

ORIGINAL RESEARCH

Safety and Efficacy of BroadBand Intense Pulsed Light Therapy for Dry Eye Disease with Meibomian Gland Dysfunction

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Background: BroadBand light intense pulsed light (BBL-IPL) therapy has shown to reduce hordeolum and blepharitis frequency. This study aims to evaluate the efficacy and safety of BBL-IPL therapy in patients with dry eye disease (DED) from meibomian gland dysfunction (MGD).

Methods: This is a retrospective, consecutive case series of 48 patients with DED from MGD who underwent BBL-IPL therapy from October 2016 to January 2019 at a single, outpatient clinic in Ontario, Canada. Clinical outcomes included first and average non-invasive keratograph tear break-up times (NIKBUT), bulbar redness (BR) scores, tear meniscus heights (TMH), visual acuity (VA) and meibograph grades. Patient-reported outcomes included the Canadian dry eye assessment (CDEA) questionnaire and patient subjective assessment (PSA) scores. Outcomes were measured at baseline and after completion of 4 monthly BBL-IPL sessions.

Results: The mean severity of dry eye symptoms as measured by the CDEA and PSA decreased significantly from 19.78 ± 9.62 to 12.08 ± 7.40 (p < 0.001) and from 7.65 ± 1.74 to 4.77 ± 2.03 (p < 0.001), respectively. Twenty-five percent of patients reported no dry eye symptoms after treatment. The meibograph grade improved significantly in both eyes (p < 0.001). Approximately 71.0% and 80.1% of patients had an improved meibograph grade in the right and left eye, respectively. Near-significant improvements were observed for BR scores and VA. There was also a trend towards improved first/average NIKBUT and TMH scores. No adverse events were noted.

Conclusion: BBL-IPL appears to be an effective and safe treatment modality in improving dry eye symptoms and meibomian gland function in patients with DED from MGD.

Keywords: BroadBand light, intense pulsed light, meibomian gland dysfunction, dry eye disease

Introduction

Dry eye disease (DED) is a multifactorial disease characterized by the loss of homeostasis of the tear film, resulting in tear film instability, hyperosmolarity and inflammation of the ocular surface. Patients with DED experience ocular discomfort, including foreign body sensation, irritation, burning, redness, and visual disturbances. DED prevalence varies between 5% and 50% across certain populations, making it one of the most common diseases encountered in ophthalmic practice. ^{2,3}

The vast majority of DED patients have evaporative dry eye caused by meibomian gland dysfunction (MGD).⁴ MGD is a chronic condition

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characterized by terminal duct obstruction and/or changes in glandular secretion affecting the stability of the tear film lipid layer. 4-6 Currently, treatment options for DED with MGD include artificial tears, warm compresses, eyelid scrubs, punctal plugs, cyclosporine drops, steroid drops, omega-3 fatty acid supplements and oral tetracycline and azithromycin. 4-7 However, many patients do not achieve complete or long-term relief with these treatments.

In the last few years, intense pulsed light (IPL) therapy has emerged as a possible treatment option for DED with MGD. IPL is widely used in treating dermatological conditions, including facial rosacea, acne, dyspigmentation and dermal vascular lesions.^{2,8-13} In 2002, Toyos et al¹⁴ reported a significant improvement in dry eye symptoms in patients treated for facial rosacea with IPL. Although the exact mechanism of action remains unknown, many studies since then have reported significant improvements in dry eye symptoms, tear break-up times, lipid layer grade and thickness, and/or meibomian gland function, with limited adverse events.^{2,15-23} These studies have used a variety of IPL devices, including M22TM (Lumenis, Israel), 17,20,22 Quadra Q4 (DermaMed Solutions, USA),^{2,14} E>Eye (E-SWIN, France),^{15,16,18,21} and customized treatment protocols, ranging in energy levels, treatment frequencies, number of treatment sessions and treatment durations.

