Intense pulsed light therapy for the treatment of evaporative dry eye disease

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Purpose of review
Evaporative dry eye disease is one of the most common types of dry eye. It is often the result of chronic meibomian gland dysfunction (MGD) and associated ocular rosacea. Evaporative dry eye and MGD significantly reduce patient's quality of life. Traditional treatments, such as artificial tears, warm compresses, and medications, such as topical cyclosporine, azithromycin, and oral doxycycline, provide some relief; however, many patients still suffer from dry eye symptoms. Intense pulsed light (IPL) therapy, which has been used extensively in dermatology to treat chronic skin conditions, is a relatively new treatment in ophthalmology for patients with evaporative dry eye disease.

Recent findings
There are very few studies published on the use of IPL in patients with dry eye disease. The present review describes the theoretical mechanisms of IPL treatment of MGD and ocular rosacea. Personal clinical experience and recently presented data are reported as well.

Summary
IPL therapy has promising results for evaporative dry eye patients. There are statistically significant improvements in clinical exam findings of dry eye disease. More importantly, patients report subjective improvement in their symptoms. More research is needed in this area to help understand the mechanism of dry eye disease and how it can be effectively treated.

Keywords
evaporative dry eye disease, intense pulsed light therapy, meibomian gland dysfunction

INTRODUCTION

Intense pulsed light (IPL) therapy, which uses light energy to affect the skin surface, is widely used in dermatology to treat a variety of conditions including dermal vascular lesions, such as port wine stains and hemangiomas, facial rosacea, and acne [1]. In addition, this technology is used in hair removal and treatment of facial skin photodamage signs, such as fine wrinkles and skin laxity [2]. In 2002, Rolando Toyos, MD, discovered the positive ophthalmic effects of IPL on his patients who underwent treatment for facial rosacea [3]. Along with decreased facial erythema, his patients developed improvement in signs and symptoms of meibomian gland dysfunction (MGD) and dry eyes. Working alongside DermaMed Solutions, he helped to develop an IPL system that was geared towards treatment of dry eye disease. Since that time, there has been a growing number of physicians across the USA that use IPL to treat MGD and dry eye.

The present review discusses the treatment of MGD and evaporative dry eye disease with IPL therapy. Although IPL is used in several eye care centers across the USA, there are only a few studies published in the literature. We describe our personal experience and also our early data.

MECHANISM OF INTENSE PULSED LIGHT TREATMENT FOR EVAPORATIVE DRY EYE

IPL is a broad spectrum, noncoherent, and polychromatic light source with a wavelength spectrum of 500–1200 nm; it can be filtered to allow only a range of wavelengths to be emitted [4]. The pivotal mechanism of IPL involves the principal of selective photothermolysis, in which light energy that comes

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KEY POINTS

- Intense pulsed light (IPL) therapy is an effective treatment for evaporative dry eye disease secondary to meibomian gland dysfunction (MGD) and ocular rosacea.
- Using the proper technique, IPL therapy for dry eye has an excellent safety profile.
- IPL should be offered to patients as a therapeutic option for patients suffering from dry eye and MGD-related symptoms.

in contact with tissue is preferentially absorbed by a chromophore and converted into heat (Fig. 1) [1]. With respect to the skin, melanin and hemoglobin are the two primary chromophores present. Light energy absorption in melanin decreases as the wavelength of light increases. Oxyhemoglobin, however, has an absorption peak at 578 nm. Yellow light wavelengths are able to pass through the upper layers of the skin without excessive absorption of the light energy by melanin. The absorption of the yellow light by oxyhemoglobin then results in conversion of the light into heat energy, leading to coagulation and ablation of blood vessels [5].

Eyelid margin telangiectasias are often seen clinically in patients with MGD and ocular rosacea. The pathophysiology of rosacea involves decreased connective tissue integrity, causing passive dilation of blood vessels (resulting in erythema and telangiectasias) and extravasation of inflammatory mediators (causing papules and pustules). IPL allows for selective ablation of these superficial vessels, which not only reduces telangiectasias and erythema but also presumably decreases inflammatory marker access

