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ORIGINAL RESEARCH

Prospective Evaluation of RedTouch Laser in the Treatment of Dry Eye Disease Secondary to Meibomian Gland Dysfunction

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Purpose: To validate the efficacy of RedTouch laser, a new 675 nm laser system in treating dry eye disease (DED) secondary to Meibomian gland dysfunction (MGD), comparing generalized periocular treatment versus direct targeting of the meibomian glands.

Patients and Methods: 70 patients with mild and moderate DED-MGD received 4 sessions of laser treatment separated by 3 weeks, with assessments before treatment, T0, and at the end, T1, after 2 months from the last session. Patients were divided randomly into 2 groups (G1 and G2) of 35 patients each to test different protocols. In G1, the eyelids and periocular area were treated with a 675 nm laser and G2, with the same treatment as in G1 but combined with a free pencil-shaped handpiece on the tarsal conjunctiva of the superior and inferior eyelids as well as on the lid margin of both eyelids.

Results: The outcomes resulted in a significant improvement in all symptoms and signs of both groups, OSDI, CFS, NITMH, NITBUT, Osmolarity and Schirmer test1. However, G2—receiving additional targeted meibomian gland treatment—showed superior outcomes across all parameters (G1 vs G2, $p < 0.001$), including the signs of the Meibomian glands and the lid margin (G1 vs G2, $p < 0.001$).

Conclusion: RedTouch laser is an effective treatment in patients with DED related to MGD, improving signs and symptoms. While periocular skin treatment alone provides clinical benefits, outcomes are significantly better when the laser is applied directly to the lid margin and tarsal conjunctiva, targeting the meibomian glands more specifically. No complications were observed.

Keywords: dry eye disease, meibomian gland dysfunction, 675 nm laser, ocular surface

Introduction

Dry eye disease (DED) associated with Meibomian Gland Dysfunction (MGD) is the most common cause of evaporative DED.[1–3] The presence of MGD and its prevalence are very high, varying with the age and sex of the patients and especially with the geographical region, from 5–20% in Western countries to 45–70% in Asian countries.[4] DED has a very significant impact on the quality of life and vision.[5]

The origin of DED-MGD is still not well known; it has been postulated that it may be caused by obstruction of the Meibomian gland operculum due to a hyperkeratinization process of the epithelium at the eyelid margin.[6,7] The retention of intraglandular meibum would degenerate into a viscous and abnormal fat that would end up damaging the Meibomian glands, causing their atrophy.[7] The lack of lipids in tears would be responsible for accelerated evaporation of the tear film, with direct exposure of the corneal-conjunctival epithelium to the air, which dries and damages it,[7–9] as well as the proliferation of commensal bacteria that contribute to damaging the ocular surface, causing irritation and more inflammation.[9,10] A vicious circle is produced, in which inflammation is the main factor in tissue damage[4,11] affecting the ocular surface and the palpebral conjunctiva, causing vasodilation of these structures. The vasodilation and extra vascularization around the eyelids contribute to their atrophy, as the Meibomian glands require certain hypoxia for their normal functioning.[12–14]

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DED-MGD current treatment has different approaches, from artificial tears without preservatives to immunosuppressants such as cyclosporine, dietary recommendations based on omega 3 and 6 fatty acid supplements, hot compresses and eyelid hygiene. More interventionist alternatives include mechanical expression of the Meibomian glands, intraductal probing of the Meibomian glands, or radiofrequency, which is not entirely satisfactory.[15–17] Intensive Pulsed Light (IPL) has shown significant efficacy, especially on the symptoms of the disease[18–21] and even in patients with rosacea with ocular involvement, improving both facial and ocular levels, decreasing the inflammation and vascularisation that characterises this disease.[22–24] Nevertheless, there is a need for new management options, especially in challenging cases.

RedTouch is a new laser that works on 675 nm wavelength, which has shown great efficacy in improving vascularization associated with pathologies such as rosacea or acne.[25,26] This laser stimulates collagen IV, increasing the thickness of the capillary wall and constricting the blood vessel, but in a different way from the IPL.[25–29] The specific frequency of the 675 nm laser is more effective and less inflammatory, with less vascular impact.[30]

We considered that the use of RedTouch applied to DED MGD could be beneficial for its effects in reducing inflammation, and also that the effects on the skin of the eyelids and periocular area could improve the dynamics of blinking, especially the amplitude of the eyelid opening. With this hypothesis, we initiated a prospective study focusing specifically on the effect of this type of laser (675 nm) in patients with DED and MGD, so we have not included a control group of patients with another type of alternative treatment.

Materials and Methods

This is a prospective study with 70 consecutive patients with mild-moderate DED-MGD, receiving the 675 nm laser (RedTouch, Deka Mela srl, Florence, Italy). The laser treatment was performed in 4 sessions, each with a 3-week interval. In each session, a general ophthalmological examination was performed to rule out possible side effects, and the study data were taken before starting the first session, T0 (2–4 days prior to treatment) and after 2 months, T1, from the last laser session.

