Long-Term Effect of Intense Pulsed Light Combined with Low-Level Light Therapy in the Treatment of Meibomian Gland Dysfunction

Efeito de Longo Prazo da Luz Pulsada Combinada com Luz de Reduzida Intensidade no Tratamento da Disfunção das Glândulas de Meibomius

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ABSTRACT

INTRODUCTION: We aim to evaluate the efficacy of intense pulsed light (IPL) combined with low-level light therapy (LLLT) in the treatment of meibomian gland dysfunction (MGD).

METHODS: A prospective, double-arm and non-randomized study; adult patients with MGD were consecutively assigned to either IPL combined with LLLT (group 1, Eye-Light® + My-Mask® by Expansione Group, Italy) or IPL therapy alone (group 2, E>Eye® by ESW vision, France), with evaluation at baseline and at 1st, 6th, 12th and 18th month after treatment. Outcomes were the variation of the validated Dry Eye Related Questionnaire (OSDI-12) and automated analysis of the ocular surface (IDRA® Ocular Surface Analyzer SBM Sistemi, Italy) such: non-invasive break-up time (NIBUT), blink rate (BR), tear meniscus height (TMH), lipid layer thickness (LLT) and loss area of meibomian glands (LAMG); tear osmolarity (Osm) by TearLab® Osmolarity System (Tearlab, San Diego, CA, USA), Schirmer's test (ST) and slit lamp examination (Oxford score) were also evaluated.

RESULTS: Sixty-two patients (124 eyes) were included: 31 in group 1 and 31 in group 2. Comparing baseline with the 18th month of follow-up, both groups showed a significant improvement in the Ocular Surface Disease Index (OSDI-12) (p<0.001), in LLT (p<0.001) and ST (group 1, p<0.001; group 2, p=0.029). There was a significant improvement in group 1 without improvement in group 2 in BR (p<0.001 *vs* p=0.618) and in TMH (p=0.040 *vs* p= 0.701). An increase in group 1 (p<0.001) with a decrease in group 2 (p=0.005) occurred in Osm; a decrease in both groups (group 1, p=0.789; group 2, p=0.133) was observed in NIBUT; no differences in both groups (group 1, p=0.659; group 2, p=0.158) were verified in Oxford score. During the follow-up, 6 eyes (group 1) and 16 eyes (group 2) were referred for retreatment.

CONCLUSION: IPL treatment is an effective and safe therapeutic choice for MGD. Both groups showed benefits in symptoms and automatic measurements even after 18 months. There was a need for earlier re-treatment in group 2, demonstrating the superiority of combined treatment in group 1, with maintenance of therapeutic benefit for a longer period.

KEYWORDS: Dry Eye Syndromes; Intense Pulsed Light Therapy; Low-Level Light Therapy; Meibomian Gland Dysfunction; Meibomian Glands.

RESUMO

INTRODUÇÃO: O objetivo do estudo foi avaliar a eficácia da luz pulsada (IPL) combinada com luz de reduzida intensidade (LLLT) no tratamento da disfunção da glândula meibomiana (MGD).

MÉTODOS: Estudo prospectivo, de braço duplo e não randomizado; doentes adultos com MGD foram consecutivamente designados para IPL combinado com LLLT (grupo 1, Eye-Light®+My-Mask® do Expansione Group, Itália) ou terapia IPL isoladamente (grupo 2, E>Eye® da ESW vision, França), com avaliação inicial e ao 1º, 6º, 12º e 18º mês após o tratamento. Os resultados foram a variação do *Ocular Surface Disease Index* (OSDI-12) e a análise automatizada da superfície ocular (IDRA® *Ocular Surface Analyzer* SBM Sistemi, Itália), tais como: *non-invasive break-up time* (NIBUT), taxa de pestanejo (BR), altura do menisco lacrimal (TMH), espessura da camada lipídica (LLT) e área de perda das glândulas meibomianas (LAMG); a osmolaridade lacrimal (Osm) pelo TearLab® *Osmolarity System* (Tearlab, San Diego, CA, EUA), teste de Schirmer (ST) e exame com lâmpada de fenda (*Oxford score*) também foram avaliados.

