Original Article

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The Effectiveness of E>Eye Intense Regulated Pulse Light Therapy in Treating Evaporative Dry Eye Disease among Southeast Asian Patients

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Abstract:

Objective: Since the effectiveness of E>Eye Intense Regulated Pulsed Light (IRPL) therapy in treating evaporative dry eye condition caused by meibomian gland dysfunction (MGD) has not been reported among the Southeast Asian population, this study aimed to retrospectively report the effectiveness of this treatment in addressing evaporative dry eye due to MGD among this population using Tear Check analyzer after three consecutive treatments.

Material and Methods: This is a retrospective study involving 71 male and 107 female patients, aged between 28 and 83 with complaints of dry eye symptoms accompanied by clinical signs of MGD who have been treated with E>Eye IRPL. All patients were treated with IRPL in three consecutive treatments where five overlapping flashes of light were administered on the lower lid and temporal part of each eye on day 1, 15, and 45. Improvement in lower meibomian gland loss, Tear Film Stability Evaluation (TFSE), and non-invasive breakup time (NIBUT) were assessed using the Tear Check analyzer at baseline and after the third treatment session.

Results: Repeated-measure ANOVA showed that the percentage of lower meibomian gland loss and TFSE score significantly improved post-treatment, indicating recovery of the meibomian gland and improved tear stability. McNemar Change Test also showed that the percentage of patients having NIBUT of lower than 6 seconds has significantly reduced post-treatment.

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Conclusion: E>Eye IRPL treatment is effective in evaporative dry eye disease caused by MGD among Southeast Asian patients after three consecutive treatments by restoring meibomian gland and tear stability post-treatment.

Keywords: dry eye, evaporative dry eye, intense regulated pulse light (IRPL), meibomian gland dysfunction (MGD)

Introduction

Dry eye is a multifactorial condition affecting homeostasis of the tear film, leading to discomfort symptoms like dryness, grittiness, burning sensations, and visual disturbances[1]. It can generally be categorized into evaporative and aqueous deficiency types, although a mixed type also exists[2]. Aqueous deficiency dry eye (ADDE) results from inadequate tear production by the lacrimal gland. On the other hand, evaporative dry eye (EDE) occurs due to increased tear evaporation caused by lid-related factors such as meibomian gland dysfunction (MGD) or abnormal blinking, or ocular-surface-related issues like abnormal mucin layers or contact-lens-related problems[3]. EDE caused by MGD has been identified as the leading cause of dry eye[4]. This occurs when the meibum production in the tears is reduced due to disturbances in meibomian glands secretion, such as inflammation of the glands or blockage of gland orifices, leading to increased evaporation of the tears[4–6]. It contributes to approximately 86% of dry eye cases reported which can be exacerbated by air pollution, contact lens wear, air-conditioned environment, and the increased use of digital devices[7,8].

Studies have shown that the prevalence of MGD varies with ethnicity, gender, age, climate, environmental factors, and socioeconomic status of the population. MGD tends to increase with age, becoming more noticeable after 40 and more prominent after 605,[9]. This was suggested to be associated with a lower level of estrogens or the imbalance of sex hormones (androgens and estrogens) with aging, which helps to regulate the metabolism and meibomian glands secretion in a younger age[6]. In addition, MGD prevalence among the Asian population was reported to be higher, ranging from 50% to 68%[10–12], compared to Caucasians with just 3.5% prevalence[13,14], possibly due to geographical factors causing differences in climate and humidity level[15], and dietary pattern[16] which can potentially influence the secretion of lipids by meibomian glands.

Various treatment options have been proposed to treat EDE caused by MGD with a more recent sophisticated treatment called Intense Regulated Pulse Light (IRPL) therapy, offering a quick option with a long-lasting effect. Intense Pulse Light (IPL) is a minimally invasive technique that has long been used in dermatology to treat chronic skin conditions, such as acne rosacea and port wine stains. It uses a polychromatic light source to generate minimal heat onto the skin, to induce selective ablation of the blood vessels[17]. Using a similar concept, ESW Vision has developed IPL with regulated pulse light that has received medical certification for application on the periocular skin to treat MGD, called E>Eye IRPL. It works by stimulating the parasympathetic nerves connected to the meibomian glands, promoting neurotransmitter release, gland secretion, and contraction to help restore the meibomian gland's function. This will result in a better flow of meibum secretion, therefore improving the oily layer of the tears and in turn, reducing tear evaporation[18].