BroadBand Light (BBLTM) is a high-quality, enhanced IPL modality that uses polychromatic, noncoherent, continuous light waves from the visible (420 nm) to the infrared (1400 nm) spectrum.²³ BBL-IPL is known for its relative safety, high skin coverage rate, and minimal recovery time.²⁰ As compared to IPL alone, BBL offers larger spot sizes, a wider range of filters and a continuous pulsing mode, which enhance the efficacy and safety of treatments.²⁴ Recently, Zhang-Nunes et al²³ reported an improvement in dry eye symptoms and blepharitis and hordeolum frequency with some temporary adverse effects after BBL-IPL treatment in patients with DED from MGD. To our knowledge, no other studies have evaluated the use of Sciton® BBL-IPL in treating DED with MGD. We carried out a single-center, retrospective study to evaluate the safety and efficacy of BBL-IPL treatment in patients diagnosed with DED with MGD.

Methods

Patient Selection

This retrospective, consecutive case-series was approved by the William Osler Health System Research Ethics Board and adhered to the Declaration of Helsinki. Medical records of patients treated for DED with MGD using BBL-IPL at a single outpatient clinic between October 2017 and January 2019 were extracted.

Inclusion criteria consisted of patients over the age of 18 diagnosed with DED from MGD by their ophthalmologist (R.M./E.S.T./H.H.C.). The diagnosis of MGD was based on anatomical features of terminal duct obstruction, meibomian gland (MG) dropout, and changes in meibum quality and outflow.^{3,4,25} MGD was classified from stage 1 to stage 4, where stage 1 represents minimal MGD and stage 4 represents severe, marked MGD.²⁵ Only patients with stages 2 to 4 MGD were included. The Fitzpatrick skin type was determined based on sun sensitivity and appearance, ²⁶ where I represents fair skin, and VI represents deeply pigmented skin. Patients with skin types I. II. III and IV were included.

Treatment Procedure

Patients received 4 sessions of IPL laser therapy using the BroadBand LightTM (Sciton[®] Palo Alto, CA, USA) IPL device. All sessions were administered by a plastic surgeon (S.A.). Before treatment, the skin of the upper and lower eyelids was prepped with povidone 5% and anesthetized with clear lidocaine hydrochloride ophthalmic gel 3.5%. Protective metal shields were placed over the patient's sclera and cornea and ultrasonic gel was applied to the skin of both eyelids. A 7-mm circular adaptor was placed on top of a rectangular sapphire crystal and treatment was directed to both eyelids with two passes and 20% overlap. Treatment settings were customized to the patient's skin type (Table 1). Each patient received approximately 30 pulses per session: 5 pulses in 6 treatment areas from the nasal to the temporal side of each eyelid. Treatment sessions were repeated approximately every month for a total of 4 sessions. Patients were advised to avoid direct exposure to sunlight during the treatment course. Patients on any active treatments for DED during the BBL-IPL course were advised to continue them as usual. Patients were advised to withhold additional treatments until after the final follow-up visit.

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Table I Customized BBL-IPL Treatment Settings Based on Patient Skin Type

Fitzpatrick Skin Type	Filter (nm)	Fluence (J/cm ²)	Pulse Width (ms)	Chill Temperature (°C)	Cumulative Dose (J/cm²)	
I–III	560	12–14	20	20	30–35	
IV–V	590	6–10	30	15	15–25	

Patient-Reported and Clinical Outcomes

Patient-reported outcomes include the Canadian Dry Eye Assessment (CDEA) questionnaire and patient subjective assessment (PSA). The 12-item CDEA questionnaire is a modification of the validated Ocular Surface Disease Index (OSDI) used to determine the severity of dry eye symptoms. 27,28 Total scores range from 0 to 48 and symptoms are interpreted as normal (<5), mild (5-20), moderate (21–30), or severe (31–48).²⁸ The question "How much do your eyes bother you?" within the CDEA was evaluated independently and named the patient subjective assessment (PSA). PSA scores range from 1 to 10, with a higher score indicating increased severity of symptoms.