RESULTADOS: Incluídos 62 doentes (124 olhos): 31 no grupo 1 e 31 no grupo 2. Comparando o baseline com o 18º mês de *follow-up*, os grupos apresentaram melhoria significativa no Índice de Doença da Superfície Ocular (OSDI-12) (p<0,001), no LLT (p<0,001) e no ST (grupo 1, p<0,001; grupo 2, p=0,029). Houve melhoria significativa no grupo 1 sem melhoria no grupo 2 no BR (p<0,001 *vs* p=0,618) e no TMH (p=0,040 *vs* p= 0,701). Houve aumento no grupo 1 (p<0,001) com diminuição no grupo 2 (p=0,005) na Osm; observada diminuição em ambos os grupos (grupo 1, p=0,789; grupo 2, p=0,133) no NIBUT; não foram verificadas diferenças em ambos os grupos (grupo 1, p=0,659; grupo 2, p=0,158) no *Oxford score*. Durante o seguimento, 6 olhos (grupo 1) e 16 olhos (grupo 2) foram encaminhados para retratamento.

CONCLUSÃO: O tratamento com IPL é uma opção terapêutica eficaz e segura para a MGD. Os grupos apresentaram benefícios nos sintomas e nos valores das medições automáticas mesmo após 18 meses. Houve necessidade de retratamento mais precoce no grupo 2, demonstrando a superioridade do tratamento combinado no grupo 1, com manutenção do benefício terapêutico por um período mais longo.

PALAVRAS-CHAVE: Disfunção das Glândulas Meibomianas; Doença Síndromes do Olho Seco; Glândulas Meibomianas; Terapia de Luz de Baixo Lível; Terapia de Luz Pulsada Intensa.

INTRODUCTION

Dry eye disease (DED) is currently recognized as a multifactorial disease in which loss of tear film homeostasis is the central pathophysiological concept.[1-3] The ocular surface, meibomian glands, the main lacrimal gland and the innervation between them form a functional unit in such a way that any of these structures are affected in DED.[4]

The prevalence of DED varies between 5% to 34% and the prevalence increases with age.[4] Risk factors may include female sex, age, history of refractive surgery, medication, hormonal dysfunction and systemic diseases.[3-5] Recent studies have demonstrated that DED is an inflammatory disease in which pro-inflammatory cytokines, chemokines and matrix metalloproteinases lead to the expansion of autoreactive helper T cells that infiltrate the ocular surface and lacrimal gland. This series of changes triggers a vicious cycle of tear film instability, excessive evaporation, hyperosmolarity and inflammation of the ocular surface.[4,6,7] The symptoms of dry eye disease include redness, burning, stinging, foreign body sensation, pruritus and photophobia.[3,8]

The NEI/Industry Report identified two main categories of dry eye as tear deficiency and evaporative deficiency and this classification was reinforced with the scheme presented by the TFOS DEWS report in 2007.[2,3,8,9] Meibomian gland dysfunction (MGD) is the main etiological factor of DED. It is a chronic, diffuse abnormality caused by an obstruction at the opening of the meibomian gland duct, due either to keratinized cells or meibum with excessively high viscosity.[3,4,6,10,11]

There has been a paradigm shift in the treatment of MGD in recent years: classical treatment (such as eyelid hygiene, warm compresses, meibomian gland expression and artificial tears) has been reinforced by topical steroids, cyclosporine, leucocyte function–associated antigen-l antagonists, secretagogues and antibiotics.[3,7,12]

Besides, new therapies are now available, and intense pulsed light (IPL) is its hallmark: It consists in non-coherent, polychromatic light pulses, with a wavelength spectrum ranging from 500 to 1200 nm, applied in the periorbital region, thereby improving dry eye symptoms, and reducing inflammation. Its underlying mechanisms involve meibum

liquefaction and collagen remodeling via thermal energy, coagulation of abnormal eyelid telangiectasia, and inhibition of inflammatory mediators, thereby reducing bacterial and parasitic growth.[2,3,11,12]

Low-level light therapy (LLLT) is a different type of photomodulation where athermal low-power monochromatic red light (wavelength spectrum ranging from 600 to 1100 nm) is applied, promoting an antioxidant effect, reducing inflammation and improving the function of normal cells.[2,10,12]

Since there is little evidence comparing IPL vs combination therapy, we aimed to compare the efficacy of IPL vs. IPL/LLLT in the treatment of MGD.