Clinical studies have demonstrated that IRPL therapy effectively reduces dry eye symptoms and clinical signs of MGD across various populations[19]. A retrospective study in Colombia[20] has reported improved dry eye symptoms alongside increased tear break-up time (TBUT) and quantity of tears, as measured with the Schirmer test in MGD patients following IRPL treatment. Using more objective assessments, a prospective study in Italy[21] reported improvement in non-invasive break-up time (NIBUT), lipid layer thickness, tear osmolarity as well as subjective dry eye symptoms based on Ocular Surface Disease Index (OSDI) score. However, among the parameters measured, they did not find any changes to meibomian gland loss which was contradicted by the earlier report by Yin et al[22] who compared the effectiveness of IRPL and lid hygiene in treating MGD in a cohort study. In a more recent study, a randomized controlled trial was conducted in New Zealand[23], to investigate the effectiveness of this therapy by comparing the symptomology, bacterial growth on the inferior lid margin, and a more extensive evaluation of the ocular surface. They reported a significant reduction in dry eye symptoms accompanied by inhibition of Corynebacterium macginleyi growth, increment in tear film lipid layer, and reduction in meibomian gland capping post-treatment. However, meibomian gland loss has not been investigated in this study despite mixed findings reported in the previous studies.

This therapy is considered relatively new in Southeast Asia countries compared to the West. Its effectiveness in treating MGD among Southeast Asian patients remains underexplored, despite the higher prevalence of MGD in this population compared to Caucasians. Considering ethnicities, and geographical and cultural differences as the causative factors in dry eye, this study aims to report the effectiveness of this therapy among Southeast Asian patients. In addition, with a larger sample size, this study also retrospectively reported ocular surface changes after the therapy, including the percentage of meibomian gland loss which was inconclusive in the previous studies.

Material and Methods

Study design and study area

This study is a retrospective study, conducted at one eye specialist center. Data was retrieved from the database among patients who came to the center for dry eye treatment between August 2022 to December 2023. The study was conducted in accordance with the Declaration of Helsinki, and was approved by ethical committee of one of the author's institution (FERC/FSK/MR/2022/0075).

Sample of the study and patient selection

Purposive sampling was used to retrospectively select the relevant data in this study. Data were collected from patients attending dry eye clinics by a single ophthalmologist at an eye specialist center who have been treated with E>Eye IRPL. All patients came with complaints of a blur of vision despite the optimum correction, unable to tolerate bright light and windy environments, having eye discomfort that affects the quality of daily living and often had red, itchy, watery, and irritated eyes. Only patients diagnosed with evaporative dry eye and presented with clinical signs of MGD based on meibomian gland assessment and tears evaluation were selected for this treatment. Patients who were uncooperative with the procedure, had unrealistic expectations from the treatment, such as hoping the condition to resolve in just one treatment or expecting a permanent effect from the treatment, were excluded from receiving the treatment. As for the retrospective collection of the data, only data from patients who met the diagnosis of MGD described above and underwent the treatment within the time frame (August 2022 to December 2023) were included in the study. On the other hand, patients who did not complete the whole course of treatment were excluded from the study.

Meibomian gland assessment that was performed to determine eligibility of the patients for IRPL treatment includes lid margin assessment and meibomian gland expression. Upon evaluation, all patients presented with lid margin abnormality. Meibomian gland expression was done by gently pressing the glands along the lower eyelids using a cotton swab or mastrota paddles to evaluate the expressed meibum quality. The grading of the expressed meibum was based on the level of opacity and viscosity of the meibum ranging from 0 to 4, with 0 indicating clear and normal viscosity, while 4 indicates no meibum expressed. Similar grading was used and explained in the previous study[24,25]. Based on the quality of the expressed meibum, only patients with meibum grade 0 (clear) to grade 2 (cloudy with debris) were included in the study. Following this, tears were evaluated using the Tear Check Analyzer by ESW Vision to evaluate non-invasive tear break-up time (NIBUT) and percentage of meibomian gland loss. Through meibography technique, Tear Check Analyzer determined the percentage of meibomian gland loss by rating the percentage of glands loss in comparison to age- and sex-matched individuals with all the glands presents. Patients who showed more than 20% of gland loss and NIBUT of less than 6 seconds were selected for IRPL treatment.

