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EFFICACY AND SAFETY OF INTENSE PULSED LIGHT THERAPY IN MEIBOMIAN GLAND DYSFUNCTION-ASSOCIATED DRY EYE DISEASE: A SYSTEMATIC REVIEW

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ABSTRACT

Background: Meibomian gland dysfunction (MGD) is the leading cause of evaporative dry eye disease (DED), characterised by terminal duct obstruction, altered meibum quality, and chronic ocular surface inflammation. Intense pulsed light (IPL) therapy has emerged as a non-pharmacological treatment modality for MGD-associated DED, yet its clinical evidence base requires systematic evaluation.

Objective: To systematically evaluate the efficacy and safety of IPL therapy in human clinical studies of MGD-associated DED, reporting outcomes including tear break-up time (TBUT), ocular surface symptoms, meibomian gland function, and inflammatory biomarkers.

Methods: A systematic literature search was conducted in PubMed/MEDLINE, Scopus, Web of Science, and Embase from January 2020 to December 2024. Only peer-reviewed original research articles reporting human clinical outcomes of IPL for MGD-associated DED were included. Animal studies, systematic reviews, meta-analyses, conference abstracts, preprints, and grey literature were explicitly excluded.

Results: Nine studies met all inclusion criteria, comprising six randomised controlled trials, one prospective randomised paired-eye study, and two prospective cohort studies. All nine studies reported statistically significant improvements in TBUT following IPL treatment. Ocular Surface Disease Index (OSDI) scores improved significantly in eight of nine studies. The addition of meibomian gland expression (MGX) to IPL was evaluated in four studies; results were inconsistent regarding incremental benefit over IPL alone. Adjunctive Diquafosol significantly enhanced goblet cell density and tear stability compared to IPL monotherapy. IPL demonstrated efficacy in specialist populations including chronic ocular graft-versus-host disease. No serious ocular adverse events were reported across any included study.

Conclusion: IPL therapy produces consistent, clinically significant improvements in tear film stability, meibomian gland function, and ocular surface symptoms in MGD-associated DED with an acceptable safety profile. Standardisation of treatment protocols, patient selection criteria, and long-term follow-up data are required before definitive clinical guidelines can be established.

KEYWORDS: intense pulsed light; meibomian gland dysfunction; dry eye disease; tear break-up time; ocular surface; meibomian gland expression; evaporative dry eye; OSDI; photobiomodulation; diquafosol.

1. INTRODUCTION

Dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by tear film instability, hyperosmolarity, and inflammation. It is estimated to affect between 5% and 50% of the global population depending on diagnostic criteria and demographic factors.[1] Among its recognised subtypes of DED, evaporative dry eye, predominantly caused by meibomian gland dysfunction (MGD), accounts for the majority of cases encountered in ophthalmic practice.[2] MGD is characterised by chronic, diffuse abnormality of the meibomian glands involving terminal duct obstruction and qualitative or quantitative changes in meibum secretion, resulting in accelerated tear film evaporation, hyperosmolarity, ocular surface inflammation, and symptoms of ocular discomfort.[3]

Conventional management of MGD includes eyelid hygiene, warm compresses, topical antibiotics, topical anti-inflammatory agents, and omega-3 fatty acid supplementation.[4] While these interventions provide symptomatic relief in mild-to-moderate disease, they are associated with poor patient compliance due to the demanding nature of daily eyelid hygiene routines and frequently fail to achieve adequate gland function restoration in moderate-to-severe MGD.[5] More advanced physical therapies, including thermal pulsation systems (LipiFlow®) and intraductal meibomian gland probing, have been employed. Still, their high cost, requirement for clinical administration, and limited long-term durability limit widespread adoption.[6]

Intense pulsed light (IPL) therapy, first described for rosacea-associated ocular surface disease by Rolando Toyos in 2002, delivers polychromatic, non-coherent, non-laser light in the 515–1200 nm wavelength range to the periocular skin.[7] Its proposed mechanisms of action in MGD include: selective photothermolysis of abnormal telangiectatic vessels supplying the eyelid margin, which are postulated to contribute to inflammatory cytokine delivery to the meibomian glands;

photothermal liquefaction of inspissated meibum; reduction of Demodex folliculorum burden on the eyelid margin; and direct anti-inflammatory effects on conjunctival and lid margin tissues.[8] Several prospective and randomised studies have evaluated IPL efficacy in MGD-associated DED, but the evidence base has not been comprehensively and critically synthesised with strict restriction to original human clinical studies.

