Efficacy of isolated treatment with Intense Pulsed Light applied directly to the eyelids of patients with Meibomian gland dysfunction: a retrospective cohort

Eficácia do tratamento isolado com luz pulsada intensa aplicada diretamente nas pálpebras de pacientes com disfunção da glândula meibomiana: uma coorte retrospectiva

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ABSTRACT

Objective: To describe the clinical benefits of intense pulsed light applied directly to the eyelids of patients with Meibomian gland dysfunction and without glandular expression.

Methods: A paired, retrospective cohort involving 16 patients diagnosed with symptomatic Meibomian gland dysfunction according to the criteria of the 2011 International Workshop on Meibomian gland dysfunction and treated with Intense Pulsed Light. The patients received three biweekly sessions on the eyelids and with the Lumenis OPT M22™ equipment. Glandular expression was not performed and after 30 days, clinical follow-up was performed with the evaluation including SPEED 2 questionnaire, meibomigraphy and glandular assessment.

Results: SPEED 2 significantly improved in 75% ($p < 0.001$) and Meibum quality improved in 84.7% ($p < 0.001$) of patients. Glandular loss decreased from 27.1% to 22.5%, without statistical significance ($p = 0.129$), but with a moderate effect size ($d = 0.452$).

Conclusion: Our findings suggest that Intense Pulsed Light applied directly to the eyelids and without glandular expression is effective in the treatment of Meibomian gland dysfunction.

RESUMO

Objetivo: Descrever os benefícios clínicos da luz intensa pulsada (LIP) aplicada diretamente nas pálpebras de pacientes com disfunção da glândula meibomiana (MGD) e sem expressão glandular.

Métodos: Coorte retrospectiva pareada envolvendo 16 pacientes diagnosticados com MGD sintomática de acordo com os critérios do International Workshop on MGD de 2011 e tratados com LIP. Os pacientes receberam 03 sessões quinzenais nas pálpebras e com o equipamento Lumenis OPT M22. A expressão glandular não foi realizada e após 30 dias foi realizado acompanhamento clínico com o questionário SPEED 2, meibomigrafia e expressão glandular.

Resultados: O SPEED 2 melhorou significativamente em 75% ($p<0{,}001$) e a qualidade do Meibum em 84,7% ($p<0{,}001$). A perda glandular diminuiu de 27,1% para 22,5%, sem importância estatística ($p=0{,}129$), mas com tamanho de efeito moderado (d =0,452).

Conclusão: Nossos achados sugerem que a LIP aplicada diretamente nas pálpebras e sem expressão glandular é eficaz no tratamento da MGD.

INTRODUCTION

Meibomian gland dysfunction (MGD) is a chronic, diffuse condition caused by obstruction of glandular orifices and alterations in meibum quantity and/or quality.[1] It is the primary cause of evaporative dry eye (EDE) disease, with prevalence varying depending on diagnostic criteria and region. In 2024, Chen et al. identified an MGD prevalence of 86% in patients with dry eye disease.[2,3]

Patients report symptoms such as burning, tearing, a sensation of a foreign body, and intermittent visual blurriness. Severe cases may lead to difficulties in everyday tasks, including reading, watching television, driving, and computer work, and may negatively affect quality of life and work performance.[4]

Current MGD treatments are divided into non-thermal (gland probing, topical/oral antibiotics, Manuka honey, emollient drops, therapeutic expression) and thermal (warm compresses, pulsed thermotherapy, and Intense Pulsed Light [IPL]).[5]

Intense Pulsed Light, initially used in dermatology for treating photoaging, rosacea, pigmented lesions, and telangiectasias, was found in 2002 by Toyos et al. to relieve symptoms of MGD in rosacea patients.[6-8] Studies confirm its efficacy in treating DED and MGD, typically applied around the eyelids in conjunction with gland expression.[9-11]

This study's primary objective is to describe the clinical benefits of IPL applied directly to the eyelids of patients with Meibomian gland dysfunction and without glandular expression.

