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ORIGINAL PAPER

Case control study of dry eye and related ocular surface abnormalities in Ibadan, Nigeria

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Abstract *Background* Tear instability is associated with symptoms of ocular discomfort and irritation. Many patients with dry eyes remain untreated due to improper diagnoses. *Objective* To identify symptoms and surface abnormalities associated with dry eyes. *Materials and methods* One hundred and fifty-six eyes of 78 subjects attending the Eye Clinic of the University College Hospital Ibadan were screened for dry eyes/tear instability using rose Bengal stain (graded 0–9), tear break-up time (TBUT), Schirmer's 1 tests, tear meniscus height and a standardised symptoms questionnaire. Grades 4–9 rose Bengal staining were considered as positive dry eye and were compared with grades 0–3 staining eyes as negative controls. *Results* Mean tear meniscus height, Schirmer's test and TBUT were lower among cases than their corresponding control eyes. The difference between the mean Schirmer's test values of cases and their controls were statistically significant ($P = 0.00$ for right eyes and $P = 0.002$ for left eyes). Rose Bengal grades were inversely correlated with the mean Schirmer's values (Pearson correlation -0.429, $P = 0.05$ for right eyes and -0.335, $P = 0.03$ for left eyes) and TBUT (Pearson correlation -0.316, $P = 0.05$ for right eyes and -0.212, $P = 0.06$ for left eyes). About 95.8% of the cases were symptomatic, as opposed to 70.4% of the controls ($P = 0.01$, Fisher's exact test) and 95.8% of dry right eyes compared to 61.1% of their controls had ocular surface abnormalities ($P = 0.001$), while 89.5% of dry left eyes compared to 62.7% of controls had surface abnormalities ($P = 0.07$). *Conclusion* A close relationship exists between ocular irritation symptoms, surface abnormalities and functional evidence of tear instability. Such patients should be treated empirically or screened for dry eyes.

Keywords Rose Bengal · Dry eye tear instability · Ocular surface abnormality · Pterygium

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Introduction

Tear instability is a disorder of the tear film due to tear deficiency or excessive evaporation and is

associated with symptoms of discomfort and ocular irritation, such as feeling hot, dry, gritty or sandy, burning, smarting sensation, itching, watering or tearing [1, 2].

Many patients with dry eyes, however, remain undiagnosed and untreated, especially in less developed economies, where it may not be possible to procure appropriate ocular surface stains. Available diagnostic tests for dry eye or tear instability include symptom assessment, contact lens and medical history, slit-lamp biomicroscopic evaluation of the eyelids, evaluation of the meibomian glands, assessment of tear film quality, tear meniscus height, assessment of blink quality, fluorescein tear break-up time (TBUT), fluorescein and rose Bengal staining of the cornea and conjunctiva, phenol red thread test, Schirmer's test and fluorescein clearance time [3, 4]. A study which compared Schirmer's 1 test, TBUT and rose Bengal staining with lysozyme, lactoferrin in tear levels and impression cytology in 165 eyes from 85 patients having Sjogren's syndrome and 80 eyes from normal controls showed that impression cytology and rose Bengal staining were the most specific and sensitive for the diagnosis of primary Sjogren syndrome [5]. Another study which compared clinical, laboratory and histological tests in patients with keratoconjunctivitis sica (KCS) observed that rose Bengal staining, osmolarity and impression cytology had high specificity and sensitivity for a correct diagnosis of KCS. Schirmer's and TBUT tests were not quite as specific or sensitive [6]. Thus, for the rational use of available sensitive and specific diagnostic tests for dry eyes in developing countries, a knowledge of symptoms and ocular surface changes and signs which correlate with appropriate stains would, therefore, help in the identification of cases that require exposure to rose Bengal or conjunctival impression cytology.

Earlier investigators found no relationship between pterygium and dry eye amongst Bantus in Africa [7]. Others in India found tear film dysfunction in patients with pterygium and other degenerative lesions of the bulbar conjunctiva, like pingueculum [8]. A study on pterygium in Ibadan in Nigeria using Schirmer's test did not find any significant tear abnormality between eyes with pterygium and control eyes [9]. Another study in Ibadan to determine the presence or absence of tear dysfunction between cases of pterygium, pingueculum and their controls found lower mean TBUT and a greater proportion of unstable tear film in eyes with pterygium compared to eyes with pingueculum and control eyes [10].

More work on dry eye and its associations is, therefore, needed in view of the conflicting results from previous studies. The objective of this study was to identify symptoms and ocular surface abnormalities associated with dry eyes.

Materials and methods

The study was carried out at the Eye Clinic of the University College Hospital Ibadan between August 2004 and February 2006.

