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Punctal Occlusion and Topical Medications for Glaucoma

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We studied the effects of punctal occlusion on the intraocular pressures of patients treated with topical medications for glaucoma. Silicone punctal plugs were used to occlude the inferior punctum of one eye in each of 19 patients treated with identical antiglaucoma eyedrops in both eyes. The intraocular pressures before and after punctal occlusion were compared. The eyes with the punctal plugs showed a statistically significant ($P < .0001$) decrease in pressure of 1.32 mm Hg after punctal occlusion when compared to that of the fellow control unplugged eyes. The intraocular pressures in the plugged eyes decreased an average of 1.82 mm Hg after punctal occlusion when compared to before punctal occlusion ($P = .001$). The intraocular pressure in the unplugged control eyes did not change significantly after punctal occlusion of the fellow treated eye.

Most topical ophthalmic medications with intraocular sites of action penetrate the eye through the cornea, conjunctiva, or sclera. The amount of medication absorbed is influenced by the amount of contact time between the medication and the ocular surfaces. Most of an eyedrop is lost to drainage within 15 to 30 seconds after instillation, which includes rapid drainage of 80% or more of the volume through the nasolacrimal system.[1] Inhibition of this rapid drainage may lengthen the contact time of the medication with the eye and increase its absorption and efficacy.

Inhibition of drainage through the nasolacrimal system may be achieved by manual occlusion with a fingertip, by placing plastic or collagen plugs into the puncta, or by permanently closing the puncta with cautery or laser. Zimmerman and Ziegler[2] have advocated nasolacrimal occlusion with fingertip pressure as a means of increasing ocular absorption of topical ocular medications. Many patients, however, are unable to practice proper manual nasolacrimal occlusion. We studied the effects of occlusion of the nasolacrimal system by using removable silicone punctal plugs on the ocular hypotensive action of topical antiglaucoma medications.

Material and Methods

Patients from the Glaucoma Service were selected for this study. Selection criteria included bilateral glaucoma or ocular hypertension with intraocular pressures controlled on glaucoma medication regimens that included one or more topical eyedrops. Both eyes of each patient were treated with identical types and dosages of medications. Exclusion criteria included past or current obstruction of the nasolacrimal system, and unwillingness or inability of the patient to give informed consent for the study.

After the nature of the study was fully explained and informed consent was obtained, a primary dye test (Jones I test) for nasolacrimal patency was performed. If no dye was recovered by this method from either side, it was assumed that the patient had a defect in the nasolacrimal system and was excluded from the study. If dye was recovered from both sides, a punctum plug was inserted into the inferior punctum of one eye. The eye in which the plug was inserted alternated between the two eyes of each subject entering the study. The fellow eye, which was not occluded, served as a control. The patients were instructed to continue their current regimen of glaucoma medications as usual. After placement of the plugs and waiting at least two days to allow equilibration to the plugs, each patient returned for three follow-up examinations on three different

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days. The times of day of the follow-up examinations were chosen to approximate those of pressure measurements that had been taken before plug placement. During these follow-up visits the intraocular pressure of both eyes were measured in a masked fashion using a Goldmann applanation tonometer and recorded along with the time of day. These measurements were performed before further examination of the eye to prevent awareness of which eye had been plugged and thus minimize bias in the pressure measurements. A slit-lamp examination was then performed to look for changes on the external ocular surfaces and in the anterior segment. The patients were monitored for side effects and complications related to the punctum plugs or to the eyedrops.

The one-sample *t*-test was used to compare the three intraocular pressure readings taken after plug placement, with the most recent three or more measurements taken during clinic visits before plug placement without intervening changes in the medical regimen. Regression analysis was used to evaluate diurnal trends in the intraocular pressure of the plugged eyes, the intraocular pressure of control eyes, and the difference in intraocular pressures between the paired eyes. Regression analysis was also used to study the differences in intraocular pressure before and after punctal occlusion among patients using one, two, or three different classes of topical antiglaucoma medications (beta-blockers, miotics, and epinephrine compounds). $P \leq .01$ was considered significant.

Results

Nineteen patients completed the study (Table 1). There were 13 women and six men. The average age was 67 years (range, 49 to 85 years). Fifteen of the patients had chronic open-angle glaucoma, two had combined mechanism glaucoma and patent peripheral iridotomies in both eyes, one had low-tension glaucoma, and one had ocular hypertension. Four patients were using only one glaucoma eyedrop; three were using two different types of eyedrops; and 12 were using three types of eyedrops, six of whom also took an oral carbonic anhydrase inhibitor. Seven patients had undergone laser treatments or surgery for glaucoma. These procedures were all performed more than six months before the study; all patients had stable glaucoma controlled with eyedrops. Ten patients had the right lower punctum occluded and nine had the left lower punctum occluded.

