DOI: 10.4274/tjo.galenos.2020.28924
Turk J Ophthalmol 2021;51:89-94

Original Article

Efficacy of Intense Pulsed Light Treatment for Moderate to Severe Acute Blepharitis or Blepharoconjunctivitis: A Retrospective Case Series

Özgün Melike Gedar Totuk*, Kerem Kabadayı**, Cihan Özkapı***, Ümit Aykan****

*Bahçeşehir University Faculty of Medicine, Department of Ophthalmology, İstanbul, Turkey
**Bahçeşehir University Faculty of Medicine, İstanbul, Turkey
***Üsküdar University, Health Services Vocational School, Department of Opticianry, İstanbul, Turkey
****Yakın Doğu University Faculty of Medicine, Department of Ophthalmology, Nicosia, Cyprus

Abstract

Objectives: We aimed to evaluate the efficacy of periocular intense pulsed light (IPL) therapy in the treatment of moderate to severe acute blepharitis or blepharoconjunctivitis.

Materials and Methods: This was a retrospective study performed in one institution. Eleven patients who received bilateral periocular IPL therapy using an IPL device (E>Eye, ESwin, Paris, France) were retrospectively evaluated. The following findings obtained at baseline and 10 weeks after the treatment were recorded: slit-lamp examinations; symptom scores of the Compression of the Eyelid (COTE) grading system and Ocular Surface Disease Index (OSDI); ocular surface staining with Oxford grading scale (OXFORD) scores; lipid layer thickness (LLT); and non-invasive tear meniscus test (TMH), non-invasive break up time measurement (NIBUT), and meibography performed by using I.C.P. Ocular Surface Analyzer (SBM System, Turin, Italy).

Results: Significant improvements in OSDI symptom scores ($p<0.0001$), LLT ($p<0.0001$), and meibography ($p<0.0001$) were obtained at 10 weeks after bilateral periocular IPL therapy. COTE and ocular surface staining scores decreased by 59.72% and 57.14% respectively, while NIBUT and TMH increased by 47.34% and 22.16%, respectively. In parallel to the improvement in OSDI, LLT, and meibography, findings of acute blepharitis or blepharoconjunctivitis improved in slit-lamp examination. There were no adverse effects.

Conclusion: Serial IPL therapy improves the clinical signs and symptoms of moderate to severe acute blepharitis or blepharoconjunctivitis, meibomian gland morphology, and secretion quality.

Keywords: Blepharitis, blepharoconjunctivitis, intense pulsed light treatment, meibography

Introduction

Meibomian gland dysfunction (MGD) refers to functional abnormalities of the meibomian glands such as chronic and diffuse terminal duct obstruction and qualitative or quantitative changes in the glandular secretion of the meibomian glands.[1,2] Blepharitis is the general term for inflammation of the eyelids as a whole. Acute blepharitis may be bacterial, viral, or parasitic in etiology. It often affects the anterior eyelid, with the most prominent changes centered on the meibomian glands.[1,2] Acute blepharitis associated with secondary conjunctival and corneal involvement is defined as acute blepharoconjunctivitis. MGD and severe chronic blepharitis may result in increased bacterial growth on the lid margin, ocular surface inflammation, and damage.[1,2]

The diagnosis of acute blepharitis or blepharoconjunctivitis is based on clinical signs and symptoms such as inflamed eyelids, anterior lid margin telangiectasia, accumulation of collarettes around the base of the cilia, recurrent episodes of chronic red eye, watering, photophobia, styes or meibomian cysts, and keratitis.

Address for Correspondence: Özgün Melike Gedar Totuk, Bahçeşehir University Faculty of Medicine, Department of Ophthalmology, İstanbul, Turkey
Phone: +90 533 336 79 86 E-mail: melikegedar@gmail.com **ORCID-ID:** orcid.org/0000-0003-1863-6501
Received: 08.12.2019 **Accepted:** 16.07.2020

Cite this article as: Gedar Totuk ÖM, Kabadayı K, Özkapı C, Aykan Ü. Efficacy of Intense Pulsed Light Treatment for Moderate to Severe Acute Blepharitis or Blepharoconjunctivitis: A Retrospective Case Series. Turk J Ophthalmol 2021;51:89-94

Clinical signs and symptoms are graded as mild, moderate, or severe.[1,2,3]