Clinical outcomes included the first and average noninvasive keratograph tear break-up times (NIKBUT), bulbar redness (BR) scores, tear meniscus heights (TMH), visual acuity (VA) and meibograph grades for both eyes. NIKBUT, BR, TMH were measured using the Keratograph® 5M (OCULUS, GmbH, Wetzlar, Germany) by a trained ophthalmic technician blinded to the treatment status.

For NIKBUT measurements, patients were instructed to keep their eyes open as long as possible. First NIKBUT was measured as the time between the last complete blink and the first perturbation of a grid projected onto the surface of the cornea, which the device detects automatically.²⁹ Average NIKBUT was calculated from the average of all break-up events. A break-up time of ≤5 seconds suggests dry eyes.³⁰

The TMH is the distance between the darker edge of the lower eyelid and the tear strip. The final TMH was calculated from the average of the TMH measurements at the left, right and center of each eyelid. A TMH of < 0.25 mm is suggestive of DED. 31

The BR score was determined by the area percentage ratio of vessels to the bulbar conjunctiva under illumination. The maximum ratio is 40%, therefore, BR scores range from 0.0 to 4.0. A higher score represents increased BR.³²

Snellen visual acuity was converted to minimum angle of resolution (logMAR) for analysis based on previous published literature.³³

Meibograph pictures of only the upper eyelids were used to grade MG dropout on a 4-point gestalt scale by an independent ophthalmologist grader (S.S.) blinded to the patient's ocular or treatment status. MG dropout was classified from grade 1 to 4 depending on severity (Figure 1).³⁴

Pre-treatment outcomes were measured approximately 30 days before the first session, while post-treatment outcomes were measured approximately 30 days after the final session.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics Version 27.0 (IBM, Armonk, NY). Continuous variables were described using proportions, means \pm standard deviations (SD), and medians with interquartile ranges (IQR). Categorical variables were described using proportions. Data normality was assessed using histograms and the Shapiro-Wilk normality test. A paired-sample t-test or Wilcoxon signed ranks test for non-normal data was used for comparisons of outcomes before and after treatment. All tests were two-tailed, and Holm-Bonferroni correction was used to confer statistical significance. Regression analyses were conducted to determine associations between gender, treatment interval and skin type and the change in outcomes. A p-value of <0.05 was used to confer statistical significance.

Results

Baseline Features

Of 80 patients treated with BBL-IPL, 48 patients met the inclusion criteria. The median age was 64 years (range 25-97), and the sample was 64.6% (31/48) female (Tables 2 and 3). The median Fitzpatrick skin type was 3 (IQR 2–4) and the median treatment interval was 136 days (IQR 116.5-204) (Table 2). All patients continued their DED medications or therapies throughout the BBL-IPL treatment course, which included lubricant drops, cyclosporine drops, antibiotic drops, steroid drops, Omega-3 supplements, oral doxycycline, as well as warm compresses and lid scrubs (Table 3). Most patients were taking at least two topical or oral medications to manage their DED symptoms (Table 3). Approximately 25.0% (12/48) patients had prior refractive

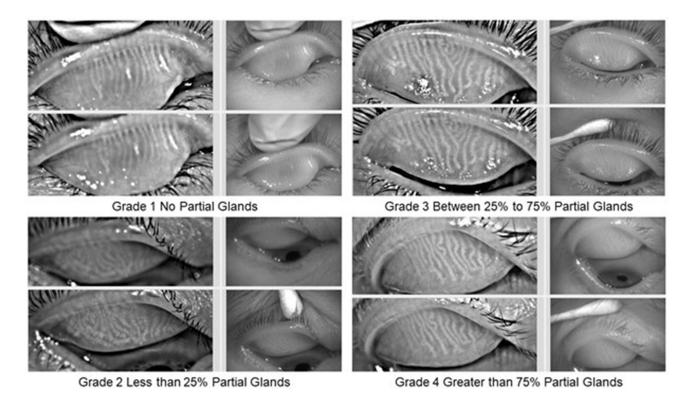


Figure I Meibograph grades based on meibomian gland dropout in upper eyelids only. Grade I represents no partial glands; Grade 2 represents less than 25% partial glands; Grade 3 represents 25% to 75% partial glands; and Grade 4 represents greater than 75% partial glands.

surgery, 2.1% (1/48) had Sjogren's disease and 14.6% (7/48) had diabetes, of which 71.4% (5/7) were being followed for diabetic retinopathy.

