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Original article

Short break-up time type dry eye has potential ocular surface abnormalities

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ABSTRACT

Purpose: To describe a case series in which corneal fluorescein staining (CFS) development occurred in short break-up time (s-BUT) dry eyes after a short period during prolonged opening of the eye.
Methods: The study was designed as a clinical case series. Ocular surface evaluations were performed on 13 individuals with s-BUT dry eye. Tear function examinations included Schirmer's test and BUT evaluation.
Results: In all 13 cases, the BUT was short, but the tear quantity was not so bad. In all cases, CFS developed following a single eye opening, and the staining was observed at sites that showed as dark spots. In several cases, the CFS disappeared later.
Conclusion: In this study, we demonstrated that CFS could develop following a single eye opening. Based on our findings, CFS is a dynamic phenomenon rather than a stable indicator of ocular surface abnormalities. Moreover, s-BUT dry eye has the potential to show ocular surface abnormalities.

1. Introduction

Dry eye is a common disease that results in symptoms such as eye fatigue, discomfort, stinging, and blurry vision. The disease is multifactorial and commonly associated with aging, hormonal dysfunction, wearing of contact lenses, systemic drug effects, Sjögren's Syndrome, and refractive surgery.[1–5] The Dry Eye Workshop definition and classification subcommittee updated the work of the National Eye Institute Workshop to create a classification system for dry eye. The subcommittee reinforced the concept of two different categories of dry eye: aqueous tear-deficient dry eye and evaporative dry eye.[5]

In the diagnosis of dry eye, the break-up time (BUT) is indicative of tear-film stability and is the simplest clinical test for this condition. BUT is measured by applying fluorescein dye to the eye and determining the time between a complete blink and the appearance of the first dry spot in the corneal tear film. Recently, a potentially new type of dry eye, termed short BUT (s-BUT) dry eye, has attracted attention.[6] A particular feature of s-BUT dry eye is a decreased tear BUT. Further, the tear quantity is normal in s-BUT dry eye patients, but the tear quality is abnormal, and patients experience a characteristic dry eye sensation. Clarifying whether s-BUT dry eye is another form of dry eye could potentially facilitate its diagnosis and treatment.

The three diagnostic criteria of dry eye syndrome are dry eye symptoms, tear abnormalities, and ocular surface abnormalities. Superficial punctate keratitis (SPK) is a hallmark of corneal epithelial abnormalities. Because s-BUT dry eye sometimes lacks SPK, it satisfies only two of the diagnostic criteria (i.e., dry eye symptoms and tear abnormalities). Thus, as stated earlier, s-BUT type is sometimes not considered to be a definite type of dry eye but rather a potential one. However, we recently observed that during prolonged eye opening, such as during BUT measurements, corneal fluorescein staining (CFS) rapidly developed in some s-BUT patients eyes, revealing ocular surface abnormalities. This CSF may be different from SPK which is generally defined, but the generic

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implication of corneal dyeing positive. This observation may potentially be an important one. In particular, if such a phenomenon is universal, CFS is not necessarily a stable indicator of a chronic dry eye condition, but is a conditional one that changes according to environmental stress, such as the simple desiccation that occurs during the prolonged absence of blinking during visual display terminal (VDT) work.[7]

The purpose of this study was to clarify whether CFS develops in a relatively short period of time during prolonged opening of the eye. To accomplish this aim, we examined patients who showed no CFS at the start of the examination but who developed CFS during BUT measurements. We found that the pattern of CFS matched exactly the pattern of tear break-up, as reflected in the location of the desiccation stress. These observations suggest that in certain dry eye patients, CFS may develop and disappear in a cyclical manner according to environmental factors.

2. Methods

2.1. Patients

This case series represents data obtained from 13 patients who were treated at Keio University and the Minamiaoyama Eye Clinic, Tokyo, Japan. The participants (10 males and 3 females) had an average age of 41.8 years (range, 20–74 years), and did not exhibit fluorescein staining at the first slit-lamp examination of their eyes. Approval for data collection and analysis was obtained from the Department of Ophthalmology, Keio University School of Medicine, and the Minamiaoyama Eye Clinic, Tokyo. We obtained informed consent from the patients.

