Original research article

EJO European Journal of Ophthalmology

Efficacy and safety of intense pulsed light of upper and lower eyelids in Meibomian gland dysfunction: A prospective multicentric study

European Journal of Ophthalmology
1–8

DOI: 10.1177/11206721231199121
journals.sagepub.com/home/ejo
Sage

Jose Manuel Benitez-del-Castillo[1,2,3], María Dolores López-Pérez[4], Antonio Cano-Ortiz[4], Cristina Peris-Martinez[5,6], Sergio Pinar-Sueiro[7,8,9], Maria Gessa-Sorroche[10,11], Carmen García-Franco-Zuñiga[12], Maria T Iradier[13], Maria A Amesty[14] and Barbara Burgos-Blasco[1]

Abstract

Purpose: To demonstrate that intense pulsed light therapy (IPL) of the upper and lower eyelids with meibomian gland expression (MGX) is effective in improving dry eye disease due to meibomian gland dysfunction (MGD).

Methods: Patients with ocular discomfort (Ocular Surface Disease Index -OSDI- above 13) and signs of MGD were recruited. All patients underwent OSDI, visual acuity (VA), intraocular pressure, Schirmer test, meibography, non-invasive tear breakup time (NITBUT), slit-lamp examination (corneal and conjunctival staining, hyperemia, gland expressibility, and meibum quality), tear osmolarity and lipid layer thickness. IPL was performed with Optima IPL (Lumenis Ltd.) following a standardized protocol on upper and lower eyelids of both eyes, with inferior eyelid MGX. Patients received four sessions separated by two weeks each. Four weeks after, examinations were repeated.

Results: 160 patients (320 eyes) were included, of which 108 (67.5%) were women and mean age was 59.2 ± 15.08 (range 20–89). After four sessions, VA, OSDI, tear osmolarity, lipid layer thickness, NITBUT, hyperemia, corneal and conjunctival staining, gland expressibility, meibum quality, inferior eyelid Meiboscore and Schirmer test improved (all, $p < 0.027$). Changes in OSDI, initial and average NITBUT increased with dry eye disease severity (according to OSDI). Increased pre-treatment OSDI, hyperemia, corneal and conjunctival staining and Schirmer test were associated with an improvement in OSDI (all, $p < 0.040$). No adverse events were noted.

Conclusions: The combination of IPL on upper and lower eyelids with MGX is safe and effective for the treatment of MGD. Patients with severe dry eye disease present greater improvements.

Keywords

Intense pulsed light therapy, dry eye disease, meibomian gland expression, upper eyelids

Date received: 1 May 2023; accepted: 7 August 2023

[1]Department of Ophthalmology, Hospital Clinico San Carlos, Madrid, Spain
[2]Universidad Complutense de Madrid, Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, Madrid, Spain
[3]Clínica Rementería, Madrid, Spain
[4]Ophthalmology Department, Unidad de córnea y segmento anterior, Hospital Arruzafa, Córdoba, Spain
[5]Aviño Peris Eye Clinic, Valencia, Spain
[6]Ophthalmology Department, University of Valencia, Valencia, Spain
[7]Ophthalmology Department, Hospital Universitario Donostia, San Sebastián, Spain
[8]Vista Instituto Oftalmológico Bilbao, Bilbao, Spain
[9]Centro Oftálmico San Sebastián (COSS), San Sebastián, Spain
[10]Ophthalmology Department, Unidad de córnea y superficie ocular, Hospital Universitario Virgen Macarena, Sevilla, Spain
[11]Unidad de córnea, catarata, refractiva y segmento anterior. Clínica Miranza Virgen de Luján, Sevilla, Spain
[12]Clínica García-Franco y Triviño, Madrid, Spain
[13]Instituto de Microcirugia Ocular (IMO), Madrid, Spain
[14]Vissum (Grupo Miranza), Alicante, Spain

Corresponding author:
Barbara Burgos-Blasco, Departmento de Oftalmología. Hospital Clinico San Carlos, Calle Prof Martin Lagos s/n, 28040, Madrid, Spain.
Email: bburgos171@hotmail.com