Clinical and Patient-Reported Outcomes

The mean CDEA score decreased significantly from 19.78 \pm 9.62 to 12.08 \pm 7.40 (p<0.001; Table 4). Approximately 86.1% (31/36) of patients reported an improved CDEA score, with 25.0% (9/36) experiencing no dry eye symptoms after treatment (Figure 2). The mean PSA score decreased significantly from 7.65 \pm 1.74 to 4.77 \pm 2.03 (p<0.001; Table 4). Approximately 93.5% (29/31) of patients reported an improved PSA score.

The first NIKBUT increased from 4.01 ± 2.71 s to 4.60 ± 2.99 s in the right eye and from 4.11 ± 3.15 s to 5.00 ± 3.64 s in

Table 2 Patient Demographics

	N	Median
Age (years)	48	64 (Range: 25–97)
Treatment Interval (days)	47	136 (IQR: 116.5–204)
Fitzpatrick Skin Type	48	3.0 (IQR: 2.0-4.0)

Abbreviations: N, number of patients; IQR, Interquartile range.

the left eye (OD: p=0.350, OS: p=0.555; Table 4). Average NIKBUT changed from 7.35 \pm 3.14s to 8.50 \pm 4.61s in the right eye and from 8.00 \pm 4.57s to 8.04 \pm 4.62s in the left eye (OD: p=0.178, OS: p=0.600; Table 4).

The mean TMH increased from 0.28 ± 0.12 mm to 0.31 ± 0.12 mm in the right eye and from 0.29 ± 0.1 mm to 0.32 ± 0.16 mm in the left eye (OD: p=0.206, OS: p=0.197; Table 4).

The mean BR decreased from 1.55 ± 0.48 to 1.33 ± 0.47 in the right eye and from 1.59 ± 0.51 to 1.39 ± 0.44 in the left eye (OD: p=0.008, OS: p=0.013; Table 4).

The mean VA improved from 0.34 ± 0.39 (Snellen 20/44) to 0.30 ± 0.41 (Snellen 20/40) in the right eye and from 0.20 ± 0.20 (Snellen 20/32) to 0.14 ± 0.18 (Snellen 20/28) in the left eye (OD: p=0.043, OS: p=0.003; Table 4).

The median meibograph grade decreased significantly from 4 (IQR 3–4) to 3 (IQR 2–3) in both eyes (p<0.001; Table 4). Approximately 71.0% (22/31) and 80.1% (25/31) of patients had an improved meibograph grade in the right and left eye, respectively (Figure 3). No patients experienced worsening in meibograph grade after treatment.

No significant correlations between gender, treatment interval and skin type and patient-reported or clinical outcomes were found (data not reported). Dovepress Murtaza et al

Table 3 Baseline Patient and Clinical Demographics

<u> </u>						
	N (%)					
Female	31 (64.6)					
Dry Eye Medications and Therapies						
Topical preservative-free lubricant drops	29 (60.4)					
Topical cyclosporine 0.05% ophthalmic drops	12 (25.0)					
Topical antibiotic ophthalmic drops (tetracycline,	3 (6.3)					
erythromycin)						
Topical steroid drops (dexamethasone 0.1% or	3 (6.3)					
tobramycin and dexamethasone 0.3%/0.1%)						
Omega 3 supplements	11 (22.9)					
Oral antibiotics (doxycycline)	2 (4.2)					
Warm compresses	16 (33.3)					
Lid scrubs, wipes, and cleansers	28 (58.3)					
Total Number of Topical and Oral Dry Eye Medications						
0 Medications	5 (10.4)					
I Medication	12 (25.0)					
2 Medications	15 (31.3)					
3+ Medications	16 (33.3)					
Fitzpatrick Skin Type						
Туре І	3 (6.3)					
Туре II	17 (35.4)					
Type III	17 (35.4)					
Type IV	11 (22.9)					
	1					

Note: Total: 48 patients.