METHODS

This non-concurrent, paired cohort study included all 46 MGD patients treated with IPL at Santa Luzia Eye Center in Guarabira between August 2019 and December 2020. It adhered to the Helsinki Declaration guidelines, and informed consent was obtained from all participants. The study was approved by the Research Ethics Committee of the *Clementino Fraga Filho* University Hospital and the Faculty of Medicine of the *Universidade Federal do Rio de Janeiro* on December 22, 2023 (approval no. 76359123.4.0000.5257).

Data extraction

All the data used were collected from information recorded in medical charts, and the information was entered into a clinical form specifically designed for the study.

The medical charts contained the following information: age, sex, meibography of the lower eyelids, quality of Meibomian secretion from 15 glands of the lower eyelid, results of the SPEED 2 questionnaire, NITBUT, and TMH. After applying the inclusion and exclusion criteria, 16 patients participated in the study.

To reduce confounding bias due to age, stratification by age group was employed (20 to 40 years, 41 to 60 years, 61 to 80 years, and ≥ 81 years).

Inclusion criteria

Patients were unresponsive to conservative treatment (lubricant eye drops, heat, and eyelid hygiene, omega-3 fatty acid supplementation) with symptomatic evaporative DED and MGD (SPEED 2 >2; NITBUT < 10 s; TMH >0.25 mm; gland loss > 25% on meibography or meibum quality classification ≥ 1, below 20 years of age and ≥ 2, above 20 years of age).

Exclusion criteria

Aqueous deficient or mixed DED (DEWS II, 2017), patients < 18 years, ongoing glaucoma drops, ocular surgeries within six months, eyelid disorders, prior DED treatments (IPL, glandular probing, pulsed thermotherapy), Fitzpatrick phototype > IV.

Procedure

IPL was administered by a single physician using the Lumenis OPT M22™ device (590 nm filter, triple pulse, 6 milliseconds duration, 50 milliseconds interval) with initial fluence of 10 J/cm², increasing by 1 J/cm² per session (Figure 1). Treatments included three sessions every 15 days with a cooled 8 x 15 mm sapphire tip handpiece applied directly to the upper and lower eyelids (Figure 2). Six (06) flashes were delivered (2 passes of 3 flashes) per eyelid (Figure 3).

Before the flashes, both eyes were anesthetized with one anesthetic eye drop (oxybuprocaine hydrochloride 0.4%, Latinofarma), and ocular shields (Surgical Steel Medium, Laser shield) were placed on each eye. The periocular skin was cleaned with micellar water (Neutrogena®). Subsequently, cleaning was completed with 2% aqueous chlorhexidine (Bioquímica). Ultrasound gel (Carbogel) was applied to both eyes' upper and lower eyelids.

After the flashes were delivered, the ultrasound gel and protective shields were removed. One drop of dexamethasone with ciprofloxacin 3 mg/mL eye drop (Latinofarma) was instilled in each eye. The eyelids were cleaned with micellar water (Neutrogena) and protected with sunscreen SPF 50 (Mantecorp).

