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EFFICACY OF INTENSE PULSED LIGHT THERAPY ON SIGNS AND SYMPTOMS OF DRY EYE DISEASE : A SYSTEMATIC REVIEW

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Abstract

Introduction: *Dry eye disease (DED) is a multifactorial disorder of the ocular surface characterized by disruption of tear film homeostasis, instability of the tear film, and inflammation of the ocular surface. Although the precise mechanism of action is still inadequately understood, numerous studies have demonstrated that IPL has the potential to alleviate both the signs and symptoms of dry eye.*

The aim: *This article showed efficacy of intense pulsed light therapy on signs and symptoms of dry eye disease.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2013 and 2023 were taken into account. Several different online reference sources, like Pubmed and SagePub, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 112 articles, whereas the results of our search on SagePub brought up 109 articles. The results of the search conducted for the last year of 2013 yielded a total 25 articles for PubMed and 19 articles for SagePub. In the end, we compiled a total of 23 papers, 14 of which came from PubMed and nine of which came from SagePub. We included sixresearch that met the criteria.*

Conclusion: *Existing research indicates that Intense Pulsed Light (IPL) therapy has the potential to alleviate the symptoms and manifestations of Dry Eye Disease (DED). Previous research did not demonstrate any significant adverse effects.*

Keyword: *Dry eye disease; Meibomian gland dysfunction; Pulsed light therapy*

INTRODUCTION

Dry eye disease (DED) is a complex ocular surface disorder that involves various factors and is defined by the disruption of tear film homeostasis, instability of the tear film, and inflammation of the ocular surface.[1] The prevalence of DED varies between 5% and 50%, contingent upon the geographical location. The aforementioned problem manifests in two primary forms, namely aqueous-deficiency and evaporative, with a frequent occurrence of both types together. Meibomian gland dysfunction (MGD) is widely recognized as the primary etiological factor contributing to evaporative dry eye disease.[2,3]

The international workshop on MGD has defined MGD as a persistent and widespread anomaly affecting the meibomian glands. This condition is typically characterized by obstruction of the terminal ducts and/or alterations in the quality and quantity of glandular secretions. MGD is associated with a decline in the quality of the meibum, disruption of the tear film's stability, exposure of the ocular surface, and ultimately, the emergence of symptoms related to dry eye. The prevalence of MGD as a contributing factor to DED has been estimated to range from 60-86%.[3]

Based on the findings of the Tear Film & Ocular Society's Dry Eye Workshop II (TFOS DEWS II), the prevalence rate of MGD among individuals aged 40 and beyond varies between 38-68%. Several therapeutic approaches for the management of MGD encompass lid hygiene, thermal pulsation, artificial tear substitutes, artificial lubricants, topical or systemic antibiotics, FDA-approved anti-inflammatory medications such as cyclosporine, autologous serum eye drops, immunosuppressant agents, Lymphocyte function-associated antigen-1 antagonists, and meibomian gland expression.[4–6]

Another therapeutic strategy that has had an increase in popularity over the last five years is the application of intense pulse light (IPL) to the skin surrounding the eyes. The IPL technique is comprised of short pulses of non-coherent and polychromatic light, encompassing wavelengths that span from 500-1200 nm. The efficacy of IPL has been demonstrated in several dermatological contexts, such as the treatment of capillary and venous malformations, telangiectasia, and erythema associated with rosacea.[7] The latter problem holds particular significance in the context of dry eye syndrome, given that approximately 80% of those diagnosed with cutaneous rosacea also experience MGD.[6,8]

Hence, it is logical to anticipate that IPL, known for its high efficacy in treating rosacea, could potentially offer benefits in the management of MGD as well.[7] While the precise mechanism of action remains poorly comprehended, numerous investigations have demonstrated that IPL has the potential to alleviate both the indications and symptoms associated with dry eye, after the groundbreaking research conducted by Toyos et al.[9] The TFOS DEWS II, in its tiered management algorithm, has suggested the utilization of this particular technology as a subsequent measure for addressing DED, following the first implementation of lid hygiene and other forms of ocular lubricants.[10]

The present investigation demonstrated the effectiveness of intense pulsed light treatment in improving both the clinical manifestations and subjective complaints associated with dry eye disease.

