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Original research article

A Hospital Based Cross-sectional Study to Evaluate Short Tear Film Breakup Time-type of Dry Eye

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Abstract

Aim: study of short tear film breakup time-type of dry eye in India

Methods: This cross-sectional study was done the Department of Ophthalmology, Nalanda Medical College and Hospital, Patna, Bihar, India for 1 year. 250 patients were selected using systematic random sampling for a comprehensive dry eye work‑up from a pool of 2500 consecutive new patients aged 18 years or more attending the corneal clinic on 3 days of the week.

Results: Of the 250 patients who underwent dry eye evaluation, there were 50 patients in the short TBUT group, 50 patients in the ATD group, 100 patients in the group with >5 but <10 s TBUT, and 50 patients in the normal group. The total and subscale scores of the OSDI questionnaire were similar between the short TBUT and ATD groups ($P > 0.05$). The number of patients with an OSDI score of ≥13 was similar ($P = 0.55$) between the short TBUT group (38%) and the ATD group (38%) and was nearly twice ($P = 0.003$) that of the patients in the group with >5 but <10 s TBUT (20%). The difference in the proportion of patients with severe symptom scores between the ATD and short TBUT groups was not significant ($P = 0.09$), but it was significant ($P = 0.0009$) between the ATD group and the group with >5 s but <10 s TBUT.Overall, there was a statistically significant difference ($P < 0.05$) in TBUT, Schirmer I test and Lissamine green staining score between the various groups. The difference in frequency was significant between the short TBUT group, ATD group ($P < 0.0001$) and the normal group ($P < 0.0001$) but not with the group with >5 but <10 s TBUT ($P = 0.11$).

Conclusion: We have described a typical group of patients with specific characteristics that distinguish them from other types of dry eye disease. This study also emphasizes the importance of measuring TBUT, particularly in patients with symptoms of eye fatigue whose complaints may not primarily be due to anomalies of accommodation and/or convergence but due to an unstable tear film.

Keywords: dry eyes, TBUT, tear film

Introduction

In 1995, Toda et al.[1] described a singular type of dry eye disease in Japan characterized by symptoms of ocular discomfort and a tear film break-up time (TBUT) of ≤5 s, but a normal tear secretion rate and absence of significant epithelial staining. In Japan, this type of dry eye condition was described as short TBUT,[2,3] and subsequent studies reported it to be fairly common in the Japanese population.[4,5] In 2015, Yokoi et al.[5] reported that short TBUT was the most common type of dry eye disease among office workers. The severity of symptoms reported by patients with short TBUT was greater than symptoms reported by those with other types of dry eye diseases. Other studies reported that patients with short TBUT type of dry eye disease had sizably more higher order aberrations with poor quality of vision,[6] which further deteriorated following prolonged visual tasks.[7,8] The severity of symptoms in short TBUT type of dry eye disease was correlated with corneal hypersensitivity to an unstable tear film,[9] and abnormalities in the mucin layer were believed to cause the unstable tear film.[10] In Japan, short TBUT type of dry eye disease was treated at par with aqueous tear deficiency (ATD) type of dry eye disease even though it did not fulfill the older (2006) Japan Dry Eye Society criteria of "definite dry eye disease."[3] However, in 2016, the society revised its guidelines, replacing vital staining of the ocular surface and Schirmer's test with a TBUT of ≤5 s as the only clinical sign necessary for the diagnosis of dry eye disease.[11] Thus, great emphasis was placed on the measurement of fluorescein TBUT, which the society felt could be comfortably performed in the general ophthalmic clinic, and make the diagnosis of dry eye disease simple and easy.[11]

However, outside Japan, there remains little recognition of short TBUT type of dry eye disease,[12] with only a few reports from other countries.[13-15] Recent findings in studies from India indicate that evaporative dry eye disease[16-18] and meibomian gland dysfunction (MGD)[19] are widely prevalent in the country. MGD, which is the most common cause of evaporative dry eye disease,[20] is also associated with short TBUT type of dry eye disease.[11] Therefore, it is plausible that the latter may also be commonly present in the Indian population, but not yet reported. The aim of this study was to describe the clinical characteristics and risk factors of short TBUT type of dry eye disease in an Indian cohort, and compare it with other types of dry eye conditions. The findings of this study will increase awareness about this type of dry eye disease among Indian ophthalmologists, thereby improving the management of patients with dry eye symptoms

Material and methods

This cross-sectional study was done the Department of Ophthalmology, Nalanda Medical College and Hospital, Patna, Bihar, India for 1 year.after taking the approval of the protocol review committee and institutional ethics committee.

In this study 250 patients were selected using systematic random sampling for a comprehensive dry eye work-up from a pool of 2500 consecutive new patients aged 18 years or more attending the corneal clinic on 3 days of the week. Exclusion criteria included red eyes, ocular trauma, anatomical abnormalities on the eyelids or ocular surface, and intraocular surgery performed within the previous 3 months.