This study was conducted following the ethical approval of our institution and the Declaration of Helsinki. The participants signed an informed consent before the beginning of the study. Subjects were enrolled from the Department of Ophthalmology of the Dexeus University Hospital (Autonomous University of Barcelona, Barcelona, Spain) between November 2022 and February 2024 (Protocol: PO-2023-03, Code: 2023/122-OFT-DEX). All participants were assessed and treated in the same center, maintaining the same conditions for all patients, with a mean room temperature of 22±0.5 °C, a relative humidity of 45±1.0% and brightness between 400 and 430 lux.

Patients were divided into 2 groups of 35 individuals. In group 1 (G1), the laser was performed with the standard handpiece in scanner mode (13x13 mm), applying it to the skin of the eyelids and the periocular area, covering an area of 5 cm around the orbital rim (Figure 1), while in group 2 (G2) the laser was performed combining the same procedure as in G1 but associating the treatment with a free pencil-shaped handpiece (3 mm single spot), on the tarsal conjunctiva of the upper and lower eyelids as well as on the lid-margin of both eyelids (Figures 2 and 3), protecting the eyelashes and the eye, with a corneal shield under the eyelids (Figure 4). For the statistical evaluation, data were taken from the eye with the highest degree of severity, when performing the test proposed in the clinical evaluation.

Patients: Inclusion and Exclusion Criteria

Inclusion criteria were DED-MGD patients with a mild to moderate degree of severity, compliant with the TFOS DEWS II Report[31] and the TFOS MGD Report,[32] which recommends performing a series of tests that establish a classification based on the severity of the results: mild, moderate, and severe. Inclusion criteria included adults between 18 and 85 years of age who accepted and signed the informed consent form and expressed their intention to follow the protocol, attended all visits, and met the inclusion and exclusion criteria.

Exclusion criteria were patients with severe DED-MGD; grade V and VI skin pigmentation on the Fitzpatrick scale, the use of photosensitizing drugs and/or the use of anticoagulant and/or immunosuppressive drugs; patients with light-triggered seizure disorders; pregnancy; patients with a personal or family history of skin cancer or with tattoos or skin conditions (eg, eczema) in the areas to be treated; patients who had been exposed to the sun for several hours in the 3 weeks before treatment.

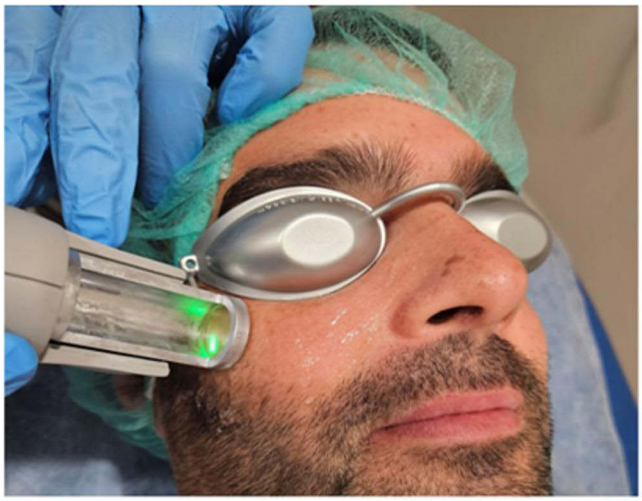

Figure 1 Laser treatment with the standard handpiece on the skin of the periocular area.

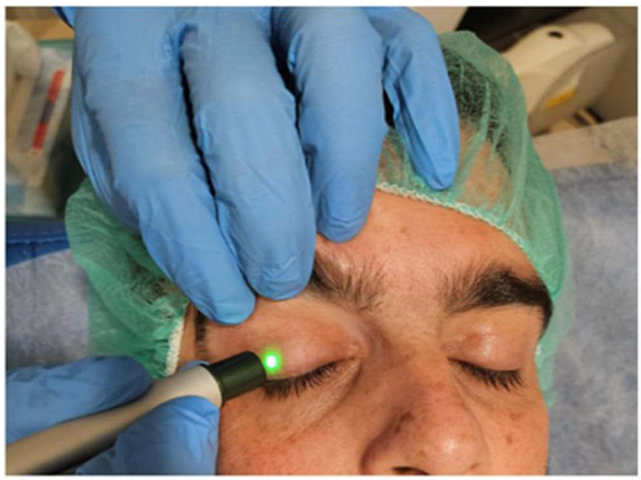

Figure 2 Laser treatment applying the pencil handpiece directly to the skin of the upper eyelid.