Mean ± S.E. intraocular pressure readings of all eyes were 16.96 ± 0.72 mm Hg before and 15.14 ± 0.70 mm Hg after punctal plug placement (Table 2). Intraocular pressure readings of all fellow eyes were 16.57 ± 0.78 mm Hg before and 16.07 ± 0.84 mm Hg after plug placement. Analysis of only the eyes with occluded puncta showed an average decrease in intraocular pressure of 1.82 mm Hg after punctal occlusion, which was statistically significant ($P = .001$) (Table 3). Comparison of the unplugged eyes alone showed no statistical change in the intraocular pressures before and after occlusion of the fellow eye ($P = .25$). Comparison of the mean differences in intraocular pressure between the plugged eye and the control fellow eye of each patient before occlusion with those differences after occlusion showed that there was an average decrease of 1.32 mm Hg after punctal occlusion. This was statistically highly significant ($P < .0001$).

Of the 57 pressure readings taken after punctal occlusion, 49 were taken at a time of day that was matched to within two hours of a corresponding measurement before occlusion. Two of the readings were between two and four hours from the before-occlusion readings. In six of the readings after occlusion, the exact time of day of the corresponding measurements before occlusion had not been recorded; however, it could be ascertained whether the patient had been seen in the morning or afternoon, and thus the timing of the measurement after occlusion was matched to either the morning or afternoon, accordingly.

Comparison of the mean differences in intraocular pressure before and after punctal occlusion among the patients using one, two, or three classes of topical antiglaucoma medications showed no statistically significant differences between the three groups. There was no significant correlation between the decrease in intraocular pressure and the number of different glaucoma medications the patient used.

Each patient was followed up for three examinations on three different days after plug placement. The length of follow-up averaged 13.8 days (range, seven to 34 days). During the follow-up period, seven patients experienced adverse reactions to the plugs, none of which were serious. Four patients complained of irritation of the eye for two days after placement, after which the discomfort abated. Two patients complained of persistent, mild, occasional itch-

TABLE 1
PATIENT CHARACTERISTICS

PATIENT NO., AGE (YRS), SEX	DIAGNOSIS	MEDICATIONS*	PREVIOUS LASER OR SURGICAL TREATMENT
1, 80, F	Chronic open-angle glaucoma	3A	None
2, 60, M	Low-tension glaucoma	1A	None
3, 65, F	Chronic open-angle glaucoma	2B	None
4, 54, M	Chronic open-angle glaucoma	1C	None
5, 65, F	Chronic open-angle glaucoma	3B	Argon laser trabeculoplasty in both eyes
6, 49, M	Chronic open-angle glaucoma	3B	None
7, 79, F	Chronic open-angle glaucoma	3A	Argon laser trabeculoplasty in both eyes
8, 65, M	Chronic open-angle glaucoma	3C	None
9, 61, F	Combined mechanism glaucoma	2A	Argon laser peripheral iridotomy in both eyes
10, 57, M	Chronic open-angle glaucoma	3B	None
11, 68, F	Chronic open-angle glaucoma	3B	Argon laser trabeculoplasty in both eyes
12, 58, M	Chronic open-angle glaucoma	3A	Argon laser trabeculoplasty in right eye, filtering surgery in right eye
13, 82, F	Chronic open-angle glaucoma	2A	None
14, 85, F	Chronic open-angle glaucoma	1B	None
15, 71, F	Chronic open-angle glaucoma	3B	None
16, 72, F	Chronic open-angle glaucoma	3A	None
17, 60, F	Chronic open-angle glaucoma	3A	Filtering surgery in the right eye
18, 69, F	Combined mechanism glaucoma	3B	Argon laser peripheral iridotomy in both eyes, argon laser trabeculoplasty in right eye
19, 75, F	Ocular hypertension	1A	None

*Medication regimen for glaucoma: 1A = beta-blocker only; 1B = miotic only; 1C = epinephrine compound only; 2A = beta-blocker and miotic; 2B = beta-blocker and epinephrine compound; 3A = beta-blocker, miotics, and epinephrine compound; 3B = beta-blocker, miotics, epinephrine compounds, and oral carbonic anhydrase inhibitor; 3C = beta-blocker, pilocarpine, and echothiophate.

TABLE 2
MEAN INTRAOCULAR PRESSURES (MM HG)*

PATIENT NO.	EYE WITH PUNCTUM PLUGGED	BEFORE PLACEMENT OF PLUG		AFTER PLACEMENT OF PLUG	
		PLUGGED EYE	FELLOW EYE	PLUGGED EYE	FELLOW EYE
1	R.E.	18.5	20.5	13.7	18.7
2	L.E.	11.2	10.5	9.0	8.7
3	R.E.	25.0	25.3	22.3	25.7
4	L.E.	14.8	13.0	15.7	14.7
5	R.E.	16.8	15.2	14.7	14.0
6	L.E.	14.8	14.2	10.3	11.0
7	R.E.	21.2	18.0	19.0	17.7
8	L.E.	17.7	17.7	16.0	17.3
9	R.E.	17.8	17.2	13.3	13.0
10	L.E.	19.0	21.0	17.7	19.0
11	R.E.	13.5	14.2	15.0	17.0
12	L.E.	15.2	13.5	15.0	13.7
13	R.E.	14.6	15.2	14.7	16.0
14	L.E.	20.2	19.8	17.0	15.0
15	R.E.	17.0	16.3	11.3	13.3
16	L.E.	17.2	16.4	16.3	15.7
17	R.E.	17.4	16.8	15.7	17.7
18	L.E.	13.5	14.0	14.0	14.7
19	R.E.	16.8	16.5	17.3	18.7

*All measurements made by applanation tonometry.