Ethical approval was obtained from the UCH-UI ethical review committee.

The subjects included all consenting new patients presenting consecutively to the eye clinic during the study period. All subjects had a voluntary written consent obtained from them after the procedures had been thoroughly explained before the commencement of the study. They were questioned using a standardised questionnaire for the presence of symptoms such as pricking, burning sensation, ocular irritation, dryness, stinging, smarting or itching of the eyes. They were also asked for the presence of ocular or systemic ailments, as well as use of ocular or systemic medications. They all had a routine eye examination and an assessment of tear function using Schirmer's test and TBUT. The conjunctival and corneal surfaces were also stained using rose Bengal and fluorescein stains, respectively.

Schirmer's test was done using 5 × 35-mm Whatman's filter paper without prior instillation of topical anaesthetic drops, and the eye was gently dried with clean tissue paper. The filter paper was folded 5 mm from one end and inserted midway between the outer and middle third of the lower lid. The patient was allowed to blink as necessary. The paper was removed after 5 min and the amount of wetting was measured from the fold.

The TBUT was measured after instilling fluorescein into the inferior conjunctival fornix and allowing the patient to blink several times before stopping. The tear film was examined with a broad beam of cobalt blue light for the appearance of black sports or lines representing areas of dryness; the time interval between the last blink and the appearance of the first

dry spot around the central cornea was the TBUT and this was recorded.

Fluorescein staining using a strip instilled into the lower fornix was done and the cornea surface examined for the presence of punctate epithelial keratopathy, filaments, mucus plaques concretions etc.

Rose Bengal staining was done using a single drop of 1% of rose Bengal stain without prior instillation of topical anaesthetic. The amount of staining was graded on a scale of 0–3, depending on the intensity (0 = no stain, 1 = mild, 2 = moderate, 3 = intense staining). The amount of staining was determined 2 min after the instilling stain so that any excess would have washed off. Grading of the staining was done at the slit lamp for each of temporal and nasal conjunctiva, as well as the cornea, to give a maximum of nine scores [11]. A cumulative score of 4 was regarded as positive, while a total score less than 4 was regarded as negative. Diagnosis of dry eye or tear instability was made only if the subject had cumulative positive rose Bengal stain grade 4 or more. Our use of grade 4 rose Bengal staining as the cut-off was in line with Van Bijsterveld, who used a cut-off point of >3.5 to obtain a sensitivity of 95% and a specificity of 96%. However, Ferris et al. in a similar study found a sensitivity of 58% and a specificity of 100% [11], suggesting that, although some cases with mild to moderate dry eye may be missed, the chances of diagnosing the absence of dry eye when it was truly not there was less likely.

Controls

Subjects with a cumulative rose Bengal staining score of 0–3 were recruited as controls.

Analysis of the data collected was done with the aid of the SPSS version 10 computer software package. The analysis was done in two phases. The first phase examined the patient as a unit and compared cases and their controls for age, sex and systemic diseases, while the second phase examined the eye as a unit and compared the ocular surface appearance between rose Bengal-positive and non-positive eyes. The frequency distribution of the variables were calculated and tabulated for cases and controls. Subsequently, mean values were calculated for tear meniscus height, Schirmer's test and TBUT. They were compared between cases and controls using the *T*-test for equality of means. The correlation between the degree of rose Bengal staining and Schirmer's test, as well as TBUT, was done by estimation of the Pearson correlation coefficients. The examination of symptoms and ocular surface abnormalities between cases and their controls was carried out by cross-tabulations using the Chi-square test (Fisher's exact test). *P*-values less than 0.05 were considered to be significant in all situations.

Results

A total of 78 subjects were included in the study. The cases had 12 males (50%) and 12 females, age range 23–69 years, mean age 47.0 ± SD 11.6 years. The control group was made up of 14 males (25.9%) and 40 females, age range 17–70 years, mean age 41.2 ± SD 14.9 years ($P = 0.04$). Other socio-demographic characteristics are as shown in Table 1.

Ocular surface abnormalities in 43 eyes (24 right eyes and 19 left eyes) that tested positive to rose Bengal stain were compared with those of 113 eyes (54 right eyes and 59 left eyes) that tested negative to rose Bengal stain.

