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Blink Test enhances ability to screen for dry eye disease

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ABSTRACT

Aim: To evaluate the patient-administered Optrex™ Dry Eye Blink Test against established clinical criteria for the diagnosis of dry eye disease (DED) and to evaluate its benefit in enhancing screening for DED.
Methods: Eighty-seven participants aged 38 ± 17 years, (44 female) were screened for DED using the Tear Film and Ocular Surface Society Dry Eye Workshop II (TFOS DEWS II) diagnostic criteria. In addition to symptoms screening with the Ocular Surface Disease Index questionnaire (≥13 cut-off score for DED), these criteria required a sign of loss of homeostasis of the tear film in the form of a non-invasive tear breakup time (NIBUT) < 10 s (Oculus Keratograph; K5M), an osmolarity reading ≥308 mOsm/L or an interocular difference in osmolarity of > 8 (Tearlab), or ocular surface staining (> 5 fluorescein corneal spots, > 9 lissamine green spots or lid wiper staining [≥2 mm length & ≥25% width]) to confirm a diagnosis of DED. The self-administered Blink Test, which requires the participant to observe an image on a computer screen and report the length of time (in seconds) that they can refrain from blinking without discomfort, was repeated three times.
Results: Using a cut-off time of 10 s, the Blink Test demonstrated sensitivity of 66%, specificity of 88%, and an area under the curve of 0.77 ($p < 0.001$), in predicting a diagnosis of DED according to the TFOS DEWS II criteria. The correlation between the Blink Test and NIBUT was $r = 0.47$ ($p < 0.001$). When combined with the screening questionnaire, the sensitivity and specificity of the Blink Test increased to 71% and 90%, respectively.
Conclusion: The Blink Test offers health professionals without advanced instrumentation, as well as patients, themselves, a rapid method of identifying possible DED.

1. Introduction

"Dry eye disease (DED) is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles" [1]. The Tear Film and Ocular Surface Society's Dry Eye Workshop II (TFOS DEWS II) provided this updated definition, which focuses on the loss of homeostasis in addition to symptoms, as the central pathophysiological concept of dry eye disease (DED). Tear film instability is considered to be a principal factor in the vicious cycle of disease, perpetuating tear film hyperosmolarity and ocular surface inflammation, leading to ocular surface damage [2].

The prevalence of DED has been estimated to be between 5% and 50% [3], however the presence of signs and symptoms has been a prerequisite of few studies, to date, and studies that conform to the new global consensus on DED diagnosis have yet to be published. Globally, the incidence of DED has been found to be higher in Asian, than in Caucasian, populations. DED prevalence increases approximately linearly with age, with a steeper rise by decade for clinical signs than for the prevalence of symptoms. Sex-related differences become significant only in older age [3].

DED causes both an economic and social burden on those affected by this chronic condition [4]. It has been shown that DED can reduce the everyday quality of life of those with the disease [5]. Mild to severe DED has been associated with anxiety and depression [6–8]. In particular, patients suffering from DED secondary to Sjögren's syndrome reportedly have a high prevalence and severity of depression [9].

The prevalence of ocular symptoms related to DED is difficult to quantify, as symptoms are not spontaneously reported by many patients unless specifically asked. Hence, non-selective use of validated questionnaires such as the 5-item Dry Eye Questionnaire (DEQ-5) [10] or Ocular Surface Disease Index (OSDI) [11] can aid in screening for DED. It's also important, through differential diagnosis, to exclude non-dry eye conditions that can mimic some of the DED signs and symptoms

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such as ocular allergy, infection and even binocular vision anomalies [12,13]. Exclusion of such non-dry eye cases, together with a positive symptom score, prompts testing to identify whether there is an accompanying loss of homeostasis, and this is most often undertaken in a specialist clinic due to the time and equipment requirements. Tests recommended by TFOS DEWS II for identifying the loss of homeostasis of the tear film are those that evaluate non-invasive breakup time (NIBUT) (with a cut-off time of < 10 s deemed to indicate DED), osmolarity (with a cut-off value for DED of ≥ 308 mOsm/L or a difference of > 8 mOsm/L between the two eyes), and ocular surface corneal staining (> 5 fluorescein spots), conjunctival staining (> 9 lissamine green spots) or lid wiper epitheliopathy at the inner eyelid margin (stained zone width with the combined dyes of ≥ 25% and length ≥ 2 mm) [12]. If any one of these tests identifies a loss of homeostasis then, in conjunction with the previously confirmed symptomology, a diagnosis of DED is made.

Since pharmacists and general practitioners most often lack access to the technology/dyes for diagnosing dry eye or monitoring treatment effects, availability of a rapid self-assessment test for dry eye could allow non-eyecare practitioners to give better advice to patients and make more appropriate referrals for a full diagnosis or differential diagnosis. Raising awareness of possible dry eye in patients themselves, might also encourage affected individuals to seek appropriate advice and management. The present investigation thus sought to validate a patient self-assessment test (Optrex™ Dry Eye Blink Test) and determine the level of certainty with which a diagnosis of DED might be made, in the absence of specialist equipment, against an established diagnosis according to TFOS DEWS II.