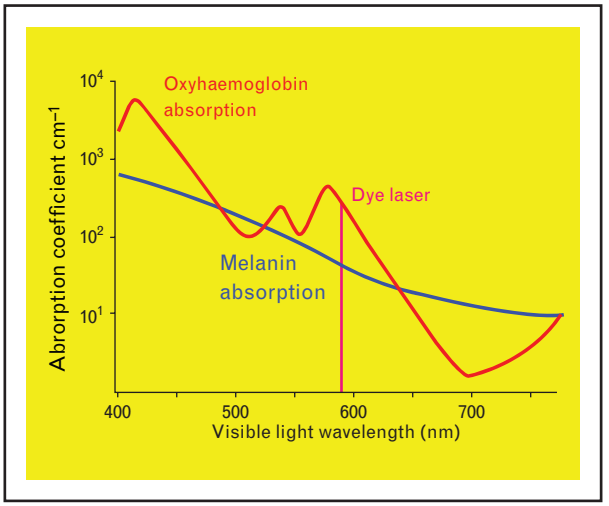

FIGURE 1. Oxyhemoglobin and melanin light absorption curves. (Reproduced by courtesy of DermaMed.).

to the meibomian glands. In addition, IPL is thought to aid collagen remodeling, which likely improves elastosis and connective tissue disorganization that occurs with rosacea and other such skin conditions [1,5].

Other potential mechanisms of action of IPL for dry eye treatment include reduction of bacteria and/or parasitic growth on the eyelids. *Demodex folliculorum* mites, which are ectoparasites living in hair follicles and sebaceous glands, retain a commensal relationship with the *Bacillus oleronius* bacterium. Together these organisms are often found in patients with facial rosacea [6]. The *B. oleronius* is a Gram-negative bacterium that has been found to cause an inflammatory response in patients with subtype 2 papulopustular rosacea [7]. Prieto *et al.* discovered coagulated *Demodex* organisms and reduced lymphocytic infiltration in patients who had undergone IPL treatment [8]. They postulated that the reduction of *Demodex*, and thereby *B. oleronius*, burden and its associated inflammation after IPL therapy helps to improve rosacea signs and symptoms. We can extrapolate this to ocular rosacea as *Demodex* has been previously cited in the literature as a potential mediator of blepharitis and MGD [9].

Another potential mechanism of IPL includes a temporary local thermal effect that warms the meibomian gland secretions. This warming effect can allow for improved manual expression of inspissated meibum within the meibomian glands after application of the light. With improved meibum secretion and viscosity, the tear film can become more stable and thus evaporative dry eye symptoms would improve.

INTENSE PULSED LIGHT PROCEDURE

Once the clinical diagnosis of MGD and dry eye have been made the patient's informed consent is obtained. IPL for MGD/dry eyes is an off label use of a United States Food and Drug Administration (US FDA) approved device. The Fitzpatrick skin type score is determined based on patient questionnaire responses about how their skin reacts to sun exposure [10]. Fair skin patients will have a lower score, whereas more deeply pigmented patients have a higher score. The Fitzpatrick score allows the physician to determine the IPL energy parameters appropriate for the degree of pigmentation. As discussed earlier, patients with more melanin (i.e., higher Fitzpatrick score) will necessitate lower energy settings to avoid risk of melanin damage and resultant hypopigmentation. For this reason, IPL treatment is generally limited to patients with Fitzpatrick skin type of four or less.

The procedure involves first placing protective IPL eye shields over the eyes. Ultrasound gel is