The common treatment approaches in moderate to advanced acute blepharitis or blepharoconjunctivitis, such as warm compresses, lid massage, daily lid hygiene, topical or systemic broad spectrum antibiotics, and topical corticosteroids, have limited efficacy.[1,2,3]

Intense pulsed light (IPL) therapy has been applied in the periocular area in dermatology for over a decade for the treatment of rosacea. During this period, it has been noticed that facial skin rosacea patients treated with IPL reported a significant improvement in their dry eye symptoms, thus the clinical application of IPL devices has been extended to include the treatment of MGD.[4,5,6,7] However, the effect of IPL treatment in patients with moderate to severe acute blepharitis or blepharoconjunctivitis has not been extensively studied.

In this study we aimed to evaluate the effect of a series of three bilateral IPL treatments, which was applied in addition to the standard clinical treatments, in patients with moderate to severe acute blepharitis or blepharoconjunctivitis.

Materials and Methods

Study Design and Patients

This was a single-center, retrospective study. Eleven patients with moderate to severe acute blepharitis or blepharoconjunctivitis who received bilateral IPL treatment using an IPL device (E>Eye, ESwin, Paris, France) in our clinic were retrospectively evaluated. Patients with moderate to severe acute blepharitis or blepharoconjunctivitis had moderate-marked hyperemia, diffuse or marked diffuse infiltration, tarsal conjunctival vessels just visible or no visible, moderate papillary hyperplasia and more than 5 follicles, as defined by Viswalingam et al.[2] None of the patients had prior treatment for acute blepharitis or blepharoconjunctivitis. Patients with excessive sun exposure in the last month, a history of herpes zoster infection, pregnancy, use of photosensitizing drugs or foods, or skin Fitzpatrick scale V/VI were excluded from the study.

Informed consent was obtained from all of the patients after explanation of the nature and possible consequences of the IPL treatment. The study was approved by the Institutional Ethics Committee of Bahçeşehir University (6 Nov 2019; 2019-16/04).

Study Procedures and Scales

The results of the following clinical evaluations performed at baseline and 10 weeks after the treatment were recorded: slit-lamp examinations; symptom scores of the Compression of the Eyelid (COTE) grading system and Ocular Surface Disease Index (OSDI); ocular surface staining with Oxford grading scale (OXFORD) scores; lipid layer thickness (LLT); and non-invasive tear meniscus height (TMH), non-invasive tear break-up time (NIBUT) measurement, and meibography performed using an I.C.P. Ocular Surface Analyzer (SBM System, Turin, Italy).

The OSDI is a self-administered questionnaire containing 12 items and scoring a range of 0 (no symptoms) to 100 (severe symptoms) points. It is evaluated using the following formula: OSDI=Dx25/E, where D is the sum of scores for all questions answered and E is the number of questions answered. A final score of 0 to 12 is interpreted as no disability, 13 to 22 as mild symptoms, 23 to 32 as moderate symptoms, and 33 to 100 as severe symptoms. The validated Turkish version of the OSDI was used in the study.

The Oxford grading scale divides corneal staining into six groups according to severity from 0 (absent) to 5 (severe).

TMH was measured using an I.C.P. Ocular Surface Analyzer with a high-power pre-shot image. Values less than 0.22 mm were considered below normal. As the tear volume was measured with TMH, we did not perform invasive Schirmer test for any of our patients.

NIBUT of the tear film was determined with a tear interferometer using the I.C.P. Ocular Surface Analyzer. The time between the last complete blink and the first indication of pattern break-up and image deformation of the Placido rings image detected with a special film in the interferometer was measured. Values equal to or greater than 10 s were considered normal.

Meibomian gland function was assessed with the COTE grading system and LLT.

The COTE test is performed at the slit lamp, using a nonpreserved, artificial tear-wetted or warm water-wetted cotton bud. On the basis of the nature and severity of expressed tarsal gland secretions, it is graded as follows: 1, clear oil; 2, easy or slow and difficult egress of pus; 3, thick toothpaste-like secretion (worm-like); 4, complete blockage of tarsal gland, no egress of secretion visualized.