METHODS

STUDY DESIGN

We conducted a prospective, observational, double-arm, non-randomized study from the outpatient clinic of the Ophthalmology Department of Centro Hospitalar Universitário de Santo António, between July 2020 and July 2023. The authors ensured that all patients' anonymity was carefully protected. Informed consent for procedures and the use of data for publication was signed by all patients. The study was conducted in accordance with the Declaration of Helsinki (1964) and its latest amendment (Brazil, 2013) and approval was obtained from the "Departamento de Ensino, Formação e Investigação" (DEFI), number 2021.143 (115-DEFI/118-CE).

PARTICIPANTS

Patients with a clinical diagnosis of MGD according to The International Workshop on Meibomian Gland Dysfunction,[13] refractory to conventional treatment and aged over 18 years were considered for treatment.

Patients were excluded from treatment if (1) they had an area of loss of meibomian glands in the lower eyelid (MGA) greater than 40% (atrophic MGD), assessed by infrared meibography with the IDRA® Ocular Surface Analyzer (SBM Sistemi, Inc., Turin, Italy); (2) history of ocular trauma (3) intraocular surgery or intraocular inflammatory disease in the last six months; (4) contact lenses wear in the last six months; (5) previous eyelid or tear surgery; (6) history of skin cancer anywhere; (7) use of photosensitizing drugs; (8) the presence of piercings in the treatment area; (9) inability to comply with treatment or follow-up regimen. If one eye met the exclusion criteria, both eyes were excluded from the study.7 Patients were allowed to use their usual artificial tears, but no changes were allowed after starting treatment.

PROTOCOL

Two groups of patients who were treated with IPL were considered:

- Group 1: Patients undergoing IPL combined with LLLT (31 patients, 62 eyes.). Each treatment session began with 5 IPL pulses (Eye-Light® with Optimal Power Energy®, Espansione Marketing S.p.A., Bologna, Italy) applied to each eye, in the periorbital region, inferiorly (4 pulses) and laterally (1 pulse). The application of a cooling gel was not necessary with the Optimal Power Energy® technology. Treatment was followed by bilateral application of LLLT (My Mask®, Espansione Marketing S.p.A., Bologna, Italy) for 15 minutes, independently of the skin pigmentation. The treatments were performed in 3 sessions 1 week apart, as recommended by the manufacturer.
- Group 2: Patients undergoing IPL therapy alone (31 patients, 62 eyes). Each treatment session consisted of 5 IPL (E>Eye, E-SWIN, Paris, France) applied to each eye, in the periorbital region, inferiorly (4 pulses) and laterally (1 pulse), over a layer of gel applied to the skin for optimized cooling and light conduction. The treatments were performed in 3 sessions, on day 0, day 15 and day 45, as recommended by the manufacturer.

Before IPL treatment, protective shields were placed over the eyes and the skin was cleaned in the areas to be treated. Hyperpigmented skin lesions were covered with a protective adhesive. Regardless of the group, the level of energy delivered was automatically set for each patient according to the degree of skin pigmentation (subjectively evaluated with skin Fitzpatrick scale) and each manufacturer recommendation. The light pulses were applied perpendicularly to the skin to minimize reflection. The clinician who applied the treatment was subject to the use of protective goggles. Between treatment sessions and during 15 days after the last treatment session, subjects were encouraged to apply sunscreen daily and avoid direct sun exposure.

