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The Impact of Eyelid Laxity on Symptoms and Signs of Dry Eye Disease

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Abstract

Purpose—To study the relationship between eyelid laxity and ocular symptoms and signs of dry eye (DE).

Methods—One hundred thirty-eight patients with normal external anatomy were prospectively recruited from a Veterans Administration hospital. Symptoms (via the DE questionnaire 5 [DEQ5] and ocular surface disease index [OSDI]) and signs of DE were assessed along with presence or absence of eyelid laxity.

Results—Seventy-one percent of participants (n=98) had clinical evidence of eyelid laxity (upper and/or lower) compared to 29% (n=40) with no eyelid laxity. Individuals with eyelid laxity were older (67±10 years vs. 55±8 years without laxity, p<0.005) and more frequently male (76% of males had laxity vs. 18% females, p<0.005). Patients with eyelid laxity had increased symptoms and signs of DE compared to their counterparts without laxity including ocular pain described as grittiness (63% vs. 45%, p=0.049), decreased tear break-up time (8.6±3 seconds vs. 10.3±4 seconds, p=0.02), increased corneal staining (2.5±3 vs. 1±2, p=0.002), decreased Schirmer's score (14±6mm vs. 17±7mm, p=0.01), meibomian gland drop out (2±1 vs. 0.8±0.8, p<0.005), increased eyelid vascularity (0.8±0.8 vs. 0.2±0.5, p<0.005), and more abnormal meibum quality (2±1.3 vs. 1.4±1.2, p=0.02). In a multivariable analysis considering both signs of DE and laxity, lower eyelid laxity remained significantly associated with OSDI scores, suggesting a direct effect of laxity on symptoms of DE.

Conclusion—The presence of eyelid laxity associates with abnormal tear parameters compared to the absence of eyelid laxity. Based on this data, it is important for clinicians to test for eyelid laxity in patients with symptoms and/or signs of DE.

Keywords

dry eye; eyelid laxity; floppy eyelid; dry eye symptoms; dry eye signs

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Introduction

Eyelid laxity refers to a clinical picture of easily distractible upper and/or lower eyelid margins away from the eye.[1] It can occur due to natural aging,[2] mechanical rubbing/forceful eyelid manipulation,[3, 4] hyperelasticity,[5] post-inflammatory response,[6] or blepharochalasis.[7, 8] Symptoms of eyelid laxity include ocular irritation, photophobia, and foreign body sensation, with increased severity upon awakening.[9] Because meibomian glands in the eyelids are known to provide the lipid component of the tear film and because blinking helps distribute tears through the ocular surface, there is biologic plausibility that eyelid laxity may have a detrimental effect on tear film function. Few studies, however, have assessed the effect of laxity on the symptoms and signs of dry eye. The largest study of 16 patients with eyelid laxity (defined as an easily everted upper eyelid) reported a correlation between the eye with worse symptoms and the eye with the more severe laxity.[10] Furthermore, these patients were also found to have a rapid tear break-up time (TBUT) (mean of 3 seconds). Another case series of 7 patients reported a relationship between eyelid laxity, dry eye symptoms (ocular irritation or foreign body sensation), and chronic papillary conjunctivitis.[11] Yet another case report suggested that meibomian gland dysfunction may be linked to floppy eyelid syndrome.[12] In all, 7 studies including 28 patients (range 1–16 in each study) have reported on symptoms and signs associated with eyelid laxity.[8,10–15] However, all these previous studies were limited by a small number of patients, lack of a control group when measuring all parameters, no differentiation between lower and upper eyelid findings, and no examination of the relationship between eyelid laxity and tear parameters on dry eye symptoms.

In a previous study, we demonstrated that eyelid laxity (in particular that of the upper eyelids) was associated with a higher frequency of severe dry eye symptoms.[16] A limitation of our study, however, was that we did not have information on tear film parameters and could therefore not assess whether the effect on symptoms was direct or mediated through abnormal tear parameters. Such knowledge is important in order to derive an evidence-based approach to treat symptoms associated with eyelid laxity. This study was conducted to build on our previous work with the aim of studying the interaction between eyelid laxity and tear parameters on dry eye symptoms.