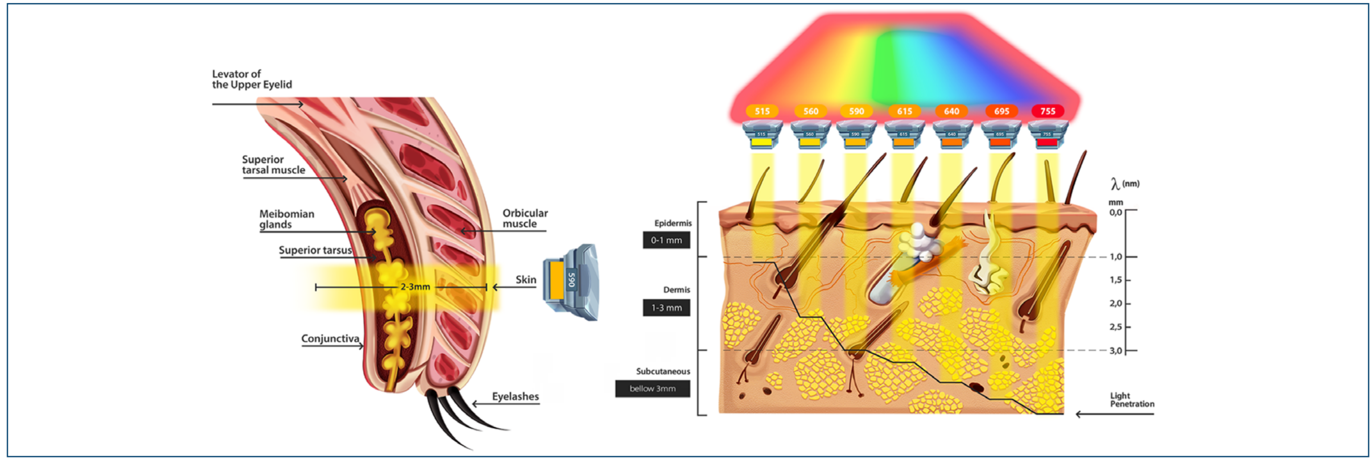

Figure 1. Intense pulsed light administration using a filter.

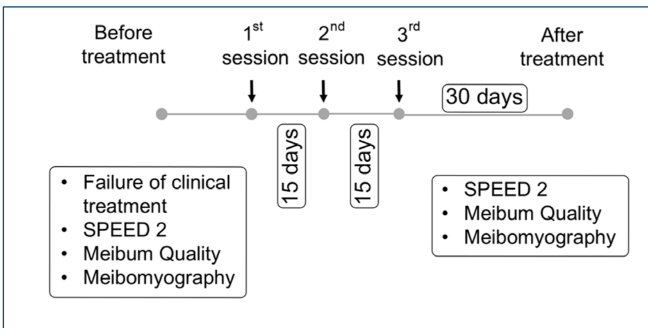

Figure 2. Frequency of clinical evaluations and the interval between intense pulsed light sessions.

As post-session care, patients were advised to avoid sun exposure for 14 days, avoid local heat for 24 hours, and use daily sunscreen protection. They were also instructed to continue using lubricating eye drops, oral omega-3 supplementation, applying warm compresses to the eyelids, and maintaining eyelid hygiene. Gland expression was not performed.

Assessments

The start time of observation for each patient (To) was defined immediately after the study inclusion criteria were fulfilled.

Approximately 30 days after the last session, all patients completed the dry eye evaluation questionnaire (SPEED 2), and the intensity of symptoms was graded on a scale for statistical analysis (Table 1). The lower eyelids were used for performing meibography and expressing the Meibomian glands (Figure 4) and the meibography (Figura 5). The CA800 equipment from Topcon was used to perform non-contact infrared meibography.

The lower eyelid was everted with a tongue depressor, images of the glands were captured, and gland dropout analysis was performed using the device software. The Pult and Nichols grading system was chosen for intensity evaluation, where a loss > 25% in patients over 20 years old and any loss in patients under 20 years old was considered positive (diseased) for MGD.

