PILOT STUDY

A Novel Combination Therapy for Patients With Dry Eye Disease: A Pilot Study

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ABSTRACT

Context • Approximately 25% of the US population suffers from dry eyes or some abnormality of the exposed ocular surface. Investigation of effective modalities for their management is needed.

Objective • The study intended to examine the efficacy of a proprietary, daily, Dry Eye Protocol consisting of daily use of a moist, heated, ocular compress and intake of an omega-3 dietary supplement in treatment of ocular surface disease.

Design • The research team designed a 4-wk, clinically based, open-label, multicenter cohort study.

Setting • The study took place at 6 private eye care practices throughout the United States: Beverly Hills, CA, USA; San Diego, CA, USA; Sunnyvale, CA, USA; Park City, UT, USA; Tarpon Spring, FL, USA; and Kennewick, WA, USA.

Participants • Participants were adults between 18 and 75 y of age who had established ocular surface disease based on clinical findings and the results of testing using the ocular surface disease index (OSDI).

Intervention • For period of 30 d, participants used a combined daily protocol that included (1) application of a moist, heated, eye compress and (2) a nutritional therapy via an omega-3 supplement in an oral triglyceride form.

Outcome Measures • Measures included the OSDI and a test of tear break-up time (TBUT).

Results • Of the original 35 participants, 33 completed the 4-wk protocol. The participants using the proprietary Dry Eye Protocol showed significant improvements from baseline, demonstrated by a 49% decrease in OSDI scores ($P = .0015$); and 46% of participants reported becoming asymptomatic of dry eye symptoms. A significant improvement was also observed in TBUT, increasing from 3.0 to 5.4 s.

Conclusions • Daily use of the proprietary Dry Eye Protocol that included a high dosage of triglyceride omega-3 and use of a moist, heated, compress daily showed significant improvement for participants in OSDI and TBUT and should be considered to be a first-line therapy for patients with dry eye disease. (*Altern Ther Health Med.* [E-pub ahead of print.])

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Approximately 25% of the US population suffers from dry eyes or some abnormality of the exposed ocular surface.[1,2] Currently, many methods exist to treat dry eye disease (DED). An International Dry Eye Workshop (DEWS) report successfully classified dry eye into 2 realms for study: (1) aqueous deficient and (2) evaporative.[3] Evaporative disorders, which relate to disorders of the Meibomian glands, have gained significant attention in recent literature and practice, and investigation of effective modalities for their management is needed.

Meibomian glands secrete a lipid and protein mixture that provides a clear optical surface for the cornea, interferes with bacterial colonization, and retards tear overflow. Secretion from these glands improves the stability and reduces the evaporation of the tear film. Dysfunction of these glands destabilizes the tear film and increases evaporation and osmolarity.[4] Meibomian gland disease (MGD) exhibits excretory duct obstruction due to hyperkeratinization of the ductal epithelium and an increased viscosity of the meibum.[5]

MGD exerts a significant effect on gene expression in the human Meibomian gland. These changes, which have not been accounted for by gender-associated differences between control and MGD patient populations, are accompanied by upregulation and downregulation of many processes

(ie, keratinization, the cell-division cycle, DNA repair, and the formation of cytoplasmic vesicles and cornified envelope components).[5,6] MGD is often considered to be a key instigator of DED[7-9] and should be targeted to reduce both symptoms and degenerative processes related to dry eye.[10,11]

Ocular warm compresses are frequently prescribed for patients with varying presentations of mild to severe Meibomian gland dysfunction and Meibomian gland obstruction, with subsequent symptoms of dry eye.[12-14] The application of heat to the external surface of the eyelid increases the temperature of the meibum in meibomian glands. This action causes the meibum to become less viscous and minimizes meibomian gland obstruction and inspissation.

Traditionally, home-based warm compresses have been limited to the use of a towel or cloth, moistened with warm water or moistened and heated using a microwave.[13] Blackie et al[15] found that the traditional compress must be replaced every minute to maintain appropriate lid temperature. Newer, moist-heat, warm compresses are able to hold warmer temperatures longer, thus providing better efficacy.

Many studies have proven the advantages of omega-3 supplementation for ocular wellness.[16-18] The American diet is heavily weighted toward omega-6 versus omega-3, which can promote more inflammatory factors and exacerbate DED.[19] The advantages of omega-3 supplementation include (1) restructuring of fatty acid chains for better interaction with transporting proteins, (2) diminished prostaglandin-induced ocular inflammation, and (3) suppression of leukocyte recruitment.[20]

A recent omega-3 supplementation study, consisting of 1419 DED patients, showed a decrease in artificial tear use, less conjunctival hyperemia, improved tear secretion, and tear film stability, adding to the considerable body of evidence linking omega-3 supplementation to improvement in DED.[21]

The current study intended to examine the efficacy of a proprietary, daily, Dry Eye Protocol consisting of daily use of a moist, heated, ocular compress and intake of an omega-3 dietary supplement in treatment of ocular surface disease.