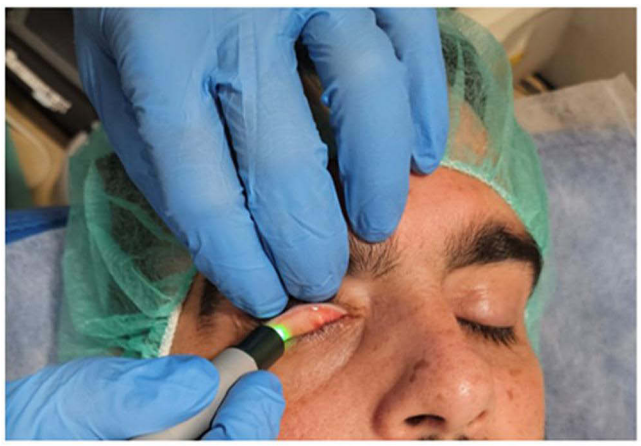

Figure 3 Laser treatment applying the pencil handpiece directly onto the tarsal conjunctiva.

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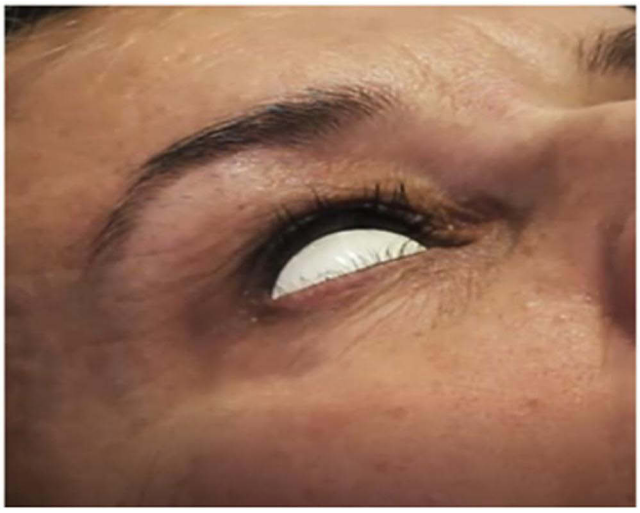

Figure 4 Detail of the eye protection (corneal shield), before performing the laser treatment.

The criteria for excluding patients in this ophthalmological study included the following:

1. A history of ocular trauma.
2. Severe ocular surface disease.
3. Active allergy or inflammatory disease affecting the ocular surface that is not related to DED or MGD.
4. Uncontrolled systemic diseases or the use of systemic medications that alter the tear film or affect the ocular surface.
5. The use of any drops other than artificial tears within the last month.
6. Recent or current treatments for DED or MGD, such as radio frequency or intense pulsed light (IPL) therapy.
7. Skin treatments within the last month.
8. Current use of punctal plugs.
9. Probing or mechanical expression of the meibomian glands in the last month.
10. Lacrimal drainage disease.
11. Pigmented lesions in the treatment area.

Additionally, patients who experienced dry eye following corneal refractive surgery (PRK or LASIK) or who wear contact lenses were excluded, as the specific nature of their dryness requires a different study approach.

Patients on standard eye care such as warm compresses, lid hygiene or eyelid massage were not excluded, but it was recommended not to continue during the study. It was only allowed to maintain lubricant eye drops but no more than 3 times a day.

Treatment Procedure

Laser treatment was performed with the device (RedTouch, Deka Mela srl, Florence, Italy) a new non-ablative red-light laser emitting system with a 675 nm wavelength through a 13×13 mm scanning system that can target collagen and melanin with precision. The laser can be optimized with a contact and temperature sensor included in the handpiece. This can produce 0.7-mm wide fractional micro- (DOT) selective thermal or subablative treatment on the skin. Through the Power and DOT pulse duration (Dwell time) parameters, each DOT is exposed to radiation from the laser source. The scanning technology partially covers the treatment area uniformly by introducing a spacing between every DOT. Each emission may safely penetrate a thermal column more than 1 mm deep because the device has a skin cooling system to avoid heat-induced damage to the epidermis and reduce downtime.

Each patient underwent an energy therapy assessment on a particular test based on their skin type and tolerance level. The endpoint was identified as mild erythema. The handpiece was gently passed over the skin's surface in locations near one another, without overlapping or treating other areas. Before each treatment, the setting parameters were selected. The intensity of the laser was adjusted in each handpiece, depending on whether the area treated was periocular and whether the lid skin, tarsal conjunctiva or lid margin was treated. The procedure started protecting the eyebrows and the eye with a corneal shield in G1 and G2 patients and protecting the lashes only in G2 patients. Ultrasound gel was applied to the periocular area and lids, and after this preparation, the laser treatment was carried out. In G1 patients, we applied the scanner handpiece on the skin of the periocular area (5 cm from the orbital rim) and lids, with a pattern scanning system (13x13 mm) with power of 10 W, Dwell time: 25 ms, spacing: 1000 mcm, Smart Stack: 1 and cooling: 10°C, Treatment was carried out by passing the handpiece over the interested areas while applying light pressure, and no overlapping. In G2 patients, the same scanning treatment was performed on the eyelids and periocular area as in G1 and was also completed by applying the small pencil handpiece (3 mm single spot), on the tarsal conjunctiva of both eyelids, after the instillation of anesthetic drops (Colirofta, 5 mg/mL eye drops solution of Tetracaine hydrochloride/Naphazoline hydrochloride), with the power of 1 W, Dewell time: 25 ms, Smart Stack: 1, at 1 mm away from the surface and without cooling, passing 3 times over the conjunctival surface and the lid-margin of the eyelids and avoiding overlapping (Figure 1). Both eyes were treated in all the 4 sessions. After the treatment, the protective shield and gel were removed, and cold water-soaked gauzes were used to cool down the skin. Post-treatment care was carried out by hydrating, soothing and protective water-based solution (Thermal water URIAGE, France), daily applied to the treated area to help restore the skin barrier and maintain an optimum moisturization, and it was also recommended to avoid sun exposure for the first 2 weeks. Side effects such as blistering, scarring, burns, hypopigmentation or hyperpigmentation were monitored during and after every treatment. The subjects received four separate treatment sessions every 3 weeks. Mechanical expression of the Meibomian glands was not performed after the laser session.