OUTCOMES

In both arms, subjects were evaluated at baseline and at 1st, 6th, 12th and 18th months after treatment. Symptoms were evaluated with the Ocular Surface Disease Index (OSDI-12), a validated questionnaire, that ranges from 0 to 100, with higher values indicating greater severity [normal (<12), mild (13–22), moderate (23–32), or severe (33–100)].[14] Automated ocular surface analysis was performed with the IDRA® Ocular Surface Analyzer (SBM Sistemi, Italy), which evaluated the non-invasive break-up time (NIBUT), the eye blink rate (BR), the tear meniscus height (TMH), the lipid layer thickness (LLT) and loss area of meibomian glands (LAMG).

The tear osmolarity (Osm) was measured with the TearLab® Osmolarity System (Tearlab, San Diego, CA, USA); the basal tear flow was assessed with the basal secretion test (Schirmer strips, after the instillation of topical anesthetic) and a slit lamp evaluation was performed, followed by the instillation of fluorescein dye to assess Oxford score for grading ocular surface staining in dry eye.[15]

STATISTICAL ANALYSIS

Statistical analysis was performed using the SPPS software (SPSS statistics, version 26.0.0 for Mac OS, IBM, Som-

ers, NY). The Kolmogorov-Smirnov test was used to assess normality. Comparison between independent continuous variables was evaluated using the Mann-Whitney U test and T-Student test. Fisher's exact test was used for nominal scaled data. Spearman's bivariate correlation test was applied to study correlations. *P* values less than 0.05 were considered statistically significant.

RESULTS

Sixty-two patients (124 eyes) were included: 31 in group 1 and 31 in group 2. A comparison of baseline demographic data and clinical data between groups is shown in Table 1.

In group 1, 48 eyes (77.4%) completed the 18 months follow-up (Table 2): in the final follow-up, 42 eyes (representing 67.7% of the initial sample) had no clinical complaints and 6 eyes (9.7%) had complaints of burning and stinging (and they were referred for retreatment with IPL).

In group 2, 46 eyes (74.2%) completed the 18 months of follow-up (Table 3): in the final of follow-up, 18 eyes (representing 20.0% of the initial sample) presented no clinical complaints; 20 eyes (representing 32.3% of the initial sample) showed improvements compared to baseline but began to start some complaints (but without the need for retreatment); 8 eyes (12.9%) demonstrated complaints of burning and itching and they were referred for IPL retreatment.

During follow-up, in group 1, 6 eyes were referred for IPL retreatment (2 eyes at 12th month and 4 eyes at 18th month) instead in group 2, 16 eyes were referred for IPL retreatment (10 eyes at 12th month and 6 eyes at 18th month); a total of 8 eyes were lost to follow-up (2 patients died and 2 patients did not attend any further appointments) in group 1 and no eye was lost during follow-up in group 2.

Comparing the baseline with the 18th month of follow-up, both groups showed a significant improvement (p<0.001) in the OSDI-12 and LLT and significant improvement with different "p-values" in ST (group 1, p<0.001; group 2, p=0.029). There was a significant improvement in group 1 without improvement in group 2 in BR (p<0.001 *vs* p=0.618) and in TMH (p=0.040 *vs* p= 0.701). An increase in group 1 (p<0.001) with a decrease in group 2 (p=0.005) occurred in Osm; a decrease in both groups (group 1, p=0.789; group 2, p=0.133) was observed in NIBUT; no differences in both groups (group 1, p=0.659; group 2, p=0.158) were verified in Oxford score.

Regarding the safety analysis, no adverse effects were noted in any group (no conjunctivitis, blistering, edema, skin pigmentation changes or loss of eyelashes).

Table 1. Baseline characteristics and univariate analysis.

