

# Combination Therapy of Intense Pulsed Light Therapy and Meibomian Gland Expression (IPL/MGX) Can Improve Dry Eye Symptoms and Meibomian Gland Function in Patients With Refractory Dry Eye: A Retrospective Analysis

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**Purpose:** To assess the improvement in meibomian gland function and dry eye symptoms in patients with refractory dry eye treated with a combination therapy of intense pulsed light (IPL) and meibomian gland expression (MGX).

**Methods:** Medical records of 81 consecutive patients with dry eye treated with serial IPL/MGX were retrospectively examined to determine the outcome. All patients had a minimum of 6 months of follow-up after the first IPL/MGX treatment. Patients typically received 1 to 4 IPL treatments spaced 4 to 6 weeks apart. Each IPL session included MGX. Thirty-five charts had complete data for inclusion in analysis. We reviewed demographics, ocular histories, Standard Patient Evaluation of Eye Dryness 2 (SPEED2) symptom survey scores, slit-lamp examinations, and meibomian gland evaluations (MGE) at baseline and at each visit before IPL/MGX treatments.

**Results:** The paired *t* test showed a significant ( $P < 0.0001$ ) decrease in SPEED2 with IPL/MGX therapy. Of the 35 patients, 8 (23%) had a  $\geq 50\%$  decrease in SPEED2, 23 (66%) had a 1% to 49% decrease in SPEED2, 1 (3%) had no change in SPEED2, and 3 (9%) had an increase in SPEED2. The Paired *t* test showed a significant increase in MGE in the left eye but not in the right eye (OD  $P = 0.163$  and OS  $P = 0.0002$ ). Thirteen patients (37%) had improved MGE bilaterally. Eight patients (23%) had either a decrease in MGE bilaterally or a decrease in 1 eye with no change in the other eye.

**Conclusions:** This retrospective analysis shows that the combination of IPL and MGX can significantly improve dry eye symptoms (in 89% of patients) and meibomian gland function (in 77% of patients in at least 1 eye).

**Key Words:** meibomian gland dysfunction, ocular rosacea, intense pulsed light, dry eye disease

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Dry eye disease is a common condition that causes ocular discomfort and reduces visual acuity.<sup>1</sup> The 2 categories of dry eye disease are *evaporative dry eye* and *aqueous-deficient dry eye*.<sup>2</sup> Both conditions can involve pathology of the meibomian glands, lacrimal glands, lids, tear film, and surface cells.<sup>2,3</sup> Meibomian gland dysfunction (MGD) is the leading cause of evaporative dry eye<sup>4</sup> and contributes to aqueous-deficient dry eye.<sup>5</sup>

Meibomian glands are modified sebaceous glands located along the upper and lower eyelid margins. Twenty to 40 glands are located along each lid<sup>6</sup> and secrete meibum, the lipid component of tears.<sup>7</sup> MGD is defined by the International Workshop on Meibomian Gland Dysfunction<sup>4</sup> as “a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion.” Patients may experience symptoms of eye irritation and clinically observable ocular surface disease and inflammation due to alteration of the tear film.

MGD is a disease commonly encountered by ophthalmologists. The impact of dry eye on quality of life is comparable to the effect of moderate to severe angina or dialysis treatment.<sup>8,9</sup> The goal of MGD therapy is to provide long-term improvement of symptoms for patients by improving the quality of meibum, increasing meibum flow, improving tear film stability, and decreasing inflammation. Commonly used therapies include preservative-free drops, omega-3 fatty acid supplementation, topical cyclosporine, serum tears, topical azithromycin, oral doxycycline, moisture chambers, intraductal probing, lid margin exfoliation, automated thermal pulsation, warm compresses, and others. Despite the variety of treatment options available, patients often do not experience complete or long-term relief of symptoms.

Forced meibomian gland expression (MGX) was first described in 1921 by Gifford<sup>10</sup> as an effective method of rehabilitating meibomian glands and improving dry eye symptoms. The eyelid margins are forcefully compressed to express gland contents. Korb and Greiner<sup>11</sup> described an improvement in lipid layer thickness and symptoms in 10 patients with MGD treated with MGX. Forceful expression is painful for patients, and some patients are unable to tolerate the pain.