METHODS

The research team designed a 4-week, clinically based, open-label, multicenter cohort study.

Participants

The study took place at 6 private eye care practices throughout the United States (Beverly Hills, CA, USA; San Diego, CA, USA; Sunnyvale, CA, USA; Park City, UT, USA; Tarpon Spring, FL, USA; and Kennewick, WA, USA) and the study protocol was implemented by the primary optometrists at each practice. Participants were adults between 18 and 75 years of age who had established ocular surface disease based on clinical findings and the results of testing using the ocular surface disease index (OSDI).

For inclusion in the study, potential participants needed to (1) be diagnosed with DED and (2) score at least 23 on the OSDI in at least 1 eye.

Potential participants were excluded if they (1) had a compromised cognitive ability that could be expected to interfere with compliance to the requirements of the study; (2) had a clinically significant eyelid deformity or eyelid movement disorder that was caused by conditions such as notch deformity, incomplete lid closure, entropion, ectropion, hordeola, or chalazia; (3) had had previous ocular disease leaving sequelae or requiring current topical eye therapy other than for DED, including, but not limited to, active corneal or conjunctival infection of the eye and ocular surface scarring; (4) had an active ocular allergy; (5) were currently taking Restasis (cyclosporine 0.05%); (6) wore contact lenses; (7) were pregnant or lactating at the time of the study; (8) were currently taking Warfarin (coumadin); (9) had a known allergy to omega-3 fatty acids; or (10) had punctal occlusion.

Informed consent was obtained from all participants before their inclusion. The study was conducted in accordance with the guidelines provided by the Declaration of Helsinki. The study was not biased in its selection of candidates based on gender, race/ethnicity, or religious background.

Procedures

A comprehensive dry eye evaluation was conducted at the participant's baseline visit, including a slit lamp evaluation of the tear lake and tear break-up time (TBUT) and a corneal staining evaluation. Participants' demographics and medical history were recorded.

Examinations were performed on both eyes, both at the initial screening at baseline and at a follow-up visit at 30 days postintervention. They included checking (1) the uncorrected and best-corrected visual acuity, using manifest refraction; (2) the lid and lash architecture, using a slit lamp evaluation, and (3) the TBUT. The research team also checked for the existence of (1) periocular lesions, (2) Meibomian gland scarring, (3) lid telangiectasia, (4) chemosis, (5) tear meniscus, and (6) corneal inflammation/edema. TBUT and corneal staining were assessed upon instillation of sodium fluorescence (NaFl) dye.

Intervention

For the period of 30 days, participants enrolled in the study were asked to (1) use the Dry Eye Compress (Solana Health Inc, Del Mar, CA, USA) heated for 30 seconds in a standard household microwave and then applied to closed eyes for 5 minutes daily; and (2) take omega-3 daily, delivered in 3 Ultra Dry Eye TG softgels (OcuSci Inc, Ultra Dry Eye TG, Del Mar, CA, USA).

Each softgel of omega-3 contained 810 mg of omega-3 polyunsaturated fatty acids in the rTG form with 390 mg of eicosapentaenoic acid (EPA) and 193 mg of acid docosahexaenoic acid (DHA). After the 30-day protocol was complete, participants returned to their associated clinics for a comprehensive dry eye evaluation following the same protocol as at baseline.

Outcome Measures

Ocular Surface Disease Index. The OSDI developed by Allergan Inc (Irvine, CA, USA) is a 12-item survey completed in office by the patient for the assessment of symptoms related to DED and their effect on vision and is one of the most frequently used survey instrument for the assessment of ocular surface disease severity in dry eye research.[20]

Participants were screened using the OSDI to assess the severity of their DED and as a benchmark for the study.[22]

Tear Break-up Time. The TBUT test is easily and quickly performed after fluorescein drops are instilled in the eye by the clinician. After the fluorescein is instilled, the patient is asked to stare without blinking. The cornea is observed under a blue light and time is counted in seconds, from the time of the last blink until a pocket of cornea appears that is no longer covered with fluorescein stained tears. The longer the TBUT, the more stable the tear film. A TBUT greater than 8 to 10 seconds is usually considered normal. Five to 10 seconds is borderline and less than 5 seconds suggests an unstable tear film and DED.[23]

Three of the 6 sites did not collect TBUT or corneal staining data, involving 17 patients in total.

Statistical Analysis

The research team performed statistical analysis including *P* values based on a paired, 2-sided *t* test comparison of mean change using Excel 2016 (Microsoft Corporation, Redmond, WA, USA) where $P < .05$ was considered significant.

RESULTS

A total of participants—26 females and 9 males between 18 and 75 years of age, with a mean age of 52 ± 12—were enrolled, of which 33 completed the 4-week protocol. Two female patients dropped out during the study, 1 due to watery eyes and sneezing and 1 to nausea.