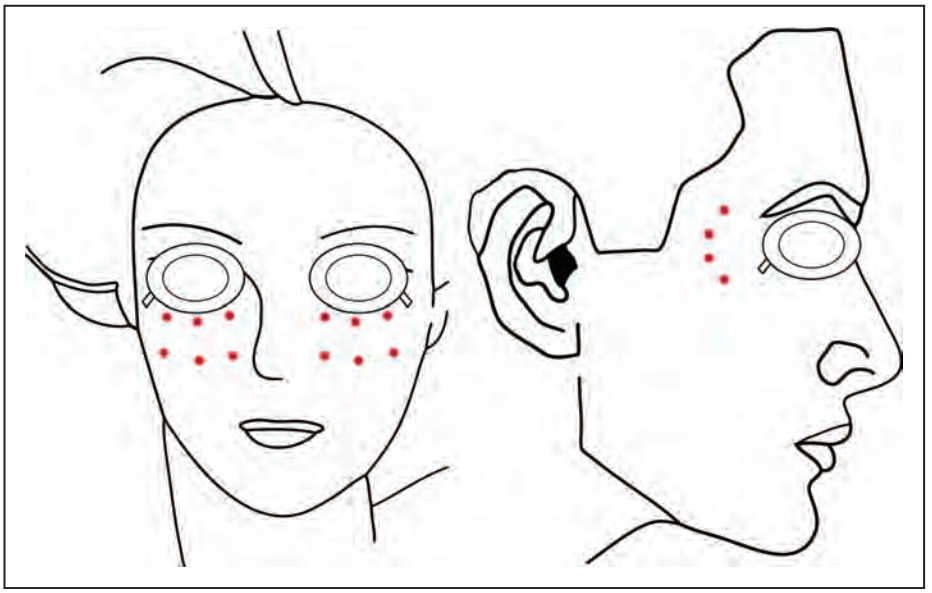

FIGURE 2. IPL treatment zone. The hand piece treats the highlighted areas for a total of 10–15 spots on each side of the face, and is then repeated in a second pass. Proper ocular protection is used.

applied on the skin to cool the treatment area. Using the DermaMed Quadra4 IPL (Lenni, PA, USA) system on the proprietary 'dry eye mode' setting, 10–15 IPL spots are placed on each side (Fig. 2). The energy parameters are determined by skin type (skin type settings 1–4, and mode A–F), along with patient tolerance and comfort. Application of the IPL is repeated for a total of two passes on each side. Only the skin inferior and lateral to the lower eyelid margin is treated. The upper eyelids are not treated directly, as there is risk of light penetration through the eyelid and absorption within the intraocular structures (i.e., pigmented iris tissue), leading to structural damage and inflammation from the broad-spectrum light. After the IPL treatment, the ultrasound gel is removed and a hot compress is placed along the eyelids for 2–3 min. Finally, the meibomian glands are manually expressed at the slit-lamp with a cotton-tip applicator. Patients then use a topical steroid, such as fluorometholone (FML) or loteprednol 0.5% one drop twice daily for 2–3 days after the procedure. With the initial series of IPL treatments, most patients undergo four treatments (range 3–6), each separated by 3–6 weeks. Subsequently, a single maintenance treatment is done every 4–12 months.

TREATMENT OUTCOMES

The treatment outcomes of IPL for facial rosacea in the dermatology literature are favorable. Schroeter *et al.* [11] reported 60 patients with 77.8% clearance of telangiectasias after an average of four IPL treatments. Papageorgiou *et al.* [5] reported 34 patients with subtype 1 erythematotelangiectatic rosacea achieved statistically significant reduction of facial erythema and telangiectasias after four IPL sessions. Of note, this study reported sustained benefits for at least 6 months. By varying the fluence and pulse duration of the IPL treatment in 102 patients, Kassir *et al.* [12] reported 80% with reduction in erythema, 78% with less flushing and better skin texture, and 72% with less acneiform flares. It should be noted that this flexibility in customizing fluence and pulse duration parameters is currently not available in the DermaMed Quadra4 IPL system using the dry eye mode; clinicians are only able to modulate energy indirectly by altering the skin type setting and the mode within the 'dry eye' mode.

In the ophthalmic literature, however, there is a paucity of published data for IPL treatment of evaporative dry eye disease. Craig *et al.* [13,14▪▪] did recently report results of a prospective placebo-controlled study of 28 patients with dry eye from MGD. One eye was treated with IPL, and the other had a placebo treatment at three time points. They reported statistically significant improvement in lipid layer grade and tear break-up time of the treated eye. Subjective symptom scores (using SPEED scoring) were improved in both eyes. Similarly, in a three-year retrospective review of 91 patients, Toyos *et al.* [15▪▪] reported significant improvement in tear break-up time in 87% of their patients. In addition, 93% of the patients reported posttreatment amelioration of symptoms.