LLT was assessed by interferometry using the I.C.P. Ocular Surface Analyzer and measured by analyzing the interference of images by using a color profile of the pre-ocular tear film in the blinking eyes. LLT was graded from F to 0 based on the comparison of the videos obtained to the classification installed in the device and seven short videos with different thicknesses of the tear film lipid layer (160-120 nm, 80-120 nm, 80 nm, 30-80 nm, 30 nm, 15 nm, <15 nm).

Meibomian gland morphological indexes were assessed by non-contact meibography using the I.C.P. Ocular Surface Analyzer.

Intense Pulsed Light Treatment

The IPL device (E>Eye, ESwin, Paris, France) has a proprietary treatment algorithm delivering light pulses with a spectral range of 580 to 1200 nm. At each treatment session, both eyes of the patient were closed with opaque safety goggles. An ultrasonic conductive gel was applied to the targeted periocular skin area reaching up to the inferior boundary of the eye shields. Four adjacent IPL flashes were administered to the skin area immediately below the lower eyelid and one IPL flash on the temple of both eyes with the E>Eye device.

Treatments were performed at baseline following baseline assessments, week 2, and week 6, adjusting the appropriate pulse intensity setting (range, 9.8-13 J/cm^2) following the

manufacturer's treatment protocol for the E>Eye device. Multiple homogenously sculpted light treatment pulse intensities were chosen based on the Fitzpatrick scale according to the manufacturer's guidelines (with very lightly pigmented Phototype 1 participants being treated at 13 J/cm^2 and individuals with dark brown complexions being treated at 9.8 J/cm^2).

Patients applied warm compresses with eyelid massage and lid hygiene with tea tree oil shampoo daily. In addition to IPL treatment, all patients received the following pharmacological treatment: 1% azithromycin ophthalmic solution (1 drop twice daily for 2 days followed by once daily dosing for 12 days) and 0.05% dexamethasone ophthalmic suspension (1 drop 4 times daily for 14 days).

Results

Twenty-two eyes of 11 patients with moderate to severe acute blepharitis or blepharoconjunctivitis (5 women and 6 men, mean age 50.54±19.39 years, age range 17-77 years) were included in the study. Cataract surgery had been performed on 4 eyes of 2 patients more than 3 years before, multiple chalazion surgeries had been performed on 6 eyes of 3 patients more than a year before, and pars plana vitrectomy surgery had been performed on 1 eye of 1 patient 7 years before the initiation of IPL therapy. Two patients had seborrheic skin type. There was no diagnosis of skin disease or previous skin therapy in any of the patients.

OSDI score (range, 0-100) was significantly improved at 10 weeks after serial IPL therapy compared with baseline score (29.73±4.58 vs. 12.36±1.40; p<0.0001). Over half of the eyes (55%) had OSDI scores higher than 12 (Table 1). Oxford grading scale (range, 0-5) did not show a significant decrease at 10 weeks after serial IPL therapy (1.91±0.75 vs. 0.82±0.39; p=0.12). However, the percentage of eyes showing an absence of corneal and ocular surface staining increased from 18% to 57.14% after serial IPL therapy (Table 1).

NIBUT (normal >10 s) was prolonged from 4.52±0.90 s to 6.66±1.50 s with serial IPL therapy, but this prolongation was not statistically significant (p=0.48, Table 1). At 10 weeks after serial IPL therapy, NIBUT was longer than 10 s in 9% eyes and the mean NIBUT increased by 47.34%. There was also an increase in the mean TMH score that was not statistically significant when compared with baseline (0.29±0.12 vs. 0.35±0.09; p=0.55) (Table 1). However, all of the eyes were within normal range (>0.22 mm) and TMH level increased by 22.16% at 10 weeks after serial IPL therapy.

LLT (range, 0-6) was significantly improved at 10 weeks after serial IPL therapy compared with baseline thickness (1.23±0.43 vs. 2.46±0.67; p<0.0001) showing improvement in all of the eyes (Table 1). In contrast, although the mean COTE score (graded 1-4) did not significantly decrease at 10 weeks after serial IPL therapy (3.27±0.77 vs. 1.32±0.48; p=0.11) (Table 1), 59.72% of eyes had decreased COTE score and 68% had clear oil secretion.

Meibomian gland loss area (range, 0-100%) significantly decreased both in upper eyelids and lower eyelids at 10 weeks after serial IPL therapy compared with baseline (p<0.0001) (Table 1). In 36% of the eyelids, meibomian gland loss completely resolved after serial IPL therapy.