Introduction

Meibomian gland dysfunction (MGD) is the leading cause of evaporative dry eye disease (DED), with an estimated prevalence of up to 70%.[1–3] It is characterized by the obstruction of the meibomian gland terminal ducts caused by increased keratinization of the terminal ducts, the presence of squamous debris and a thickening of the meibum. Changes in their glandular secretion result in tear film evaporation, ocular surface inflammation, and dry eye symptoms.[4,5]

Initial treatment options include warm compresses and lid hygiene, along with antibiotics, anti-inflammatory agents and essential fatty acid supplementation. These treatments have been only somewhat effective, suggesting that a multi-faceted treatment approach may be necessary.[5,6]

Intense pulsed light therapy (IPL) has been recently presented as a new therapeutic option in MGD. It consists of light sources of high-intensity that produce polychromatic and noncoherent light with a particular wavelength. Light energy is selectively absorbed by a chromophore and converted to heat, targeting specific tissue without damaging its surrounding structures. It has been widely used in dermatology to treat multiple conditions including vascular skin lesions, facial rosacea, and acne.[7] In 2002, Dr. Toyos serendipitously noted the beneficial effects of IPL on his patients who underwent treatment for facial rosacea. Along with an improvement of facial erythema, the patients also showed improvement in signs and symptoms of MGD and DED, increasing the interest in IPL as a potential therapeutic option for MGD. IPL devices have been modified since in order to reduce side effects and expand its indications, along with different IPL protocols.[8]

The purpose of the current prospective study is to further demonstrate the efficacy and safety of IPL treatment for DED due to MGD in a multi-site study performed on a Spanish population. Our aim is to show that IPL combined with meibomian gland expression (MGX) is effective in improving the signs and symptoms of DED due to MGD. The main objective was to investigate the symptomatic improvement in Ocular Surface Disease Index (OSDI) after IPL. Secondary objectives were to analyze the non-invasive tear breakup time (NITBUT), corneal and conjunctival staining, hyperemia, tear osmolarity, lipid layer thickness, quality of the meibum, meibomian gland atrophy and meibomian gland expressibility after IPL, along with the factors associated with a greater improvement.

Methods

Patients

This open prospective cohort study including patients with DED due to MGD took place at seven clinics in Spain: Hospital Arruzafa in Córdoba, Aviño Peris Eye Clinic in Valencia, Vista Instituto Oftalmológico Bilbao (IOB) in Bilbao, Clínica Miranza Virgen de Luján in Sevilla, Clínica García-Franco y Triviño in Madrid, Instituto de Microcirugia Ocular (IMO) in Madrid and Vissum in Alicante.

Patients with ocular discomfort, signs and symptoms of DED and who met the inclusion criteria and no exclusion criteria were recruited. In order to participate, written informed consent was obtained from all participants. This study was performed with the approval of the Hospital Clinico San Carlos' Ethics Committee (21/429-EC_P) and in accordance with the Declaration of Helsinki.

The inclusion criteria were: over 18 years of age, skin phototype between I and V according to the Fitzpatrick classification, OSDI above 13, clinical signs of altered expressibility of the Meibomian Glands, first NITBUT below 10 s and clinical signs of MGD (meibomian orifice plugging, eyelid margin foaminess, hyperemia or telangiectasias). As for exclusion criteria, the following were considered: signs of acute ocular surface inflammation, ocular surgery or trauma within the previous month, eyelid malpositions (lagophthalmos, entropion, or ectropion), pregnancy, breastfeeding, systemic immune-mediated diseases (Sjögren's Syndrome, Stevens-Johnson Syndrome or pemphigoid), pre-cancerous skin lesions, skin cancer or other specific pathology history in the treatment area, changes in ocular treatment in the month prior or during the study and other ocular pathologies that may affect the study according to the investigator.

Clinical protocol

Before IPL treatment, all patients underwent the Fitzpatrick questionnaire to evaluate skin phototype, OSDI questionnaire, best-corrected visual acuity (BCVA) measured on a decimal scale, intraocular pressure, 5-min Schirmer 1 test, NITBUT (initial and average), meibography and slit-lamp examination. Also, tear osmolarity was assessed with the TearLab Osmolarity System (TearLab Inc, United States) and LipiView Ocular Surface Interferometer (Johnson & Johnson, United States) measured the lipid layer thickness.