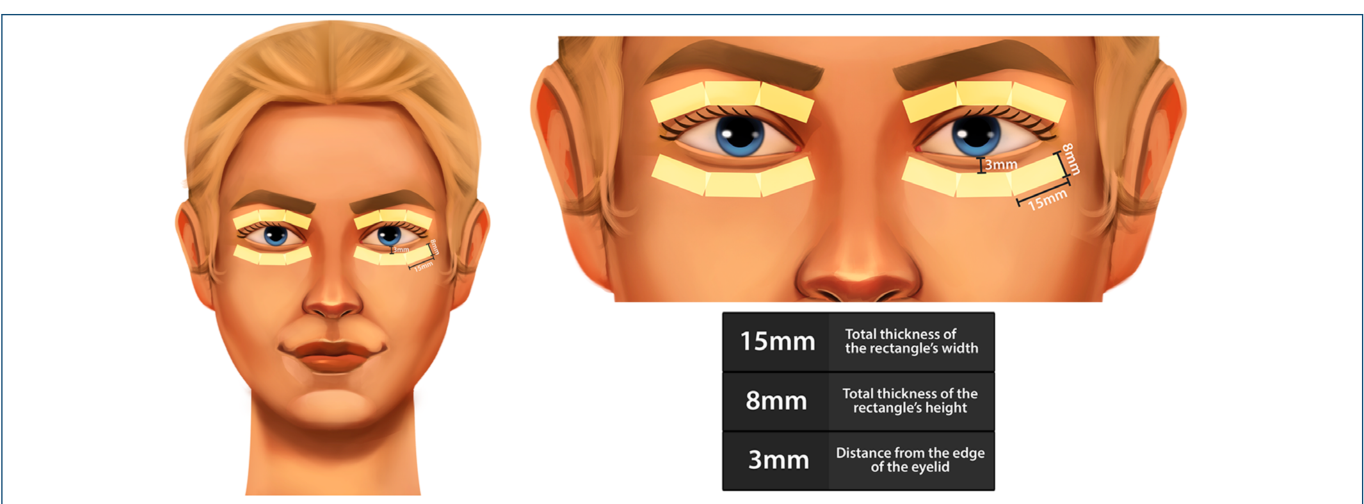

Figure 3. Positioning of the sapphire tip over the eyelids.

Table 1. Score for symptom intensity

Classification	SPEED	Grade
Normal	≤03	0
Mild	≤06	1
Moderate	≤10	2
Severe	≤28	3

The CA800 Topcon equipment was used to quantify NITBUT in seconds and TMH in mm. The patient was examined in a dimly lit room with the air conditioning unit turned off. They were asked to blink, and the TMH was immediately measured at the lower corneal level (6 hours). For the NITBUT, the patient was asked to blink three times, and three images were captured; the equipment's software then chose the average of the images.

Finally, 15 Meibomian glands in the lower eyelids were expressed using Arita forceps (Figure 4). Obstruction or poorer meibum quality was then analyzed. A patient was considered having the disease with a grade ≥ 1 for those under 20 years old or ≥ 2 for those over 20 years old (Table 2).

Statistical analysis

The right eye (RE) was selected for statistical analysis, which was performed using the Jamovi software, version 2.3.28.0 (www.jamovi.org). Data normality was verified using the Shapiro-Wilk test. The non-parametric Wilcoxon test was used to compare meibum quality, while the paired Student's t-test was employed to evaluate SPEED 2 results and gland dropout in meibography. A p-value less than 0.05 was considered statistically significant.

All analyses were conducted before and after a 4-week period following the last session of IPL treatment.

A univariate logistic analysis was performed to identify predictors that could affect symptom improvement and be included in the initial model of the multivariate logistic analysis. A p-value less than 0.20 (univariate logistic analysis) and/or a p-value less than 0.05 (multivariate logistic regression) was considered statistically significant.

RESULTS

Among all patients with MGD and treated with IPL at the Santa Luzia Eye Center during the study period, 30 patients were not included in the analysis: 6 patients were asymptomatic, 4 had a NITBUT > 10 seconds, 1 patient was younger than 20 years, 9 patients had TMH < 0.25 mm, 2 patients had meibomyography < 25% and 8 patients answered a different questionnaire (Ocular Surface Disease Index [OSDI]).

This study included 16 eyes from 16 patients (10 women) with symptomatic MGD. The mean age was 60.4 ± 18.4 years, ranging from 27 to 85 (Table 3).

Primary outcome

The treated patients showed a statistically significant improvement in their symptoms, with 75% becoming asymptomatic and/or reporting mild symptoms (change 7.31; 95% of confidence interval [95%CI] 4.19-9.18; p < 0.001) (Figure 6A).