Clinical Evaluation

Clinical assessments were conducted at the beginning of the study (T0) and at the final visit (T1), which occurred 2 months after the last laser session. The assessments included the following:

1. Symptoms Evaluation: Symptoms were assessed using the Ocular Surface Disease Index (OSDI) questionnaire, which consists of 12 items evaluating ocular discomfort, the effects on visual function and the impact of environmental triggers. Scores range from 0 (none) to 100 (maximum), with a cutoff value of <13 indicating potential issues.
2. Tear Osmolarity (TO): This was evaluated bilaterally from the inferior lateral tear meniscus using the Tear Lab system (Tear Lab Corp, San Diego, CA). Participants were instructed not to use eye drops for at least 2 hours prior to testing. A TO cutoff value of ≥310 mOsm/L and an inter-eye difference of ≥8 mOsm/L were defined as indicators of DED.
3. Non-Invasive Tear Meniscus Height (NITMH): NITMH was measured using the Keratograph 5M (Oculus, Wetzlar, Germany), which captures infrared images of the tear meniscus. Three zones of the tear river in the lower eyelid (temporal, central, and nasal) were evaluated, and the average of these measurements was calculated. A value of <20 μm was considered the cut-off for the diagnosis of DED.
4. Non-Invasive Tear Break-Up Time (NIBUT): Also measured with the Keratograph 5M, patients were instructed to blink gently three times before focusing on a fixation point. The device analyzed the reflection of Placido rings on the cornea and recorded the time until the first break in the tear film occurred. Three measurements were taken for each eye to ensure reliability. A normal cutoff for NIBUT was >10 seconds, while <5 seconds indicated dry eye diagnosis.
5. Corneal Fluorescein Staining (CFS): This assessment was performed using a slit lamp under blue light illumination with a yellow filter. After instilling 2% sodium fluorescein into the bulbar conjunctiva, patients blinked naturally three to five times and then were instructed to look straight ahead without blinking. CFS was evaluated using the Baylor grading scheme across five zones of the cornea (central, temporal, nasal, superior, and inferior), with scores

ranging from 0 (absent) to 4 (extensive staining). The degree of CFS severity was categorized as 0=absent, 1=mild (grades 1 and 2), 2=moderate (grade 3), and 3=severe (grade 4).

6. Eyelid Margin and Meibomian Gland Assessments: Evaluations were conducted with a slit lamp and the Keratograph 5M based on the TFOS MGD Report recommendations. The eyelid margin was assessed for rounding, irregularity, telangiectasia/vascularity, and blepharitis, each scored from 0 (normal) to 3 (severe). Meibomian gland assessments involved multiple subscores, including the number of plugged orifices, expressed secretion quality, expressibility, and gland dropout. The Arita scoring system (meiboscore) was used to evaluate gland loss, with scores ranging from 0 (no loss) to 3 (loss of more than two-thirds of the area).
7. Blinking Study: We evaluated blinking dynamics, the blink amplitude and inter-blink time (IBT) using a video recorded with the Keratograph 5M. Patients were asked to maintain relaxation and look at the device's central fixation point while blinking naturally. The blink amplitude was measured by determining the maximum distance between the superior and inferior eyelid margins, expressed in millimeters. IBT was calculated as the average time from the end of one blink to the start of the next. The coefficient of variation (CV) for IBT was also assessed to reflect the regularity of the blinking pattern.

Safety evaluations were conducted at every visit to assess both local and systemic adverse events.

Statistical Analysis

Data was analyzed with IBM SPSS Statistics for Windows (Version 29.0. Armonk, NY: IBM Corp). Descriptive statistics for all patient data were obtained and expressed as mean ± standard deviation (SD). In each treatment group, G1 and G2, the comparative analysis was performed at the beginning of the treatment, T0, and at the end, T1, using the non-parametric Wilcoxon signed-rank test. For the comparative analysis of results at the end of the study, T1, between the 2 treatment groups, G1 vs G2, the non-parametric Mann–Whitney *U*-test was used. Finally, to analyze the correlation between different tests in evaluating the patients, the Spearman's rank correlation coefficient test was used for non-parametric continuous variables and the Chi-square test (χ^2) when the variables were categorical. Results were considered statistically significant for $p < 0.05$.