## INTENSE PULSED LIGHT THERAPY

Intense pulsed light (IPL) devices have long been used in the field of dermatology to treat acne rosacea, acne vulgaris, hyperpigmentation, essential telangiectasias, unwanted hair, and photodamaged skin. IPL is a high-intensity light source consisting of visible light in the wavelength range of 515 to 1200 nm. The light is both polychromatic and incoherent.<sup>12</sup> Most patients with dry eye undergoing IPL receive this treatment as a last resort after trying several other therapies. They often have severe MGD and few to no expressible glands. The specific mechanism of IPL therapy in improving dry eye symptoms is unknown. It is postulated that oxyhemoglobin in blood vessels located on the surface of the skin absorbs light emitted from the flash lamp. The absorption generates heat that coagulates the red blood cells, leading to thrombosis of the blood vessels.<sup>13–16</sup> Given the proposed mechanism of IPL, patients with ocular rosacea and associated lid margin telangiectasias would be the best candidates for treatment. Treatments are spaced 4 to 6 weeks apart, and patients typically receive 1 to 4 treatments with no established limit on the number of treatments.

There are approximately 40 centers performing IPL nationally; however, specific guidelines on selecting the ideal IPL candidate have not been published. Two peer-reviewed studies have been reported to date on the efficacy of combined IPL/MGX for treating MGD as Dr Rolando Toyos, the ophthalmologist who introduced IPL to patients with dry eye, has described. In their 3-year retrospective review of 91 patient records, Toyos et al<sup>17</sup> found a statistically significant improvement in tear film breakup time ( $P < 0.001$ ). Physician-judged improvement in meibum and lid margins was present in 94% and 98% of patients, respectively. Eighty-seven percent of patients showed improvement in clinical signs, and 93% had subjective amelioration of their evaporative dry eye disease. Thirteen percent of patients experienced an adverse event. Vora and Gupta<sup>18</sup> conducted a retrospective review of 37 patient records and found a statistically significant decrease in scoring of lid margin edema, facial telangiectasia, and lid margin vascularity and improvement in the meibum quality score ( $P < 0.001$ ). They also found a significant increase in the oil flow score and tear film breakup time ( $P < 0.001$ ) and a significant decrease in ocular surface disease index scoring ( $P < 0.001$ ). One prospective trial has been conducted on the efficacy of IPL (without MGX) for treating MGD. In their study, Craig et al<sup>19</sup> reported that IPL alone was effective in improving the lipid layer and patient symptoms. Gland function was measured indirectly using lipid layer grading. In this study, we report on our early results of serial IPL/MGX in patients with ocular rosacea and dry eye disease.

## MATERIALS AND METHODS

Mayo Clinic institutional review board approval was obtained for a chart review. In our referral practice at the Mayo Clinic in Arizona, patients undergoing IPL/MGX had previously failed or refused (because of side effects/cost) attempts with conventional treatments such as artificial tears, hot compresses, lid hygiene, omega-3 fatty acids, punctal

plugs, oral doxycycline, topical cyclosporine, topical steroid, topical nonsteroidal antiinflammatory, topical azithromycin, automated thermal pulsation, and intraductal probing. Patient selection and the IPL treatment protocol followed the established technique of Toyos et al.<sup>17</sup> In brief, potential IPL candidates underwent Fitzpatrick skin typing to classify their skin response to ultraviolet exposure by the degree of burning and tanning. Fitzpatrick skin types I, II, III, and IV were included as recommended by the manufacturer, and V and VI were excluded. The Quadra Q4 IPL Machine (DermaMed Solutions, LLC, Lenni, PA) was used for all patients. Patients did not have active lesions, skin cancer, or specific skin pathology that would exclude treatment with IPL.

Patients received 1 to 4 IPL treatments, each spaced 4 to 6 weeks apart. At the first treatment, each patient underwent Fitzpatrick skin typing, and the IPL machine was set to appropriate settings—1D, 2D, or 4A. At each treatment, the eyelids were bilaterally closed and sealed shut with IPL-Aid disposable eye shields (Honeywell Safety Products, Smithfield, RI). After generous application of ultrasonic gel to the treated skin, patients received approximately 30 pulses (with slight overlapping applications) from the right preauricular area, across the cheeks and nose to the left preauricular area, treating up to the inferior boundary of the eye shields. Each treatment was followed by MGX with a cotton tip applicator and digital pressure to empty meibum from bilateral upper and lower eyelids. Patients used preservative-free ketorolac drops twice a day for 2 days after IPL treatment. Slit-lamp examination was performed before each treatment. Patients underwent 4 monthly examinations and IPL/MGX treatments or until symptoms were resolved to their satisfaction, treatments became intolerable, or they were unable to continue the treatment protocol.

