First-in-human Clinical Trial of a Novel Eyelid Warming Device in Meibomian Gland Dysfunction

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ABSTRACT **Background:** Meibomian gland dysfunction (MGD) causes significant patient morbidity as well as economic burden.
Objectives: To evaluate a novel eyelid warming and a neuro-stimulating device that delivers heat via low-level infrared radiation to the eyelids of patients with MGD.
Methods: In this prospective interventional study, patients with MGD were recruited at a single medical center. The main outcome measures included changes in tear break-up time (TBUT), Schirmer's test, and Ocular Surface Disease Index (OSDI), overall satisfaction, and corneal signs of dry eye. Patients were instructed to use the device twice daily for 5 minutes on each eye for a total of 14 days. Follow-up assessments were performed after the 2-week treatment.
Results: A total of 10 patients were included; mean age was 67 ± 16 years; six males (60%). Changes in pre- vs. post-treatment TBUT (5.0–6.11), OSDI (28.1–23.9), and Schirmer score (8.67–7.11) were not statistically significant. Over a course of 243 treatments, 131 (54%) demonstrated improvement in symptoms, 40% found no change, and 6% experienced worsening of symptoms. General satisfaction was observed overall in 80% of the patients. No adverse events were observed.
Conclusions: In this first study of a novel eyelid warming device, overall subjective satisfaction was reported in 80% of patients. Potential advantages of this user-friendly device include its ability to improve MGD and tear film stability, as well as symptomatic relief, while allowing the user to continue with normal daily functioning while undergoing treatment.
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KEY WORDS: dry eye disease (DED), eyelid warming device, infrared radiation, meibomian gland dysfunction (MGD)

Dry eye disease (DED) is a chronic disorder characterized by tear film instability, which can lead to ocular dryness, inflammation, and irritation symptoms [1]. Studies have demonstrated that up to 10% of people, mostly older adults, present with DED, with increasing prevalence due to the aging population [2]. DED has been associated with significant economic burden due to frequent eye clinic visits, as well as reduced quality of life, with the impact of severe disease comparable to angina pectoris [1,3,4]. DED can be categorized by the underlying etiology, generally classified as aqueous deficient due to lacrimal gland dysfunction, evaporative as a result of meibomian gland dysfunction (MGD), or a mixture of both [1].

In MGD, dysfunction of the meibomian glands in the inner eyelids limits the release of lipids (meibum) that form the outer layer of the tear film, thus reducing evaporation of the aqueous tear layer [5]. Treatment of MGD focuses on alleviating this obstruction, typically via lid hygiene and warm compresses, which enhance lipid secretions by reducing the viscosity of the meibum. This treatment facilitates outflow, thereby improving the consistency of the tear film lipid layer and augmenting its consistency [5]. However, treatment with warm compresses is non-standardized, compliance is low, and the applied temperature varies with time. These variations result in poor resolution of symptoms [6-8]. Therefore, various electronic in clinic-use heating devices, as well as commercial products, have been developed to help address this problem [5-7,9,10].

The purpose of this study was to test the safety and effectiveness of a novel infrared radiation eyelid warming device that is worn on one side of a spectacle frame during a 5-minute treatment.

PATIENTS AND METHODS

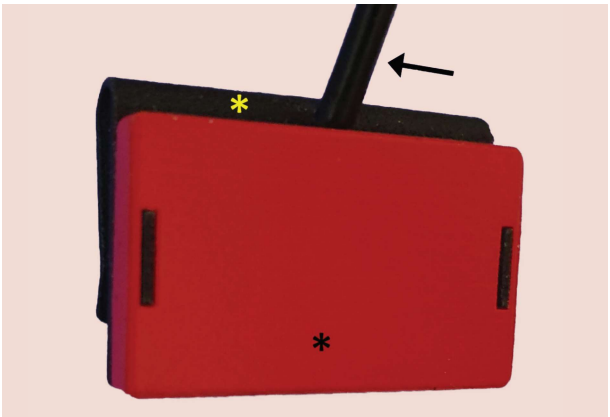
In this prospective study, we recruited 12 patients who presented with MGD between March 2022 and July 2022 to the Goldschleger Eye Institute at Sheba Medical Center. Patient consent was obtained prior to the recruitment.