In our own retrospective review, 37 patients with a diagnosis of evaporative dry eye disease

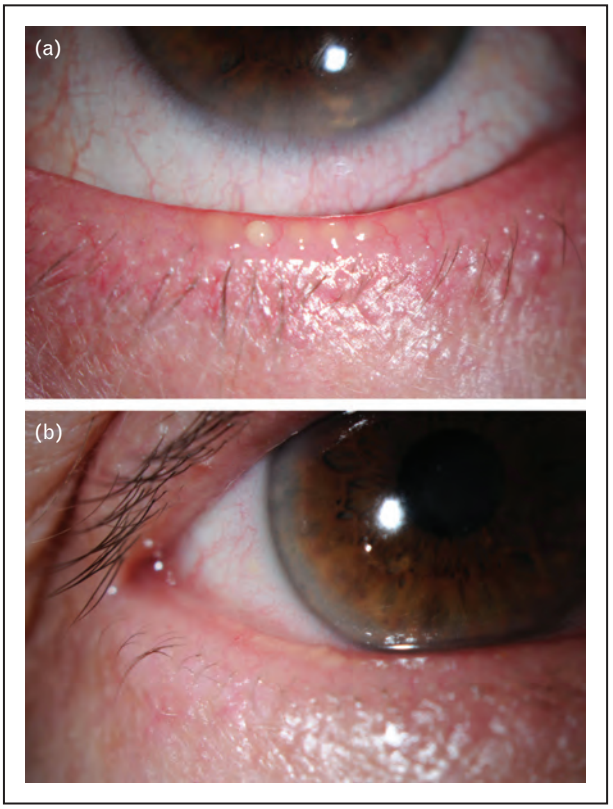

FIGURE 3. (a) Pretreatment: meibomian glands are inspissated with thick oil and fine telangiectasias. (b) Immediate posttreatment and manual expression: meibomian glands are expressed and oils are more liquefied.

underwent three or more IPL treatments [16]. Patients were examined at each visit for tear break-up time, and grading of eyelid and facial vascularity, eyelid margin edema, meibomian gland oil flow, and oil quality as described previously by Mathers [17]. In addition, each patient completed an Ocular Surface Disease Index (OSDI) questionaire to assess for subjective symptoms of dry eye disease. The OSDI score has been shown to be a valid and reliable measurement of the subjective symptoms of dry eye disease [18]. On average, the patients in our study had moderate–severe dry eye symptoms prior to IPL treatment as scored by the OSDI questionnaire. From first to last follow-up visit, there was a significant decrease in clinical signs of MGD. There was a decrease in scoring of lid margin edema, facial telangiectasia, lid margin vascularity, and improvement in meibum quality score, all with $P < 0.001$ (Fig. 3). Furthermore, there was a significant increase in oil flow score and tear break-up time, both $P < 0.001$. Subjective symptoms of dry eye disease also improved, and there was a statistically significant decrease in OSDI scoring ($P < 0.001$). Although not statistically significant, there was a general trend in reduction of the amount of artificial tear usage. Similar to the Papageorgiou study, our patients usually get lasting relief for several months. Oftentimes, maintenance treatments are necessary every 6–12 months. [16]

SAFETY PROFILE

Although IPL has a relatively good safety profile, some ocular complications have been reported when used without proper eye protection. Lee *et al.* [19] reported two patients with anterior uveitis, permanent iris atrophy and pupillary defects causing long-lasting photophobia and pain after receiving periorbital IPL treatment. The pigmented iris tissue absorbs light energy emitted from the IPL flash lamp, thereby posing as a vulnerable structure. Similar cases of uveitis and iris damage have been reported elsewhere in the literature [20–23]. Another case was reported of corneal pigment deposition in a patient who underwent IPL while wearing colored contact lenses [24]. The pigmentation resolved after superficial keratectomy. With proper eye protection, periocular IPL is safe. Our study had no adverse events aside from the normal postprocedure temporary discomfort and erythema that may occur.

CONCLUSION

IPL therapy is a safe and effective treatment for evaporative dry eye disease from MGD and rosacea. After an average of four treatments, patients develop relief from their chronic symptoms. Additional treatments are often required every 6–12 months to maintain symptom relief. More research is needed with more patients and longer follow-up time to assess the long-term outcomes of IPL treatment.

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Conflicts of interest

Dr P.K.G. is a consultant to Tear Science, Shire, Allergan, Biotissue, and Novabay. There were no conflicts of interest for the other author.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- ■ of special interest
- ■■ of outstanding interest

1. Piccolo D, Di Marcantonio D, Crisman G, *et al.* Unconventional use of intense pulsed light. Biomed Res Int 2014; 2014:618206.