Discussion

In the present study, we primarily found that the subjective symptoms and objective signs of acute blepharitis or blepharoconjunctivitis were significantly improved after a series of IPL treatments combined with short-term medical therapy.

MGD is an important clinical condition which can lead to hyperosmolarity and instability of the tear film, increased bacterial growth on the lid margin, eye irritation, ocular surface inflammation, and dry eye.[8] MGD causes more viscous meibum production than usual, and patients can experience severe inflammation and bacterial overgrowth that exacerbates abnormal meibum production.[1,2] Inflammation of the meibomian glands leads to acute blepharitis or blepharoconjunctivitis, which can be treated with warm compresses, lid massage, and topical antibiotics.[4,5,6] Treatment modalities for blepharitis include eyelid hygiene (i.e., warm compresses, eyelid massage, and eyelid scrubs), meibomian gland expression and probing, topical corticosteroid drops to decrease inflammation in acute exacerbations, topical antibiotics for up to eight weeks for staphylococcal and seborrheic blepharitis, and increasing dietary intake of essential fatty acids, specifically omega-3 fatty acid, in cases of mild-to-severe MGD.[3] For severe cases, topical steroids and systemic antibiotics are needed. Most acute blepharitis or blepharoconjunctivitis cases result from underlying MGD. Treatment is often long-term and requires patient adherence, yet despite diverse treatment modalities, complete and lasting relief of the signs and symptoms of MGD could not be obtained.[9] Recurrence during follow-up is common and requires repeating the treatment.[10,11,12,13] Additionally, long-term antibiotic and

Table 1. Signs and symptom scores before and 10 weeks after serial intense pulsed light (IPL) therapy

Score (range)	Baseline	10 weeks post-IPL	p value[a]
COTE grade (1-4)	3.27±0.77	1.32±0.48	0.11
OSDI score (0-100)	29.73±4.58	12.36±1.40	<0.0001
OXFORD scale (0-5)	1.91±0.75	0.82±0.39	0.12
NIBUT (> or <10 s)	4.52±0.90	6.66±1.50	0.48
LLT (0-F[b])	1.23±0.43	2.46±0.67	<0.0001
MGL (0-100%)			
UL	31.86±13.08	9.82±10.58	<0.0001
LL	26.59±9.94	7.41±7.56	<0.0001
TMH (> or <0.22 mm)	0.29±0.12	0.35±0.09	0.55

COTE: Compression of the Eyelid, OSDI: Ocular Surface Disease Index, OXFORD: Ocular surface staining with Oxford grading scale, NIBUT: Non-invasive break-up time, LLT: Lipid layer thickness, MGL: Meibomian gland loss, UL: Upper eyelids, LL: Lower eyelids, TMH: Tear meniscus height; [a]Paired t test. [b]LLT is scored as follows: A=1, B=2, C=3, D=4, E=5, and F=6

corticosteroid therapy bears the potential risk of serious side effects.[9] Although there is no standard concomitant medical therapy after IPL procedure, our patients were treated with warm compresses with eyelid massage, lid hygiene with tea tree oil shampoo daily, and short-term topical antibiotic and corticosteroid drops. The decreased number of medications is a critical factor increasing patients' adherence to treatment and decreasing the risk of potential side effects of systemic medications. Although the cost of IPL therapy is relatively high and not covered by health insurance, it is balanced by reduced medication costs.

Since IPL therapy was accidentally found to treat dry eye due to MGD during its use for the treatment of facial rosacea, IPL has been used as an effective and well-tolerated treatment option for improvement of subjective symptoms and objective findings of mild to moderate MGD or dry eye.[4,5,13,14,15,16] This relatively novel treatment modality utilizes non-coherent, polychromatic light in a wavelength spectrum of 500-1200 nm applied to the periocular skin for selective thermolysis. The light absorbed by chromophores (e.g., melanin), hemoglobin, and water in the skin transforms into heat, causing thrombosis and ablation of superficial blood vessels.[17]

The mechanisms underlying the effect of IPL treatment in MGD are not clearly understood. Multiple possible mechanisms of action have been proposed:

1. Thrombosis of abnormal erythematous blood vessels removes the major source of inflammation in the eyelids and meibomian glands through facial artery and orbital vessels.[17]