Table 1 Characteristics of the subjects studied for tear instability

Characteristic	Cases ($n = 24$)	Number %	Controls ($n = 54$)	Number %
Sex				
Male	12	50.0	14	25.9
Female	12	50.0	40	74.1
Systemic disease				
Hypertension	7	29.2	9	16.7
Hypertension and diabetes	1	4.2	2	3.7
Diabetes	-	-	6	11.1
History of allergy	10	41.7	16	29.6
Arthritis	2	8.3	3	5.6

The mean tear meniscus height, Schirmer's test and TBUT values were lower among cases when compared to the corresponding controls' eyes. The difference between the mean Schirmer's test values of cases and their controls when the cut-off point for the diagnosis of cases was initially fixed at three points of rose Bengal staining was not statistically significant, but it became statistically significant when the diagnostic criteria was made more stringent by elevating the degree of rose Bengal staining required for diagnosis from 3 to 4 ($P = 0.00$ for right eyes and $P = 0.002$ for left eyes). The difference between the mean TBUT and the tear meniscus height amongst cases and controls, however, remained statistically insignificant details in Tables 2 and 3.

Examination of the correlation between the degree of rose Bengal staining and Schirmer's test, as well as TBUT values, showed that the rose Bengal grades were inversely correlated with the mean Schirmer's values (Pearson correlation -0.429, $P = 0.05$) and TBUT (Pearson correlation -0.316, $P = 0.05$) for right eyes and the mean Schirmer's values (Pearson correlation -0.335, $P = 0.03$) and TBUT (Pearson correlation -0.212, $P = 0.06$) for left eyes. A review of the symptoms and signs exhibited by the subjects studied showed that the majority or 95.8% of the cases had symptoms, as opposed to 70.4% of the controls ($P = 0.01$, Fisher's exact χ^2). Itching of the eyes was the most common symptom, accounting for 70.8% of symptoms among cases and 38.9% among controls. Less common complaints included pricking and itching (12.5% of cases and 13.0% of controls). About 95.8% of dry right eyes compared to 61.1% of their controls had ocular surface abnormalities or signs ($P = 0.001$), while 89.5% of dry left eyes

Table 2 Ocular surface staining and tear function of subjects studied for tear instability—right eyes

Tear function/ocular surface staining	Cases ($n = 24$)	Controls ($n = 54$)	*P*-value
Tear meniscus			
Mean	0.26	0.26	0.20
Min.	0.10	0.10	
Max.	1.00	1.00	
SD	0.19	0.22	
Schirmer's test			
Mean	9.4	19.1	0.00
Min.	0.0	0.0	
Max.	30.0	55.0	
SD	8.6	13.45	
TBUT			
Mean	9.7	11.57	0.22
Min.	0.0	5.0	
Max.	30.0	25.0	
SD	6.1	5.1	

Ocular surface staining	Number	%	Number	%
Debris in tear film	5	20.8	5	9.3
Fluorescein stain				
SPK	6	25.0	7	13.0
Filaments	0	0.0	3	5.6
Plaque	1	4.2	0	0.0

Inverse correlation between rose Bengal grades and mean Schirmer's values (Pearson correlation -0.429, $P < 0.05$) as well as TBUT (Pearson correlation -0.316, $P < 0.05$)

Table 3 Ocular surface staining and tear function of subjects studied for tear instability—left eyes

Tear function/ocular surface stain	Cases ($n = 19$)	Control ($n = 59$)	*P*-value
Tear meniscus			
Mean	0.19	0.24	0.11
Min.	0.1	0.1	
Max.	0.2	1.0	
SD	0.02	0.17	
Schirmer's test			
Mean	10.26	17.2	0.002
Min.	1.0	0	
Max.	30.0	55.0	
SD	9.38	13.0	
TBUT			
Mean	7.95	11.3	0.08
Min.	0.0	5.0	
Max.	15.0	25.0	
SD	4.8	4.9	

Ocular surface staining	Number	%	Number	%
Debris in tear film				
Fluorescein stain				
SPK	6	31.6	7	11.9
Filaments	0	0.0	3	5.1
Plaque	1	5.3	0	0.0

Inverse correlation between rose Bengal grades and mean Schirmer's values (Pearson correlation -0.335, $P = 0.03$) and TBUT (Pearson correlation -0.212, $P = 0.06$)

Table 4 Symptoms and signs exhibited by subjects studied for tear instability

Symptoms/signs	Cases		Controls	
Symptoms	Number (24)	%	Number (54)	%
Itching	17	70.0	21	38.9
Pricking, itching and stinging	1	4.2	0	0.0
Pricking and itching	3	12.5	7	13.0
Itching and others	1	4.2	3	5.6
Others	2	8.3	1	1.9
Pricking	1	4.2	1	1.9
Stinging and itching	1	4.2	0	0.0
Burning, dryness, stinging and itching	0	0.0	1	1.9
Dryness	0	0.0	1	1.9
No symptoms	1	4.2	16	29.6
Signs	Number (43 eyes)	%	Number (113 eyes)	%
Pingueculum	26	60.5	56	49.6
Pterygium	9	20.9	6	5.3
Tortuous conjunctival vessels	7	16.3	4	3.5
Brownish conjunctiva	5	11.6	15	13.3
Blepharitis	2	4.7	0	0.0
Redundant conjunctiva	0	0.0	2	1.8

compared to 62.7% of controls had these abnormalities ($P = 0.07$). Surface abnormalities exhibited by the subjects included pingueculum (60.5% of cases as opposed to 49.6% of controls), pterygium (20% of cases as opposed to 5.3% of controls) and tortuous conjunctival vessels (16.3% of cases and 3.5% of controls). Details of the presenting symptoms and signs are shown in Table 4.