The Meiboscore Classification was used to classify the upper and lower meibography in grade 0 (no loss of meibomian glands), grade 1 (loss of less than one-third of the total surface area of the meibomian glands), grade 2 (loss of one to two-thirds of the total surface) and grade 3 (loss of more than two-thirds of the surface). In the slit lamp examination, the following were evaluated: fluorescein corneal staining (Oxford modified scale), lissamine green conjunctival staining (Oxford modified scale), conjunctival hyperemia (McMonnies classification) and quality of meibomian secretion assessed in the central lower eyelid on a scale of 0–3 (0 being clear meibomian discharge, 1 turbid meibomian discharge, 2 cloudy with granules and 3 being like toothpaste). Gland expressibility was measured using the following scale: 1 (light), 2 (moderate) and 3 (high pressure).

Four weeks after the last IPL session, the patients underwent the same tests and examinations as before IPL treatment. The same variables and the presence of adverse effects were registered.

IPL treatment sessions

The IPL treatment was performed with the Optima IPL (Lumenis Ltd., Israel), by only one person per center and following a standardized protocol on the upper and lower eyelids of both eyes. Every patient received four IPL sessions separated by two weeks each. The treatment was applied in the malar region and on the upper and lower eyelids, with fluences between 10 J/cm^2 and 14 J/cm^2 depending on the skin phototype. After applying a thick layer of cold IPL gel, a double pass technique was performed. The face was treated from temple to temple, including the nose, with the 15 × 35 mm light guide with a total of 12 impacts and then, with the 8 × 15 mm light guide, the upper eyelids were treated with 3 impacts each (Figure 1). Finally, we performed the expression of the inferior eyelid meibomian glands using Collins meibomian gland forceps with topical anaesthesia (tetracaine hydrocholoride 0.1% and oxybuprocaine hydrocholoride 0.4%, Double anaesthetic, Alcon, United States). Post-session treatment was netilmicin 0.3% and dexamethasone 0.1% (Netdex, SIFI, Italy) three times a day for three days.

Data analysis

Statistical analysis was performed using the software package SPSS® (Statistical Package for Social Sciences, v25.0; SPSS Inc., Chicago, IL, USA). Mean and standard deviation are used to depict quantitative data, while qualitative data are expressed as frequency distributions. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of data. Parameters were non-normally distributed. Wilcoxon signed-rank test was employed to evaluate differences between pretreatment and posttreatment variables. Changes in variables were calculated as posttreatment value minus pretreatment value, so an increase resulted in a positive value. Spearman's rank correlation coefficient was used to investigate associations. Statistical significance was considered when $p < 0.05$.

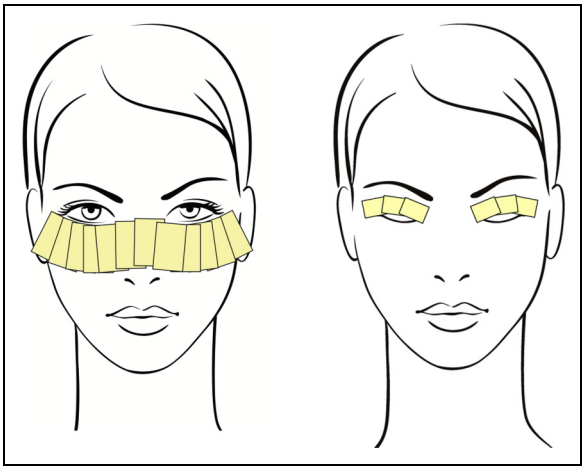

Figure 1. Using the Optima IPL (Lumenis Ltd., Israel) and after applying a thick layer of cold IPL gel, the face was treated from temple to temple with the 15 × 35 mm guide (12 impacts) and then, with the 8 × 15 mm guide, the upper eyelids were treated (3 impacts each). Fluences varied between 10 J/cm^2 and 14 J/cm^2 depending on the skin phototype and a double pass technique was performed.

Results

The study population comprised 160 patients (320 eyes), of which 108 patients (67.5%) were women and 52 patients (32.5%) were men. The mean age was 59.2 ± 15.08 (range 20–89). Fitzpatrick skin types of the patients were as follows: I 8 patients (5%), II 84 patients (53%), III 59 patients (37%) and IV 8 patients (5%) and V 1 patient (1%).