TABLE 3
MEAN ± S.E. INTRAOCULAR PRESSURE (MM HG)

EYES	BEFORE PLACEMENT OF PLUG	AFTER PLACEMENT OF PLUG	CHANGE IN PRESSURE FROM BEFORE TO AFTER PLACEMENT OF PLUG	P VALUE
Plugged eyes	16.96 ± 0.72	15.14 ± 0.70	decrease 1.82 ± 0.46	.001
Unplugged eyes	16.57 ± 0.78	16.07 ± 0.84	decrease 0.50 ± 0.42	.25
Difference in pressure (plugged eye−unplugged eye)	0.39 ± 0.29	−0.93 ± 0.36	decrease 1.32 ± 0.25	<.0001

ing, but one of the two had preexisting chronic blepharitis. One patient complained of bothersome persistent epiphora of the occluded eye which necessitated wiping her eye several times a day. In one patient the plug extruded just hours before she came in for her final follow-up visit when she rubbed her eyes. No evidence of infection, persistent conjunctivitis, or corneal epitheliopathy was noted in any of the patients.

Discussion

This study suggests that occlusion of the lacrimal puncta may result in an increased efficacy of antiglaucoma eyedrops, as shown by a decrease in intraocular pressure. The mechanism responsible for this increased efficacy is probably that the punctal plugs inhibit drainage of the eyedrops through the nasolacrimal system, thus keeping the medication in contact with the ocular surfaces for a longer time. Because of this increased contact time, more of the medication is absorbed into the eye, resulting in increased efficacy. Our results are consistent with those of Zimmerman and associates[3] who showed that nasolacrimal occlusion increases intraocular absorption of topically applied fluorescein.

The decrease in intraocular pressure, although highly statistically significant, was less than 2 mm Hg. Therefore, we cannot determine from this study whether the decrease in intraocular pressure was clinically significant. We chose to occlude only the lower punctum, leaving the upper punctum patent, to avoid inducing excessive epiphora in our patients. Perhaps if both puncta had been occluded, the decrease in intraocular pressure would have been even greater. However, the incidence of epiphora also might have increased.

The punctal plugs were generally well tolerated by most patients. The two patients who reported mild, occasional itching showed no objective signs of changes on their external ocular surfaces. These two patients tolerated the mild ocular irritation without difficulty. The plug extruded in only one of the 19 patients (5.3%). In this patient, the plug could be placed only half-way into the punctum, and it extruded nine days after placement. This incidence of extrusion is lower than the 28% (nine of 32 eyes)[4] and 22% (three of 14 eyes)[5] reported previously in studies using similar plugs. Subsequent to our study, the manufacturer of the silicone plugs used in this study (Eagle Vision, Inc.) developed plugs shorter in overall length and shorter in the height of the dome that remains exposed after plug placement. The use of these newer plugs may decrease ocular irritation and extrusion. Only one of our 19 patients (5.3%) reported epiphora with just the lower punctum occluded. Willis and associates[5] reported a series of 18 patients with dry eyes who underwent occlusion of all four puncta with removable punctal plugs. Three of their patients (17%) complained of epiphora. Only one of our patients (5.3%), the one who experienced epiphora, had an adverse effect that was significant enough to contraindicate plug placement.

Noncompliance in the treatment of glaucoma has been called a "leading cause of glaucoma blindness."[6] Kass and associates showed that patients actually administered only 76% of their prescribed doses of pilocarpine[7] and only 83% of their prescribed doses of a beta-blocker.[8] It is likely that some patients would be even more noncompliant in practicing proper manual punctal occlusion for five minutes after instilling each eyedrop since it requires even more effort than instilling eyedrops. Occlusion of the puncta with punctal plugs may be a simple method of maximizing the effects of topical medications in these patients.

Another potential benefit of punctal occlusion is the reduction of systemic absorption of topical medications, which may result in fewer

systemic side effects. Zimmerman and associates[3] showed that nasolacrimal occlusion reduced the amount of systemic absorption of topical timolol maleate by more than 60%. In our series no patient reported any systemic side effects attributable to their eyedrops before or after plug placement. This may be because we selected patients who had been controlled with the same medications for an extended period of time. Patients who experienced significant side effects would have required modifications of their medication regimen and thus would not have been included in our study.

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