Methods

Study Population

This study was conducted with adherence to the tenets of the Declaration of Helsinki and with approval from the University of Miami's Institutional Review Board. Patients were prospectively recruited from various practitioners at the Miami Veterans Administration Ophthalmology Clinic between January 2014 and January 2015. Patients returned to clinic on a separate day and informed consent was obtained from each patient after explanation of the nature and possible consequences of this study. Patients with a spectrum of dry eye symptoms (none to severe) and signs (none, aqueous tear deficiency, evaporative deficiency) were included so as to be able to evaluate the association of each of these individual facets of dry eye with eyelid laxity. Exclusion criteria included infection, eyelid malposition, prior retina, glaucoma, or refractive surgery, cataract surgery in the last 6 months, glaucoma, the

use of ocular medications (except artificial tears), and contact lenses wear. Additionally, patients with inflammatory or immune conditions (i.e. sarcoidosis, graft-versus host disease, collagen vascular disease, human immunodeficiency virus) were excluded. Subjects were split into groups based on the presence (or absence) of any/upper/lower eyelid laxity. All subsequent analyses were conducted based on these groupings.

Data Collection

Demographic information for each patient was collected, including age, gender, race, ethnicity, smoking status, and health status (assessed by asking patients "How would you describe your current health status?" Answer choices included excellent, good, fair, or poor). Further medical history was recorded via questionnaire, which included diagnoses of diabetes mellitus, hypertension, hypercholesterolemia, benign prostate hyperplasia (BPH), and sleep apnea.

Dry eye symptoms were assessed via the Ocular Surface Disease Index (OSDI), which assesses visual function in the setting of dry eye, and the Dry Eye Questionnaire Score 5 (DEQ5), which assesses specific discomforts (dryness, discomfort, tearing) independent of visual function.[17, 18] Patients were also asked about descriptors of eye pain (presence or absence of grittiness, dryness, soreness, and irritation), and the most bothersome ocular symptom (pain, blurry vision, and/or tearing).

The presence and location of eyelid laxity was assessed via slit lamp examination by the same optometrist (ALM), who was blinded to patient symptoms (OSDI and DEQ5). The presence of lower eyelid laxity was determined by the snap-back test. A delay of 2 to 5 seconds for the lower lid to return to its native state, or the need to blink to return to normal state (indicating persistent separation) was recorded positive, while laxity within normal limits was recorded as negative. Upper eyelid laxity was determined by the lid distraction test. Greater than 7mm of distraction was recorded as positive, while laxity within normal limits was recorded as negative.[16] Each eye was graded seperately for upper and lower eyelid laxity.

Ocular presence and location of conjunctivochalasis (Cch) was documented in the following manner: nasal-Cch, non-nasal Cch (medial, temporal, and/or both), or no-Cch.[19] Further ocular surface examination for dry eye signs included, in the order performed, measurement of tear osmolarity, TBUT, corneal staining, Schirmer's score, meibomian gland drop out, eyelid vascularity, and meibum quality. Tear osmolarity was measured once in each eye (TearLAB, San Diego, CA), TBUT was measured 3 times in each eye and averaged, corneal staining was assessed in 5 areas of the cornea and scored 0–3 in each (National Eye Institute scale), Schirmer's score was performed with Schirmer strips with anesthesia, meibomian gland drop out was measured via meibography (a technique that uses transillumation to evaluate degree of area loss of glands according to the Meiboscale[20]), eyelid vascularity was graded on a scale of 0 to 3 (0 = none; 1 = mild engorgement; 2 = moderate engorgement; 3 = severe engorgement),[18] and meibum quality on a scale of 0 to 4 (0 = clear consistency; 1 = cloudy consistency; 2 = granular consistency; 3 = toothpaste; 4 = no meibum expressed[21] using digital pressure). The above testing was all performed by the same optometrist (ALM).

Statistical Analysis

All statistical analyses were performed using SPSS Version 22 (SPSS Inc., Chicago, Illinois USA) statistical package. The relationship between dry eye and any eyelid laxity (in the worst eye) was first examined, followed by analyses separating the effects of upper and lower laxity on dry eye symptoms and signs. Analyses included linear regression, chi-squared test for nominal variables and analysis of variance and student's independent t-test for continuous variables. A p-value less than 0.05 was considered statistically significant. In our study, we had 98 subjects with any eyelid laxity and 40 subjects without laxity. With these sample sizes and an alpha error of 0.05, we had >80% power to detect a difference in means that was 0.55 times the magnitude of the sample standard deviation and proportions of 30% if the proportion in cases without laxity was 25% (both medium effect sizes in the terminology of Cohen[22]).