Dry Eye Work-up

All subjects underwent a comprehensive eye examination that included history-taking, slit-lamp examination, visual acuity measurement, applanation tonometry, and fundus evaluation. Information on age, gender, place of residence, dietary preferences, use of smartphones or video display terminals (VDT), use of air-conditioning, presence of systemic comorbidities, and in female patients, a history of menopause were recorded. All clinical examinations were performed in a single examination room where the temperature (20–22°C) and humidity (50–60%) were uniformly maintained. The sequence of dry eye tests was history

of generic symptoms, Ocular Surface Disease Index (OSDI), fluorescein TBUT, Schirmer I test without the use of a topical anesthetic agent, Lissamine green staining score as per the Oxford scale, and meibomian gland expression. All the dry eye tests were carried out as per recommended guidelines.[19-25]

Diagnoses

Based on the findings of the dry eye evaluation, patients were classified into the following four groups: short TBUT group, ATD group, patients with >5 but <10 s TBUT group, and normal group. The details of all operational diagnoses are given in Appendix III. Briefly, dry eye disease (symptoms and any one clinical sign as per DEWS II report) was diagnosed if the OSDI score was ≥13, with either TBUT being <10 s or Lissamine green staining score ≥2.[26] Patients were diagnosed with short TBUT based on the following criteria: TBUT ≤5 s, Schirmer I test without the use of a topical anesthetic agent >5 mm and Lissamine green staining score <2.[1,2] In our study, we also considered patients with a TBUT >5 but <10 s with a normal Schirmer I test and no signs of epithelial staining as a separate group. The severity of symptoms was categorized as none (OSDI score 0–12), mild (OSDI score 13–22), moderate (OSDI score 23–32), and severe (OSDI score 33–100).[23]

Statistical analysis All quantitative and qualitative variables have been expressed as mean ± standard deviation and percentages, respectively. The normality of the data was tested using the Shapiro–Wilk test. Dry eye tests between the groups were compared with the Kruskal–Wallis test and the Mann–Whitney U test. Categorical data was analyzed using the Pearson's Chi-square test. A linear logistic regression analysis was done to identify risk factors for short TBUT type of dry eye disease. The age-adjusted prevalence data was calculated by considering the census data of India in 2011.[27] All tests were computed using the software Statistical Package for Social Sciences version 23.0 for Macintosh (IBM Corporation, New York, USA). A two-tailed P value of less than 0.05 was considered statistically significant.

Results

Of the 250 patients who underwent dry eye evaluation, there were 50 patients in the short TBUT group, 50 patients in the ATD group, 100 patients in the group with >5 but <10 s TBUT, and 50 patients in the normal group. All these patients had a positive symptom score (OSDI score ≥13), but their dry eye tests were normal.

The demographic and lifestyle characteristics of the four groups are given in Table 1. There was a significant intergroup difference in the age distribution (P = 0.002), use of VDTs (P = 0.03), and time spent in air-conditioning (P = 0.02). The patients with short TBUT type of dry eye disease were younger [Table 1] than the other dry eye groups, but the difference was statistically not significant. Across all the groups, there were more patients from an urban background, but the difference was only significant when comparing the short TBUT and ATD groups (P = 0.009). Similarly, the proportion of women who had attained menopause was higher in all the dry eye groups compared to the normal group (P = 0.01).

The distribution of the most commonly reported symptoms by the patients, while a more detailed analysis is provided in Appendix V. Symptoms like eye fatigue, heaviness in the eye, and uncomfortable sensations were more commonly reported in patients in the short TBUT group, while light sensitivity, dryness, burning sensation, foreign body sensation, and blurring of vision were more commonly reported in patients with ATD. Eye pain or soreness was reported equally between both the groups.

The total and subscale scores of the OSDI questionnaire [Table 2] were similar between the short TBUT and ATD groups (P > 0.05). The number of patients with an OSDI score of ≥13 was similar (P = 0.55) between the short TBUT group (38%) and the ATD group (38%) and was nearly twice (P = 0.003) that of the patients in the group with >5 but <10 s TBUT (20%). There were (16%) patients with mild symptoms, (10%) patients with moderate symptoms, and (12%) patients with severe symptoms according to the OSDI questionnaire score in the short TBUT group, and (8%), (14%), and (24%) patients with mild, moderate, and severe symptoms, respectively, in the ATD group [Appendix VI]. The difference in the proportion of patients with severe symptom scores between the ATD and short TBUT groups was not significant (P = 0.09), but it was significant (P = 0.0009) between the ATD group and the group with >5 s but <10 s TBUT.