Results

This is a prospective, longitudinal and open-label study with 70 consecutive patients, divided into two groups of 35 patients each with comparable demographic data and degree of severity (Table 1), receiving a different laser treatment protocol, periocular treatment (G1) versus direct targeting of the meibomian glands (G2).

The results showed significant improvement in all symptoms and signs evaluated, OSDI, CFS, NITMH, NITBUT, Osmolarity and Schirmer test1, both in G1 and G2, but with better results in G2 (G1 vs G2, $p < 0.001$), when adding laser treatment in the tarsal conjunctiva and lid-margin. Regarding the signs of the Meibomian glands and the lid-margin, there is also a significant improvement in the 2 groups but more important in G2 (G1 vs G2, $p < 0.001$). The blinking analysis also showed improvement in both groups, and again, when comparing G1 vs G2, G2 was better ($p < 0.001$). Table 2 details.

Table 1 Demographic Data (n, Mean and Standard Deviation) of Patients in Both Groups of Treatment, G1 (Laser on the Skin of the Eyelids and Periocular Area) and G2 (Laser as in G1 Combined with Laser on the Lid Margin and the Upper and Lower Tarsal Conjunctiva)

Group/Degree of Severity	**G1 n:35**	**G2 n:35**
	22 Women	21 Women
	Age: 25–83 years, 55.0±14.02	Age: 18–80 years, 54.01±55.17
Mild	n:16, 10 Women, 56.0±13.5 y	n: 14, 9 Women, 54.17±15.1
Moderate	n: 19, 14 Women, 54.4±14.7 y	n: 21, 16 Women, 53.9±16.5 y

Table 2 Results (Mean and Standard Deviation) of Patients in Both Groups of Treatment, G1 (Laser on the Skin of the Eyelids and Periocular Area) and G2 (Laser as in G1 Combined with Laser on the Lid Margin and the Upper and Lower Tarsal Conjunctiva), with the Statistical Analysis, Expressed with the "P" of Each Test, in Each Treatment Group and with the Comparison of G1 vs G2. We Considered Significant $p < 0.05$.

Groups/ Clinical Results	G1			G2			G1 vs G2
	T0	T1	p	T0	T1	p	p
OSDI	55.9±12.5 (28–80)	36.6±11.5 (8–50)	<0.001	46.5±17.5 (8–89)	14.9±7.5 (2–26)	<0.0001	<0.001
CFS	1.37±0.5	0.5±0.5	<0.001	1.65±0.7	0.32±0.5	<0.0001	<0.001
NITMH	12.03±4.1 (6–19)	15.43±4.61 (8–26)	<0.001	11.91±5.5 (4–28)	21.68±4.4 (12–29)	<0.0005	<0.003
NITBUT	7.06±2.6 (3–16)	10.08±2.6 (6–17)	<0.0007	6.6±2.4 (2–12)	14.4±2.3 (10–20)	<0.0001	<0.005
Osmolarity	318.68±9.25 (290–342)	311.85±9.94 (293–320)	<0.005	315.82±6.94 (290–328)	292.74±6.5 (295–309)	<0.0001	<0.001
Schirmer T1	5.97±2.2 (3–12)	8.57±1.9 (5–14)	<0.001	6.6±4.17 (1–23)	13.30±1.93 (8–25)	<0.0001	<0.001

Abbreviations: OSDI, Ocular Surface Disease Index; CFS, Corneal Fluorescein Staining; NITMH, Non-Invasive Tear Meniscus Height; NITBUT, Non-Invasive Break Time.

The improvement values from the initial values in % were significant in all aspects, being more relevant for the G2 group; in OSDI (Ocular Surface Disease Index) was for G1: 34.5% and for G2: 67.9%; in CFS (Corneal Fluorescein Staining) was for G1: 63.5% and for G2: 80.6%. The improvement in NITMH (Non-Invasive Tear Meniscus Height) was for G1: 28.3% and for G2: 82.1%, and in NITBUT (Non-Invasive Tear Break-Up Time) was for G1: 42.8% and for G2: 118.2%. The Osmolarity changes were G1: 2.1% and G2: 7.3%. The Schirmer T1 improvement was in G1: 43.6% and in G2: 101.5%.

The analysis of symptoms OSDI is in Table 2, and we can observe a significant improvement in both groups, with a gain of more than 20 points after laser, 54.3% in G1 and 80% in G2. The improvement in the OSDI was reflected in the subjective questionnaire of symptoms, related to the sensation of dryness and pain and in the aspects related to vision. In G1, the score decreased from 55.9 ± 12.5 to 36.6 ± 11.5 ($p < 0.001$), corresponding to a reduction in dry eye symptoms, more clearly in G2, with scores dropping from 46.5 ± 17.5 to 14.9 ± 7.5 ($p < 0.0001$). The comparison between the two groups revealed that G2 experienced a significantly greater improvement ($p < 0.001$).