METHODS

In accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 standards, the researcher of this study undertook measures to assure strict adherence to these criteria. The adoption of this method is meant to ensure the correctness of the investigation's outcomes. The primary goal of this review was to demonstrate the efficacy of strong pulsed light treatment on the signs and symptoms of dry eye illness. The fundamental goal of this work is to highlight the significance of the aforementioned issues discussed in the text.

To be eligible for participation in the study, researchers had to meet the following criteria: the article's composition should be in English, and its focus should be on the efficacy of intense pulsed light therapy on signs and symptoms of dry eye disease. Both of these criteria must be met by the paper in order for it to be published. A number of the articles under consideration were published between 2013 and the predetermined timeframe deemed relevant for this systematic review. Editorials, submissions without a Digital Object Identifier (DOI), previously published review articles, and entries that are effectively duplicates of previously published journal pieces are all disallowed.

We used “intense”; “pulsed light therapy”; and “dry eye disease” as keywords.The search for studies to be included in the systematic review was carried out from August, 9th 2023 using the PubMed and SagePub databases by inputting the words: *((“intense pulsed light therapy”[MeSH Terms] OR (“intense”[All Fields] AND “pulsed”[All Fields] AND “light”[All Fields] AND “therapy”[All Fields]) OR “intense pulsed light therapy”[All Fields]) AND (“dry eye syndromes”[MeSH Terms] OR (“dry”[All Fields] AND “eye”[All Fields] AND “syndromes”[All Fields]) OR “dry eye syndromes”[All Fields] OR (“dry”[All Fields] AND “eye”[All Fields] AND “disease”[All Fields]) OR “dry eye disease”[All Fields])) AND ((y_10[Filter]) AND (clinicaltrial[Filter]))* used in searching the literature.