More than half of the enrolled patients (54%) were considered to have severe DED based on the OSDI scoring, with a mean starting score of 57 ± 19.3 (Figure 1). Participants showed significant improvements between baseline and postintervention, demonstrated by a decrease in OSDI scores of 28 points (49%) to an average of 29 ± 21.1, with $P = .0015$. Furthermore, 45% of patients reported becoming asymptomatic of dry eye symptoms.

TBUT was collected at 3 of the 6 participating clinics for a total of 18 participants, and although the data did not reach statistical significance due to the small sample size, TBUT, as measured in seconds, improved by 2.4 seconds (81%), with $P = .55$, moving from a mean of 3.0 ± 1.4 seconds to 5.4 ± 3.5 seconds at 30 days postintervention, as shown in Figure 2.

Figure 1. Change in Ocular Surface Disease Index

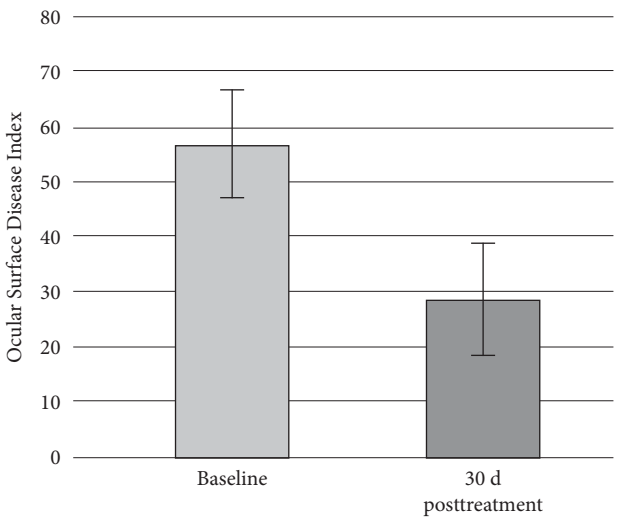
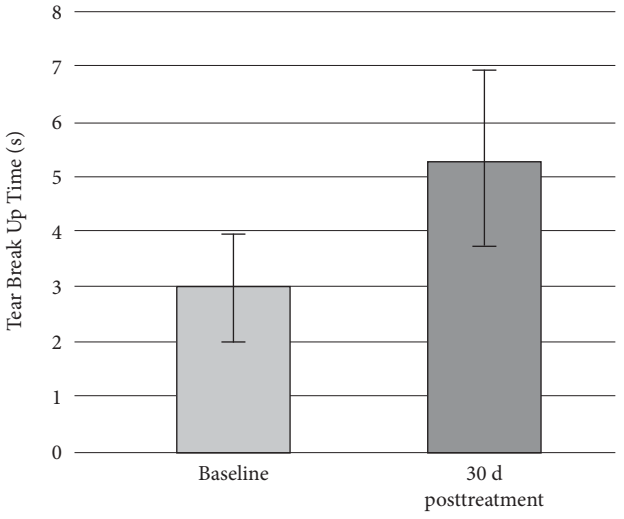


Figure 2. Change in Tear Break Up Time



DISCUSSION

Tear-film improvement highly correlates with the OSDI scale where the function of the Meibomian glands and the stabilization of the lipid layer greatly reduce patient's symptoms.[4] In the current study, daily use of the proprietary Dry Eye Protocol that included a high dosage of triglyceride omega-3 and use of a moist, heated, compress daily showed significant decreases for participants in OSDI scores and increases in TBUT scores and should be considered to be a first-line therapy for patients with DED.

It is well known that medication adherence decreases with increased dosages.[24,25] Hobbs et al[26] have discussed this matter specifically when referring to omega-3 fatty acid supplements with regard to hypercholesterolemia. The concentration and dosage of the omega-3 supplement used in the current study meets the therapeutic dosage of omega-3 for DED treatment[27] and also increases compliance by limiting dosage frequency to 3 pills per day versus the 4 per day required in other studies.

The current study had limitations because no randomization occurred, and no control was used regarding the oral omega-3 supplement. Some new technologies involve more invasive treatments that may deter patients' interest.

Compliance may be poor as more complex treatments are implemented, such as prescriptions of multiple ophthalmic medications and/or rigorous daily care regimens. The current study may prove to offer relief for patients suffering from DED who are unable to initiate other forms of treatment

CONCLUSIONS

With a very conservative and efficient protocol of fewer than 7 minutes per day, the current research team was able to reduce participants' symptoms of DED significantly and to offer a low-risk therapy for patients and clinicians. Because DED is a chronic disease, the ease of use of the proprietary Dry Eye Protocol may enable better long-term dry eye management by improving patients' compliance. Patients' education in DED and understanding of the best strategy for the individual is imperative in achieving long-term success in overcoming this epidemic.

AUTHOR DISCLOSURE STATEMENT

The product for the study was supplied at no charge by OcuSci and Solana Health, and no remuneration was provided to investigators or patients.

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