Results

Participants were first classified into 2 groups by the presence of any eyelid laxity (upper and/or lower in either eye; n=98) and no eyelid laxity (n=40). In those with laxity, the finding was bilateral in all cases. Individuals with eyelid laxity were older (67±10 years vs. 55±8 years without laxity; p<0.005), more frequently male (96 of 127 males, 76% had laxity vs. 2 of 11 females, 18%; p<0.005), and more frequently of white race (58 of 74 white race had laxity, 78%, vs 38 of 62 black race, 61%; p=0.05). Table 1 lists the frequencies of demographics and co-morbidities between those with any laxity versus those without laxity.

Patients were further sub-classified by the presence of upper eyelid laxity in either eye (n=78) and no upper eyelid laxity (n=60), and the presence of lower eyelid laxity in either eye (n=71) and no lower eyelid laxity (n=67). Patients with upper (compared to no upper) and lower (compared to no lower) eyelid laxity were older and more frequently male, of white race, and diagnosed with BPH. In addition, those with upper eyelid laxity more often reported to be in excellent/good health and more frequently had hypercholesterolemia compared to those without upper eyelid laxity.

Looking at dry eye symptoms globally, patients with eyelid laxity reported similar DEQ5 and OSDI scores than patients without laxity (Table 2). Patients with eyelid laxity more frequently characterized their ocular dysesthias as "grittiness." In a sub-group analysis (results not shown), patients with upper eyelid laxity had increased DEQ5 scores compared to patients without upper eyelid laxity (12±5 vs. 10±6 respectively, p=0.04). Although "grittiness" was again a common complaint both in those with upper and lower laxity, this descriptor did not reach statistical significance in the subgroup analyses (n=42, 66% upper laxity vs. n=29, 48% no upper laxity, p=0.052; n=41, 67% lower laxity vs. n=34, 51% no lower laxity, p=0.059).

With regards to ocular examination findings, the presence of eyelid laxity was associated with the presence of Cch (nasal and non-nasal) (Table 3). Moreover, patients with eyelid laxity had worse TBUT, corneal staining, Schirmer's score, meibum gland drop out, eyelid vascularity, and meibum quality compared to patients without eyelid laxity (Table 3).

Similar findings were seen in the sub-group analyses of both upper and lower eyelid laxity which independently associated with abnormal dry eye signs.

In a multivariable model considering age, gender, worst ocular sign from either eye (osmolarity, TBUT, corneal staining, Schirmer's score, meibomian gland dropout, vascularity, meibum quality, Cch, and eyelid laxity (upper/no upper and lower/no lower)), 15% (R=0.39) of variability in OSDI scores were explained by age, gender, and ocular surface variables. Ocular surface variables that remained significantly associated in the model included Schirmer's score: Beta=−0.22, p=0.047; and lower/no lower laxity: Beta=0.25, p=0.028).

Discussion

Eyelid laxity (easily distractible upper and/or lower eyelid margins away from the eye) was described as a component of floppy eyelid syndrome (FES) by Culbertson and Ostler in 1981.[23] The definition of FES in this original paper was chronic upper eyelid papillary conjunctivitis and floppy upper eyelids seen in a cohort of overweight men. Since this description, FES has been expanded to include women,[24] children,[25] non-obese individuals, and to have variable degrees of papillary conjunctivitis (none to severe).[10, 13] Based on the evolving terminology, in this manuscript, we examined the relationship between eyelid laxity (without necessitating the presence of papillary conjunctivitis) and dry eye symptoms and signs.