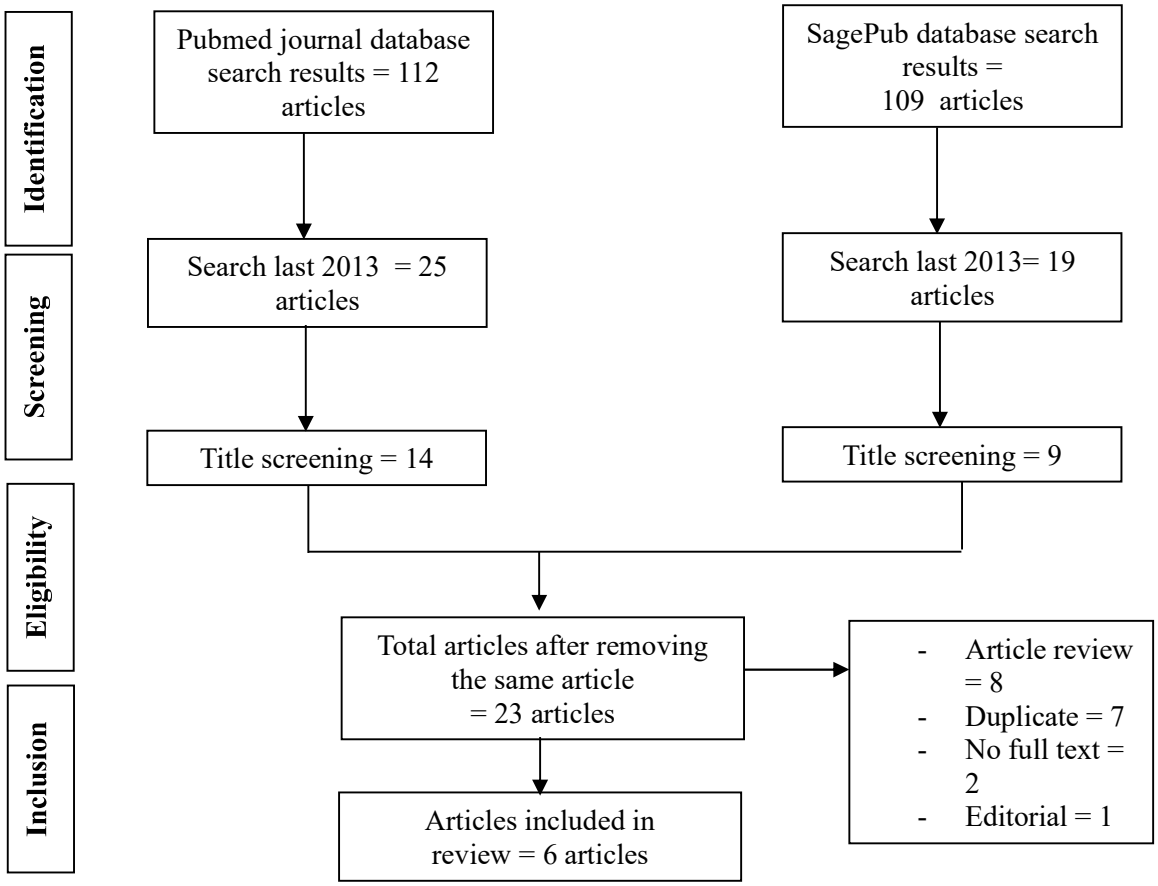

Figure 1. Article search flowchart

The authors evaluated each study's abstract and title to determine if it met the inclusion criteria. The authors then determined which prior studies would serve as the article's sources and selected those studies. Numerous studies that appeared to indicate the same trend were analyzed in order to reach this conclusion. All submissions must be written in English and unpublished before submission. Only publications satisfying all inclusion criteria were considered for the systematic review. This reduces the number of search results to only those that are relevant to your query. We disregard any study's results that do not meet our criteria. The research findings will then be thoroughly analyzed.

This study's investigation revealed the following: names, authors, publication dates, location, study activities, and parameters. Before deciding which publications to investigate further, each author performed independent research on the research included in the publication's title and abstract. The subsequent step is to evaluate all of the articles that satisfy the inclusion criteria for the review. Then, we will choose which articles to include in the review based on the findings. This criterion is used to select documents for additional examination. To facilitate as much as possible the selection of papers for evaluation. This section discusses the prior studies conducted and the aspects of those studies that justified their inclusion in the review.

RESULT

In the PubMed database, the results of our search brought up 112 articles, whereas the results of our search on SagePub brought up 109 articles. The results of the search conducted for the last year of 2013 yielded a total 25 articles for PubMed and 19 articles for SagePub. In the end, we compiled a total of 23 papers, 14 of which came from PubMed and nine of which came from SagePub. We included sixresearch that met the criteria.

Toyos, et al (2022)[9] showed tear breakup time (TBUT) increased from 3.8 ± 0.2 to 4.5 ± 0.3 seconds in the control arm and from 4.0 ± 0.2 to 6.00. ± 3 seconds in the study arm ($p < 0.01$). Other signs / symptoms that improved in both arms but were more pronounced in the study arm were Meibomian gland score (MGS) ($P < 0.01$), Eye Dryness Score (EDS) ($P < 0.01$), the number of expressible glands in the lower and upper eyelids ($P < 0.01$), the predominant meibum quality in the lower and upper eyelids ($P < 0.01$), and the level of meibomian gland expression (MGX)-related pain ($P < 0.01$).

Ocular Surface Disease Index (OSDI) ($P = 0.99$) and the daily use of artificial tears ($P = 0.82$) were outcome measures that improved in both categories with no significant differences between them. Meibography, daily use of warm compresses, and the severity of cutaneous rosacea did not demonstrate statistically significant differences between the two arms. There were no substantial adverse events observed. There was a modest tendency for the control group to experience more adverse events ($P = 0.06$).[9]

Yan, et al (2021)[11] showed total efficacy rates of the experimental and control groups were 90.2% and 80%, respectively, and the therapeutic effects of the experimental group were superior to those of the control group (P <0.05). Time decreased the eyelid gland quality score for moderate and severe abnormality, the lacrimal river height measurements 0.35 mm, and the tear secretion measurements 5 mm in the generalized estimation equation (P <0.05). In addition, moderate and severe aberrant eyelid gland quality scores, lacrimal river height measurements 0.35 mm, and tear secretion measurements 5 mm were significantly lower in the experimental group compared to the control group (P <0.05). The incidence of adverse events did not differ significantly between the two groups during treatment (P >0.05).