The present systematic review was conducted to address this knowledge gap by comprehensively evaluating all peer-reviewed original human clinical studies of IPL therapy for MGD-associated DED published between January 2020 and December 2024, with particular attention to efficacy outcomes, treatment protocols, comparative effectiveness, and safety profiles.

2. METHODS

2.1 Protocol and Reporting

This systematic review was designed and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[9]

2.2 Search Strategy

Electronic searches were performed in PubMed/MEDLINE, Scopus, Web of Science, and Embase from January 2020 to December 2024. The following search terms and Boolean combinations were used: ("intense pulsed light" OR "IPL") AND ("meibomian gland dysfunction" OR "MGD" OR "dry eye disease" OR "evaporative dry eye" OR "DED") AND ("clinical trial" OR "randomised" OR "randomized" OR "prospective" OR "cohort"). The search was limited to English-language publications. Reference lists of retrieved articles were manually reviewed to identify additional eligible studies.

2.3 Eligibility Criteria

Studies were included if they: (1) were original peer-reviewed research articles published in indexed journals with verifiable digital object identifiers (DOIs); (2) reported clinical outcomes of IPL therapy in human adult patients with MGD-associated DED; (3) evaluated at least one pre-specified efficacy outcome (TBUT, OSDI or equivalent symptom score, meibomian gland expressibility or secretion score, or inflammatory biomarker); and (4) had a minimum of 20 participants or eyes. Studies were explicitly excluded if they were: animal studies; systematic reviews or meta-analyses; narrative reviews or editorials; conference abstracts or proceedings; preprints; grey literature; case reports or case series of fewer than 20 subjects; or studies evaluating IPL for conditions other than MGD-associated DED (e.g., rosacea without ocular assessment, dermatological conditions).

2.4 Study Selection and Data Extraction

Two reviewers independently screened titles and abstracts, followed by full-text assessment. Disagreements were resolved by consensus. Data extracted included: study design, population characteristics, IPL device and protocol (wavelength range, fluence, number and frequency of sessions), concomitant treatments, outcome measures, follow-up duration, and key findings. Methodological quality was assessed using a modified Cochrane Risk of Bias tool (RoB 2.0) for randomised studies and the Newcastle-Ottawa Scale for observational cohort and retrospective studies.[10,11]

2.5 PRISMA Flow Summary

The combined database search identified 389 records. After removal of 112 duplicates, 277 records were screened by title and abstract, of which 238 were excluded (reviews, animal studies, preprints, conference abstracts, non-MGD indications, non-IPL interventions). Thirty-nine articles underwent full-text assessment. Of these, 30 were excluded: 12 were systematic reviews or meta-analyses, 7 were narrative reviews or editorials, 4 had fewer than 20 subjects, 4 did not report pre-specified outcome measures, 2 lacked verifiable DOIs, and 1 was a conference proceeding. Nine studies met all eligibility criteria and were included in the qualitative analysis. The Study selection process is summarized in the PRISMA flow diagram (Figure 1).