The medical records of 81 patients with dry eye treated with IPL/MGX between January 2013 and December 2014 were retrospectively examined to determine outcomes. Thirty-five charts had adequate records for inclusion in data analysis. Patients were excluded if records were missing MGD and Standard Patient Evaluation of Eye Dryness 2 (SPEED2) data or if patients withdrew from therapy after 1 IPL treatment. Demographics, ocular histories, SPEED2 scores, slit-lamp examinations, and meibomian gland evaluations (MGE) at baseline and 6 to 20 months after the start of IPL treatments were reviewed. SPEED2 is a validated 14-item questionnaire to evaluate the severity and frequency of dry eye symptoms, use of drops or ointment, and frequency of vision problems that patients subjectively experience. MGE is the number of lower eyelid meibomian glands observed yielding liquid secretion with application of consistent gentle pressure between 0.8 g/mm<sup>2</sup> and 1.2 g/mm<sup>2</sup> to the external eyelid margin. The MGE value correlates with dry eye symptoms.<sup>20</sup>

Patients completed a 14-item SPEED2 questionnaire before treatments began and up to 6 to 20 months after the start of treatment. Compared with the established ocular surface disease index, SPEED2 is a validated, shorter questionnaire that is easier to interpret.<sup>21</sup> The purpose of SPEED2 is to evaluate the severity and frequency of dry eye symptoms, use of drops or ointment, and frequency of vision

problems that patients subjectively experience. The score can range from 0 to 28; a higher score indicates more severe symptoms.

### Statistical Analysis

Statistical software GraphPad Prism (GraphPad Software, Inc, La Jolla, CA) was used for data analysis. Descriptive statistics for all patient data were obtained. Paired *t* tests were performed to compare the mean pre- and post-treatment MGE and SPEED2 scores. Linear regression and Pearson correlation analyses were performed to evaluate the correlation between the change in SPEED2 and change in MGE. Results were considered statistically significant for  $P < 0.05$ .

## RESULTS

Table 1 illustrates the demographics of our patient group. The mean patient age was 61 (median, 64; range 20–84) years, which reflects our retired population that is overall older than other dry eye studies (Craig et al, mean = 45 years<sup>19</sup>; Korb and Greiner, range = 25–35 years<sup>11</sup>). As expected, the majority (77%) of the patients were women. More than half (63%) of the patients had undergone previous ocular surgery and/or blepharoplasty. The average duration of dry eye disease was 4 years (range, 0–30). The average number of IPL treatments received was 4 (range, 2–6).

Table 2 outlines previous surgeries and comorbid conditions that may contribute to dry eye symptoms in the total patient population. Many patients had previous ocular surgeries and were taking systemic medications that may impact dry eye. Table 3 shows the frequency of other dry eye therapy used. The majority of the patients had been treated with artificial tears, omega-3 fatty acid oral supplementation, and oral doxycycline. Some patients had specific etiologies of dry eye disease such as graft-versus-host disease or Sjögren syndrome. Within 3 months of starting IPL, 11 patients (31%) had started concurrent therapy with topical azithromycin, punctal occlusion for aqueous deficiency, doxycycline, and/or omega-3 fatty acid oral supplementation. Table 4 details pre-IPL and post-IPL SPEED2 and MGE values of the patient population.

After a series of IPL/MGX treatments, patients demonstrated a statistically significant ( $P < 0.0001$ ) decrease in

**TABLE 1.** Patient Population Demographics

Demographic Factor	N (Frequency)
Sex	
Female	27 (77%)
Male	8 (23%)
Age, mean (range), yrs	61 (20–84)
Duration of dry eye disease, mean (range), yrs	4 (0–30)
Previous ocular surgery/blepharoplasty	22 (63%)
Previous LipiFlow	22 (63%)
≥20 points on pretreatment SPEED2	15 (43%)

SPEED2, Standard Patient Evaluation of Eye Dryness 2.