	Group 1 (n=62 eyes)	Group 2 (n=62 eyes)	Total (n=124 eyes)	*p*-value
Demographic characteristics				
Mean age, years±SD	66.9 ± 9.1	64.4 ± 11.0	65.7 ± 10.1	0.168[1]
Male, n (%)	24 (63.2)	14 (36.8)	38 (30.6)	0.051[2]
Comorbidities				
History of diabetes, n (%)	58 (93.5)	40 (64.5)	98 (79.0)	**<0.001**[2]
History of arterial hypertension, n (%)	40 (64.5)	20 (32.3)	60 (48.4)	**<0.001**[2]
Ophthalmic history				
Previous cataract surgery, n (%)	11 (17.7)	26 (41.9)	37 (29.8)	**0.003**[2]
Use of anti-hypertensive eye drops, n (%)	12 (19.4)	8 (12.9)	20 (16.1)	0.329[2]
Use of lubricant eye drops, n (%)	47 (75.8)	42 (67.7)	89 (71.8)	0.318[2]
Use of eye drops with preservatives, n (%)	22 (35.5)	30 (48.4)	52 (41.9)	0.145[2]
Ocular surface parameters				
Non-invasive break-up time, mean±SD	10.2±4.5	9.9±3.6	10.0 ± 4.1	0.658[1]
Blink rate* (median, IQR)	100 (2)	60 (48)	100 (43)	**<0.001**[3]
Tear meniscus height, mean±SD	0.3±0.2	0.3±0.1	0.3±0.1	**0.016**[1]
Lipid layer thickness* (median, IQR)	55 (25)	55 (44)	55 (25)	0.360[3]
Loss area of meibomian glands* (median, IQR)	3 (16)	10.5 (15)	7 (17)	**0.037**[3]
Tear osmolarity, mean±SD	298.1±11.3	314.7±19.5	306.4±17.9	**<0.001**[1]
Schirmer's test, mean±SD	9.6±5.5	10.4±6.8	10.0±6.2	0.4691
Oxford score, mean±SD	1.0±1.2	1.5±1.5	1.2±1.4	0.616
OSDI score, mean±SD	45.0±21.2	42.1±24.6	43.5±22.9	0.474[1]
OSDI score grade, n (%)				
Normal	6 (9.7)	8 (12.9)	14 (11.3)	0.347[2]
Mild	4 (6.5)	6 (9.7)	10 (8.1)	
Moderate	5 (8.1)	10 (16.1)	15 (12.1)	
Severe	47 (75.8)	38 (61.3)	85 (68.5)	

[1] Student T-Test; [2] Chi-Square; [3] Mann-Whitney U; * Do not have normal distribution by visual analysis of the histogram; Statistically significant values are highlighted in **bold (p<0.05).** SD: standard deviation; OSDI: Ocular Surface Disease Index.

Table 2. Baseline and follow-up assessments at 12 and 18 months of group 1.

	Baseline (n=62 eyes)	12th month (n=48 eyes)	*p*-value (baseline vs 12th month)	18th month (n=48 eyes)	*p*-value (baseline vs 18th month)
Non-invasive break-up time, mean±SD	10.2±4.5	10.0±2.1	0.834	9.8±1.7	0.789
Blink rate* (median, IQR)	100.0 (2)	56.0 (18)	<0.001	55 (12)	**<0.001**
Tear meniscus height, mean±SD	0.3±0.2	0.3±0.2	0.863	0.3±0.1	**0.040**
Lipid layer thickness* (median, IQR)	55.0 (25)	90.0 (20)	<0.001	80 (20)	**<0.001**
Loss area of meibomian glands* (median, IQR)	3.0 (16)	9.0 (20)	0.334	10 (14)	0.600
Tear osmolarity, mean±SD	298.1±11.3	309.3±16.4	<0.001	307.8±11.6	**<0.001**
Schirmer's test, mean±SD	9.6±5.5	13.0±6.7	<0.001	13±6.0	**<0.001**
Oxford score, mean±SD	1.0±1.2	0.42±0.8	0.601	0.42±1.0	0.659
OSDI score, mean±SD	45.0±21.2	12.3±13.4	<0.001	12.1±14.6	**<0.001**

[1] Paired Samples T-Test; [2] Wilcoxon Signed Ranks Test; [3] McNemar Test; *4 missings; Statistically significant values are highlighted in **bold (*p*<0.05).** SD: standard deviation; OSDI: Ocular Surface Disease Index.