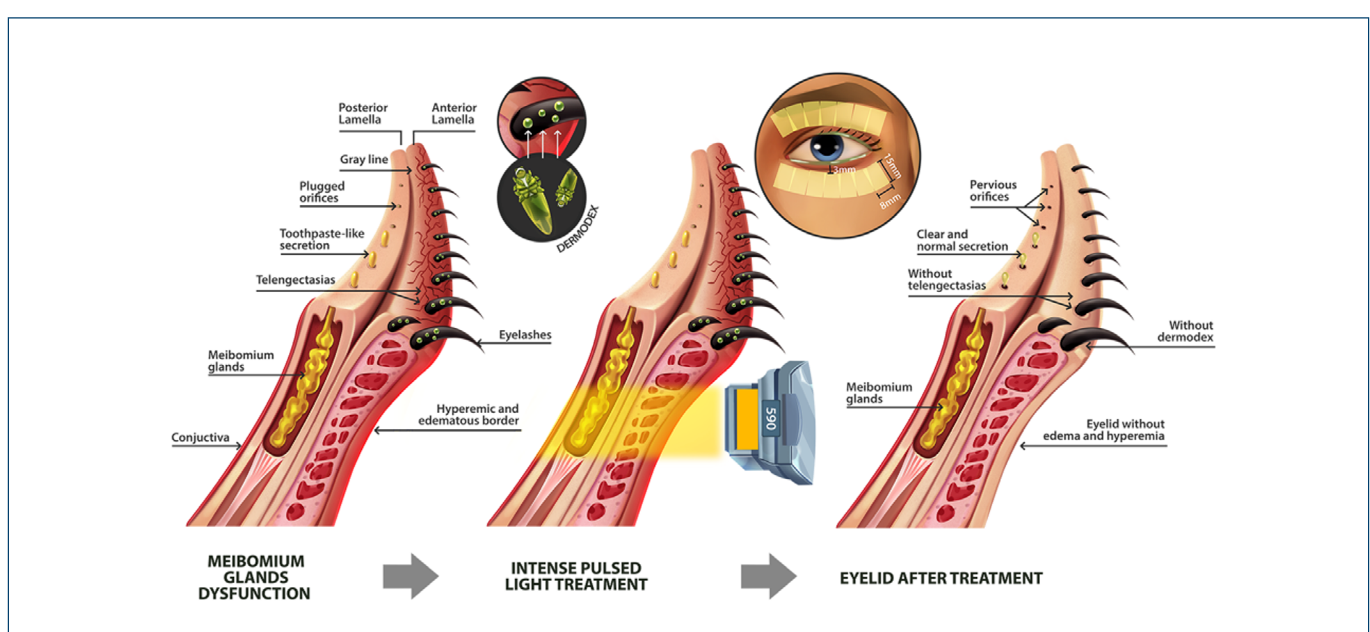

Figure 4. Mechanism of action of intense pulsed light in the treatment of Meibomian gland disease.

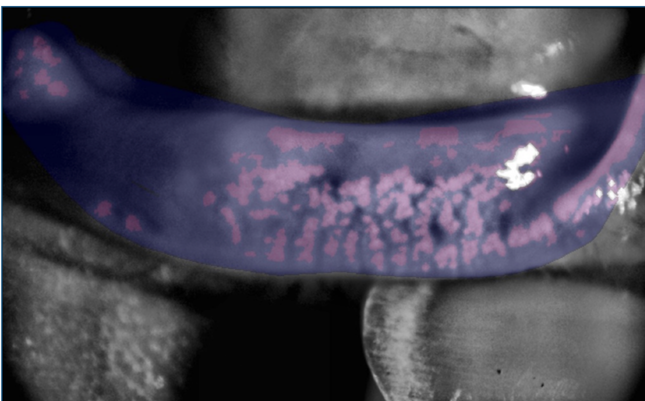

Figure 5. Analysis of gland dropout using meibography with the CA-800 device.

Table 2. Meibum quality and glandular dropout score

Grade	Meibum quality	Glandular drop out on meibomyogram in %
0	Oily	0
1	Yellow	≤25
2	Hardened yellow	≤50
3	Toothpaste	≤75
4	Absence of secretion	≤100

None of the analyzed predictors (sex, p = 0.374; age, p = 0.980; meibum quality, p = 0.726; meibography, p = 0.764) influenced the response to treatment.

Secondary outcomes

The quality of the meibum showed a statistically significant improvement with treatment (Mdn 0.00; IQ 0-2; $p < 0.001$), with 68.8% of patients presenting oily or yellowish secretion without granules (Figure 6B).

A reduction in gland dropout was observed but did not reach statistical significance (change 4.85; 95%CI -1.63-11.3; p = 0.129), with the mean dropout decreasing from 27.1% to 22.5%, with a moderate effect size (d = 0.452) (Figure 6C).