In contrast to our previous findings,[16] dry eye symptom scores generated using standardized questionnaires were not significantly different in those with any laxity compared to those without. In a sub-group analysis, however, and similar to our previous findings, those with upper eyelid laxity had higher DEQ5 scores than those without upper laxity. With regards to dry eye signs, patients with upper and/or lower laxity uniformly had more abnormal ocular surface metrics, suggesting the laxity may underlie abnormal tear parameters in some individuals. Interestingly, when considering both the effects of eyelid laxity and DE signs on symptoms, we found that lower eyelid laxity remained significantly associated with OSDI scores, suggesting that along with affecting tear parameters, laxity may also have a direct effect of symptoms of DE. When comparing our two studies, we did find several differences between them, most notably that sleep apnea did not remain associated with laxity in the latter study. This may be explained by differences in our study populations. For our first study, we included all comers from geriatric and ophthalmology clinics, including those with ocular co-morbidities. In our more recent study, we had stringent exclusion criteria and included only those with normal external anatomy and no ocular surface comorbidities (e.g. pterygium, glaucoma).

Our study is the first to stringently evaluate the relationship between eyelid laxity and ocular surface symptoms and signs and the first to include a control group when assessing all studied parameters. In our study, we aimed to evaluate the effect of laxity on global symptoms of dry eye and as such, evaluated the relationship between laxity in the worst eye and patient reported symptoms. The largest previous study evaluated 16 patients with upper eyelid laxity and found a positive correlation between the eye with the worst symptoms

(defined as nonspecific chronic ocular irritation) and the eye with the more severe upper eyelid laxity.[10] Numerous small case series further commented on symptoms in patients with eyelid laxity. For example, Goldberg et al. reported on 2 patients with chronic irritative ocular symptoms,[8] McNab et al. on a patient with tearing,[14] and Belliveau et al. on a patient with redness and irritation.[15] Symptoms were worse on the side the patients' slept on, presumably due to eyelid eversion upon pillow contact. A review article by Mastrota K.M. further described unilateral or bilateral ocular irritation, dryness, tearing, redness, burning, and foreign body sensation in patients with FES (defined as lax and easily everted lids associated with chronic papillary conjunctivitis).[13]

Regarding ocular surface signs, our findings agree with those of smaller series that patients with laxity have abnormal tear film parameters. The largest case series of patients with laxity (n=16) found that 15 patients had abnormal TBUT and all 16 patients displayed lipid abnormalities (longer spread time of 1.12±0.67 seconds compared to the published normal spread time of 0.43±0.22 seconds).[10] In smaller studies, Goldberg et al. reported 2 patients with FES (eyelid laxity associated with papillary conjunctivitis) had global punctate fluorescein staining and poor tear film quality, but normal Schirmer's scores (≥20 mm).[8] Another case series, in contrast, found lower Schirmer's scores (≤ 5mm) in 3 out of 5 FES (eyelid laxity associated with papillary conjunctivitis) patients.[11] As above, a limitation of all these studies is the limited numbers of patients and lack of a control group with which to compare all the findings.

There is biologic plausibility to the noted relationship between laxity and abnormal ocular signs given that eyelids function for ocular protection and tear film maintenance. With each blink, tear fluid filled with lipids from meibomian glands, aqueous fluid from lacrimal glands, and mucin from epithelial cells nourish the ocular surface. Therefore, damaged or loose eyelid tissue not only disrupts the flow of tears, but can also alter the composition of tear fluid, highlighting the importance of eyelid laxity in ocular surface health.

With respect to treatment options for patients with eyelid laxity, conservative treatment has been advocated such as lubrication with artificial tears, preventing eyelid eversion during sleep with patching, and treatment with anti-inflammatory agents.[11, 13, 23] Our findings support these treatment options, as we found poor tear fluid quality in patients with eyelid laxity. When conservative treatment fails, surgical techniques involving horizontal eyelid shortening have been shown to improve symptoms, corneal signs, and eyelid tone.[8, 26]

As with all studies, our findings must be considered along with its limitations. Our study was conducted at a Veterans Affair Hospital and therefore our population consisted of predominantly older males. While the results of our study may not therefore extrapolate to women, men are an understudied population in regards to dry eye and therefore, symptoms, signs, and anatomic disturbances in this population of patients are important to characterize. Also, our study was cross-sectional in design and therefore the duration and stability of eyelid laxity in our population is unknown as is its temporal relationship to the symptoms and signs of dry eye. Finally, patients' medical diagnoses were self-reported; they were not verified with formal testing (e.g. sleep studies), and other lid metrics such as marginal reflex distance, lagophthalmos, and orbicular tone were not assessed.