Table 3. Baseline and follow-up assessments at 12 and 18 months of group 2.

	Baseline (n=62 eyes)	12th month (n=52 eyes)	*p*-value (baseline vs 12th month)	18th month (n=46 eyes)	*p*-value (baseline vs 18th month)
Non-invasive break-up time, mean±SD	10.2±4.5	10.0±2.1	0.834	9.8±1.7	0.789
Blink rate* (median, IQR)	100.0 (2)	56.0 (18)	<0.001	55 (12)	<0.001
Tear meniscus height, mean±SD	0.3±0.2	0.3±0.2	0.863	0.3±0.1	0.040
Lipid layer thickness* (median, IQR)	55.0 (25)	90.0 (20)	<0.001	80 (20)	<0.001
Loss area of meibomian glands* median, IQR)	3.0 (16)	9.0 (20)	0.334	10 (14)	0.600
Tear osmolarity, mean±SD	298.1±11.3	309.3±16.4	<0.001	307.8±11.6	<0.001
Schirmer's test, mean±SD	9.6±5.5	13.0±6.7	<0.001	13±6.0	<0.001
Oxford score, mean±SD	1.0±1.2	0.42±0.8	0.601	0.42±1.0	0.659
OSDI score, mean±SD	45.0±21.2	12.3±13.4	<0.001	12.1±14.6	<0.001

[1] Paired Samples T-Test; [2] Wilcoxon Signed Ranks Test; [3] McNemar Test; Statistically significant values are highlighted in **bold (*p*<0.05).** SD: standard deviation; OSDI: Ocular Surface Disease Index.

DISCUSSION

To our knowledge, this is the first comparative study investigating the effects of IPL alone vs. combined IPL/LLLT therapy for the treatment of MGD during an 18-month follow-up.

Previous literature demonstrates the efficacy and safety of both treatment modalities. However, its long-term efficacy is unknown: a 2020 Cochrane meta-analysis found uncertain evidence for the efficacy and safety of IPL as a treatment for MGD.[16] The differences in inclusion criteria and methodologies may limit the comparison of several studies.[10]

Our study demonstrates objective and subjective long-term-efficacy in the treatment of patients with dry eye and MGD treated either with IPL alone or with combined IPL/LLLT therapy, which is in line with previous publications.[2,7,10-12]

Regarding the reported symptoms, there was a significant improvement in the OSDI-12 score in both groups that persisted at the 18-month follow-up, with greater improvement in group 1.

Compared with combined therapy, in group 2, the IPL alone effect may wane after a 12-month follow-up, which is demonstrated by the worsening of burning and itching symptoms and the greater need for retreatment in this group. These data are corroborated by the fact that eyes in group 2 presented clinical complaints during follow-up in more than three times the cases compared to eyes in group 1 (n=44, 71.0% *vs* n=12, 19.4% in group 2 and group 1, respectively). Pérez-Silguero *et al* reported that in studies with longer follow-up, a decline of improvement was observed 3–4 months after the last session, in contrast to the data obtained in our study.[12]

Regarding the analysis of the ocular surface, there was a significant LLT improvement in both groups ($p<0.001$), in line with some of the existing literature: this improvement was greater at the 12th month in group 1; on the other hand, the improvement obtained by group 2 at the 12th month remained stable until the 18th month. The improvement in LLT occurs through a global improvement in the function of the meibomian glands and consequently an improvement in the consistency of secretions, in both cases promoted by the IPL action, an action that is present in both groups. Marques *et al* demonstrated significant improvements 3 weeks after the last treatment session in the combined treatment of IPL with LLLT[7] and Marta *et al* also demonstrated a significant improvement after 6 months of treatment.[2]