The study adhered to the tenets of the Declaration of Helsinki. The study was HIPAA compliant, and institutional review board (IRB) approval was obtained. Inclusion criteria included patients with MGD referred to our institution. Patients who were not using glasses suitable for mounting the device received non-optical frames. Dry eye disease was confirmed by ocular history, clinical assessment, and standard slit lamp examination with tear function, including tear fluorescein break-up time (TBUT) and Schirmer's test. For subjective assessment, all patients completed the Ocular Surface Disease Index (OSDI) questionnaire, a standardized 12-item questionnaire that evaluates symptoms of ocular irritation caused by DED as well their impact on daily life [11]. Scores ranged between 0 and 100, with higher scores correlating with more severe symptoms [12]. Exclusion criteria included patients younger than 18 years of age, non-compliant patients, and patients lost to follow up. All measures were evaluated twice, with the first assessment at the pre-treatment visit, and the second visit performed 2 weeks following the trial. Overall satisfaction from the device was recorded at the post-treatment visit.

THE EYELID WARMING DEVICE

The innovative home eyelid warming device enables stable controlled heating of the eyelid in a more comfortable way for the patient [Figure 1]. The device is mounted on the frame of the glasses in front of one eye at a time [Figure 2], thereby allowing the contralateral eye to function freely; therefore, the use of the device is possible without interruption of routine daily functions, including reading or screen usage. The device heats the eyelid using low power infrared radiation produced by light emitting diodes (LEDs) with a wavelength of 960 nm. The device was tested by the Israel Standards Institute and classified under the exempt category, corresponding to safe usage.

Figure 1. The eyelid warming device with spectacle clamp (yellow asterisk), plate facing eyelid (black asterisk), and power cable (arrow)



The easy-to-use device touches the eyelids after being clipped to a spectacle frame, and then heats the eyelids to a constant temperature of 42°C. It operates from an external mobile 5-volts power bank that utilizes a battery as its power source.

Figure 2. The eyelid warming device attached to the glasses frame (A) front view (B) top view

[A] Front view

[B] Top view

CLINICAL METHODS

At the baseline visit, patient characteristics were collected, and a slit lamp examination was performed. Over the course of 14 days, patients were instructed to use the device twice a day for 5 minutes each time, with patient compliance as well as daily subjective interpretation measured via a standardized form. Follow-up assessments were reviewed at the post-treatment visit.

STATISTICAL ANALYSIS

Non-parametric tests were used to compare means of continuous variables such as OSDI, TBUT, visual acuity, and Schirmer test results. For statistical analysis, the right eye was arbitrarily evaluated for each patient, to prevent the inter-eye correlation erroneous effects on the results. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 26 (SPSS, IBM Corp, Armonk, NY, USA). All results are presented as mean ± standard deviation (SD).

RESULTS

Twelve patients were recruited for this study. Two patients were lost to follow-up, leaving a total of 10 patients at the post-treatment visit. The mean age of the cohort was 67 ± 16 years and included six males and four females. All but two patients used over-the-counter eye drops for symptomatic relief prior to using the device. Patients used the device an average of 89% ± 12.4% of the required times. Over a course of 243 treatments, 54% demonstrated immediate improvement in symptoms, 40% no change, and 6% worsening of symptoms. Patients reported overall satisfaction with the use of the device in eight cases (80%).

On clinical examination at baseline visit, visual acuity (VA) was 20/25, punctate epithelial erosions (PEEs) were demonstrated in 8 of the 10 patients, mean ± SD TBUT of 5.0 ± 2.24 seconds, Schirmer 9.10 ± 6.0 millimeters, and OSDI score of 28.1 ± 18.5. Post treatment indices were VA 20/23, TBUT 5.8 ± 3.1 seconds, Schirmer 7.1 ± 4.2, and OSDI score 23.9 ± 20.9. The differences between pre- and post-treatment values were non-significant for all (related-samples Wilcoxon Signed Rank test).

During the study, we found that heating the eyelids with infrared radiation induced immediate tear secretion, possibly due to direct stimulation of the local nerves demonstrated in other applications of infrared neural stimulation [13]. No adverse events occurred during the 2-week trial period.

DISCUSSION

DED significantly impacts millions of individuals, with a substantial burden on quality of life. It is a leading cause of seeking eye care [2]. As the population ages, the prevalence of DED continues to grow, necessitating new advances in treatment [12]. In this study, we examined the first-in-human use of a simple, home-use eyelid heating device, whose novelty lies in its ability to heat eyelids via low-level infrared radiation rather than direct heat. This treatment provides a constant and regulated temperature, a feature limited by most home treatment DED devices. The portable device treats one eye at a time, thus allowing continuation of normal activities. as well as preventing the need for binocular eyelid closure during each use. After a 2-week course of using the device, patient satisfaction was positive, with 8 of the 10 patients subjectively reporting overall improvement in symptoms.

