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Reflex epiphora in patients with dry eye symptoms: Role of variable time Schirmer-1 test

G. SINGH BHINDER, H. SINGH BHINDER

Guru Gobind Singh International Eye Research and Cure Centre, New Delhi - India

PURPOSE. To report reflex epiphora in patients with dry eye symptoms and describe the role of variable time Schirmer-1 test.

METHODS. The study was conducted in 16 consecutive dry eye patients (32 eyes), nine male and seven female, aged 16 to 73 years (mean 48.56±16.68 years), presenting with reflex epiphora. Each eye was subjected to Schirmer-1 test and the time elapsed in total wetting of the 35 mm strip from its placement into the conjunctiva was noted and test was graded. This was compared with symptomatology, closed chamber infrared thermometry, humidity, fluorescein tear break-up time (FTBUT), fluorescein stain test, and Lissamine green stain.

RESULTS. Schirmer-1 test differentiated reflex epiphora in dry eye patients into groups 0 to 4 based on time it took to wet the 35 mm strip (Group 0 = ≤5 min; Group 1 = ≤2 min; Group 2 = ≤1.5 min; Group 3= ≤1 min; Group 4 = ≤1/2 min). The score was –0.04 in 8 eyes, –0.03 in 10 eyes, –0.02 in 2 eyes, –0.01 in 6 eyes, and 0.00 in 6 eyes in Groups 4, 3, 2, 1, and 0, respectively. Reflex epiphora had a statistically significant correlation to the symptomatology ($p<0.001$), lissamine green staining ($p<0.001$), closed chamber humidity difference ($p<0.001$), and FTBUT score ($p=0.001$). Fluorescein stain test and difference in infrared thermometry did not show any correlation. A statistically significant correlation existed between severe and mild to moderate reflex epiphora ($p=0.002$). However, the two groups separately failed to show any statistically significant relationship with the symptomatology ($p=0.16$), Lissamine green ($p=0.69$), humidity difference from close to open eye position ($p=0.17$), and FTBUT ($p=0.25$). Thermometry and fluorescein stain test showed no relationship.

CONCLUSIONS. Schirmer-1 test with variable time quantifies reflex epiphora in dry eye patients, which was significantly related to the other tear function tests. (Eur J Ophthalmol 2005; 15: 429-33)

KEY WORDS. Fluorescein tear break-up time, Fluorescein stain test, Infrared thermometry, Closed chamber, Humidity, Dry eyes, Schirmer-1 variable time test, Reflex epiphora

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INTRODUCTION

Some cases of dry eye disease initially present to the ophthalmologist as reflex epiphora. To grade such cases by the existing Schirmer-1 test appears illogical as wetting of 35 mm tear strip occurs very rapidly and the clinician is compelled to label such cases as normal. However, such cases may not be normal. Tsubota et al (1) noted reflex tearing by irritating the nasal mucosa of 297 dry eye patients with a cotton swab and measured the wetting using Schirmer-1 test paper that was 75 mm long. To assess grade of reflex epiphora, we evaluated the time of wetting of 35 mm Schirmer-1 strip and evaluated its use relative to other tear function tests.

MATERIALS AND METHODS

The study comprised 16 cases (32 eyes), nine male and seven female, aged 16 to 73 years (mean 48.56 ± 16.68),

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who presented to us in a consecutive study of 250 dry eyes (126 cases) at G.G.S.I. Eye Research and Cure Centre between 1999 and 2003. The criteria for diagnosis of dry eye were symptomatology score (>2), fluorescein tear break-up time (FTBUT) (<10 seconds), lissamine green stain score (>2), fluorescein staining score (>1), the difference from close to open eyes position in infrared thermometry (temperature = 0.00 °C), and difference in humidity (≥1 RH%).

Variable time Schirmer-1 test

Variable time Schirmer-1 test was carried out using Whartmann filter paper 41, 5 mm x 35 mm. The filter paper's bent 5 mm tip was was placed into lower fornix at the junction of outer 1/3 to inner 2/3 of lower lid and the patient kept the eyes open. The time elapsed from placement into the inner tarsal conjunctiva to its full 35 mm wetting was noted, which was used for the scoring from 0.0 to –0.04 (0.0 = <5 min; –0.01 = ≤2 min; –0.02 = ≤1.5 min; –0.03 = ≤1 min; –0.04 = ≤1/2 min).

Closed chamber infrared thermometry and humidity

The tests were performed as reported earlier by us (2) in which humidity difference score diagnostic values were grouped into four groups (1 = 1–1.5 RH%; 2 = >1.5–2.0 RH%; 3 = >2–2.5 RH%; 4 = >2.5 RH%) and infrared thermometry score showing no change in temperature from close to open eye positions was diagnostic of dry eye disease.

Fluorescein tear break-up time

In all these eyes, FTBUT was carried out by touching the temporal conjunctiva with a wet fluorescein strip and asking the patient to blink two to three times and using cobalt blue filter of a slit lamp with 10x magnification; the time elapsed between last blink to the appearance of a dark spot in the tear film with an average of three readings was taken as FTBUT in seconds. It was graded from 0 to 4 on Oxford scale (0 = >10 sec; 1 = 5–10 sec; 2 = 3–5 sec; 3 = 2–3 sec; 4 = <2 sec).