On the other hand, there was a significant improvement in blink rate ($p<0.001$) and tear meniscus height ($p=0.040$) only in group 1. Some of the postulated mechanisms for the effec-

tiveness of LLLT are its cellular photoactivation, inducing the activation of mitochondria and anti-inflammatory processes, through the regulation of reactive oxygen species[12]; on the other hand, it is postulated that lacrimal gland secretion may improve through the effect of LLLT, since it is the only treatment that was applied directly to the upper eyelid, which may be responsible for the improvement observed in the quality of blinking or the quality of film tearing.[2]

In our study, there was a tendency for improvement in the production of aqueous tears assessed by the Schirmer test, as previously reported by Marta *et al* at a 6-month follow-up study.[2] This improvement, although more pronounced in group 1, was statistically significant in both groups, whose peak was at the 12th month, maintaining at least until 18 months.

Regarding tear osmolarity, a different behavior was observed in both groups: there was a statistically significant increase (p<0.001) in group 1 and a statistically significant decrease (p=0.005) in group 2. The study by Marta *et al*[2] demonstrated that the mean tear osmolarity was higher 6 months after treatment and this can be explained by the higher increment on the lipid layer (solute) compared to the increment on the aqueous layer (solvent). However, in some studies of IPL without LLLT,[17,18] tear osmolarity was reported to be reduced, as observed in group 2 of our study. In our point of view, in dry eye disease, there is not always a concordance between the improvement of symptoms and the improvement in Osm. Since dry eye is a multifactorial and complex disease, the Osm assessment may not be a good indicator to assess improvement in symptoms or response to treatment.

Finally, in the Oxford score, there were no significant differences in the 18th month as reported in some studies.[7,2] However, in group 2, at 6th month, there was a clinically significant improvement. This finding may be a consequence of the non-significant, but unequal distribution of diabetic patients between the groups, with greater frequency in group 1, and this parameter may be a confounding factor, since there may be an underlying diabetic keratopathy component, leading to a greater propensity for keratitis.[2,7]

To our knowledge, this is the longest follow-up study evaluating the effects of IPL combined with LLLT therapy. Furthermore, this study included eyes with different severities of DED with DGM and a multimodal assessment.

This prospective study with a good sample size allowed control, through a validated multimodal assessment (objective) and questionnaire (subjective), and to evaluate the response to innovative therapeutic regimens, for a long period of follow-up.

The biggest limitation of this study is that it is a non-randomized study. The ideal would be to treat one eye being the other eye the control in the same patient, avoiding the tendency in dry eye studies of subjective improvement with any treatment. However, the mask used for LLLT treatment (MY MASK-E®) makes it impossible to treat just one eye. Furthermore, the two eyes are not always the same in the same person. Another limitation is losses during follow-up. Comparative studies with larger samples and follow-up are needed to validate these results.

It was decided to set the maximum follow-up limit for our sample at 18 months. A longer follow-up period would not be representative of our sample due to losses to follow-up by the patients.

The results of this study show some differences between the groups, namely in the need for retreatment, which was earlier in group 2, highlighting the superiority of combined treatment in group 1, with maintenance of therapeutic benefit for longer. This may possibly be related to the use of a mask with a more comprehensive LLLT effect, allowing stimulation of other cells/glands with consequent improvement in aqueous secretion.

CONCLUSION

IPL treatment is an effective and safe therapeutic choice for DED. DED is a multifactorial and difficult-to-treat disease and, in this sense, IPL appeared as an emerging technology, but very safe and effective in relieving symptoms. Other therapies such as LLLT, more recently, have also demonstrated potential usefulness in refractory cases, and in co-adjuvant treatments with IPL.

In our study, both treatment groups showed benefits in terms of symptoms and automatic measurements even after 18 months, with a need for earlier retreatment in group 2. Thus, this study demonstrated the superiority of combined treatment in group 1, with maintenance of therapeutic benefit for a longer period.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

JL, IB: Drafting the manuscript.
BBR, JHM, PS, SP, PM and IB: Critical revision.
All authors approved the final version to be published.

JL, IB: Elaboração do manuscrito.
BBR, JHM, PS, SP, PM and IB: Revisão crítica.
Todos os autores aprovaram a versão final a ser publicada.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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