Overall baseline characteristics and changes after IPL treatment are shown in Table 1. After 4 IPL sessions, BCVA, OSDI, tear osmolarity, lipid layer thickness, NITBUT, hyperemia, corneal staining, conjunctival staining, gland expressibility, meibum quality, inferior eyelid Meiboscore and Schirmer test improved (all, $p < 0.027$). Most of these differences remained when patients were divided according to the severity of the symptoms (mild: 13–22 points; moderate: 23–32 points, and severe 33–100 points; Table 2).

Changes in OSDI, initial NITBUT and average NITBUT increased with DED severity (Table 3). Increased pretreatment OSDI, hyperemia, corneal staining, conjunctival staining and Schirmer test were associated with an improvement in OSDI (all, $p < 0.040$, Table 4).

No adverse events following IPL were noted, including intraocular inflammation, iris transillumination, lens injury, skin burns, ocular hypertension, fundus abnormalities or visual loss.

Discussion

IPL sessions performed with two-week intervals for two months resulted in a significant improvement in multiple DED and MGD parameters compared with pretreatment values. Our findings thus prove that IPL including upper eyelid treatment and MGX is an effective therapeutic approach for patients with MGD.

Multiple studies in MGD patients have shown that IPL is useful in improving ocular outcomes.[6,7,9] A randomized controlled study performed by Toyos et al. included 88 patients and compared IPL (4 sessions at 2-week intervals) combined with MGX with MGX alone. NITBUT increased 2.0 [IC95% 1.4, 2.6] seconds in the study arm, the difference between both arms being statistically significant. Other signs

Table 1. Baseline characteristics and changes after Intense Pulsed Light (IPL) treatment.

Variable	Pre-treatment		Post-treatment		p (Wilcoxon signed-rank test)
	Mean	SD	Mean	SD	
Visual acuity (decimal scale)	0.85	0.23	0.88	0.22	**<0.001**
Intraocular pressure (mmHg)	14.65	3.01	14.69	2.95	0.415
OSDI	27.27	12.51	18.99	10.96	**<0.001**
Tear osmolarity (mOsm/L)	319.20	8.37	302.13	13.28	**<0.001**
Lipid layer thickness (mm)	82.74	17.98	90.44	14.81	**<0.001**
First NITBUT (seconds)	9.63	4.08	10.64	4.37	**<0.001**
Average NITBUT (seconds)	7.97	3.82	8.74	3.72	**<0.001**
Hyperemia	1.81	1.08	0.88	0.74	**<0.001**
Corneal staining	0.87	0.97	0.30	0.53	**<0.001**
Conjunctival staining	0.69	0.86	0.25	0.49	**<0.001**
Gland expressibility	2.11	0.66	1.19	0.43	**<0.001**
Meibum quality	1.86	0.81	0.78	0.61	**<0.001**
Inferior Eyelid Meiboscore	0.85	0.69	0.75	0.59	**0.027**
Superior Eyelid Meiboscore	0.47	0.74	0.46	0.70	0.467
Schirmer test (seconds)	8.67	6.33	10.20	6.56	**<0.001**

SD: standard deviation; OSDI: ocular surface disease index; NITBUT: non-invasive tear break-up time. Statistically significant differences are marked in bold.

and symptoms which improved in both arms but were greater in the study arm included Meibomian gland score, Eye Dryness Score, the number of expressible glands and the meibum quality. Interestingly, the OSDI score improved similarly in both groups.[10] Our findings further prove that IPL is beneficial for MGD, improving OSDI, tear osmolarity, lipid layer thickness, NITBUT, hyperemia, corneal and conjunctival staining, gland expressibility, meibum quality, Meiboscore and Schirmer's test.