2. IPL therapy causes a temperature increase up to 45-70 °C in small blood vessels, which in turn raises the eyelid skin temperature above the phase-transition temperature, which is 4 °C higher in MGD patients than healthy subjects. This thermal response unclogs the meibomian glands, liquefies the meibum and facilitates distribution over the ocular surface.[18,19]

3. The reduction in epithelial turnover with IPL therapy decreases the accumulation of debris on the lid margin and eliminates the risk of physical meibomian gland obstruction.[20]

4. Photomodulation (intracellular changes at the gene and protein levels by means of visible and infrared light induction) starts a cascade of excitation of cytochrome C oxidase, induction of redox potentials of mitochondrial respiratory chain and electron transfer, increase in cytoplasmic ATP levels, and finally increase in intracellular free calcium concentration, which stimulates specific physiological reactions for cell development and growth.[21,22,23]

5. Photomodulation increases the proliferation rate of fibroblasts and enhances the synthesis of collagen genes.[23,24]

6. The light delivered during IPL therapy is absorbed by pigmented chromophores in the exoskeleton of *Demodex folliculum*, a potential mediator of blepharitis, causing coagulation and necrosis of the ectoparasite.[25,26] Eradication of *Demodex* decreases the microbial load, particularly commensal bacteria *Bacillus olerinus,* which contributes to chronic inflammation of the eyelids.[27]

7. IPL therapy interferes with the positive feedback loop underlying the inflammatory cycle by upregulating anti-inflammatory agents like interleukin (IL)-10 and transforming growth factor beta (TGF-β) and/or downregulation of proinflammatory ones like IL-6 and tumor necrosis factor alpha (TNF-α).[28,29,30]

8. IPL indirectly suppresses one of the major protein families in the pathogenesis of dry eye disease, matrix metalloproteinases, by downregulating TNF-α.[31]

9. High-dose light irradiation causes attenuation of reactive oxygen species levels and decreases oxidative stress and inflammation.[7,32]

The E>Eye device, which we used in our study, is one of the specifically configured periocular IPL therapy devices (intense regulated pulsed light, IRPL) with regulated wavelengths, pulse duration, pulse intervals, and fluence depending on the patient's skin Fitzpatrick score. IPL therapy is not recommended for patients with a Fitzpatrick score higher than IV to avoid the risk of melanin damage and hypopigmentation.[33,34]

The non-invasive nature of the IPL device is favorable for both patient and ophthalmologist. However, incorrect use can cause devastating intraocular complications such as acute iridocyclitis due to neglecting the use of eye shields, permanent iris atrophy, posterior synechia, pupillary block, and secondary angle closure glaucoma due to absorption of light by the pigmented iris.[35,36,37,38,39] Other side effects are transient blistering, cheek swelling, conjunctival cyst, floaters, hair loss on the brow and forehead, light sensitivity, redness of face, purpura, and hyperpigmentation.[16,33,40] We observed no adverse effects in any of our patients.

Toyos et al.[16] reported that tear break-up time (TBUT) and meibum secretion were improved in 86% and 94% of patients with MGD-associated dry eye disease treated with IPL and meibomian gland expression (MGX), and the rate of patient satisfaction with treatment was 93%. Gupta et al.[41] showed a significant decrease in meibum viscosity and OSDI score and a significant increase in meibum flow and TBUT in MGD patients who underwent IPL therapy. Mejía et al.[42] demonstrated that IPL therapy effectively improves dry eye symptoms and objective scores of TBUT, Schirmer test, ocular surface staining in both evaporative and aqueous-deficient dry eye disease. Albietz and Schmid[43] reported sustained improvements in meibum expression, TBUT, ocular surface staining, and OSDI 6 weeks after final treatment with IPL/MGX, but not in Schirmer test or tear osmolarity. Arita et al.[15] showed significant improvement in Standard Patient Evaluation of Eye Dryness (SPEED) score, NIBUT, TBUT, meibum grade, and ocular surface staining in refractory MGD cases at 6 to 32 weeks of IPL/MGX. Choi et al.[44] reported that in addition to improvements in meibum score, TBUT, ocular surface staining, and OSDI, there is a correlation between meibomian gland function in patients with MGD and decreased inflammatory cytokines levels after IPL therapy. Dell et al.[45] reported that TBUT, corneal staining, tear film osmolarity, SPEED score, and meibomian gland score were improved but LLT was unchanged after 4 sessions of IPL/MGX in moderate