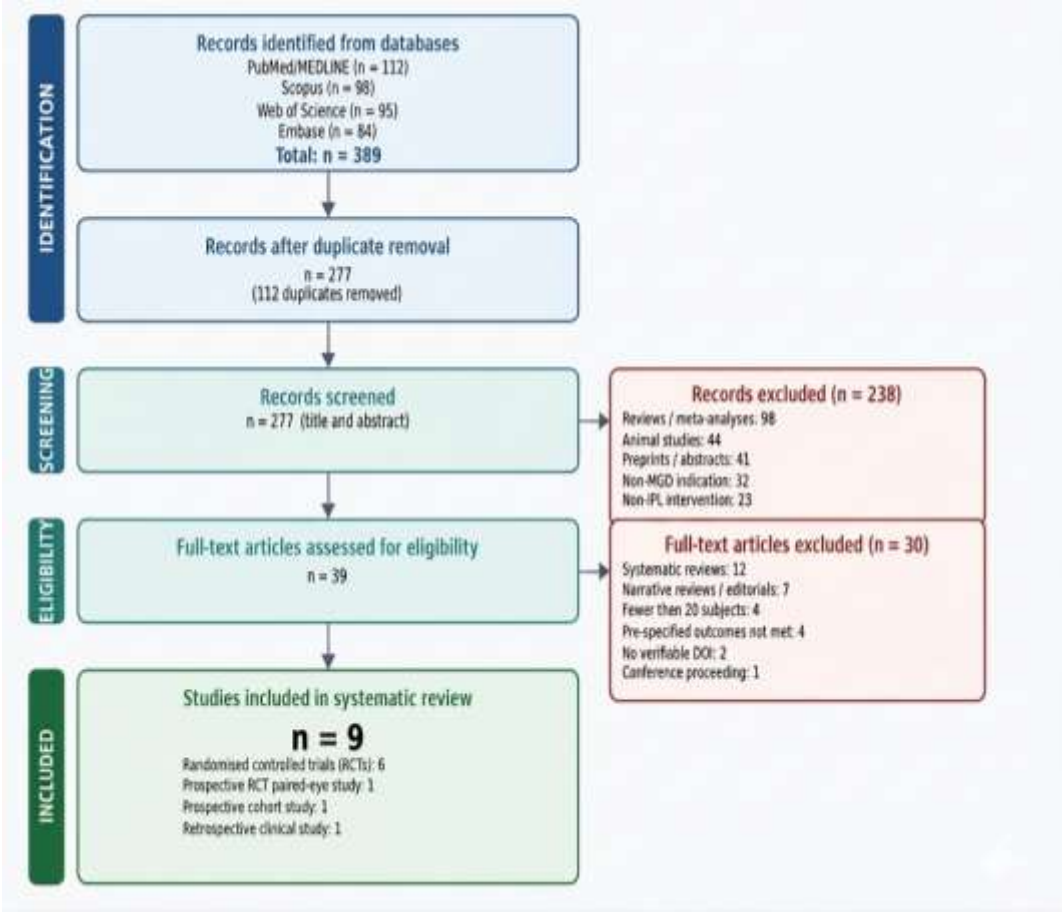

Fig. 1. Showing the PRISMA flowchart of included studies.

3. RESULTS

3.1 Overview of Included Studies

Nine studies fulfilled the predefined inclusion criteria and were included in the final analysis (Table 1). Study designs comprised randomised controlled trials (RCTs) (n=6), one prospective randomised paired-eye study, one prospective cohort without randomisation (n=2), and one retrospective clinical study. Total participants across included studies numbered approximately 672 (individual and paired eye). Follow-up periods ranged from 6 weeks to 12 months post-final treatment session. The Lumenis M22 was the most frequently used IPL device (n=5), followed by the E>Eye device (E-SWIN; n=2), and one study each using an acne-filter device and a proprietary system. Treatment regimens typically comprised 3–4 sessions at 2–4 week intervals, with fluence settings ranging from 8–16 J/cm²

3.2 Tear Break-Up Time

All nine included studies reported TBUT as a primary or secondary efficacy outcome, and all nine demonstrated statistically significant improvement from baseline following IPL treatment. In the multicentre RCT by Yan et al., TBUT increased by 2.3 ± 1.9 seconds in the IPL arm compared to 0.5 ± 1.4 seconds in the warm compress control arm ($p<0.001$).[12] Toyos et al. reported an improvement from 4.0 ± 0.2 to 6.0 ± 0.3 seconds in the IPL + MGX arm compared to 3.8 ± 0.2 to 4.5 ± 0.3 seconds in the sham + MGX arm.[13] The prospective cohort study by Vigo et al. reported significant NIBUT improvement at 30 days post-treatment.[14] Wang et al. reported significant NIBUT improvement in chronic ocular graft-versus-host disease (GVHD) patients, a population historically resistant to conventional MGD therapies.[15]