2. Bitter PH. Noninvasive rejuvenation of photodamaged skin using serial, full-face intense pulsed light treatments. Dermatol Surg 2000; 26:835–842.
3. Kent C. Intense pulsed light: for treating dry eye. Rev Ophthalmol 2010; http://www.reviewofophthalmology.com/content/d/technology_update/i/1353/c/25857/.
4. Campolmi P, Bonan P, Cannarozzo G, *et al.* Intense pulsed light in the treatment of nonaesthetic facial and neck vascular lesions: report of 85 cases. J Eur Acad Dermatol Venereol 2011; 25:68–73.
5. Papageorgiou P, Clayton W, Norwood S, *et al.* Treatment of rosacea with intense pulsed light: significant improvement and long-lasting results. Br J Dermatol 2008; 159:628–632.
6. Li J, O'Reilly N, Sheha H, *et al.* Correlation between ocular *Demodex* infestation and serum immunoreactivity to *Bacillus* proteins in patients with facial rosacea. Ophthalmology 2010; 117:870–877; e1.
7. Lacey N, Delaney S, Kavanagh K, *et al.* Mite-related bacterial antigens stimulate inflammatory cells in rosacea. Br J Dermatol 2007; 157:474–481.
8. Prieto VG, Sadick N, Lloreta J, *et al.* Effects of intense pulsed light on sun-damaged human skin, routine, and ultrastructural analysis. Lasers Surg Med 2002; 30:82–85.
9. Liu J, Sheha H, Tseng SC. Pathogenic role of *Demodex* mites in blepharitis. Curr Opin Allergy Clin Immunol 2010; 10:505–510.
10. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. Arch Dermatol 1988; 124:869–871.
11. Schroeter CA, Haaf-von Below S, Neumann HA. Effective treatment of rosacea using intense pulsed light systems. Dermatol Surg 2005; 31:1285–1289.
12. Kassir R, Kolluru A, Kassir M. Intense pulsed light for the treatment of rosacea and telangiectasias. J Cosmet Laser Ther 2011; 13:216–222.
13. Craig J, Chen A, Turnbull PR. Prospective evaluation of intense pulsed light (IPL) therapy for meibomian gland dysfunction (MGD). Acta Ophthalmol 2014; 92:2014; Suppl 253:1965–1970.
14. ■■ Craig JP, Chen YH, Turnbull PR. Prospective trial of intense pulsed light for the treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci 2015; 56:1965–1970.

This study is the first published prospective, placebo-controlled study of IPL on MGD. They tested one eye of 28 patients with IPL and the other with sham. They reported objective and subjective improvements in the patients' condition.

15. ■■ 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.

This study is a retrospective review with the largest number of patients ($n = 91$) with dry eye disease having undergone IPL over 3 years. A majority of the patients showed improvement in clinical signs (87%) and subjective amelioration (93%) of their evaporative dry eye disease.

16. Gupta PK, Vora GK, Stinett S. Outcomes of intense pulsed light therapy for treatment of evaporative dry eye disease. Boston, MA: American Society of Cataract and Refractive Surgery; 2014.
17. Mathers WD, Shields WJ, Sachdev MS, *et al.* Meibomian gland dysfunction in chronic blepharitis. Cornea 1991; 10:277–285.
18. Schiffman RM, Christianson MD, Jacobsen G, *et al.* Reliability and validity of the Ocular Surface Disease Index. Arch Ophthalmol 2000; 118:615–621.
19. Lee WW, Murdock J, Albini TA, *et al.* Ocular damage secondary to intense pulse light therapy to the face. Ophthal Plast Reconstr Surg 2011; 27:263–265.
20. Jewsbury H, Morgan F. Uveitis and iris photoablation secondary to intense pulsed light therapy. Can J Ophthalmol 2012; 47:e13–e14.
21. Crabb M, Chan WO, Taranath D, *et al.* Intense pulsed light therapy (IPL) induced iritis following treatment for a medial canthal capillary malformation. Australas J Dermatol 2014; 55:289–291.
22. Pang AL, Wells K. Bilateral anterior uveitis after intense pulsed light therapy for pigmented eyelid lesions. Dermatol Surg 2008; 34:1276–1279.
23. Javey G, Schwartz SG, Albini TA. Ocular complication of intense pulsed light therapy: iris photoablation. Dermatol Surg 2010; 36:1466–1468.
24. Hong S, Lee JR, Lim T. Pigment deposition of cosmetic contact lenses on the cornea after intense pulsed-light treatment. Korean J Ophthalmol 2010; 24:367–370.