Fluorescein stain of the cornea was noted after 2 minutes of FTBUT and graded from 0 to 4 depending on the part of staining of the cornea (<0 = no staining; 1 = 1/4th; 2 = 2/4th; 3 = 3/4th; 4 = whole).

Lissamine green stain was performed by touching dye impregnated wet strip (Akorn Inc., Buffalo Grove, IL) to the temporal conjunctiva and asking the patient to blink a few times; the staining of the conjunctiva and cornea were noted with the slit lamp using proper light contrast between 30 seconds and 2 minutes duration. A 0–4 score was used to evaluate the results in each of the four quadrants of conjunctival sac and cornea (0 = no stain; 1 = stippled; 2 = 2 mm staining dots; 3 = lesion bigger than 3 mm; 4 = confluent lesion about ≥4 mm). The maximum score in each quadrant was 4 and total score including cornea was 20. The average score was calculated by dividing the sum total of scores by five.

The exclusion criteria for the study were as follows: evidence of infection of conjunctiva or lid in the week preceding the tests, intraocular surgery or severe ocular trauma 2 months preceding the tests, defects of the conjunctival sac sufficient to preclude retention, abnormality of lid position, patient currently wearing contact lens, history of dendritic keratitis, history of retinal detachment, exophthalmos, enophthalmos, lid coloboma, lid entropion, iridocyclitis, orbital cellulitis, ocular growth, severe purulent conjunctivitis, sloughing corneal ulcers, and infection of nose and nasolacrimal passages.

Statistical analysis

The data of all the patients were managed on Microsoft Excel spreadsheet. All the entries were checked for any possible keyboard error and analyzed with STATISTICA 5.0. All the cases were subjected to analysis by descriptive statistics: t-test for independent samples, Wilcoxon matched pairs test, and multiple regression analysis. In this study, p less than 0.05 was considered statistically significant.

RESULTS

The data profile is given in Tables I–IV.

The variable time Schirmer-1 test was useful to quantify 32 out of 250 cases (12%) of reflex epiphora due to dry eyes. In 8 eyes (25%) the score was –0.04; in 10 eyes (31.25%) it was –0.03. However, –0.02 score was seen only in 2 eyes (6.25%); in 12 eyes (37.5%) the grades ranged from 0.0 to –0.01. The diagnostic value of Schirmer-1 test in cases of epiphora with dry eyes was

TABLE I - SCHIRMER TEST IN REFLEX EPIPHORA IN PATIENTS WITH DRY EYE SYMPTOMS

Score	No. of eyes	%
-0.04	8	25.00
-0.03	10	31.25
-0.02	2	6.25
-0.01	6	18.75
0.0	6	18.75
Total	**32**	**100**

TABLE II - TEAR TESTS DETECTION RATE OF DRY EYE IN REFLEX EPIPHORA

	Tearing group	
	No. of cases	%
Schirmer-1 test	0	0.00
Humidity	32	100.00
Thermometry	32	100.00
FST	2	6.25
Lissamine green	28	87.50
FTBUT	30	93.75

FST= Fluorescein staining test; FTBUT = Fluorescein tear break-up time

TABLE III - RELATION OF VARIABLE TIME SCHIRMER-1 TEST WITH OTHER TEAR FUNCTION TESTS IN REFLEX EPIPHORA IN PATIENTS WITH DRY EYE SYMPTOMS

		Symptomatology	FST	Lissamine green	FTBUT	Humidity difference	Thermometry difference
Group 4	No.	8	8	8	8	8	8
	Range	2–4	0–0	0.4–3.2	3–4	1.5–4	4–4
	Mean	3.13±0.94	0.0±0.0	2.25±1.19	3.25±0.46	2.24±0.88	4.0±0.0
	p value	0.001	—	0.001	0.001	0.001	—
Group 3	No.	10	10	10	10	10	10
	Range	2–4	0–0	2.1–3.5	2–4	1.3–4.1	4–4
	Mean	3.2±0.79	0.0+0.0	2.73±0.54	3.0±0.67	2.05±0.81	4.0±0.0
	p value	0.001	—	0.001	0.001	0.001	—
Group 2	No.	2	2	2	2	2	2
	Range	4–4	0–0	2–2	4–4	2.2–4.2	4–4
	Mean	4.0±0.0	0.0±0.0	2.73±0.54	3.0±0.67	2.05±0.81	4.0±0.0
	p value	0.001	—	0.001	0.001	0.001	—
Group 1	No.	6	6	6	0	0	6
	Range	2–3	0–1	0.0–3.5	3–4	1.5–3.0	4–4
	Mean	2.67±0.52	0.33±52	2.23±1.74	3.67±0.52	1.92±0.58	4.0±0.0
	p value	0.001	0.134	0.010	0.001	<0.001	—
Group 0	No.	6	6	6	0	0	6
	Range	2–4	0–0	2–3	3–4	1.2–2.0	4–4
	Mean	3.17±0.75	0.0±0.0	2.43±0.46	3.33±0.52	1.57±0.27	4.0±0.0
	p value	0.001	—	0.001	0.001	<0.001	—