to severe MGD. Jiang et al.[46] reported significant improvement in symptom scores, TBUT, and meibomian gland score in MGD eyes, with no adverse effects. Karaca et al.[47] also reported improvement in Schirmer test, TBUT, OSDI, and SPEED scores, but not in Oxford scale or meibomian gland score after 3 sessions of IPL therapy in patients with MGD. Li et al.[40] observed a larger increase in TBUT and OSDI scores in younger MGD patients with Fitzpatrick skin types III-IV after IPL therapy. Seo et al.[5] indicated that improvements in meibomian gland score and ocular symptoms persisted for 12 months in patients with rosacea-associated MGD after 4 sessions of IPL treatment. Craig et al.[48] reported significant increase in LLT and NIBUT, but not in TMH or tear evaporation rate in MGD eyes treated with IPL.

To our knowledge, this is the first study in the English literature showing the effects of IPL therapy on moderate to severe acute blepharitis or blepharoconjunctivitis. We primarily observed clinical improvement in moderate to severe acute blepharitis or blepharoconjunctivitis patients without any side effects. We also found that ocular surface indexes (OSDI scores, ocular surface staining, non-invasive TMH, and NIBUT), meibomian gland functional indexes (COTE grading system and LLT), and meibomian gland morphological indexes determined using the non-contact meibography system with I.C.P. Ocular Surface Analyzer were improved, consistent with the literature.

Study Limitations

The main limitations of the study are its retrospective and single-arm design, small number of patients, concomitant drug treatment, and short follow-up time. Further prospective controlled studies with larger sample size and longer follow-up duration will be necessary to assess the long-term effectiveness and safety of IPL treatment for acute blepharitis or blepharoconjunctivitis.

Conclusion

In conclusion, our results suggest that in patients with moderate to severe acute blepharitis or blepharoconjunctivitis, serial IPL therapy in addition to conventional treatments effectively improves clinical signs, meibomian gland morphology, and secretion quality.