However, different protocols to the one hereby presented have also been used and even a session alone has proven beneficial.[11] Arita et al. performed a controlled study comparing the combination of IPL and MGX with MGX alone as a control.[12] The protocol consisted of a series of eight IPL sessions at 3-week intervals. The eyes that underwent IPL and MGX showed a significantly better improvement in NITBUT, plugging and meibum grade compared with those in the control group. Qin et al. used 3 sessions separated by 3 weeks each in severe DED patients, obtaining excellent results.[13] In general, current evidence suggests that the efficacy of IPL combined with MGX is positively correlated with the number of sessions and declines with increased observation time.[7]

In addition, to similar findings presented by other groups, we found a decrease in tear osmolarity with IPL. Albietz and Schmid obtained no differences in tear osmolarity, although it was evaluated after 3 sessions with another device (E-Eye, E-Swin, Paris, France).[14] However, other groups have indeed demonstrated a decrease in tear osmolarity with IPL sessions. Furthermore, Iradier et al. showed that this change in osmolarity correlated significantly with the baseline osmolarity in both eyes.[15–17]

Multiple pretreatment factors have been shown to correlate with clinical outcomes. In the present study, increased pre-treatment OSDI, hyperemia, corneal staining, conjunctival staining and Schirmer test were significantly associated with an improvement in symptoms (OSDI). In agreement, Iradier et al. noted that the change in OSDI was significantly correlated with the baseline value of OSDI ($r = -0.489$, $p < 0.001$) and the same occurred with the change in osmolarity (right $r = -0.636$, left $r = -0.620$, $p < 0.001$). They developed a linear predicting model of the change in OSDI with IPL, which included OSDI, NITBUT and meibum quality.[17] Similarly, Qin et al. reported excellent results in severe DED.[13] In another study, the improvement in the OSDI score was related to the baseline meibomian gland expressibility; the poorer the initial meibomian gland expressibility, the greater the improvement of the ODSI scores.[14]

Several potential mechanisms have been proposed for the improvement of ocular surface signs and symptoms with IPL in these patients. Firstly, IPL warms meibomian glands through the periocular skin, thus melting the meibum. Secondly, the energy is absorbed by chromophores in hemoglobin and closes telangiectasias in the eyelid margin, preventing the release of inflammatory mediators by these vessels. The levels of multiple inflammatory markers such as TNF-A, IL-17A, IL-6 and IL-4 decrease with IPL sessions, along with a downregulation of prostaglandin E2. The reduction in telangiectasias may result in hypoxia, which promotes the function of human meibomian gland epithelial cells mediated by the hypoxia-inducible factor 1α.[18,19] Thirdly, IPL may relieve inflammatory or neurogenic pain. Also, IPL can have an antibacterial effect and reduce the bacterial load on the eyelid margin.[12,20–22]

Adverse effects of IPL have been reported in some studies, most resolving spontaneously within one week. Adverse events in Toyos et al.'s series of 91 patients

Table 2. Baseline characteristics and changes after Intense Pulsed Light (IPL) treatment according to dry eye disease severity.

	Mild (n = 128)					Moderate (n = 120)					Severe (n = 27)				
Variable	Mean	SD	Mean	SD	p (Wilcoxon signed-rank test)	Mean	SD	Mean	SD	p (Wilcoxon signed-rank test)	Mean	SD	Mean	SD	p (Wilcoxon signed-rank test)
OSDI	17.32	2.94	13.59	6.11	**<0.001**	26.90	2.99	19.14	6.58	**<0.001**	45.57	12.41	28.57	15.89	**<0.001**
Tear osmolarity (mOsm/L)	319.24	4.71	301.57	6.81	**<0.001**	324.41	4.96	302.75	19.82	**<0.001**	305.17	10.66	302.67	11.32	0.759
Lipid layer thickness (mm)	89.14	13.00	95.78	7.16	**<0.001**	70.61	20.50	86.33	19.75	**0.008**	82.06	18.40	83.89	17.21	0.438
First NITBUT (seconds)	11.08	4.01	11.51	4.50	**0.013**	9.04	4.05	10.84	4.35	**<0.001**	8.03	3.40	8.81	3.63	**0.005**
Average NITBUT (seconds)	8.47	4.71	7.61	3.48	0.319	7.50	3.64	9.09	3.46	**<0.001**	8.15	3.33	9.14	4.01	**0.003**
Hyperemia	1.71	1.02	0.64	0.72	**<0.001**	1.98	1.21	1.05	0.78	**<0.001**	1.69	0.93	0.93	0.62	**<0.001**
Corneal staining	0.80	0.83	0.18	0.39	**<0.001**	1.01	1.11	0.38	0.60	**<0.001**	0.75	0.93	0.39	0.60	**<0.001**
Conjunctival staining	0.45	0.58	0.15	0.36	**<0.001**	0.86	0.98	0.24	0.49	**<0.001**	0.74	0.91	0.40	0.60	**<0.001**
Gland expressibility	2.27	0.60	1.17	0.38	**<0.001**	2.16	0.67	1.23	0.51	**<0.001**	1.80	0.65	1.19	0.39	**<0.001**
Meibum quality	1.95	0.77	0.56	0.67	**<0.001**	2.01	0.80	0.82	0.53	**<0.001**	1.58	0.82	0.95	0.59	**<0.001**
Inferior Eyelid Meiboscore	0.95	0.79	0.76	0.70	**0.008**	0.80	0.66	0.71	0.53	0.544	0.81	0.60	0.78	0.54	0.653
Superior Eyelid Meiboscore	0.82	0.92	0.80	0.86	0.564	0.26	0.54	0.22	0.42	0.157	0.34	0.60	0.36	0.63	0.564
Schirmer test (seconds)	9.94	6.04	10.91	5.39	**<0.001**	7.59	5.09	9.28	6.15	**<0.001**	7.90	8.23	10.21	8.91	**<0.001**