The ocular surface and tear film results are shown in Table 2, improving CFS, TMH, NITBUT and Osmolarity. The results from the clinical parameters demonstrate significant improvements in both groups (G1 and G2) across several measures. In terms of CFS, G1 showed a reduction from 1.37 to 0.5 ($p < 0.001$), while G2 experienced a more significant improvement, decreasing from 1.65 to 0.32 ($p < 0.0001$). The difference between G1 and G2 was also significant ($p < 0.001$), with G2 showing a more substantial reduction. Regarding NITMH, G1 increased from 12.03 to 15.43 ($p < 0.001$), and G2 had a larger improvement, rising from 11.91 to 21.68 ($p < 0.0005$). The difference between the two groups was significant ($p < 0.003$), with G2 demonstrating a greater increase in tear meniscus height. For NITBUT, G1 showed an increase from 7.06 to 10.08 ($p < 0.0007$), while G2 experienced a more pronounced improvement, rising from 6.6 to 14.4 ($p < 0.0001$). The difference between the two groups was significant ($p < 0.005$), with G2 again showing a greater improvement. In Osmolarity, G1 demonstrated a small decrease from 318.68 to 311.85 ($p < 0.005$), whereas G2 had a larger reduction, from 315.82 to 292.74 ($p < 0.0001$). The difference between the two groups was significant ($p < 0.001$), with G2 showing a more notable change. Finally, Schirmer T1 results showed G1 improving from 5.97 to 8.57 ($p < 0.001$), and G2 exhibiting a larger improvement, from 6.6 to 13.30 ($p < 0.0001$). The difference between G1 and G2 was significant ($p < 0.001$), with G2 demonstrating a more significant increase in tear production.

The analysis of the eyelid and lid-margin characteristics revealed significant improvements in both groups (G1 and G2), Table 3. Thickness, regularity, vascularization and blepharitis, evaluating the qualitative grade of severity, where 0 = absent, 1 = mild, 2 = moderate and 3 = severe. In lid-margin thickness, G1 showed a reduction from 1.51 ± 0.61 at T0 (range 1–3) to 0.97 ± 0.62 at T1 (range 0–2), with a significant improvement ($p < 0.001$). G2 also showed improvement, from 1.54 ± 0.61 at T0 (range 1–3) to 0.97 ± 0.62 at T1 (range 0–3), with a highly significant change ($p < 0.0001$). No significant differences were found between the groups at T1. For lid-margin regularity, G1 improved

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Table 3 Results (Mean and Standard Deviation) of the Lid-Margin in Both Groups of Treatment, G1 (Laser on the Skin of the Eyelids and Periocular Area) and G2 (Laser as in G1 Combined with Laser on the Lid Margin and the Upper and Lower Tarsal Conjunctiva), with the Statistical Analysis, Expressed with the "P" of Each Test, in Each Treatment Group and with the Comparison of G1 vs G2. We Consider Significant $p < 0.05$

Groups/Lid Margin	G1			G2			G1 vs G2
	T0	T1	p	T0	T1	p	p
Thickness	1.51±0.61 (1–3)	0.97±0.62 (0–2)	<0.001	1.54±0.61 (1–3)	0.97±0.62 (0–2)	<0.001	NS
Regularity	1.63±0.6 (1–3)	1.26±0.56 (0–3)	<0.005	1.51±0.66 (1–3)	0.97±0.62 (0–3)	<0.001	<0.03
Vascularization	1.86±0.65 (1–3)	0.91±0.51 (0–2)	<0.0005	1.48±0.61 (0–3)	1.0±0.59 (0–2)	<0.0001	<0.01
Blepharitis	1.71±0.62 (1–3)	0.86±0.49 (0–2)	<0.001	1.94±0.64 (1–3)	0.60±0.55 (0–2)	<0.0001	<0.001

from 1.63 ± 0.60 at T0 (range 1–3) to 1.26 ± 0.56 at T1 (range 0–3, $p < 0.005$), while G2 showed improvement from 1.51 ± 0.66 at T0 (range 0–3) to 0.97 ± 0.62 at T1 (range 0–3, $p < 0.001$). Comparing the two groups at T1, G2 had slightly better results ($p < 0.03$). Vascularization in the lid-margin decreased in G1 from 1.86 ± 0.65 at T0 (range 1–3) to 0.91 ± 0.51 at T1 (range 0–2, $p < 0.0005$), while G2 improved from 1.48 ± 0.61 at T0 (range 0–3) to 1.00 ± 0.59 at T1 (range 0–2, $p < 0.0001$). At T1, G2 had slightly better results than G1 ($p < 0.01$).

In terms of blepharitis, G1 showed an improvement from 1.71±0.62 at T0 (range 1–3) to 0.86±0.49 at T1 (range 0–2), with a significant improvement ($p<0.001$). G2 also showed a notable improvement, from 1.94±0.64 at T0 (range 1–3) to 0.60±0.55 at T1 (range 0–2), with a highly significant reduction ($p<0.0001$). When comparing G1 and G2 at T1, G2 had better results, with a significant difference ($p<0.001$).