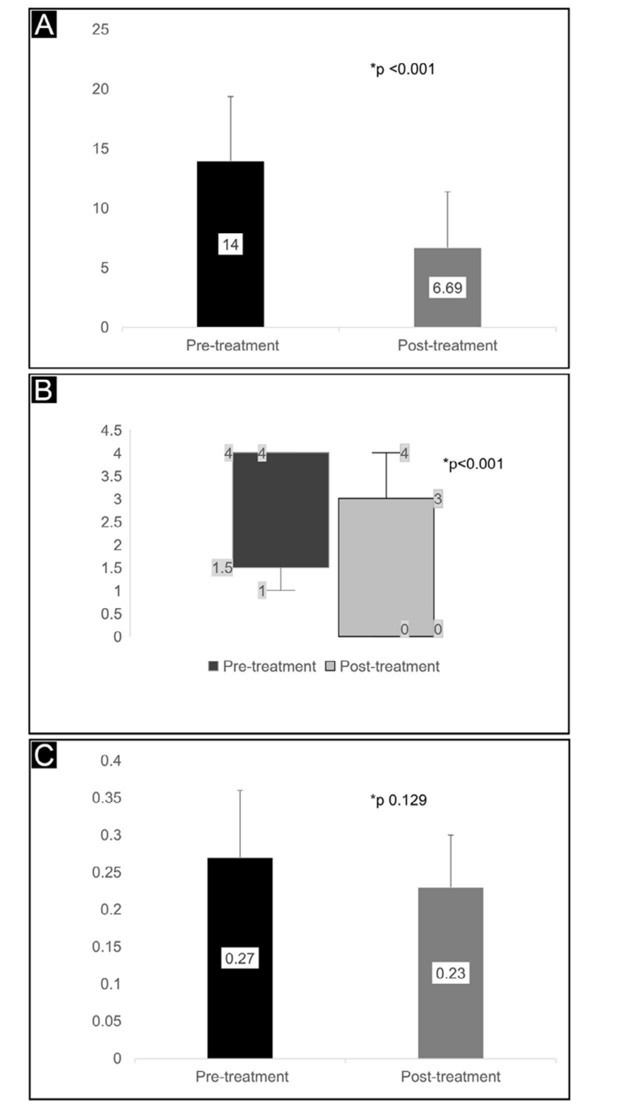

Figure 6. (A) Behavior of SPEED 2 in 16 patients treated with Intense Pulsed Light. (B) Behavior of meibum quality in 16 patients treated with Intense Pulsed Light. (C) Behavior of gland dropout in 16 patients treated with Intense Pulsed Light.

Table 3. Demographic characteristics and clinical examinations of 16 patients undergoing Intense Pulsed Light treatment

Patient	Sex	Age	SPEED 2 (before treatment)	Meibography (before)	Meibum (before)	SPEED 2 (after treatment)	Meibography (after)	Meibum (after)
1	M	59	14	25	4	4	31	0
2	M	49	14	19	4	4	25	0
3	M	44	18	13	4	2	29	0
4	F	75	6	38	4	4	30	1
5	F	85	16	25	1	5	15	2
6	M	27	7	29	4	7	12	4
7	F	74	12	51	4	2	28	2
8	F	81	16	32	4	16	23	4
9	F	68	15	22	4	15	18	3
10	M	82	5	24	4	4	17	2
11	F	74	7	22	4	4	16	2
12	M	72	21	30	4	6	19	0
13	F	43	4	28	2	12	33	3
14	F	53	22	30	2	11	25	0
15	F	32	16	17	1	4	19	0
16	F	49	21	28	2	10	30	0

M: male; F: female.