SD: standard deviation; OSDI: ocular surface disease index; NITBUT: non-invasive tear break-up time. Statistically significant differences are marked in bold.

Table 3. Changes in symptoms and tear break-up time after intense pulsed light (IPL) treatment.

	Total (n = 320)		Mild (n = 128)		Moderate (n = 120)		Severe (n = 72)		
Change in variables	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p
Change in OSDI	−8,48	11,23	−3,91	6,32	−7,89	7,02	−17,72	16,91	**<0,001**
Change in first NITBUT	0,95	3,80	0,38	3,44	1,70	3,80	0,77	4,23	**0,002**
Change in average NITBUT	0,71	4,73	−1,04	4,43	1,54	4,44	0,99	4,96	**0,003**

SD: standard deviation; OSDI: ocular surface disease index; NITBUT: non-invasive tear break-up time. Statistically significant differences are marked in bold.

Table 4. Factors associated with a greater improvement in OSDI and NITBUT.

	Change in OSDI		Change in first NITBUT		Change in average NITBUT	
Baseline variables	Correlation coefficient	p	Correlation coefficient	p	Correlation coefficient	p
OSDI	−0.483	**<0.001**	0.114	**0.045**	0.191	**0.009**
Tear osmolarity	−0.014	0.894	−0.161	0.130	−0.453	0.104
Lipid layer thickness	0.160	0.180	−0.230	0.052	0.241	0.258
First NITBUT	0.102	0.083	−0.286	**<0.001**	−0.548	**<0.001**
Average NITBUT	0.025	0.753	−0.504	**<0.001**	−0.587	**<0.001**
Hyperemia	−0.166	**0.009**	0.238	**<0.001**	0.053	0.476
Corneal staining	−0.141	**0.016**	0.301	**<0.001**	0.114	0.123
Conjunctival staining	−0.261	**<0.001**	0.165	**0.008**	0.120	0.107
Gland expressibility	−0.040	0.535	0.104	0.109	0.123	0.187
Meibum quality	−0.055	0.450	0.207	**0.004**	0.104	0.265
Inferior Eyelid Meiboscore	0.043	0.530	−0.010	0.875	−0.043	0.563
Superior Eyelid Meiboscore	−0.114	0.152	−0.135	0.090	0.090	0.349
Schirmer test	−0.136	**0.040**	−0.088	0.184	0.224	**0.023**

OSDI: ocular surface disease index; NITBUT: non-invasive tear break-up time. Statistically significant differences are marked in bold.

included blistering, cheek swelling, conjunctival cyst, floaters, hair loss at brow and forehead, light sensitivity, and redness of the face.[8] In a series of 2,282 patients who received IPL and MGX, there were 74 adverse events, with an incidence of 3.24%.[23] There are also case reports of uveitis and iris damage secondary to IPL, particularly associated with incorrect ocular protection when applying cosmetic IPL therapy on the upper eyelids by non-ophthalmologic health care workers.[24–26] Pain associated with MGX may be a concern for some patients, but MGX has shown to be more tolerable after IPL, possibly because it softens meibum and thereby reduces the pain.[12]