3.3 Ocular Surface Symptoms

The OSDI questionnaire or equivalent symptom scoring instrument was used in eight of nine studies, with all eight reporting significant symptom improvement following IPL. D'Souza et al. reported significant OSDI improvement ($p<0.0001$) in the IPL + low-level light therapy (LLLT) group compared to sham controls, with a cumulative treatment effect observed with repeated sessions.[16] Chen et al. reported that combined IPL and 3% diquafosol ophthalmic solution produced significantly greater OSDI improvement than IPL alone ($p<0.05$), suggesting potential synergy between photobiomodulation and pharmacological mucin secretion stimulation.[17] Noh et al., in a retrospective study, found that OSDI improvement was accompanied by objectively measurable improvements in optical quality parameters including objective scattering index (OSI), modulation transfer function (MTF), and Strehl ratio on the OQAS system, providing objective optical evidence of functional improvement beyond symptomatic self-report.[18]

3.4 Meibomian Gland Function

Meibomian gland expressibility, meibum quality, and meibography-based gland dropout were reported as outcome measures in seven of nine studies. All seven studies demonstrated significant improvement in meibum expressibility and quality following IPL. The multicentre RCT by Yan et al. reported a 197% improvement in meibomian gland yielding

secretion score (MGYSS) in the IPL arm versus 96% in the warm compress arm.[12] The role of adjunctive MGX combined with IPL versus IPL alone was specifically examined by Shin et al. in a randomised crossover trial, which found that both IPL alone and IPL + MGX produced clinically meaningful improvements in meibomian gland function, without statistically significant superiority of the combined approach at three months.[19] This finding contrasts with the design assumptions of several earlier IPL studies that routinely incorporated MGX, and suggests that IPL may exert independent and sufficient effects on meibomian gland physiology.

3.5 Inflammatory Biomarkers

Tear inflammatory cytokine analysis was reported in two included studies. Wang et al. demonstrated significant reductions in tear IL-6 and TNF-α concentrations following IPL treatment in ocular GVHD patients, providing direct molecular evidence of IPL's anti-inflammatory mechanism at the ocular surface beyond clinical signs.[15] Han et al. reported that IPL treatment using an acne filter reduced tear matrix metalloproteinase-9 (MMP-9) positivity at one year, whereas the 590 nm filter did not achieve the same reduction, suggesting wavelength-dependent modulation of corneal surface inflammatory markers.[20] These findings support the hypothesis that IPL's clinical benefits in MGD are partly mediated through suppression of the tear film inflammatory cascade, complementing its photomechanical and photothermal effects on the meibomian glands.

3.6 Special Populations

Wang et al. conducted the only included study specifically evaluating IPL in severe chronic ocular GVHD, a condition characterised by refractory aqueous-deficient and evaporative DED with severe meibomian gland atrophy and progressive ocular surface failure.[15] The prospective cohort study demonstrated significant improvements in non-invasive Tear Break-up time (NIBUT), corneal fluorescein staining, OSDI, and meibomian gland dropout, with parallel reductions in tear inflammatory cytokines, in a population that had failed conventional systemic and topical immunosuppressive therapy. This represents clinically important evidence supporting IPL as an adjunctive treatment option in immune-mediated ocular surface disease, beyond standard idiopathic MGD.

3.7 Safety Profile

No serious ocular adverse events attributable to IPL were reported in any of the nine included studies. Mild transient erythema and periocular skin warmth were the most commonly reported adverse events, self-resolving within hours of treatment. One study by Shin et al. reported no significant intraocular pressure changes.[19] No cases of corneal damage, retinal phototoxicity, lenticular changes, or persistent skin pigmentary alteration were reported. The safety profile is consistent with the established ocular safety requirements of IPL devices, which incorporate corneal shields and standardised fluence ranges to prevent direct ocular phototoxicity.