DISCUSSION

This study was the first to demonstrate the efficacy of standalone IPL therapy applied directly to the eyelids in improving symptoms and glandular function in patients with MGD. In 2020, Xue et al., when treating 87 patients with IPL without eyelid massage in the tragus region, achieved improvement in symptoms (OSDI) mean: 21 ± 17 and SPEED mean: 9 ± 5; p < 0.001), but without statistically significant differences in meibum quality (Mdn: 2; IQR: 1-2; p = 0.28) or meibography (Mdn: 1; IQR: 0-2; p = 0.29), with results inferior to this study.[10]

In 2021, Shin et al. [12] conducted a comparative study of patients treated with standalone IPL versus those with therapeutic expression, concluding that expression alone did not improve symptoms (p = 0.84) or Meibomian gland quality (p = 0.731). In 2022, Martínez-Hergueta et al. applied IPL directly to the eyelids, combined with glandular expression, and reported improvement in meibography (M: 1.40 ± 0.74; p = 0.024).[13] Toyos et al. confirmed that IPL combined with glandular expression improved meibum quality (p < 0.0001).[14]

Meibomian gland dysfunction is characterized by obstruction and alterations in secretion quality, often accompanied by telangiectasias and secondary Demodex infestations. Treatments targeting these alterations, including IPL, are effective.[5,15]

Intense Pulsed Light is a non-coherent, scattered, pulsed light beam with wavelengths between 400 and 1200 nm. Its tissue action is based on selective photothermolysis, targeting chromophores (hemoglobin, melanin, or water) using specific filters (Figure 7).[16]

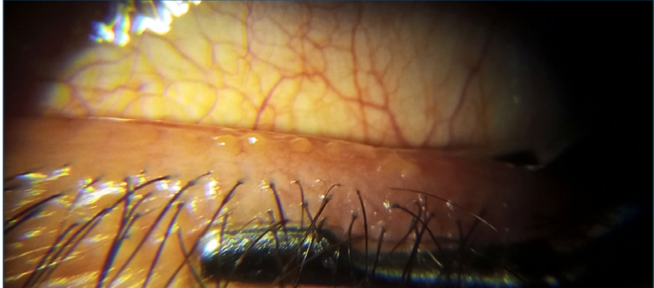

Figure 7. Glandular expression for meibum quality classification.

In 2015, dermatologist Rolando Toyos et al. observed that his facial rosacea patients treated with IPL experienced improvement in dry eye symptoms. Since then, IPL has gained prominence in the treatment of dry eye.[8,14]

The likely mechanisms of action of IPL therapy involve several processes. First, the local heat generated by the IPL flash raises tissue temperature to approximately 50ºC, sufficient to liquefy glandular secretions and facilitate drainage, thereby reducing gland dropout. However, many IPL devices lack small tips designed for direct eyelid application, resulting in protocols being applied to the face, as seen in rosacea treatment, even in patients with MGD alone. Some researchers have noted that IPL may not sufficiently elevate eyelid temperature to melt glandular secretions effectively.[14]

Another mechanism is the occlusion of small vessels at the eyelid margin. Meibomian glands function optimally in low-oxygen environments, and small ships at the eyelid margin increase oxygen delivery, impairing gland function. Intense Pulsed Light coagulates hemoglobin in these vessels, creating the anaerobic environment essential for gland efficiency.[17]

Intense Pulsed Light also aids in the elimination of *Demodex folliculorum* and *Demodex brevis*, which contribute to the inflammatory cycle in dry eye syndrome by releasing toxins on the ocular surface. The IPL treatment increases porphyrin production in the mitochondria of *Demodex* mites, leading to their destruction.[18]

Furthermore, IPL reduces pro-inflammatory mediators such as interleukin (IL) 17A, IL-6, and prostaglandin E2 while combating blepharitis.[19] It also induces photobiomodulation by altering intracellular gene and protein expression, which improves cellular function. IPL's effect on fibroblasts enhances collagen synthesis, improving eyelid tone and elasticity. This results in more efficient blinking, improved Meibomian gland expression, reduced tear evaporation, enhanced ductal gland architecture, and activation of germinative cells, thereby improving secretion quality.[20]

Lastly, IPL exerts neurological effects by stimulating two branches of the parasympathetic nerve in the lower eyelid, improving the function of the Meibomian and lacrimal glands. These combined mechanisms contribute to the therapeutic efficacy of IPL in treating MGD and associated conditions.[21]

In this study, IPL treatment was performed on the lower eyelid, as in most studies, and on the upper eyelid.[8,13,21-23] Meibomian gland dysfunction is not exclusive to the lower eyelid. Unfortunately, the initial indication for this therapy was for dermatological patients with dry eyes and facial rosacea. The initial machines had large tips, which made it impossible to treat the upper eyelid without causing harmful effects, leading many doctors to avoid treating it.