Abbreviation: N, number of patients.

Adverse Events

No temporary or permanent adverse events were noted.

Discussion

With the recent US Food and Drug Administration approval of the M22TM Lumenis IPL device for treatment of DED, the use of IPL therapy is expected to rise in routine ophthalmic practice. Our study demonstrates that BB-IPL, an enhanced IPL modality, can improve dry eye symptoms and meibomian gland function in patients with DED due to MGD.

After four monthly sessions of BBL-IPL, there was a significant improvement in CDEA and PSA scores. Over 85% of patients reported an improvement in dry eye symptoms, which concurs with improvements seen with IPL therapy alone. The use of patient-reported outcomes in dry eye research is an area of ongoing development. Although the reliability and validity of the CDEA are yet to be established, some studies have found no correlations between symptoms reported in dry eye

questionnaires and clinical tests for dry eye, such as tear break-up time (TBUT), TMH and MG structure. ^{27,35} However, we observed improvements in both patient-reported and clinical outcomes.

We observed a significant improvement in the meibograph grades in both eyes. Nearly two-thirds of our patients had severe MG dropout at baseline, yet over 70% experienced an improvement after treatment. In contrast to IPL, BBL-IPL uses continuous pulsed light in the red and infrared spectrum to provide more evenly distributed heat to the skin and subcutaneous tissues.24 We believe the heat generated from continuous pulsed light has a two-fold effect in improving MG structure and function. Firstly, as the melting point of meibum is higher in patients with MGD, 4,39 BBL-IPL can stimulate MGs making meibum less viscous, and thereby promoting outflow. 15,16,21,22 Secondly, heat from BBL-IPL may reduce harmful bacteria and Demodex mite infection in the eyelids and ocular surface, and limit inflammation and obstruction of MG orifices. 2,15,16,18,23

We also found a trend towards improved NIKBUT and TMH in both eyes, which is consistent with findings in literature on IPL therapy alone. ^{2,14–21} A low NIKBUT contributes to blurred vision, therefore the improvements in first and average NIKBUT values may explain the improvements in VA in both eyes. ^{15,16} Despite significant improvements in meibomian gland structure, four sessions of BBL-IPL therapy may not have produced significant functional improvements in tear quality and volume. We may see further improvements in tear quality and volume with additional sessions.

We found a near-significant decrease in BR, which can explain the significant improvements reported in dry eye symptoms. Through selective photo thermolysis, IPL induces thrombosis of abnormal vascularization in the eyelid margin and conjunctiva. ^{2,15,22} The reduction in redness and inflammation is attributed to the limited access of inflammatory precursor molecules causing tear film instability at the ocular surface. ^{6,23,38} Studies have reported a significant reduction in pro-inflammatory cytokines, including IL-4, IL-6, IL-10, IL-17A, PGE2, and TNF-alpha in tears of patients treated with IPL therapy. ^{2,12,17,20} Improvements in patient-reported visual symptoms may also be explained by the effects of IPL in the 600–950 nm spectrum in relieving chronic inflammatory pain and neurogenic sensitivity. ^{36,37}