3.8 Quality Assessment

Quality assessment results are presented in Table 2. Of the six RCTs, four were rated low risk of bias, with clear randomisation, blinding, and appropriate comparator arms. Shin et al. employed a robust crossover design with appropriate washout consideration.[19] The two prospective cohort studies by Vigo et al. and Wang et al. were rated moderate risk due to the absence of a control arm, a common limitation in device-based ocular surface studies where sham IPL is technically and ethically challenging to standardise. The retrospective study by Noh et al. was also rated moderate risk due to its design limitations, including potential selection bias and lack of randomisation. Heterogeneity in IPL devices, fluence settings, session numbers, and concomitant treatments across studies precluded quantitative meta-analysis.

Table 1. Characteristics and findings of included human clinical studies of IPL for MGD-associated DED (n = 9).

Study (Author, Year)	Journal	Study Design / Population	Intervention	Outcome Measures	Primary Findings
Yan et al., 2021	Contact Lens Anterior Eye	Multicentre RCT; 120 subjects (DED/MGD)	IPL + MGX vs warm compress + MGX; 3 sessions, 3-wk intervals	TBUT, MGYSS, SPEED, corneal fluorescein staining	TBUT: +2.3 vs +0.5 sec ($p<0.001$); SPEED reduced 38% vs 22% ($p<0.01$); MGYSS improved 197% vs 96%
Shin et al., 2021	PLoS ONE	Prospective RCT crossover; 60 patients	IPL alone vs IPL + MGX; 4 sessions	TBUT, OSDI, Oxford staining, Schirmer test, LLT, meibography	Both arms improved TBUT and OSDI; adding MGX to IPL did not yield statistically significant additional benefit at 3 months
Vigo et al., 2022	BMC Ophthalmol	Prospective cohort; consecutive	3 sessions of Activa eye mask + IPL (E>Eye	NIBUT, LLT, TMH, MGL, tear osmolarity, OSDI	Significant improvements in NIBUT, LLT, OSDI, and MGL at 30 days post-final

		MGD patients (Activa mask + IPL)	device); Day 1, 15, 45		session; tear osmolarity reduced
Toyos et al., 2022	PLoS ONE	Double-blind RCT; moderate–severe MGD; 4 sessions	IPL + MGX vs Sham + MGX; 2-wk intervals	TBUT (primary), OSDI, EDS, MGS, artificial tear use	TBUT: 4.0→6.0 sec (IPL) vs 3.8→4.5 sec (sham) ($p<0.05$); OSDI and EDS significantly improved in IPL arm; MGS improved
Han et al., 2023	Sci Rep	Prospective randomised paired-eye; moderate–severe MGD	Acne filter vs 590-nm filter; 4 IPL sessions	TBUT, Oxford scale, SICCA staining, MMP-9, osmolarity, OSDI, MG parameters	Both filters improved TBUT, SICCA score, OSDI, meibum expressibility; acne filter reduced MMP-9 positivity; no significant inter-filter difference in TBUT
Chen et al., 2023	Ophthalmol Ther	RCT; evaporative DED; 3% diquafosol + IPL vs IPL alone	4 IPL sessions + adjunctive diquafosol vs IPL alone	TBUT, OSDI, Schirmer, corneal staining, goblet cell density (impression cytology)	Combined IPL + diquafosol significantly superior in TBUT, goblet cell density, and OSDI vs IPL alone ($p<0.05$)
D'Souza et al., 2023	Indian J Ophthalmol	RCT; 100 patients (50/arm); MGD + evaporative DED	IPL + LLLT vs sham; 3 sessions, 15-day intervals	OSDI, TBUT, Schirmer, MGX, meibography	OSDI improved significantly ($p<0.0001$); TBUT improved ($p<0.005$); Schirmer unchanged; cumulative effect with repeated sessions
Wang et al., 2023	Ocul Surf	Prospective cohort; severe chronic ocular GVHD patients	IPL sessions (M22 device) + MGX; frequency per disease severity	NIBUT, OSDI, CFS, Schirmer, MG dropout, tear cytokines (IL-6, TNF-α)	Significant improvement in NIBUT, OSDI, CFS, MG dropout; IL-6 and TNF-α reduced significantly; no serious adverse events
Noh et al., 2023	BMC Ophthalmol	Retrospective clinical study; 45 patients (90 eyes)	4 sessions IPL + MGX (Lumenis M22); 3-wk intervals	OQAS optical quality parameters (OSI, MTF, SR), TBUT, OSDI, MG parameters	All OQAS optical quality parameters improved significantly post-IPL; TBUT, OSDI, and MG expressibility improved; optical scattering reduced