2.2. Tear function examinations

BUT measurements were performed after instillation of 2 μL of 1% fluorescein solution into the conjunctival sac of each patient's eye(s) using a micropipette. A cobalt blue filter was used to measure the BUT. The patients were then instructed to blink several times for a few seconds to ensure adequate mixing of the dye with the tear film. The interval between the last complete blink and the appearance of the first corneal black spot in the stained tear film was measured three times, and the mean value of the measurements was calculated. A BUT value of $\leq$ 5 seconds was considered abnormal. The BUT measurements were obtained by the same doctor each time.

2.3. Schirmer's I test

In Schirmer's test, a 35 mm $\times$ 5 mm strip of filter paper was used to measure the amount of tears produced over a period of 5 minutes under ambient light. The strip was then placed at the junction of the middle and lateral thirds of the lower eyelid without anesthetic eye drops, and the patient was instructed to close his/her eyes. Patients were considered to have dry eyes when the wetting values were < 5 mm during the 5-minute period, as defined by Japanese criteria for the diagnosis of dry eye syndrome. This test was performed after obtaining the BUT measurements.

3. Results

All of the patients had relatively severe dry eye symptoms. The results of the BUT and Schirmer's tests are shown in Table 1. The tear BUT was < 5 seconds in all of the patients, thus revealing abnormalities in the tear dynamics. In contrast, none of the individuals had wetting values of < 5 mm according to the Schirmer's I test, revealing that the patient's eyes did not have a tear deficiency.

Table 1
Patient descriptions and the results of diagnostic tests for dry eye disease.

	Age (y)/sex	Schirmer's I test (mm)	BUT (s)
Case 1	36/F	8	3
Case 2	36/M	11	3
Case 3	20/M	10	3
Case 4	37/M	9	2
Case 5	50/F	8	3
Case 6	41/M	11	3
Case 7	74/M	9	1
Case 8	45/M	8	2
Case 9	39/M	10	3
Case 10	29/F	8	4
Case 11	50/M	9	3
Case 12	20/M	11	4
Case 13	67/M	7	3

BUT = break-up time.

In all 13 cases, CFS developed in only a single BUT measurement in each case. Some images of representative cases are shown in Figs. 1 and 2. The initial examination showed no CFS (Figs. 1A and 2A). After the patients held their eyes open for several seconds, the eyes developed tear break-up (Figs. 1B and 2B). Strikingly, as seen in Figs. 1C and 2C, CFS developed in only a single BUT measurement in each case, and matched exactly the tear break-up pattern. We also provide a movie of another case (Video 1).

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Among the 13 patients, five cases (Cases 9–13) were followed for an additional ~30 minutes and reexamined for CFS. These cases showed weak or nearly absent CFS (Fig. 2D).

At the first visit, the 13 patients were diagnosed with probable dry eye because they satisfied two out of three diagnostic criteria, the presence of dry eye symptoms and abnormal tear dynamics (s-BUT). However, we were unable to make a definite diagnosis of dry eye because the eye condition of these patients did not satisfy the third criteria of ocular surface abnormalities. However, based on the development of CFS during the BUT examinations, all 13 patients may fulfill the three diagnostic criteria of dry eye syndrome.

4. Discussion

To maintain a stable tear film, the ocular surface employs a unique strategy of defense involving both compositional and hydrodynamic factors. Even when normal tear components are present, a stable tear film cannot be formed without the kinetic movement that occurs during blinking. Blinking also facilitates the expression of meibum at the margin of the eyelid and refreshing of the tear fluid. In addition, blinking causes the open-eye state to be intermittently turned off by eyelid closure, thus helping to minimize evaporation of the tear fluid and drying of the eye. Blinking frequency and the completeness of eyelid closure during a blink ensures the establishment of a stable tear film between blinks.

Aqueous tear-deficient dry eye disease is caused by a failure of lachrymal tear secretion.[8,9] Evaporative dry eye disease, by contrast, may be caused by intrinsic factors such as compromised eyelid health or extrinsic factors such as topical medications. These categories of dry eye disease are not mutually exclusive and dry eye beginning as one major type may coexist with the other type or lead to events that cause dry eye by another mechanism.

Different diagnostic tests are best correlated to the subsets of dry eye disease. However, tear osmolality is currently believed to be a global indicator of the disease, independent of its etiology.[5] Unlike disease subset markers, which suffer from excessive scatter (Schirmer's test, meibomian scoring, and ocular surface disease