Table 4 Clinical and Patient-Reported Outcomes Before and After BBL-IPL Therapy

			Pre-Treatment		Post-Treatment		Treatment Difference
		N	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	P
CDEA (0-48)		36	19.78 ± 9.62	16.00 (13.25–28.50)	12.08 ± 7.40	11.50 (6.50–16.00)	<0.001*
PSA (I-I0)		31	7.65 ± 1.74	8.00 (7.00–9.00)	4.77 ± 2.03	5.00 (3.00–7.00)	<0.001*
NIKBUT (s)	First OD	40	4.01 ± 2.71	3.19 (2.17–5.76)	4.60 ± 2.99	3.63 (2.58–6.02)	0.350
	First OS	37	4.11 ± 3.15	3.50 (2.20–5.10)	5.00 ± 3.64	3.64 (2.62–6.79)	0.555
	Average OD	40	7.35 ± 3.14	7.10 (5.17–9.00)	8.50 ± 4.61	6.82 (5.31–11.92)	0.178
	Average OS	36	8.00 ± 4.57	6.66 (4.94–9.80)	8.04 ± 4.62	7.31 (3.73–11.57)	0.600
BR (0.0-4.0)	OD	29	1.55 ± 0.48	1.60 (1.20–1.80)	1.33 ± 0.47	1.30 (1.05–1.50)	0.008
	OS	30	1.59 ± 0.51	1.40 (1.10–1.63)	1.39 ± 0.44	1.40 (1.10–1.63)	0.013
TMH (mm)	OD	43	0.28 ± 0.12	0.28 (0.21–0.35)	0.31 ± 0.12	0.30 (0.20–0.40)	0.206
	OS	43	0.29 ± 0.10	0.28 (0.21–0.35)	0.32 ± 0.16	0.14 (0.10–0.37)	0.197
VA (logMAR)	OD	26	0.34 ± 0.39	0.18 (0.10-0.30)	0.30 ± 0.41	0.10 (0.00–0.18)	0.043
	OS	26	0.20 ± 0.20	0.18 (0.10-0.30)	0.14 ± 0.18	0.18 (0.0–0.21)	0.003
Meibograph Grade (I–4)	OD	31	3.52 ± 0.71	4.0 (3.0–4.0)	2.81 ± 0.86	3.0 (2.0–3.0)	<0.001*
	OS	31	3.45 ± 0.71	4.0 (3.0–4.0)	2.55 ± 0.76	3.0 (2.0–3.0)	<0.001*

Notes: p values were determined by Wilcoxon signed rank test or paired t-test with Holm-Bonferroni correction (significance indicated by *). Treatment differences for CDEA, First NIKBUT OS, Average NIKBUT OD, BR OD, TMH OD/OS, VA OD/OS and MG OD/OS were determined using a Wilcoxon signed rank test. **Abbreviations**: CDEA, Canadian Dry Eye Assessment; PSA, Patient Subjective Assessment; NIKBUT, Non-Invasive Keratographic Tear Break-up Time; BR, Bulbar Redness; TMH, Tear Meniscus Height; VA, Visual Acuity OD, Right; OS, Left; MD, mean difference; SD, standard deviation; IQR, inter quartile range.

Safety

Zhang-Nunes et al²³ reported reduced blepharitis and hordeolum frequency after one to four sessions of BBL-IPL treatment. However, four of their patients experienced temporary adverse effects including corneal abrasion, hyperpigmentation, and eyelash thinning.²³ Despite two patients using oral doxycycline, a known skin-sensitizing agent, we observed no temporary or permanent adverse events. We also did not observe worsening in VA after treatment. Some studies suggest limiting IPL exposure to only the lower eyelids and Fitzpatrick skin types I–IV.^{2,14} Even though BBL-IPL therapy delivers more evenly distributed heat than IPL alone, our findings support the safety of BBL-IPL in Fitzpatrick skin types I–IV and both eyelids in the context of adequate eye protection for improving MG function.

Overall, BBL-IPL therapy offers similar functional benefits as IPL therapy alone with respect to dry eye symptoms, tear film quality and quantity, conjunctival injection, visual acuity, and meibomian gland health. However, we believe that in routine practice, BBL-IPL is superior to IPL because continuous pulsed light delivers more evenly distributed energy and heat, without compromising safety. Furthermore, BBL-IPL has a wider range of spot sizes and filters allowing for targeted treatment and a better safety profile for darker skin types.²⁴ Interestingly, some recent photobiomodulation modalities, such as low-level light therapy (LLT), which involves athermal photoactivation, have also been shown to improve dry eye symptoms, tear breakup times, and meibomian gland structure with minimal side effects.^{41,42} Future research can compare the effects of BBL-IPL with other athermal treatment modalities like LLT on the improvement of DED from MGD.