The analysis of Meibomian gland expression, secretion quality, number of occluded opercula, and gland dropout showed improvements in both G1 and G2 (Table 4). For Meibomian glands expression, G1 improved from 1.17±0.39 at T0 (range 1–2) to 0.88±0.40 at T1 (range 0–2, $p<0.001$), while G2 improved significantly from 1.66±0.59 at T0 (range 1–3) to 0.57±0.59 at T1 (range 1–3, $p<0.0001$). G2 showed better results than G1 at T1 ($p<0.001$). In secretion quality, G1 improved from 1.23±0.43 at T0 (range 1–2) to 0.68±0.58 at T1 (range 1–2, $p<0.0007$), while G2 improved from 1.37 ±0.55 at T0 (range 1–3) to 0.54±0.50 at T1 (range 1–3, $p<0.0001$), with G2 showing better results at T1 ($p<0.005$). Regarding the number of occluded opercula, G1 improved from 1.2±0.40 at T0 (range 1–2) to 0.83±0.51 at T1 (range 0–2, $p<0.001$), while G2 improved from 1.34±0.55 at T0 (range 1–2) to 0.40±0.49 at T1 (range 0–1, $p<0.0001$), with G2 showing better results at T1 ($p<0.001$). For gland dropout, G1 showed improvement from 1.51±0.61 at T0 (range 1–3) to 1.14±0.49 at T1 (range 1–3, $p<0.005$), and G2 improved from 1.26±0.50 at T0 (range 0–2) to 1.03±0.68 at T1 (range 1–2, $p<0.005$), with no significant differences between groups at T1.

Table 4 Results (Mean and Standard Deviation) of the Meibomian Glands in Both Treatment Groups, G1 (Laser on the Skin of the Eyelids and Periocular Area) and G2 (Laser as in G1 Combined with Laser on the Lid Margin and the Upper and Lower Tarsal Conjunctiva), with the Statistical Analysis, Expressed with the "P" of Each Test, in Each Treatment Group and with the Comparison of G1 vs G2, Considering Statistically Significant $p < 0.05$

Groups/Meibomian Glands	G1			G2			G1 vs G2
	T0	T1	p	T0	T1	p	p
Expression	1.17±0.39 (1–2)	0.88±0.40 (0–2)	<0.001	1.66±0.59 (1–3)	0.57±0.59 (1–3)	<0.0001	<0.001
Secretion Quality	1.23±0.43 (1–2)	0.68±0.58 (1–2)	<0.0007	1.37±0.55 (1–3)	0.54±0.5 (1–3)	<0.0001	<0.005
Occluded Opercula	1.2±0.40 (1–2)	0.83±0.51 (0–2)	<0.001	1.34±0.55 (1–2)	04±0.49 (0–1)	<0.0001	<0.001
Meibomian Gland Drop	1.51±0.61 (1–3)	1.14±0.49 (1–3)	<0.005	1.26±0.5 (1–3)	1.03±0.68 (1–2)	<0.005	NS

Table 5 Results (Mean and Standard Deviation) of Blink Dynamics in Both Groups of Treatment, G1 (Laser on the Skin of the Eyelids and Periocular Area) and G2 (Laser as in G1 Combined with Laser on the Lid Margin and the Upper and Lower Tarsal Conjunctiva), with the Statistical Analysis, Expressed with the "P" of Each Test, in Each Treatment Group and with the Comparison of G1 vs G2, Considering Statistically Significant $p < 0.05$

Groups/Blink Dynamics	G1			G2			G1 vs G2
	T0	T1	p	T0	T1	p	p
Eyelid opening (mm)	8.56±0.55 (7.2–9.4)	0.88±0.63 (7.2–9.7)	<0.005	8.83±0.41 (7.2–9.4)	0.57±0.59 (7.8–9.7)	<0.0003	<0.001
Interblinking time IBT (sec)	2.0±0.57 (0.9–3.6)	3.47±0.5 (2.4–4.5)	<0.001	1.82±0.63 (0.3–3.4)	3.74±0.8 (1.1–5.5)	<0.0001	<0.001
IBT CV%	16.4	17.1		14.6	15.1		

The study also analyzed blinking dynamics, Table 5, focusing on the maximum interpalpebral distance (eyelid opening) and the interblinking time (IBT), as well as the coefficient of variation (CV%) of IBT. In G1, at T0, the eyelid opening was 8.56±0.55 mm (range 7.2–9.4 mm), which improved to 8.88±0.63 mm (range 7.2–9.7 mm) at T1, showing significant improvement ($p<0.005$). In G2, at T0, the eyelid opening was 8.83±0.41 mm (range 7.2–9.4 mm), improving to 9.31±1.59 mm (range 7.8–9.7 mm) at T1, with a very significant improvement ($p<0.0003$). G2 showed better results than G1 at T1 ($p<0.001$). For blinking time, G1's T0 values were 2.05±0.57 s (range 0.9–3.6 s, CV 16.4%), improving to 3.47±0.50 s (range 2.4–4.5 s, CV 17.1%) at T1 ($p<0.001$). In G2, T0 values were 1.82±0.63 s (range 0.3–3.4 s, CV 14.6%), improving to 3.74±0.80 s (range 1.1–5.5 s, CV 15.1%) at T1 ($p<0.0001$). Again, G2 showed better results than G1 at T1 ($p<0.001$).