Dry eye tests

Overall, there was a statistically significant difference (P < 0.05) in TBUT, Schirmer I test and Lissamine green staining score between the various groups [Table 2]. As expected, TBUT was the least in the short TBUT group, and Schirmer I test was the least in the ATD group. The patients in the short TBUT and ATD groups differed significantly in TBUT, Schirmer I test, and Lissamine green staining scores. The patients in the group with >5 but <10 s TBUT time differed significantly (P < 0.05) in all the dry eye parameters as compared with the normal group.

The difference in frequency was significant between the short TBUT group, ATD group (P < 0.0001) and the normal group (P < 0.0001) but not with the group with >5 but <10 s TBUT (P = 0.11).

Dry eye disease (symptoms and signs) was present in (36%) patients in the short TBUT group, (34%) patients in the ATD group, and (20%) patients in the group with >5 but <10 s TBUT. The difference was statistically significant between the short TBUT group and the group with >5 but <10 s TBUT (P = 0.003) and the short TBUT and normal groups (P < 0.0001), but not between the short TBUT and ATD groups (P = 0.86). The difference was also significant between the ATD group and the group with >5 but <10 s TBUT (P = 0.006), and between the group with >5 but <10 s TBUT and the normal group (P < 0.0001).

Table 1: Comparison of demographic characteristics in patients with different categories of tear film abnormalities

	n=50	**n=50**	**n=100**	**n=50**	**Between all groups**	**Group 1 vs Group 2**	**Group 1 vs Group 3**	**Group 1 vs Group 4**	**Group 3 vs Group 4**	**Group 2 vs Group 3**
Age in years	48.9±15.9	51.8±15.7	50.6±16.6	43.5±15.0	0.002	0.200	0.183	0.066	<0.001	0.200
Sex										
Male	24 (48)	23 (46)	53 (53)	30 (60)	0.259	0.744	0.501	0.187	0.760	0.243
Female	26 (52)	27 (54)	47(47)	20 (40)						
Residence										
Urban	42 (84)	33 (66)	75(75)	39(78)	0.053	0.009	0.110	0.401	0.761	0.107
Rural	8 (16)	17 (34)	25(25)	11 (22)						
Diet										
Non-vegetarian	25 (50)	26 (52)	49 (49)	31 (62)	0.259	0.870	0.893	0.185	0.051	0.697
Vegetarian	25 (50)	24 (48)	51(51)	19 (38)						
Menstrual cycle										
Regular	16 (32)	13 (26)	47(47)	28(58)	0.011	0.500	0.131	0.034	0.255	0.017
Menopause	34 (68)	37 (74)	53(53)	21 (42)						
Use of VDT (in hours)	4.2±3.8	3.5±2.2	3.7±3.0	4.3±2.7	0.038	0.837	0.683	0.147	0.004	0.837

Stay in air-conditioning (in hr)	2.1±3.9	0.5±2.0	1.3±2.9	1.1±3.0	0.028	0.006	0.361	0.113	0.258	0.006

Table 2: The total and subscale scores of the OSDI questionnaire

Variables	Group 1 n=50	Group 2 n=50	Group 3 n=100	Group 4 n=50	P-value					
					Between all groups *	Group 1 vs Group 2	Group 1 vs Group 3	Group 1 vs Group 4	Group 3 vs Group 4	Group 2 vs Group 3
OSDI Ocular symptom subscale	2.4±2.7	3.5±4.0	1.5±2.5	0.5±1.0	<0.0001	0.238	<0.0001	<0.0001	0.005	<0.0001
OSDI Vision-function-related subscale	1.1±2.1	1.2±2.1	0.8±2.0	0.4±1.1	0.016	0.572	0.125	0.034	0.274	0.017
OSDI Environmental trigger subscale	0.7±1.4	1.0±1.0	0.5±1.2	0.3±0.6	0.019	0.277	0.206	0.164	0.682	0.005
OSDI Total score	10.8±11.6	15.5±18.2	7.1±11.4	2.9±3.9	<0.0001	0.238	0.001	<0.0001	0.134	<0.0001
Tear film breakup time (seconds)	3.7±1.0	6.1±3.6	7.2±1.3	13.1±1.7	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Schirmer's 1 test (mm)	20.5±9.5	5.6±5.9	23.3±9.4	27.5±8.5	<0.0001	<0.0001	0.024	<0.0001	0.001	<0.0001
Lissamine green score	0.3±0.4	0.9±1.1	0.2±0.4	0.1±0.3	<0.0001	0.003	0.274	0.005	0.021	<0.0001