FST = Fluorescein staining test; FTBUT = Fluorescein tear break-up time

TABLE IV - RELATIONSHIP OF DEGREE OF REFLEX EPIPHORA WITH OTHER TEAR FUNCTION TESTS

	Severe reflex epiphora	Mild to moderate reflex epiphora	p value*
Symptomatology	3.44±0.60	2.61±0.63	<0.161
Fluoresceinstain test	0.00±0.00	0.16+0.22	—
Lissamine green stain	2.57±0.75	2.33±1.10	<0.686
Fluorescein tear break up time	3.08±0.66	3.50±0.52	<0.249
Closed chamber humidity difference	2.11±0.83	1.74±0.42	<0.168
Closed chamber infrared thermometry difference	0.00±0.00	0.00±0.00	—

*Wilcoxon matched pairs test

negligible (0%) as compared to humidity (100%), thermometry (100%), FTBUT (93.75%), lissamine green (87.5%), and fluorescein stain test (6.25%). Reflex epiphora had statistically significant correlation to the symptomatology ($p<0.001$), lissamine green staining ($p<0.001$), closed chamber humidity difference ($p<0.001$), and FTBUT score ($p=0.001$). FST and difference in infrared thermometry did not show any correlation to the reflex epiphora.

The reflex epiphora was divided into severe reflex epiphora (Groups 4, 3, 2) and mild to moderate reflex epiphora (Groups 1 and 0) based on the values of variable time Schirmer-1 test. It was found that the two groups showed a statistically significant correlation with each other ($p=0.002$). However, analysis by Wilcoxon matched pairs test, t-test for independent samples, and multiple regression test revealed no statistical difference in the two groups of variable time Schirmer-1 test concerning symptomatology ($p=0.161$), lissamine green staining ($p=0.686$), humidity difference from closed to open eye position ($p=0.168$), or FTBUT ($p=0.249$). Infrared thermometry and fluorescein staining test revealed no difference in both groups.

DISCUSSION

A decrease in tear production is a common finding in many types of dry eyes. However, reflex epiphora was a chief symptom in 32 out of 250 cases (12%) in this study. Although tearing in the eyes as a complaint in a questionnaire on population based studies (3-6) has been included, cases of spontaneous reflex epiphora as reported in this study have not been reported earlier. Tsubota et al (1) reported cases of induced reflex tearing by irritation of nasal mucosa in Schirmer-1 test but did not report cases as in the present study. There is no test to quantify reflex epiphora in dry eyes. Tsubota et al (1) deviated from the routine Schirmer-1 test by using a Whartmann filter paper of 75 mm length. We believed that the testing room environment would affect the results in a longer paper and errors would be created due to unconventional paper size. Therefore, in our study we used the standard strip of 35 mm and noted the time required to wet a length of 35 mm strip. We observed that the wetting was complete in <2 minutes in 26 eyes (81.25%). In 6 eyes (18.75%) it took more than 2 minutes and less than 5 minutes. We tried to correlate the finding with the severity of the dry eyes but found that the wetting of Whartmann paper was quicker in severe reflex epiphora as compared to mild and moderate reflex epiphora ($p<0.002$). We further noted that reflex epiphora was directly related to symptomatology score ($p<0.001$), ocular surface staining by lissamine green ($p<0.001$), difference in closed chamber humidity ($p<0.001$), and FTBUT ($p<0.001$). However, fluorescein staining test score ($p<0.134$) and infrared thermometry had no correlation to reflex epiphora.

Although there is no diagnostic value of this test in cases of dry eyes as compared to humidity and thermometry, which has 100% specificity and sensitivity, yet this quantifies the maximum reflex epiphora in certain cases.

Although variable time Schirmer-1 test quantified the reflex epiphora, the degree of wetting did not show any significant correlation with symptomatology, lissamine green staining, FTBUT, and humidity difference. Fluorescein staining and thermometry did not show any relationship to severity of wetting.

It is presumed that a correlation exists between tear functions measured by Schirmer-1 test and ocular surface abnormalities detected by vital stains. However, there is still a controversy about the correlation between the Schirmer-1 test and ocular surface conditions. Paschides et al (7) reported that there was no correlation between the Schirmer test results and squamous metaplasia of ocular surface. However, Tsubota et al (1) noted that Schirmer-1 test correlated more with rose Bengal staining than fluorescein stain. Since lissamine green and rose Bengal staining reflected epithelial cells deprived of mucin, whereas fluorescein staining reflected the destruction of cell to cell junctions, the two factors reflected different pathologic conditions (8, 9). Conjunctival mucin expression may be related more to the deficiency of tear component while corneal permeability may be related more to the accumulation of inflammatory cytokines or cytotoxic factors as a result of poor clearance.

Reprint requests to:
Gurbax Singh Bhinder, MD
31, Defence Enclave
Vikas Marg
New Delhi 110 092, India
gurbax_s@yahoo.com
info@visioncareindia.com
www.visioncareindia.com

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