Discussion

We realize that our use of grade 4 rose Bengal staining as the cut-off for dry eye may have reduced the sensitivity of this diagnostic tool, especially with regards to mild to moderate cases of dry eye, some of which we may have classified as controls. We have done this in line with previous studies by Van Bijsterveld and by Ferris et al. [11]. We, however, believe that a strict diagnostic criterion such as what we have done ensures that the specificity is kept as high as possible and very few false-negatives would be wrongly diagnosed and treated as dry eyes.

The study observed a statistically significant higher age amongst persons with tear instability than their controls. Those diagnosed with tear instability were also more likely to have systemic diseases such as hypertension, allergy and arthritis, except for diabetes alone, which was found to be more common amongst the controls. These findings are in keeping with a previous population study which observed a higher incidence of dry eyes amongst older people, the presence of systemic disease and the use of diuretics and other medications [12]. It, however, differs from a previous study which had observed abnormal ocular surface and tear function amongst diabetics [13]. Diabetics are expected to have abnormal ocular surface since they have been reported to have functional as well as structural surface abnormalities with unstable tear film and higher tear osmolarity than non-diabetics [14] and, therefore, are more susceptible to staining by rose Bengal. Our findings could have been influenced by our stringent definition of dry eye, which may have considered diabetics with mild dry eye as controls.

A statistically significant difference was observed to be present between the mean Schirmer's test values of cases and controls when the diagnostic criteria was made more stringent from grade 3 to grade 4 rose Bengal staining. The same relationship was, however, not obtained for TBUT and tear meniscus height, although both TBUT and Schirmer's test were inversely correlated with the degree of rose Bengal staining. This would suggest that rose Bengal stain and Schirmer's test examination would be more reliable tests than TBUT and tear meniscus for the diagnosis and evaluation of tear instability/dry eye in our setting. Use of grade 4 rose Bengal staining as the cut-off rather than grade 3 would also ensure an improvement in the specificity as a diagnostic tool. This is similar to a European community study group findings on their examination of the diagnostic criteria for Sjogren's syndrome from 22 centres in 11 countries. They reported that Schirmer's test (which showed the best balance between sensitivity, 76.9%, and specificity, 72.4%) and rose Bengal tests (specificity 81.7%) gave the best concordance results, while tear fluid lactoferrin levels and TBUT gave less reliable results which were not concordant with each other or with other ocular tests [15].

The majority (95.8%) of subjects with positive rose Bengal stain were observed to have ocular irritation symptoms, with itching being the most common symptom; however, these symptoms were also present in 70.4% of those subjects who did not have positive rose Bengal staining and, although the difference was statistically significant, the presence of symptoms amongst controls suggests that the presence of symptoms are not always indicative of dry eye; they may also suggest that the patient only has mild to moderate dry eye, which could be missed when the diagnostic criteria is made stringent. Their presence should, therefore, raise a clinician's suspicions of the possibility of existing dry eye so that appropriate and more specific diagnostic tests can be carried out. Itching is more commonly associated with allergy, which was evenly distributed between cases and controls in the study. It has poor specificity for diagnosing dry eye, as shown by previous studies [16, 17].

We found ocular surface abnormalities to be significantly associated with dry right eyes and also to be more common among dry left eyes than their controls. The abnormalities included superficial punctuate keratopathy, corneal plaque, pterygium, pingueculum, tortuous conjunctival vessels and blepharitis. Blepharitis alone was limited to the dry eye group. This shows its strong association with meibomian gland dysfunction-related tear instability [18], indicating its importance as a localising sign for the diagnosis of dry eye and tear instability. Pterygium more than pingueculum was more commonly seen amongst dry eyes cases than controls, as in previous studies [8–10]. Thus, the observation of surface abnormalities, such as pterygium, pingueculum and tortuous conjunctival vessels, should arouse suspicion and subsequent testing for dry eye, especially amongst symptomatic patients.

Conclusion

A close relationship exists between ocular irritation symptoms, surface abnormalities and functional evidence of tear instability. Such patients should be treated empirically for dry eyes or promptly screened and adequate treatment given.

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