Some limitations of the current study should be acknowledged. First, this study did not involve randomization nor a placebo 'treated' control group. Due to the proven efficacy of IPL in MGD, we considered it unethical. In addition, direct comparison with many studies is difficult due to different study designs, diagnostic criteria, cohort ethnicity, skin type and IPL protocols. Nevertheless, we present an extensive and objective evaluation of the effects of IPL on multiple ocular parameters, including tear osmolarity. Results show that IPL including treatment of the upper eyelids combined with MGX results in NITBUT, OSDI and improvement of DED symptoms and signs. There is still significant heterogeneity between the available studies regarding spot sizes, treatment schedules, number of patients, follow-up regimens and devices.

In conclusion, the present study demonstrated that the combination of IPL including upper eyelid treatment and MGX is safe and effective for the treatment of MGD. Further studies are necessary to develop and establish the most adequate number of sessions and define the predictive factors associated to a greater effect in order to develop evidence-based clinical guidelines for the use of IPL to treat MGD.

Acknowledgements

We would like to thank Yvonne Hernández for her important role coordinating and supporting the study.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Jose Manuel Benitez-del-Castillo https://orcid.org/0000-0002-2010-1701
Antonio Cano-Ortiz https://orcid.org/0000-0003-3587-7892
Barbara Burgos-Blasco https://orcid.org/0000-0003-2178-6164