Yan, et al (2021)[12] showed all outcome measures improved in both arms, but in general, the improvement was significantly larger in the IPL arm. Tear break up time increased by 2.3±1.9 and 0.5±1.4 sec, in the IPL and control arms respectively (P<0.001). SPEED was reduced by 38% and 22% in the IPL and control arms, respectively (P<0.01). Meibomian Gland Yielding Secretion Score was improved by 197% in the IPL arm and 96% in the control arm. Corneal fluorescein staining also decreased by 51% and 24% in the IPL and control arms respectively, but the differences between the two arms were not statistically significant (P=0.61). A composite score of lid margin abnormalities improved in both arms, but more in the IPL arm (P<0.05).

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Intervention	Result
Toyos, 2022[9]	United State of America	Randomized controlled study	82 patients presenting with severe dry eye syndrome	4 sessions of intense pulse light + MGX at 2-week intervals, or 4 sessions of Sham + MGX at 2-week intervals	The findings of this study indicate that the utilization of a combined treatment regimen involving intense pulse light (IPL) and meibomian gland expression (MGX) may present a viable and secure strategy for ameliorating clinical manifestations associated with dry eye disease (DED) resulting from meibomian gland dysfunction (MGD) in individuals exhibiting moderate to severe symptoms.
Yan, 2021[11]	China	Randomized controlled study	132 patients with dry eye caused by MGD	Intense pulsed light (IPL) and hot water compress	The efficacy of Intense Pulsed Light (IPL) surpasses that of a conventional combination therapy involving eyelid gland massage and hot compress in the treatment of dry eye caused by eyelid gland dysfunction. Intense Pulsed Light (IPL) has demonstrated efficacy in enhancing ocular function and mitigating clinical symptoms, while also exhibiting a favorable safety profile. Consequently, IPL has promise for potential therapeutic utilization and widespread adoption.
Yan, 2021[12]	China	Randomized controlled study	120 subjects with DED due to MGD	Intense pulsed light (IPL) and hot water compress	The combination of intense pulsed light (IPL) and MGX therapy shown a significantly higher efficacy compared to the application of immediate warm compresses followed by MGX. This observation implies that the IPL component has a significant role in enhancing the manifestations and indications of DED.
Toyos, 2019[13]	United State of America	Randomized controlled study	88 patients presenting with severe dry eye syndrome	IPL treatment consisting of four treatments spaced no fewer than 2 weeks apart and no longer than 4 weeks apart	The findings of this preliminary investigation indicate that the utilization of a novel specialized 6 mm cylindrical handpiece for the M22 Lumenis IPL machine exhibits both safety and efficacy in enhancing tear breakup time as measured by physicians. Additionally, this intervention demonstrates positive effects on various scales assessing symptoms associated with ocular dryness, encompassing global symptoms, frequency of symptoms, and occurrence of ocular dryness within the 24-hour period preceding the study visit.
Toyos, 2015[14]	United State of America	Retrospective cohort study	91 patients presenting with severe dry eye syndrome	Intense-pulsed-light therapy and gland expression at a single outpatient clinic over a 30-month study	The initial findings of a study investigating the efficacy of intense-pulsed-light therapy as a treatment for dry eye syndrome resulting from meibomian gland dysfunction show encouraging results.
Craig, 2015[15]	New Zealand	Randomized controlled study	Twenty-eight participants underwent IPL treatment	Homogeneously sequenced light pulses delivered to one eye and placebo treatment to the partner control eye at 1, 15, and 45 days	The therapeutic promise of intense pulsed light (IPL) with several shaped pulses in the treatment of meibomian gland dysfunction (MGD) is evident, since it has been shown to enhance tear film quality and alleviate symptoms associated with dry eye.