2. Methods

This study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the institutional ethics committees of Aston University, Birmingham, United Kingdom and the University of Auckland, Auckland, New Zealand. Study participants were recruited from both centres and were enrolled following explanation of the procedures and after providing written informed consent. Eighty-seven adults, ranging in age from 19 to 87 years old (mean age 38 ± 17) (43 males, 44 females) were enrolled in the study. All subjects were in good general health and were able to participate in the test sessions without difficulty. Subjects with any active ocular disease or currently using ocular medications were excluded. None of the subjects were contact lens wearers. In particular, the study sought to recruit subjects across a range of DED severities in order to test the discriminatory ability of the Blink Test.

Room conditions were maintained at a temperature of 20.8 ± 2.1 °C and relative humidity of 46.1 ± 9.2%, and subjects spent a minimum of 10 min acclimatising to the study room conditions before testing. The participants were asked to answer the DEQ-5 questionnaire which scores eye discomfort and eye dryness frequency from 0 (never) to 4 (constantly) and intensity from 0 (never have it) to 5 (very intense) along with watery eye frequency. In addition they completed the 12-item OSDI questionnaire, which scores experience of 3 ocular symptom questions, 6 visual function-related questions and 3 environmental trigger questions during their previous week from 0 (none of the time) to 4 (all of the time). The final score is calculated with the following formula;

$$\text{OSDI} = \frac{(sum\ of\ scores)x\ 25}{(number\ of\ questions\ answered)}$$

DED signs were assessed from only the right eyes of subjects, in the following order. NIBUT was assessed objectively with the Keratograph 5M (Oculus, Wetzlar, Germany) using the infrared light setting, after two non-forceful blinks, from automated detection of disruption of a projected mire pattern reflected from the tear film surface, during a period of non-blinking [14,15]. A mean of three 'first breakup time measurements was recorded each time.

The mean values of three consecutive Blink Test measurements were obtained (although the manufacturer's instructions does not specify repetition). Test instructions were displayed on a 15-inch thin-film-transistor liquid-crystal display digital screen positioned at ~40 cm from the participant. The patient was requested to make 2 non-forceful blinks, before ceasing blinking, and to press a timer button on the screen when discomfort was noted (Fig. 1).

Tear film osmolarity was measured at the inferior tear meniscus with an impedance-based, low volume osmometer (TearLab, San Diego, USA) [16]. Daily instrument calibration was performed and stability in temperature ensured in accordance with the manufacturer's instructions [12]. Measures were collected non-invasively from each eye, and the maximum osmolarity and interocular difference recorded.

Conjunctival damage was evaluated with the aid of lissamine green dye (Green Glo, HUB Pharmaceuticals LLC, Rancho Carcamonga, CA, USA). The strip was wet with saline and the lissamine green solution instilled at the temporal canthus, after a period of 5 s to ensure an

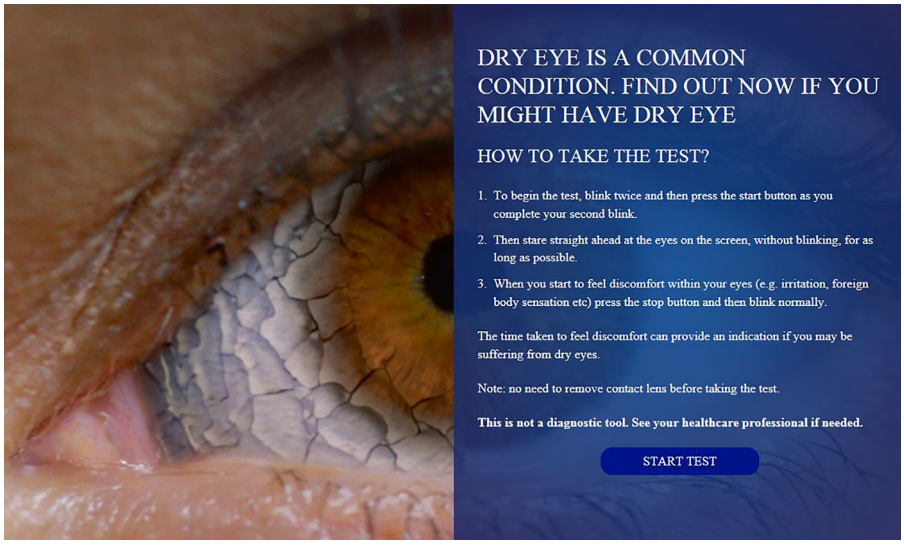

Fig. 1. The Optrex™ Dry Eye Blink Test (with permission from Reckitt Benckiser).