References

1. Hassanzadeh S, Varmaghani M, Zarei-Ghanavati S, et al. Global prevalence of meibomian gland dysfunction: a systematic review and meta-analysis. *Ocul Immunol Inflamm [Internet]* 2021; 29: 66–75. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32589483.
2. McCann P, Abraham AG, Mukhopadhyay A, et al. Prevalence and incidence of dry eye and Meibomian gland dysfunction in the United States: a systematic review and meta-analysis. *JAMA Ophthalmol [Internet]* 2022; 140: 1181–1192. Available from: http://www.ncbi.nlm.nih.gov/pubmed/36301551.
3. Yadav S, Gupta N, Makwana T, et al. Noninvasive ocular surface analyzer as an adjunct in diagnosis and estimating prevalence of meibomian gland dysfunction: hospital-based comparative study. *Indian J Ophthalmol [Internet]* 2022; 70: 1539–1545. Available from: http://www.ncbi.nlm.nih.gov/pubmed/35502020.
4. Rabensteiner DF, Aminfar H, Boldin I, et al. The prevalence of meibomian gland dysfunction, tear film and ocular surface parameters in an Austrian dry eye clinic population. *Acta Ophthalmol [Internet]* 2018; 96: e707–e711. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29656524.
5. Nichols KK, Foulks GN, Bron AJ, et al. The international workshop on meibomian gland dysfunction: executive summary. *Investig Ophthalmol Vis Sci* 2011; 52: 1922–1929.
6. Lam PY, Shih KC, Fong PY, et al. A review on evidence-based treatments for Meibomian gland dysfunction. *Eye Contact Lens* 2020; 46: 3–16.
7. Barbosa Ribeiro B, Marta A, Ponces Ramalhão J, et al. Pulsed light therapy in the Management of dry eye disease: current perspectives. *Clin Ophthalmol* 2022; 16: 3883–3893.
8. Toyos R, McGill W and Briscoe D. Intense pulsed light treatment for dry eye disease due to meibomian gland dysfunction; a 3-year retrospective study. *Photomed Laser Surg [Internet]* 2015; 33: 41–46. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25594770.
9. Leng X, Shi M, Liu X, et al. Intense pulsed light for meibomian gland dysfunction: a systematic review and meta-analysis. *Graefe's Arch Clin Exp Ophthalmol [Internet]* 2021; 259: 1–10. Available from: https://link.springer.com/10.1007/s00417-020-04834-1.
10. Toyos R, Desai NR, Toyos M, et al. Intense pulsed light improves signs and symptoms of dry eye disease due to meibomian gland dysfunction: a randomized controlled study. *PLoS One [Internet]* 2022; 17: 1–23. Available from: https://dx.doi.org/10.1371/journal.pone.0270268.
11. Yan S and Wu Y. Efficacy and safety of intense pulsed light therapy for dry eye caused by meibomian gland dysfunction: a randomised trial. *Ann Palliat Med [Internet]* 2021; 10: 7857–7865. Available from: https://apm.amegroups.com/article/view/75154/html.
12. Arita R, Fukuoka S and Morishige N. Therapeutic efficacy of intense pulsed light in patients with refractory meibomian gland dysfunction. *Ocul Surf [Internet]* 2019; 17: 104–110. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1542012418302222.
13. Qin G, Chen J, Li L, et al. Managing severe evaporative dry eye with intense pulsed light therapy. *Ophthalmol Ther* 2023; 12: 1059–1071.
14. Albietz JM and Schmid KL. Intense pulsed light treatment and meibomian gland expression for moderate to advanced meibomian gland dysfunction. *Clin Exp Optom* 2018; 101: 23–33.
15. Zarei-Ghanavati S, Hassanzadeh S, Khorasani AA, et al. The effect of Meibomian gland dysfunction treatment on sleep quality. *J Curr Ophthalmol [Internet]* 2021; 33: 272–276. Available from: http://www.ncbi.nlm.nih.gov/pubmed/34765814.
16. Zarei-Ghanavati S, Hassanzadeh S, Azimi Khorasani A, et al. Efficacy of five-flash intense pulsed light therapy technique in patients with meibomian gland dysfunction. *Clin Exp Optom [Internet]* 2022; 105: 687–693. Available from: http://www.ncbi.nlm.nih.gov/pubmed/34538227.
17. Iradier MT, Del Buey MÁ, Peris-martínez C, et al. Characterization and prediction of the clinical outcome of intense pulsed light-based treatment in dry eye associated to meibomian gland dysfunction. *J Clin Med* 2021; 10: 3573.
18. Liu Y, Chen D, Chen X, et al. Hypoxia: a breath of fresh air for the meibomian gland. *Ocul Surf [Internet]* 2019; 17: 310–317. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30528291.
19. Liu Y, Wang J, Chen D, et al. The role of hypoxia-inducible factor 1α in the regulation of human Meibomian gland epithelial cells. *Invest Ophthalmol Vis Sci [Internet]* 2020; 61: 1. Available from: http://www.ncbi.nlm.nih.gov/pubmed/32150252.
20. Yu H, Zeng W, Zhao G, et al. Response of tear cytokines following intense pulsed light combined with meibomian gland expression for treating meibomian gland dysfunction-related dry eye. *Front Endocrinol (Lausanne) [Internet]* 2022; 13: 973962. Available from: http://www.ncbi.nlm.nih.gov/pubmed/36187125.
21. Choi M, Han SJ, Ji YW, et al. Meibum expressibility improvement as a therapeutic target of intense pulsed light treatment in Meibomian gland dysfunction and its association with tear inflammatory cytokines. *Sci Rep [Internet]* 2019; 9: 7648. Available from: https://www.nature.com/articles/s41598-019-44000-0.
22. Liu R, Rong B, Tu P, et al. Analysis of cytokine levels in tears and clinical correlations after intense pulsed light treating Meibomian gland dysfunction. *Am J Ophthalmol [Internet]* 2017; 183: 81–90. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0002939417303756.
23. Qiao C, Li L, Wang H, et al. Adverse events of intense pulsed light combined with Meibomian gland expression versus meibomian gland expression in the treatment of meibomian gland dysfunction. *Lasers Surg Med [Internet]* 2021; 53: 664–670. Available from: http://www.ncbi.nlm.nih.gov/pubmed/33161597.

24. Jewsbury H and Morgan F. Uveitis and iris photoablation secondary to intense pulsed light therapy. *Can J Ophthalmol [Internet]* 2012; 47: e13–e14. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22883855.
25. Pang ALY and Wells K. Bilateral anterior uveitis after intense pulsed light therapy for pigmented eyelid lesions. *Dermatol Surg [Internet]* 2008; 34: 1276–1279. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18554285.
26. Lee WW, Murdock J, Albini TA, et al. Ocular damage secondary to intense pulse light therapy to the face. *Ophthal Plast Reconstr Surg [Internet]* 2011; 27: 263–265. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21346668.