Craig, et al (2015)[15] showed grade of the lipid layer improved significantly from baseline to Day (D) 45 in the treated eye ($P < 0.01$), but not in control ($P = 0.71$), with 82% of treated eyes exhibiting at least one lipid layer grade (LLG) improvement. Noninvasive tear break-up time improved significantly from baseline to D45 in the treated eye ($P < 0.01$), but not in control ($P = 0.056$), and was significantly longer than in the treated eye at D45 (14.1 ± 9.8 vs. 8.6 ± 0.8 seconds, $P < 0.01$). The height of the tear meniscus did not differ from baseline in either eye ($P > 0.05$). By D45, 86% of participants reported reduced symptoms in the treated eye ($P = 0.015$) but not in the control eye ($P = 0.245$), as measured by the Visual Analog Scale (VAS).

DISCUSSION

The mechanism through which IPL treats DED caused by MGD is unknown. IPL may seal aberrant telangiectasia and prevent their inflammatory mediators. Therefore, a major cause of peri-orbital irritation is removed. The fact that IPL dramatically lowers tear cytokines supports this mechanism.[14] IPL may also stimulate cells by photobiomodulation. Light, especially red and near infrared light, is absorbed by mitochondrial cytochrome C oxidase in PBM, increasing ATP synthesis and calcium levels.[16,17]

PBM can increase anti-oxidant defenses, reduce reactive oxygen species in oxidative stressed cells, lower pro-inflammatory cytokines in activated inflammatory cells, and change the phenotype of macrophages from bacteria and pathogen killers to protein debris removers and healers. IPL may also reduce melanogenic gene upregulation and UVB-induced cytokine expression.[18] All of these may minimize inflammation and stimulate ocular surface and meibomian gland repair. Third, IPL may produce heat-shock in skin cells. IPL may also decrease Demodex mites, another MGD-related risk factor for DED.[19]

Other findings suggested relative hypoxia affects meibomian gland health. These researchers found that loss of hypoxic circumstances causes MGD, while IPL's thrombotic effects close excessive blood vessels, restoring hypoxic conditions for meibomian gland activity. Finally, IPL may heat malfunctioning meibomian gland secretions to soften them. This last explanation is contentious. Some researchers believe that brief IPL pulses can transport heat to the eyelids, dissolve abnormally inspissated meibum in the meibomian glands, and enhance their production. Other study showed IPL only causes short-term thermal effects with minor skin surface temperature changes.[13,15]

IPL pulses are too short to cause prolonged meibum alterations, according to this theory. Study support several of these theories. First, although IPL was administered below the lower eyelids, the higher eyelids also responded positively: nearly one third of the rise in expressible eyelids was in the upper lids. This suggests that beneficial molecules (anti-inflammatory agents, antioxidants, heat shock proteins, etc.) are circulating via the orbital vasculature or heat transfer through skin and connective tissues some distance from the IPL application site. Another intriguing finding was that study participants reported less MGX pain than control patients. The vigorous MGX process might be painful. Even with local anesthetics, some individuals have poor procedure tolerance.[20]

Thus, monotherapy MGX may not work for such patients. Arita and colleagues found that 3 of their study patients (7%) refused MGX alone due to pain, but none of those treated with IPL + MGX complained. To explain these results, Arita and colleagues proposed that IPL heats the meibomian glands, dissolving the meibum, reducing expression pressure and MGX pain. As said, this hypothesis is not universally accepted. Another explanation is that PBM processes increase meibum quality between treatments. This would lessen MGX pain at the next IPL treatment.[9]

CONCLUSION

Existing research indicates that Intense Pulsed Light (IPL) therapy has the potential to alleviate the symptoms and manifestations of Dry Eye Disease (DED). Previous research did not demonstrate any significant adverse effects.