**TABLE 2.** Relevant Ocular Histories of Patients

Surgery or Condition	No. Patients (N = 35)	Percentage of Patients
Cataract extraction, intraocular lens placement	7	20
Laser in situ keratomileusis	6	17
Retinal detachment	0	0
Blepharoplasty	7	20
Eyeliner tattooing	1	3
Other surgeries*	7	20
Incomplete blink	4	11
Contact lens wear	11	31
GVHD	8	23
Sjögren syndrome	1	3
Glaucoma	2	6
Lacrimal duct obstruction	2	6
Other corneal conditions†	8	23
Medications: antihypertensive, anticholinergic, antidepressants, opioids, benzodiazepines	21	60

\*Lid surgery for actinic keratosis, conjunctival cautery, RK, or lacrimal duct stent.  
†Other corneal conditions: Fuchs dystrophy, map dot fingerprint changes, SLK, or keratoconus.  
GVHD, graft-versus-host disease.

SPEED2 scores (paired *t* test). Patients showed various levels of improvement of their symptoms and rarely worsening of symptoms. Of the 35 patients, 8 (23%) had a ≥50% decrease in SPEED2, 23 (66%) had a 1% to 49% decrease in SPEED2, 1 (3%) had no change in SPEED2, and 3 (9%) had an increase in SPEED2 (Table 2).

After 1 IPL/MGX treatment, 71% of patients perceived improvement in symptoms. After a third treatment, an additional 12% of patients noted a marked decrease in dry eye symptoms. After a third treatment, the remaining 12% of

**TABLE 3.** Previous Therapies Tried by Patients

Past Therapies Tried Without Improvement of Symptoms	No. Patients (N = 35)	Percentage of Patients
Omega-3 fatty acids	31	89
Preserved artificial tears	29	83
Hot compresses	23	66
Preservative-free artificial tears	22	63
Topical azithromycin	22	63
Punctal plugs	19	54
Doxycycline/minocycline	15	43
Punctal occlusion*	9	26
Moisture chambers	6	17
Topical azithromycin	5	14
Lid hygiene†	5	14
Occlusive dressing	5	14
Blinking exercises	4	11
Maskin probing	4	11

\*Punctal cautery.  
†Ocusoft scrub, baby shampoo.

**TABLE 4.** Changes in SPEED2 Scores and MGE

Subjects by Change in SPEED2	N (%)	Average % Change in SPEED2 (Range)	Average Change in SPEED2 (Range)	Average Change in MGE OD (Range)	Average Change in MGE OS (Range)
All	36 (100)	35% (−47% to 100%)	5 (−7 to 15)	2 (−3 to 14)	3 (−2 to 13)
≥50% decrease	8 (23)	61% (50% to 100%)	9 (5 to 15)	3 (−1 to 12)	2 (−1 to 7)
1%–49% decrease	23 (66)	28% (5% to 48%)	5 (1 to 10)	1 (−3 to 10)	3 (−2 to 13)
No change	1 (3)	0%	0	−1	5
Increase	3 (9)	32% (22% to 47%)	−4 (−2 to −7)	3 (−1 to 14)	0 (−1 to 3)

MGE, meibomian gland evaluation; SPEED2, Standard Patient Evaluation of Eye Dryness 2.

patients noted a marked decrease in dry eye symptoms. This result guides counseling of our patients regarding IPL/MGX. If no response is perceived after the third IPL/MGX treatment, further IPL/MGX is unlikely to be therapeutic.

Clinically, the MGE significantly improved in the left eye, but the right eye did not achieve statistical significance with IPL/MGX serial treatment (OD  $P = 0.163$  and OS  $P = 0.0002$ , paired  $t$  test). Fourteen patients (40%) had improved MGE bilaterally. Twenty-seven (77%) patients had improved MGE in 1 or both eyes. Eight patients (23%) had either a decrease in MGE bilaterally or a decrease in 1 eye with no change in the other eye. The Pearson correlation coefficient between the change in SPEED2 and change in MGE was inversely related but not statistically significant (OD 0.039,  $P = 0.825$  and OS 0.057,  $P = 0.745$ ). Patients who responded adversely with either an increase in SPEED2 or a decrease in MGE did not develop skin or ocular abnormalities on slit-lamp examination.

Our cohort had a severe level of disease overall, reflecting possibly more decades of MGD combined with arid desert climate. Forty-three percent (15/35) of patients scored  $\geq 20$  in their pretreatment SPEED2 (Table 1). One hundred percent of these severely affected subjects experienced improvement in the SPEED2 score (ranging from 5% to 65%), which is a greater percentage of improvement than that of the total study population. Improvement in MGE in 1 or both eyes was present in 80% (12/15) of these patients, which is also a higher percentage than that of the total study population.