Ethics

Ethics Committee Approval: The study was approved by the Institutional Ethics Committee of Bahçeşehir University (6 Nov 2019; 2019-16/04).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.M.G.T., Concept: Ö.M.G.T., Ü.A., Design: Ö.M.G.T., Ü.A., Data Collection or Processing: Ö.M.G.T., K.K., C.Ö., Analysis or Interpretation: Ö.M.G.T., K.K., C.Ö., Ü.A., Literature Search: Ö.M.G.T., K.K., C.Ö., Writing: Ö.M.G.T., Ü.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Nelson JD, Shimazaki J, Benitez-del-Castillo JM, Craig JP, McCulley JP, Den S, Foulks GN. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52:1930-1937.
2. Viswalingam M, Rauz S, Morlet N, Dart JKG. Blepharokeratoconjunctivitis in children: diagnosis and treatment. Br J Ophthalmol. 2005;89:400-403.
3. Lindsley K, Matsumura S, Hatef E, Akpek EK. Interventions for chronic blepharitis. Cochrane Database Syst Rev. 2012:CD005556.
4. Rong B, Tang Y, Liu R, Tu P, Qiao J, Song W, Yan X. Long-term effects of ıntense pulsed light combined with meibomian gland expression in the treatment of meibomian gland dysfunction. Photomed Laser Surg. 2018;36:562-567.
5. Seo KY, Kang SM, Ha DY, Chin HS, Jung JW. Long-term effects of intense pulsed light treatment on the ocular surface in patients with rosacea-associated meibomian gland dysfunction. Cont Lens Anterior Eye. 2018;41:430-435.
6. Vegunta S, Patel D, Shen JF. Combination therapy of ıntense pulsed light therapy and meibomian gland expression (IPL/MGX) can improve dry eye symptoms and meibomian gland function in patients with refractory dry eye: a retrospective analysis. Cornea. 2016;35:318-322.
7. Dell SJ. Intense pulsed light for evaporative dry eye disease. Clin Ophthalmol. 2017;11:1167-1173.
8. Küçümen RB, Utine CA, Görgün E, Yenerel NM, Ziylan S, Çiftçi F. Evaluation of tear film osmolarity in cases with chronic belpharitis. [In Turkish] Turk J Ophthalmol. 2015;45:5-8.
9. Alves M, Fonseca EC, Alves MF, Malki LT, Arruda GV, Reinach PS, Rocha EM. Dry eye disease treatment: a systematic review of published trials and a critical appraisal of therapeutic strategies. Ocul Surf. 2013;11:181-192.
10. Torkildsen GL, Cockrum P, Meier E, Hammonds WM, Silverstein B, Silverstein S. Evaluation of clinical efficacy and safety of tobramycin/dexamethasone ophthalmic suspension 0.3%/0.05% compared to azithromycin ophthalmic solution 1% in the treatment of moderate to severe acute blepharitis/blepharoconjunctivitis. Curr Med Res Opin. 2011;27:171-178.
11. Thode AR, Latkany RA. Current and emerging therapeutic strategies for the treatment of meibomian gland dysfunction. Drugs. 2015;75:1177-1185.
12. Akova YA, Asena L. Meibomian Gland Dysfunction: Review. Turkiye Klinikleri J Ophthalmol. 2014;23:172-183.
13. Geerling G, Tauber J, Baudouin C, Goto E, Matsumoto Y, O'Brien T, Rolando M, Tsubota K, Nichols KK. The International Workshop on Meibomian Gland Dysfunction: report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011;52:2050-2064.
14. Yin Y, Liu N, Gong L, Song N. Changes in the meibomian gland after exposure to intense pulsed light in meibomian gland dysfunction (MGD) patients. Curr Eye Res. 2018;43:308-313.
15. Arita R, Mizoguchi T, Fukuoka S, Morishige N. Multicenter study of intense pulsed light therapy for patients with refractory meibomian gland dysfunction. Cornea. 2018;37:1566-1571.
16. Toyos R, McGill W, Briscoe D. Intense pulsed light treatment for dry eye disease due to meibomian gland dysfunction; a 3-year retrospective study. Photomed Laser Surg. 2015;33:41-46.
17. Papageorgiou P, Clayton W, Norwood S, Chopra S, Rustin M. Treatment of rosacea with intense pulsed light: significant improvement and long-lasting results. Br J Dermatol. 2008;159:628-632.
18. Borchman D, Foulks G, Yappert M, Bell J, Wells E, Neravetla S, Greenstone V. Human meibum lipid conformation and thermodynamic changes with meibomian-gland dysfunction. IOVS. 2011;52:3805-3817.
19. Bäumler W, Vural E, Landthaler M, Muzzi F, Shafirstein G. The effects of intense pulsed light (IPL) on blood vessels investigated by mathematical modeling. Lasers Surg Med. 2007;39:132-139.