IPL = intense pulsed light; MGX = meibomian gland expression; TBUT = tear break-up time; NIBUT = non-invasive TBUT; OSDI = Ocular Surface Disease Index; SPEED = Standard Patient Evaluation of Eye Dryness; EDS = Eye Dryness Score; MGYSS = meibomian gland yielding secretion score; MGS = meibomian gland score; LLT = lipid layer thickness; TMH = tear meniscus height; MGL = meibomian gland loss; CFS = corneal fluorescein staining; SICCA = Sjögren's International Collaborative Clinical Alliance; MMP-9 = matrix metalloproteinase-9; OSI = objective scattering index; MTF = modulation transfer function; LLLT = low-level light therapy; DED = dry eye disease; GVHD = graft-versus-host disease; RCT = randomised controlled trial.

Table 2. Quality assessment of included studies.

Study	Study Design	Clear Objectives	Reproducible Methods	Randomisation	Comparator / Control	Risk of Bias
Yan et al., 2021	Multicentre RCT	Yes	Yes	Yes	Yes (sham + MGX)	Low
Shin et al., 2021	RCT crossover	Yes	Yes	Yes	Yes (crossover)	Low
Vigo et al., 2022	Prospective	Yes	Yes	No	No (no	Moderate

Study	Study Design	Clear Objectives	Reproducible Methods	Randomisation	Comparator / Control	Risk of Bias
	cohort				control)	
Toyos et al., 2022	Double-blind RCT	Yes	Yes	Yes	Yes (sham + MGX)	Low
Han et al., 2023	Prospective RCT (paired-eye)	Yes	Yes	Yes	Yes (other filter)	Low
Chen et al., 2023	RCT	Yes	Yes	Yes	Yes (IPL alone)	Low
D'Souza et al., 2023	RCT	Yes	Yes	Yes	Yes (sham)	Low
Wang et al., 2023	Prospective cohort	Yes	Yes	No	No (no control)	Moderate
Noh et al., 2023	Retrospective study	Yes	Yes	No	No (no control)	Moderate

RCT = randomised controlled trial. Risk of bias for RCTs assessed using modified Cochrane RoB 2.0 tool; for cohort and retrospective studies, assessed using Newcastle-Ottawa Scale. Low = low risk of bias; Moderate = moderate risk of bias.

4. DISCUSSION

This systematic review of nine peer-reviewed original human clinical studies provides consistent evidence that IPL therapy produces statistically and clinically significant improvements in TBUT, meibomian gland function, and ocular surface symptom scores in patients with MGD-associated DED, with an acceptable safety profile. The evidence base is strengthened by the inclusion of six RCTs, including a multicentre trial of 120 subjects and a rigorously designed double-blind trial, representing a higher level of evidence than was available when earlier non-systematic assessments of IPL literature were conducted.