Strengths

Unlike previous studies that used customized treatment protocols, a major strength of our study is that we used a standardized treatment protocol that can be easily implemented into routine clinical practice and give

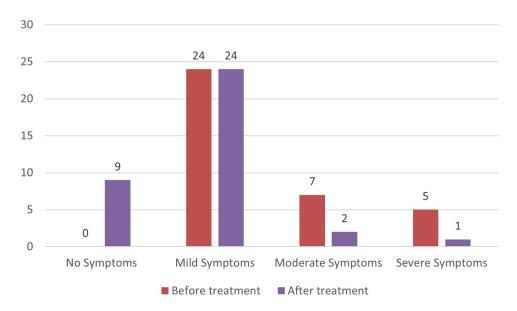


Figure 2 Dry eye symptom severity according to the Canadian Dry Eye Assessment (CDEA) questionnaire before and after BBL-IPL therapy. Total scores for the CDEA questionnaire range from 0 to 48 and are interpreted as no dry eye symptoms or normal (<5), mild dry eye symptoms (5–20), moderate dry eye symptoms (21–30), or severe dry eye symptoms (31–48).

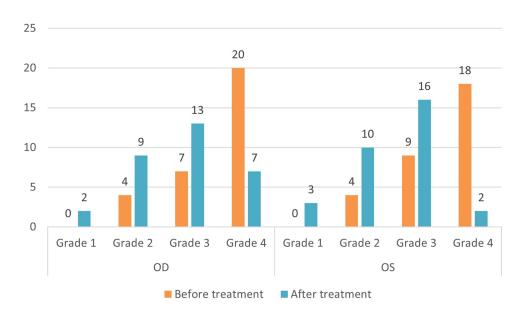


Figure 3 Meibograph grades before and after BBL-IPL therapy. Meibograph grades (1 to 4) were assigned based on the severity of meibomian gland dropout in the upper eyelids only. A higher grade represents increased severity.

reproducible results. We also used objective DED metrics as measured by the Keratograph 5M, which have been found to correlate with dry eye symptoms. ^{32,40} The meibograph grade was assessed by an ophthalmologist (S.S.) blinded to treatment status, thereby improving the internal validity of findings, and limiting investigator bias.

Furthermore, some studies measured post-treatment results on the same day or shortly after an IPL session, ^{15,16} while our post-treatment results were measured at least 30 days after the last session. Therefore, our study findings demonstrate the sustained effects of BBL-IPL treatment. Lastly, we used PSA as an additional

patient-reported measure to better ascertain the effects of BBL-IPL therapy on the severity of dry eye symptoms.

Limitations

The retrospective design and a small sample size with no comparison group weaken the validity of study findings. Given the significant improvement in meibograph grade but non-significant improvements in NIKBUT and TMH scores, other variables of tear film quality and stability, such as lipid-layer grade and thickness, tear evaporation rate, tear film osmolarity, and matrix metalloproteinases levels, could also be investigated. To better isolate the effects of BBL-IPL treatment on the tear film, lid margin debridement could have been performed before sessions. Generally, studies with larger patient samples, variable treatment sessions and longer follow-up periods are needed to better evaluate the efficacy and safety of BBL-IPL therapy for DED with MGD.

Conclusion

BBL-IPL appears to be a safe and effective treatment modality for dry eye disease with meibomian gland dysfunction. Patients experienced an improvement in dry eye symptoms, tear break-up times, bulbar redness, visual acuity and meibomian gland function after 4 monthly sessions of BBL-IPL therapy, without any temporary or permanent adverse effects.

Ethical Corrections

Patient consent to review medical records was not required by the William Osler Health System Research Ethics Board as this was a retrospective case series. All efforts were made to protect patient confidentiality. This research project adhered to the Declaration of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

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