Discussion

DED-MGD is clinically relevant, with a growing need for treatments. In this study, we showed the clinical improvement with RedTouch laser in signs and symptoms in all patients, with a benefit of adding laser treatment in the tarsal conjunctiva and lid margin, targeting the meibomian glands, although we do not have a control group to compare the results. There is a tendency for better outcomes in patients over 60 years.

The laser improved the Meibomian glands analysis in gland expression, opercula occlusion and secretion quality. The 675 nm laser would reduce the internal diameter of the capillary by increasing the collagen layer of its wall, reducing the lumen and, consequently, the blood flux.[26] By reducing blood flow, hypoxic conditions around the Meibomian glands are restored, thus their functionality. This mechanism of reducing blood flow by constricting the caliber of the capillaries does not generate inflammation and it is more physiological and better tolerated by the surrounding tissues, with better outcomes than microcoagulation produced by IPLs.[21–25] Moreover, Mathew-Steiner et al,[27] reported that some types of collagen show anti-angiogenic properties, inhibiting the migration and proliferation of endothelial cells and inducing apoptosis.[27–29] These effects are probably influenced and amplified by the presence of collagen in the surrounding environment (connective tissue), which contributes to the constriction of the capillaries and reduces blood flow.[28,29]

Red light (600–760 nm), in particular, the 675 nm wavelength shows a high affinity for collagen fibers and melanin,[30,33] with minimal interaction with hemoglobin. RedTouch acts directly on the collagen component, promoting new collagen production via fibroblast activation and the rearrangement of elastic fibers.[33] Due to its high affinity to collagen, the 675 nm laser has also been used for the treatment of other collagen-rich lesions, like acne scars, with good outcomes[26] and for an anti-ageing effect.[34,35] Although a more marked improvement is observed in the elderly population, the benefits are also observed in the younger population.[36]

The blinking dynamics showed an improvement in the interpalpebral distance and the blinking time. These results can be explained, in part, by the action of the laser on the lid dermis and on the collagen of these structures.[33] The most significant benefits were seen in patients older than 60 years. The effect of the laser on the skin would be more relevant in older patients who have a higher laxity of the eyelid skin, and a certain degree of blepharochalasia with a lower eyelid aperture. This would result in an improvement in palpebral dynamics, and a better and more effective blink contributes to better tear film formation and stability,[30] as reflected in the NITBUT values and tear osmolarity results.

Limitations

This study has several limitations, especially in the interpretation of the results obtained, since this is the first time that laser technology has been used in the treatment of DED-MGD. The time of evaluation of the patients, 2 months after the last laser session, limits the duration of the results obtained, as the efficacy of this treatment needs to be validated over time. Some changes in the eyelid margin and the skin may require more time to appear and may not have been detected in the study. Moreover, we did only one analysis at the end of the treatment period, and we are not aware of the progression of improvement. Another important limitation of this study is the lack of a control group to compare the results of the 675 nm laser with other alternative treatments, such as high-intensity pulsed light (IPL). Finally, the hypothesis of the improvement related to inflammation should be validated with the study of the inflammatory biomarkers. Also, the theory of the improvement of the Meibomian glands, by the action of vascularization, and the effect on the oxygen supply should be confirmed by histological studies.

Conclusion

In this study, the RedTouch 675nm laser demonstrates clinical improvement in treating Dry Eye Disease associated with Meibomian Gland Dysfunction, leading to enhanced signs and symptoms. The treatment was carried out in 4 sessions separated by 3 weeks each, and in no case were significant complications observed. The results are consistently better in the group that received the combined laser treatment on the skin of the eyelids and periocular area, with the application of laser directly on the lid margin of the eyelids and the tarsal conjunctiva of both eyelids.

Abbreviations

DED, Dry eye disease; MGD, Meibomian Gland Dysfunction; IPL, Intensive Pulsed Light; TO, tear osmolarity; NITMH, non-invasive tear meniscus height; NIBUT, non-invasive tear break-up time; CFS, corneal fluorescein staining; ST1, Schirmer test; IBT, the interblinking time; CFS, Corneal Fluorescein Staining; SD, standard deviation; MG, Meibomian glands; HIF1α, hypoxia-inducible factor1 α.

Data Sharing Statement

Data that support the study findings are available at the request of the corresponding author.

Ethics Approval and Consent to Participate

All procedures of this study were in accordance with the tenets of the Declaration of Helsinki and approved by the medical ethics committee: Department of Ophthalmology of the Dexeus University Hospital (Autonomous University of Barcelona, Barcelona, Spain) Protocol: PO-2023-03, Code: 2023/122-OFT-DEX.

Patient Consent for Publication

A signed informed consent form was obtained from all participants before starting the study. The patients in the figures provided informed consent for the images to be published.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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