*		*Difference*	*p**
		Mean	*S.D.*	*Mean*	*S.D.*		
1	OD	21.4	± 4.4	18.4	± 3.14	3.0	<0.01
	OS	18.8	± 4.2	15.8	± 2.1	3.0	<0.01
2	OD	26.9	± 5.0	17	± 2.8	9.9	<0.001
	OS	40.4	± 8.7	27.8	± 4.5	12.6	<0.001
3	OD	24	± 4.3	14.6	± 1.5	9.4	<0.001
	OS	40	± 10.7	16.4	± 2.6	23.6	<0.001
4	OD	23.4	± 6.8	16.1	± 1.5	7.3	<0.001
	OS	27.8	± 9.6	18.5	± 2.9	9.3	<0.001
5	OD	18.8	± 3.1	14.4	± 1.9	4.4	<0.001
	OS	20.5	± 3.0	14.9	± 2.0	5.6	<0.001
6	OD	22.5	± 3.6	16.5	± 2.6	6.0	<0.001
	OS	24.9	± 4.6	118.9	± 3.4	6.0	<0.001
7	OD	28.2	± 6.0	14.4	± 2.8	13.8	<0.001
	OS	25.1	± 5.0	14.1	± 3.3	11	<0.001

*Paired t test.

highest pressures between 9 and 15 hours and lowest between 24 and 3 hours. The exception was Patient 7 who had a drop in pressure at both 6 and 15 hours. The diurnal intraocular pressure variation was lessened in all patients with pilocarpine therapy.

Table I lists the single highest and lowest pressure for each eye during both the control and pilocarpine treatment periods. During the control period, the mean high and low pressures were 35.5 ± 11.1 mm. Hg and 17.1 ± 4.3 mm. Hg, for a mean diurnal variation maximum of 18.4 ± 8.4 mm. Hg. The same values for the pilocarpine treatment period were 21.8 ± 4.7 for the mean highest pressure and 13.2 ± 2.8 for the mean lowest pressure, with a mean diurnal variation maximum of 8.6 ± 2.6.

The greatest diurnal variation during the control period occurred in the left eye of Patient 4 which varied 36 mm. Hg (15 to 51 mm. Hg) and the least in the left eye of Patient 5 which varied 8 mm. Hg (16 to 24 mm. Hg). During the pilocarpine treatment the greatest variation was 15 mm. Hg in the left eye of Patient 2 (20 to 35 mm. Hg) and the least in patients 3 and 4 which varied only 6 mm. Hg (12 to 18 and 13 to 19 mm. Hg).

Table II lists the mean and standard deviation values for intraocular pressure for each patient over the 2 days of control and pilocarpine treatment. Paired t tests showed a significant difference in the means at $p < 0.001$ for all but Patient 1 where the significance was $p < 0.01$. Therefore, pilocarpine had a significant pressure-lowering effect in each patient. The mean of all mean pressures during the control period was 26 mm. Hg and during the pilocarpine treatment period it dropped to 17 mm. Hg for an overall mean drop for all readings (over 3,000) of 9 mm. Hg.

Fig. 1 shows the comparison in diurnal curve

among all eyes between the control and pilocarpine treatment periods. The curve during pilocarpine treatment drops (mean pressure of 26 mm. Hg dropped to 17 mm. Hg) and flattens out (mean variation dropped from 18.5 to 8.5 mm. Hg). The difference at each point is significant at $p < 0.02$ by the paired t test and is significant at $p < 0.001$ between 9 and 18 hours.

Discussion. The patients in this study have glaucoma as defined by optic nerve damage with field loss. They demonstrated a wide swing in intraocular pressure while on no treatment (mean pressure of 26 mm. Hg and a mean maximum diurnal variation of 18.5 mm. Hg), which lessened on pilocarpine treatment (mean pressure of 17 mm. Hg and mean maximum diurnal variation of 8.5 mm. Hg). This therapeutic response to pilocarpine was most gratifying from the standpoint of both flattening the curve and dropping the average pressure. It was reassuring to note that the peak pressures occurred during the usual working hours (9 to 18) and that the patients in this study had normally lower pressures during the sleeping hours. It was also reassuring to see that the pilocarpine effect appeared to carry over into the sleeping hours. All pressures in this study were measured with the patients sitting. Supine values would be higher.

Future studies might involve a continuous-delivery system like the Ocusert therapeutic system[5] in hopes of a greater flattening of the diurnal curve and even lower pressures during sleep.

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Key Words: diurnal, intraocular pressure, noncontact tonometer, pilocarpine.

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