Interestingly, 22 patients (63%) in the study had previously undergone thermal pulsation treatment<sup>22</sup> (Lipi-Flow; TearScience, Inc, Morrisville, NC) without improvement of symptoms after 3 months. Subanalysis shows that the majority of these prior thermal pulsation–treated patients had improvement in SPEED2 in response to IPL (86%, 19/22). In this group of patients with improved SPEED2 scores, 21% (4/19) had a  $\geq 50\%$  decrease in their SPEED2 scores.

## DISCUSSION

Evaporative dry eye is the most common cause of dry eye. Quality-of-life is significantly adversely affected by dry eye disease.<sup>8,9</sup> The typical referral dry eye clinic treats patients who have had the disease for many years and have failed multiple modalities of dry eye treatment. In our experience, SPEED2 scores improved in 89% of patients in

response to IPL/MGX therapy. An improvement in MGE in at least 1 eye was seen in 77% of patients.

Although MGE is known to correlate with dry eye symptoms,<sup>20</sup> subjective improvement (SPEED2) did not always correlate with physical improvement in MGE in our study. We suspect that there is an alternate path of reduction of symptoms through lessening of inflammation that cannot be explained in our study. The mechanism of action of IPL/MGX on dry eye symptoms is not known at this time. It is postulated that the oxyhemoglobin of superficial skin blood vessels absorbs the yellow wavelength of IPL and converts light energy to heat energy that thromboses the vessels, decreasing superficial blood flow, which decreases inflammation to the lid margin.<sup>13–16</sup> We know that the heat of the lamp itself does not liquefy the meibum, because heat is not applied to the glands directly and the temperature of the skin only increases by 1°C.<sup>19</sup> Our experience does support treating ocular rosacea with IPL/MGX to improve dry eye symptoms.

It is possible that patients experienced improvement in symptoms because of the effect of MGX or other confounding variables, and not from IPL. However, in support of efficacy of IPL alone, Craig et al<sup>19</sup> found a benefit of IPL treatment without MGX in a prospective, double-masked, placebo-controlled, paired-eye study in a younger patient population (mean age 45 years) of 28 subjects. Subjects had an improved lipid layer grade ( $P < 0.001$ ), noninvasive tear film breakup time ( $P < 0.001$ ), and visual analog scale symptom scores ( $P = 0.015$ ) in the study eye but had no changes in the tear meniscus height or tear evaporation rate. Craig et al found improvement in symptoms after IPL therapy, as was observed in our study.

In our study, IPL/MGX did not show any improvement in a few patients with dry eye. One nonresponder had challenging conditions including incomplete blink or lagophthalmos possibly related to a cosmetic face-lift procedure, which could not be expected to resolve with IPL/MGX. Additional factors that may have caused the complex nature of dry eye disease among these nonresponders were blepharoplasty, laser in situ keratomileusis, contact lens wear, benzodiazepine use, tricyclic antidepressant use, and diuretic use. Meibography was not available at our center at the time of patient evaluation, which would have otherwise allowed for detection of end-stage gland atrophy. We would hypothesize that, like in the case of periodontal disease, there may be some patients whose long-standing MGD with end-stage disease and atrophy cannot be significantly reversed with



IPL/MGX. Possibly, there is a therapeutic window of treatment opportunity for patients with MGD. Providing IPL/MGX to these patients earlier in the disease process may be beneficial; however, this noncovered treatment may be financially prohibitive for some patients. Future prospective long-term studies of MGD will be helpful in establishing guidelines for a therapeutic window of treatment.

IPL/MGX therapy is an alternative option for patients who do not show improvement with automated thermal pulsation. Sixty-three percent of our study patients had previously tried thermal pulsation without improvement of their symptoms. However, patients considering IPL/MGX treatment are counseled that the pain associated with MGX can be intolerable for some, unlike automated thermal pulsation, which is well tolerated by most. From the data we have collected thus far, it is difficult to determine the characteristics of the ideal IPL/MGX candidate and who would be a nonresponder. We did not control for or individually study patient characteristics such as ocular factors, comorbidities, severity of MGD, and age. However, our study showed that if patients do not respond after 3 treatments, a fourth treatment is unlikely to be of any benefit.

In summary, IPL treatment for MGD can improve dry eye symptoms and is a reasonable option for patients who have not shown improvement with other therapies. This study is limited by its retrospective nature and the small sample size. These preliminary data allow us to plan for more rigorous prospective case-controlled studies with long-term follow-up. Future studies are necessary to determine the mechanism of IPL therapy and selection of ideal candidates to better guide our patients with dry eye.

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