The upper eyelid has an average of 30 Meibomian glands, while the lower has 25. These glands produce an

average of 26 and 13 μL of secretion, respectively.[24] Thus, the upper eyelid's reservoir of meibum is significant and should not be neglected.

Unfortunately, most IPL machines have large tips, typically 35 mm x 15 mm, which are unsuitable for eyelid dimensions. This mismatch can cause burns, loss of eyebrows and eyelashes, uveitis, and iris transillumination defects.[7,13,15,25,26]

Despite treatment on the upper and lower eyelids, meibomography and meibum evaluation were performed only on the lower eyelid due to technical limitations, as they already represent the disease.

Direct IPL treatment on the eyelids did not increase gland dropout percentages, a significant concern for proponents of pulsed thermotherapy, given that eyelid temperature can exceed 50°C.[13,26,27] Improvements in meibography averages (Figure 6C) may be attributed to the photobiomodulatory effects of IPL on the acinar units of Meibomian glands, which liquefy meibum, facilitate drainage, reduce ductal pressure, and slow down acinar apoptosis and gland dropout.[13,20]

The therapy resulted in symptom improvement, with 75% of patients becoming asymptomatic or reporting mild symptoms, achieving statistical significance ($p<0.001$) and a substantial effect size ($d = 1.44$). In 2024, Elbakary et al. treated 15 patients with moderate-to-severe EDE using IPL and achieved 73% of asymptomatic and mild cases, which is similar to the values we found. A significant improvement in patients' quality of life (QOL) was noticed in all patients treated with IPL, with a reduction of the mean OSDI score from 56.9 ± 11.1(moderate-to-severe) to 22.9 ± 16.4(asymptomatic-to-mild).[28]

Additionally, 68.8% exhibited clear or yellowish meibum, with an important effect size (rpb 0.889). These results demonstrate clinical relevance and justify the standalone use of IPL for treating patients with refractory MGD.

Neither sex nor age influenced treatment response as they did not meet the assumptions for the initial multiple linear regression model. This was unexpected, given that age and sex are significant risk factors for MGD, likely due to glandular loss with age and hormonal changes.[29-31]

This study employed a retrospective cohort design, with data collected from medical records. This led to information loss. Another limitation was the transformation of numerical data into ordinal variables for statistical analysis, which reduced the study's power.

The treatment period coincided with the COVID-19 pandemic, which discouraged patient follow-up. Several patients reported significant symptom improvement but did not attend the post-therapy control examinations, affecting the sample size. Adverse effects included eyelash loss in two patients and localized burning sensation for a few hours.[7,31,32]

The sample size was small, and follow-up was short, only 30 days post-treatment. Longer follow-up would be necessary to assess the duration of the therapy's effects on glandular secretion, symptom improvement, and glandular loss.

An interesting observation was made in patients using prostaglandin analogs for the management of glaucoma. Long-term use of these medications leads to orbital fat atrophy, eyelid stiffening, and darkening. Following IPL sessions, skin lightening and improved eyelid tone were observed, thereby enhancing periocular aesthetics.[6,33]

CONCLUSION

Our findings suggest that concomitant treatment of the upper and lower eyelids was associated with statistically and clinically significant improvements in symptoms, demonstrating the possible irrelevance of associating glandular expression with Intense Pulsed Light. The quality of meibum secretion also enhanced, with no worsening of gland dropout in meibography, thereby, contributing to the reduction of the disease's progression.

AUTHORS' CONTRIBUTION

George Luiz Soares de Oliveira, Laura Pires Soares de Oliveira, Sofia Pires Soares de Oliveira, Dillan Cunha Amaral, Filipi Fim Andreão, José Eduardo Ferreira Manso, Mário Luiz Ribeiro Monteiro, Milton Ruiz Alves, Ricardo Noguera Louzada: substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; 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.

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