20. Henriquez A, Korb D. Meibomian glands and contact lens wear. Br J Ophthalmol. 1981;65:108-111.
21. Karu T. Primary and secondary mechanisms of action of visible to near-IR radiation on cells. J Photochem Photobiol B. 1999;49:1-17.
22. Farivar S, Malekshahabi T, Shiari R. Biological effects of low level laser therapy. J Lasers Med Sci. 2014;5:58-62.
23. Takezaki S, Omi T, Sato S, Kawana S. Ultrastructural observations of human skin following irradiation with visible red light-emitting diodes (LEDs): a preliminary in vivo report. Laser Ther. 2005;14:153-160.
24. Cuerda-Galindo E, Díaz-Gil G, Palomar-Gallego M, Linares-GarcíaValdecasas R. Increased fibroblast proliferation and activity after applying intense pulsed light 800–1200 nm. Ann Anat. 2015;198:66-72.
25. Prieto V, Sadick N, Lloreta J, Nicholson J, Shea C. Effects of intense pulsed light on sun-damaged human skin, routine, and ultrastructural analysis. Lasers Surg Med. 2002;30:82-85.
26. Kirn T. Intense pulsed light eradicates Demodex mites. Skin Allergy News. 2002;33:37.
27. O'Reilly N, Menezes N, Kavanagh K. Positive correlation between serum immunoreactivity to Demodex-associated Bacillus proteins and erythematotelangiectatic rosacea. Br J Dermatol. 2012;167:1032-1036.
28. Byun J, Choi H, Myung K, Choi Y. Expression of IL-10, TGF-β1 and TNF-α in cultured keratinocytes (HaCaT Cells) after IPL treatment or ALA-IPL photodynamic treatment. Ann Dermatol. 2009;21:12-17.
29. Lee S, Park K, Choi J, Kwon J, Lee DR, Shin MS, Lee JS, You CE, Park MY. A prospective, randomized, placebo-controlled, double-blinded, and split-face clinical study on LED phototherapy for skin rejuvenation: clinical, profilometric, histologic, ultrastructural, and biochemical evaluations and comparison of three different treatment settings. J Photochem Photobiol B. 2007;88:51-67.
30. Taylor M, Porter R, Gonzalez M. Intense pulsed light may improve inflammatory acne through TNF-α down-regulation. J Cosmet Laser Ther. 2014;16:96-103.
31. Wong WR, Shyu WL, Tsai JW, Hsu KH, Lee HY, Pang JH. Intense pulsed light modulates the expressions of MMP-2, MMP-14 and TIMP-2 in skin dermal fibroblasts cultured within contracted collagen lattices. J Dermatol Sci. 2008;51:70-73.
32. Lubart R, Lavi R, Friedmann H, Rochkind S. Photochemistry and photobiology of light absorption by living cells. Photomed Laser Surg. 2006;24:179-185.
33. Guilloto Caballero S, García Madrona JL, Colmenero Reina E. Effect of pulsed laser light in patients with dry eye syndrome. Arch Soc Esp Oftalmol. 2017;92:509-515.
34. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol. 1988;124:869-871.
35. Crabb M, Chan WO, Taranath D, Huilgol SC. Intense pulsed light therapy (IPL) induced iritis following treatment for a medial canthal capillary malformation. Australas J Dermatol. 2014;55:289-291.
36. Lee WW, Murdock J, Albini TA, O'Brien TP, Levine ML. Ocular damage secondary to intense pulse light therapy to the face. Ophthal Plast Reconstr Surg. 2011;27:263-265.
37. Pang AL, Wells K. Bilateral anterior uveitis after intense pulsed light therapy for pigmented eyelid lesions. Dermatol Surg. 2008;34:1276-1279.
38. Goldman MP, Weiss RA, Weiss MA. Intense pulsed light as a nonablative approach to photoaging. Dermatol Surg. 2005;31:1179-1187.
39. Javey G, Schwartz SG, Albini TA. Ocular complication of intense. pulsed light therapy: iris photoablation. Dermatol Surg. 2010;36:1466-1468.
40. Li D, Lin S, Cheng B. Intense pulsed light treatment for meibomian gland dysfunction in skin types III/IV. Photobiomodul Photomed Laser Surg. 2019;37:70-76.
41. Gupta PK, Vora GK, Matossian C, Kim M, Stinnett S. Outcomes of intense pulsed light therapy for treatment of evaporative dry eye disease. Can J Ophthalmol. 2016;51:249-253.
42. Mejía LF, Gil JC, Jaramillo M. Intense pulsed light therapy: a promising complementary treatment for dry eye disease. Arch Soc Esp Oftalmol. 2019;94:331-336.
43. Albietz JM, Schmid KL. Intense pulsed light treatment and meibomian gland expression for moderate to advanced meibomian gland dysfunction. Clin Exp Optom. 2018;101:23-33.
44. Choi M, Han SJ, Ji YW, Choi YJ, Jun I, Alotaibi MH, Ko BY, Kim EK, Kim T, Nam SM, Seo KY. Meibum Expressibility improvement as a therapeutic target of intense pulsed light treatment in meibomian gland dysfunction and its association with tear infammatory cytokines. Sci Rep. 2019;9:1-8.
45. Dell SJ, Gaster RN, Barbarino SC, Cunningham DN. Prospective evaluation of intense pulsed light and meibomian gland expression efficacy on relieving signs and symptoms of dry eye disease due to meibomian gland dysfunction. Clin Ophthalmol. 2017;11:817-882.
46. Jiang X, Lv H, Song H, Zhang M, Liu Y, Hu X, Li X, Wang W. Evaluation of the safety and effectiveness of intense pulsed light in the treatment of meibomian gland dysfunction. J Ophthalmol. 2016;1910694.
47. Karaca EE, Kemer OE, Özek D. Intense regulated pulse light for the meibomian gland dysfunction. Eur J Ophthalmol. 2018;1-4.
48. Craig JP, Chen YH, Turnbull PRK. Prospective trial of intense pulsed light for the treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2015;56:1965-1970.