Discussion

In this study, we report a cohort of dry eye patients with short TBUT type of dry eye disease, who have clinical features distinct from other types of dry eyes, namely, a very unstable tear film (TBUT ≤5 s), no significant epithelial staining and a normal tear production. While the dry eye-related symptom severity was not very different from patients with ATD, the pattern was distinctive. Our patients were largely middle-aged adults of both sexes, and a significant proportion of the female patients had attained menopause. These clinical features distinguished short TBUT type of dry eye disease as a distinct subtype of evaporative dry eye disease, which was previously reported mostly from Japan, but now seems to be present outside that country. One of the reasons why the short TBUT type of dry eye disease is regarded with importance in Japan[2] is its high prevalence in the urban population.[4,5] The age-adjusted prevalence of short TBUT type of dry eye disease in our study was less than the prevalence rate (43%) reported in a Japanese study conducted among office workers.[5] However, the prevalence of symptomatic disease (5%) in our study was not greatly different from the prevalence rate of symptomatic disease (9%) in the Japanese study. The larger proportion of asymptomatic patients in our study may represent a preclinical disease stage. It is now hypothesized that chronic dry eye causes neurotrophic keratopathy.[28] Therefore, dry eye symptoms may be masked in these patients. Moreover, in elderly patients, there is reduced corneal sensitivity, which also masks symptoms of dry eye.[29] This may explain the high proportion of asymptomatic patients in the study.

Although the severity of symptoms between short TBUT type of dry eye and ATD type of dry eye did not seem to differ in this study, the pattern of symptoms was different. Eye fatigue, heaviness in the eyes, and uncomfortable sensations were present to a greater extent in the short TBUT group, while dryness, light sensitivity, burning or foreign body sensation, and blurred vision were largely present in the ATD group. Some of these differences were of borderline statistical difference. This difference in the pattern of symptoms appears to be related to different pathological mechanisms causing the two conditions – reduced tear secretion versus an unstable tear film. Symptoms like dryness, foreign body, and burning sensation have been predominant symptoms reported by patients with primary and secondary Sjogren's disease,[30]

where there is reduced tear secretion. In contrast, eye fatigue, dry eye sensation, and uncomfortable sensation have been more commonly reported in patients with short TBUT type of dry eye,[5] where tear secretion is normal, but the tear film is unstable. Eye fatigue and its related symptoms, which are predominantly experienced in short TBUT type of dry eyes, are thought to be related to accommodation fatigue,[7-10] caused by the continuous effort of the ciliary muscles to focus the image (degraded due to an unstable tear film) on the retina.[15,31] A routine orthoptic examination was not done in patients complaining of eye fatigue. However, measurement of TBUT may play a diagnostic role in young adults complaining of eye fatigue. It is possible that some of these patients may have unrecognized short TBUT type of dry eyes and they may benefit if the unstable tear film is addressed. A measurement of functional visual acuity[8] in these patients may provide a better understanding of the mechanisms underlying their symptoms.

In their initial paper, Toda et al.[1] had described allergic conjunctivitis as a risk factor for short TBUT type of dry eye disease because of increased secretion of immunoglobulin-E and the presence of mucin abnormalities in their patients. In our study, the female sex were identified as independent risk factors. Tear film stability is maintained by both the lipid and the mucin layers.[20,32] postmenopausal women,[19,20] and at the same time, mucin abnormality has also been reported more frequently in postmenopausal women with dry eye disease.[32] There are also reports that meibomian glands may regulate mucin secretion from the lacrimal glands and conjunctival goblet cells.[33,34] Therefore, multiple interrelated pathways may lead to a short TBUT type of dry eye state.

In this study, patients with a TBUT >5 but <10 s comprised the largest group of patients. They had a mild form of the disease as compared with the short TBUT type of dry eye disease but differed significantly from normal patients in the pattern of symptoms, severity, and dry eye test results. There were more reports of symptoms such as light sensitivity, dryness, eye pain, blurred vision, burning sensation, and foreign body sensation from these patients than those in the normal group. Interestingly, the dry eye diagnostic criteria of the Asia/Japanese dry eye society,[11] but not the DEWS II report,[25] exclude patients with a TBUT >5 s from the ambit of dry eye disease. In light of our findings, we believe that patients with a TBUT >5 but <10 s represent a preclinical or milder form of short TBUT type of dry eye disease, and excluding such patients may be counterproductive. Monitoring and treating these patients may prevent disease progression.

The cross-sectional clinic-based design of this study is a limitation in predicting the temporal course of the disease or generalizing the findings to the community. In our study, the association between short TBUT type of dry eye disease and the use of VDTs or other environmental factors were weak unlike the Japanese studies.[5,10] Our study included patients from both urban and rural settings, and this heterogeneous composition of the sample population may have mitigated the effect of urbanization and associated lifestyle risks. Despite these limitations, the findings of the present study bring forth a different perspective to our understanding of dry eye disease in India.

Conclusion

We have described a typical group of patients with specific characteristics that distinguish them from other types of dry eye disease. This study also emphasizes the importance of measuring TBUT, particularly in patients with symptoms of eye fatigue whose complaints may not primarily be due to anomalies of accommodation and/or convergence but due to an unstable tear film.

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