Despite these limitations, this study provides clinicians with a broad description of the dry eye symptoms and signs associated with eyelid laxity and demonstrates the importance of testing for laxity as part of the dry eye evaluation. It is interesting that in our population, no differences were seen in overall symptoms of dry eye but signs were almost uniformly abnormal in those with laxity. These findings are important as they suggest that medical management is a reasonable first option in patients with laxity to address various aspect of tear function. However, the approach to dry eye must be individualized and in those with more severe forms of laxity (i.e. those with an associated papillary conjunctivitis), surgical intervention may be considered at an earlier stage.

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Table 1

Demographics and co-morbidities of the Study Population

		Eyelid Laxity (any upper or lower)	No Eyelid Laxity	p value
n (n, %)		98 (71%)	40 (29%)	
Age (mean±SD)		67±10	55±8	<0.005
Gender (n, %)	male	96 (98%)	31 (78%)	<0.005
Race (n, %)	white	58 (59%)	16 (40%)	0.05
	black	38 (39%)	24 (60%)	
Ethnicity (n, %)	Hispanic	22 (22%)	15 (38%)	0.07
Smoking Status (n, %)	never	15 (15%)	8 (20%)	0.53
	past	52 (53%)	23 (58%)	
	current	31 (32%)	9 (22%)	
Self- Reported Health Status (n, %)	*excellent+good*	60 (61%)	31 (78%)	0.06
	fair+poor	38 (39%)	9 (22%)	
Diabetes mellitus (n, %)		34 (35%)	17 (43%)	0.39
Hypertension (n, %)		79 (81%)	27 (68%)	0.10
Hypercholesterolemia (n, %)		67 (68%)	22 (55%)	0.14
Benign prostatic hyperplasia (n, %)		19 (19%)	3 (8%)	0.08
Sleep apnea (n, %)		16 (16%)	9 (23%)	0.39

Table 2

Ocular Symptoms of the Study Population

		Eyelid Laxity (any upper or lower)	No Eyelid Laxity	p value
DEQ5 (mean±SD)		11.8±5	10.4±6	0.16
DEQ5 ≥12 (n, %)		55 (56%)	19 (48%)	0.36
OSDI (mean±SD)		36.2±28	35.4±26	0.85
OSDI ≥20 (n, %)		62 (63%)	28 (70%)	0.45
Description of Ocular Pain (n, %)	*Grittiness*	62 (63%)	18 (45%)	0.049
	Dryness	75 (77%)	28 (70%)	0.424
	Soreness	53 (54%)	18 (45%)	0.333
	Irritating	71 (72%)	28 (70%)	0.772
Symptoms that Bother Most (n, %)	*Pain*	39 (48%)	12 (36%)	0.27
	Visual Disturbance	28 (34%)	12 (36%)	0.82
	Tearing	20 (24%)	7 (21%)	0.72

Dry eye questionnaire 5 (DEQ5); Ocular surface disease index (OSDI)

Table 3

Ocular Examination Findings of the Study Population

		Eyelid Laxity (any upper or lower)	No Eyelid Laxity	p value
Conjunctivochalasis (n, %)	*nasal*	40 (44%)	6 (16%)	<0.005
	non-nasal	39 (43%)	16 (42%)	
	none	11 (12%)	16 (42%)	
Osmolarity (mOsm/L)		303.9±16	309±22	0.13
TBUT (seconds) (mean±SD)		8.6±3	10.3±4	0.02
Corneal staining (mean±SD)		2.5±3	1±2	0.002
Corneal staining ≥2 (n, %)		52 (53%)	9 (23%)	0.001
Schirmer's score (mm) (mean±SD)		14±6	17±7	0.01
Meibomian gland drop out (mean±SD)		1.9±0.99	0.8±0.8	<0.005
Meibomian gland drop out ≥2 (n, %)		63 (64%)	4 (10%)	<0.005
Eyelid vascularity (mean±SD)		0.8±0.8	0.2±0.5	<0.005
Eyelid vascularity ≥2 (n, %)		23 (24%)	1 (3%)	0.003
Meibum quality (mean±SD)		2±1.3	1.4±1.2	0.022
Meibum quality ≥2 (n, %)		55 (61%)	18 (49%)	0.120

Tear break-up time (TBUT)

*All ocular examination findings reflect the value of the more severely affected eye.