At home warm compresses remain the conventional treatment for addressing MGD, however are limited by patient compliance, lack of standardization, and temperature regulation [7]. Several methods of hot towel applications have been investigated that have shown to improve symptoms of dry eye disease and aim to achieve a regulated temperature between 40°C and 45°C without exceeding 48°C to prevent thermal injury [7,14]. However, a recent review demonstrated the need for constant reheating or towel replacement to maintain this desired temperature, which can impact patient compliance [14]. Furthermore, without reheating every few minutes, hot towel treatment becomes ineffective in achieving symptomatic relief [14,15]. The novel eyelid heating device maintains a constant temperature of 42°C through LEDs, thereby alleviating the need for constant reheating, and allowing the user to maintain daily activities.

Various commercial devices that target meibomian gland dysfunction via heating mechanisms have been developed to address the growing burden of MGD. For example, LipiFlow®, an in-office FDA approved medical device delivers heat in peristaltic motion to the eyelid to alleviate gland obstruction and improve outflow of meibomian secretions. Various studies have demonstrated the effectiveness of the LipiFlow device. Lane et al. [9] demonstrated improved measurements in meibomian gland secretions, TBUT, and OSDI with LipiFlow compared to using iHeat, a portable warm compress at a 2-week follow-up. LipiFlow users demonstrated an overall improvement of 76% in dry eye symptoms [6,9]. Another randomized control trial demonstrated that a single LipiFlow treatment resulted in up to 9 months of sustained improvement in dry symptoms and tear film indices [16]. Other in-office heating devices have been developed, such as TearCare® (Sight Sciences, USA), and iLux® (Alcon, USA), with promising results [5,6]. A randomized, open-label, controlled, multicenter clinical trial demonstrated subjective improvement at 4 weeks in OSDI scores following treatment with iLux® and LipiFlow® of 50.7 ± 18.6 to 19.5 ± 17.0 and 50.6 ± 18.7 to 22.6 ± 19.8, respectively [17]. Overall, these devices are limited by availability as well as cost, with most devices not covered by United States insurance policies [5,6].

New commercial at-home heating devices are available that have demonstrated improved heat delivery and regulation with significant reduction in dry eye symptoms [8,18,19]. A randomized control trial investigating the efficacy and safety of the MGDRx EyeBag® eyelid warming device (EyeBag Company Ltd, Halifax, UK) in 25 patients demonstrated an increase in ocular comfort scores over a 2-week treatment period compared to control eyes. It also showed an overall improvement in non-invasive TBUT time and corneal staining patterns [19]. Another randomized control trial compared standard warm towel treatment to warming devices EyeGiene® (Eyedetec Medical Inc., Danville, CA, USA) and Blephasteam® (Spectrum Thea Pharmaceuticals LTD, Macclesfield, UK) over a course of 3 months of treatment. While subjective improvement was demonstrated in all groups (45.5%, 41.2%, and 78.3%, respectively), no significant change was shown in TBUT (change of 0.2, -0.1, 0.8, respectively; $P = 0.612$) or Schirmer's score. Furthermore, eight withdrawals were demonstrated in the EyeGiene® group due to warming technical difficulties [8]. Overall, many of these devices are limited by patient compliance, expense, and necessity to close both eyes [18,20]. The device addresses patient compliance by retaining heat in a regulated fashion via infrared technology to the treated eye, while allowing normal functioning with the contralateral eye. We demonstrated generally good compliance as well as overall satisfaction with the device and improvement in most dry eye indices.

The limitations in the study include the small sample size. The lack of statistical significance in this patient cohort may be due to the small cohort size. Future, large prospective trials with longer follow-up periods are recommended to evaluate the effectiveness of the device.

CONCLUSIONS

The novel eyelid-warming device addresses meibomian gland dysfunction that treats one eye at a time, allowing the user to function normally using the non-treated contralateral eye. Preliminary results in 10 patients who used the device over a course of 2 weeks demonstrated overall patient satisfaction with no adverse effects. Future studies can be conducted with a larger population to further prove efficacy.

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