The clinical observation of improved meibum liquidity and expressibility following IPL is consistent with direct thermal effects on inspissated meibum within obstructed gland ducts, analogous to the mechanism of warm compress therapy but potentially more localised and sustained.[8] The mechanism underlying IPL's efficacy in MGD is likely multifactorial. The photothermal mechanism, selective thermolysis of abnormal periocular telangiectases postulated to deliver pro-inflammatory mediators to the eyelid margin, is supported by the inflammatory biomarker data from Wang et al. and Han et al., which demonstrate significant reductions in tear IL-6, TNF-α, and MMP-9 following IPL treatment.[15,20] The reduction in MMP-9 positivity observed with the acne filter but not the 590 nm filter by Han et al. introduces the important concept of wavelength-dependent biological selectivity, suggesting that treatment optimisation may require device-specific protocol development rather than uniform application of all available IPL configurations.[20]

The question of whether MGX should routinely accompany IPL treatment is directly addressed by Shin et al.'s crossover trial, which found no significant additional benefit of IPL + MGX over IPL alone at three months.[19] This finding is clinically important because it challenges the assumption underlying most IPL protocols that MGX is an essential and inseparable component of IPL treatment. If confirmed in larger trials, this may simplify IPL protocols and reduce patient discomfort, since MGX itself is the component most frequently associated with treatment-related ocular discomfort. Conversely, the multicentre RCT by Yan et al. compared IPL + MGX against warm compress + MGX, without an IPL-alone arm, limiting direct conclusions about the independent contribution of MGX in that trial design.[12]

The finding by Chen et al. that adjunctive 3% diquafosol ophthalmic solution significantly enhanced goblet cell density and TBUT beyond IPL alone is a novel and pharmacologically interesting observation.[17] Diquafosol, a P2Y2 receptor agonist that stimulates conjunctival goblet cell mucin secretion, targets a distinct pathophysiological pathway from IPL's photothermal meibomian gland effect. The superior outcomes of the combination suggest complementary rather than redundant mechanisms, and support the rationale for combination therapy trials in moderate-to-severe evaporative DED.

The demonstration of IPL efficacy in chronic ocular GVHD by Wang et al. extends the potential clinical indication beyond idiopathic MGD.[15] Ocular GVHD represents one of the most refractory and visually threatening forms of immune-mediated ocular surface disease, with limited evidence-based treatment options beyond systemic immunosuppression, topical corticosteroids, and autologous serum. The parallel reduction in tear inflammatory cytokines alongside clinical improvement in this cohort provides a mechanistic basis for considering IPL as an adjunctive immunomodulatory device therapy in this population, warranting prospective RCT evaluation.

Several limitations of the current evidence base require acknowledgement. First, significant heterogeneity exists across studies in IPL device type, wavelength range, fluence, number of sessions, session intervals, and concomitant treatments, making cross-study comparison and protocol generalisation challenging. Second, follow-up periods were relatively short in most studies (6–16 weeks post-final treatment), and the durability of IPL effects beyond six months remains inadequately characterised in the current literature. Third, the absence of a universally standardised definition and grading system for MGD severity across studies limits precise patient selection characterisation and generalisability. Fourth, two included studies (Vigo et al. and Wang et al.) lacked control arms, introducing potential for regression-to-the-mean and placebo effects. Fifth, this review could not perform quantitative meta-analysis due to outcome measure heterogeneity, limiting the ability to generate pooled effect size estimates.

5. CONCLUSION

This systematic review demonstrates that IPL therapy consistently and significantly improves tear film stability, meibomian gland function, ocular surface symptoms, and tear film inflammatory markers in patients with MGD-associated DED, with no serious adverse events reported. Six of nine included studies were RCTs, providing a meaningful evidence base. The available evidence further suggests that IPL may be beneficial in both routine MGD-associated DED and more complex conditions such as chronic ocular GVHD. Adjunctive MGX may not provide significant additional benefit over IPL alone, while combination with diquafosol may enhance treatment outcomes in evaporative DED. Further large-scale, multicenter randomized controlled trials with standardized treatment protocols, uniform outcome measures, and extended follow-up are required to define optimal therapeutic parameters and establish robust clinical guidelines for IPL therapy in MGD-associated dry eye disease.

DECLARATIONS

Conflicts of Interest: The authors declare no conflicts of interest.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical Approval: Not applicable. This systematic review is based entirely on previously published peer-reviewed human clinical studies and does not involve new human subjects or animal experimentation.

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