REFERENCES

[1]. Nelson JD, Craig JP, Akpek EK, Azar DT, Belmonte C, Bron AJ, et al. TFOS DEWS II Introduction. Ocul Surf. 2017 Jul;15(3):269–75.
[2]. Shimazaki J. Definition and Diagnostic Criteria of Dry Eye Disease: Historical Overview and Future Directions. Invest Ophthalmol Vis Sci. 2018 Nov;59(14):DES7–12.
[3]. Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS II Epidemiology Report. Ocul Surf. 2017 Jul;15(3):334–65.
[4]. Bron AJ, de Paiva CS, Chauhan SK, Bonini S, Gabison EE, Jain S, et al. TFOS DEWS II pathophysiology report. Ocul Surf. 2017 Jul;15(3):438–510.
[5]. Nelson JD, Shimazaki J, Benitez-del-Castillo JM, Craig JP, McCulley JP, Den S, et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011 Mar;52(4):1930–7.
[6]. Kaiserman I, Rabina G, Mimouni M, Sadi Optom NB, Duvdevan N, Levartovsky S, et al. The effect of therapeutic meibomian glands expression on evaporative dry eye: a prospective randomized controlled trial. Curr Eye Res. 2021;46(2):195–201.
[7]. Viso E, Millán AC, Rodríguez-Ares MT. Rosacea-associated meibomian gland dysfunction—an epidemiological perspective. Eur Ophthalmic Rev. 2014;8(1):13–6.

[8]. Wat H, Wu DC, Rao J, Goldman MP. Application of intense pulsed light in the treatment of dermatologic disease: a systematic review. Dermatologic Surg Off Publ Am Soc Dermatologic Surg [et al]. 2014 Apr;40(4):359–77.
[9]. Toyos R, Desai NR, Toyos M, Dell SJ. Intense pulsed light improves signs and symptoms of dry eye disease due to meibomian gland dysfunction: A randomized controlled study. PLoS One. 2022;17(6):e0270268.
[10]. Jones L, Downie LE, Korb D, Benitez-del-Castillo JM, Dana R, Deng SX, et al. TFOS DEWS II management and therapy report. Ocul Surf. 2017;15(3):575–628.
[11]. Yan S, Wu Y. Efficacy and safety of Intense pulsed light therapy for dry eye caused by meibomian gland dysfunction: a randomised trial. Ann Palliat Med. 2021 Jul;10(7):7857–65.
[12]. Yan X, Hong J, Jin X, Chen W, Rong B, Feng Y, et al. The Efficacy of Intense Pulsed Light Combined With Meibomian Gland Expression for the Treatment of Dry Eye Disease Due to Meibomian Gland Dysfunction: A Multicenter, Randomized Controlled Trial. Eye Contact Lens. 2021 Jan;47(1):45–53.
[13]. Toyos R, Toyos M, Willcox J, Mulliniks H, Hoover J. Evaluation of the Safety and Efficacy of Intense Pulsed Light Treatment with Meibomian Gland Expression of the Upper Eyelids for Dry Eye Disease. Photobiomodulation, photomedicine, laser Surg. 2019 Sep;37(9):527–31.
[14]. 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 Jan;33(1):41–6.
[15]. Craig JP, Chen Y-H, Turnbull PRK. Prospective trial of intense pulsed light for the treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2015 Feb;56(3):1965–70.
[16]. Liu R, Rong B, Tu P, Tang Y, Song W, Toyos R, et al. Analysis of Cytokine Levels in Tears and Clinical Correlations After Intense Pulsed Light Treating Meibomian Gland Dysfunction. Am J Ophthalmol. 2017 Nov;183:81–90.
[17]. Calderhead RG. The photobiological basics behind light-emitting diode (LED) phototherapy. Laser Ther. 2007;16(2):97–108.
[18]. Kim J, Lee J, Choi H. Intense pulsed light attenuates UV-induced hyperimmune response and pigmentation in human skin cells. Int J Mol Sci. 2021;22(6):3173.
[19]. Prieto VG, Diwan AH, Shea CR, Zhang P, Sadick NS. Effects of intense pulsed light and the 1,064 nm Nd:YAG laser on sun-damaged human skin: histologic and immunohistochemical analysis. Dermatologic Surg Off Publ Am Soc Dermatologic Surg [et al]. 2005 May;31(5):522–5.
[20]. Arita R, Fukuoka S, Morishige N. Therapeutic efficacy of intense pulsed light in patients with refractory meibomian gland dysfunction. Ocul Surf. 2019 Jan;17(1):104–10.