Procedure

Pre and post-treatment evaluation

To evaluate the effectiveness of IRPL treatment on EDE caused by MGD, the ocular surface was evaluated twice which were during pre and post-treatment evaluation on day 1 before the treatment, and on day 45 after the treatment, respectively. The ocular surface evaluation was done using the Tear Check Analyzer (E-Swin, ESW Vision), an instrument with a 2D high-resolution camera that is fixed to a table with a chin and headrest. It offers a non-invasive and quick evaluation of several ocular surface parameters. Although several parameters can be measured using the Tear Check Analyzer, only the percentage of lower meibomian gland loss, Tear Film Stability Evaluation (TFSE), and NIBUT were included in this retrospective study as we were unable to retrieve the remaining parameters due to technical issues.

During the procedure, participants were asked to rest their chin and head on the chinrest and headrest provided. They were asked to look at the camera for 60 seconds and were allowed to blink naturally while the measurements were taken. Measurements were taken separately for each eye by the instrument once initiated by the examiner. For TFSE and NIBUT measurements, participants were asked to blink twice, before their eyes were then recorded for 10 seconds for the instrument to analyze TFSE and NIBUT scores. While NIBUT indicates the major event appears on the tear's surface, which is seen as the rupture of the film (tear break-up), TFSE scores reveal the subtle changes happening on the surface offering a closer investigation of the tear’s stability. Therefore, both measurements were compared in this study to signify the change in tear stability after the treatment. Similar measurements were also performed in the previous studies investigating the efficiency of IPL on dry eye[26,27].

Tear Check Analyzer measures TFSE by assessing the number and intensity of micro-deformation of the tear film surface over 10 seconds. A healthy eye is expected to have fewer and lower intensity of tears micro-deformations compared with dry eye with a greater lipid deficiency. The micro-deformations were computed by the software and converted into a score ranging from 18 to 1200 points, with the increase in number and intensity of deformations reflect lesser tear stability which was denoted by a higher TFSE score. On the other hand, the NIBUT shows where and when the tear film surface is rupture, indicating the point where tears become unstable. This is measured by Tear Check Analyzer three times per second throughout the 10 seconds imaging of the tear film.

This was followed by an examination of the meibomian glands on the upper and lower eyelids of each eye. The eyelid flipping tool enclosed with the instrument was used to help expose the eyelid, particularly the meibomian glands areas to examine the percentage of the glands present. Then, the examiner marked the area of interest (the meibomian glands) directly on the screen captured by the instrument using a digital pen provided to refine and confirm the meibomian gland areas before the percentage of the glands is analyzed. The percentage of meibomian gland loss was automatically calculated and determined by the software, which may include partial loss or truncation of the glands. However, since this study is a retrospective study, there were some corrupted data that cannot be retrieved from the (Tear Check Analyzer) which include upper meibomian gland loss. Therefore, only lower meibomian gland loss was included and reported in the analysis.

IRPL therapy

All patients included in this study were treated with E>Eye IRPL using the E>Eye device (E-Swin, Paris, France) in three consecutive visits which were done on day 1 (after pretreatment evaluation of the ocular surface), day 15, and day 45 as per manufacturer recommendation (Figure 1). Before beginning the treatment, patients were seated comfortably on a chair in a slightly reclined position. They were asked to wear a protective eye mask provided and treatment gel was applied onto their cheekbone and temporal areas to protect the eyes and ensure their comfort during the treatment. E>Eye IRPL was then used to generate polychromatic pulsed light with specific energy, spectrum, wavelength, and duration to stimulate the nerves that are connected to meibomian glands. This instrument was used to generate four overlapping flashes of light on the cheek (starting from the inner canthus to the temporal canthus) and one flash at the temporal part of the eye to stimulate the meibomian glands. The gel was then wiped off after five flashes of light were administered to both eyes. The whole procedure took only a few minutes per session to complete for both eyes (Figure 2). During the treatment, patients received no other adjunct treatment for MGD.

IRPL=Intense Regulated Pulse Light

Figure 1 E>Eye IRPL by ESW Vision

Data analysis

Data was analyzed retrospectively using Statistics Package for Social Sciences (SPSS) version 29 for Mac (IBM Corp., Armonk, NY). Descriptive analysis was used to describe demographic information and the three ocular surface parameters measured in this study. Repeated-measure ANOVA was used to compare the percentage of lower meibomian gland loss and TFSE score between pre- and post-treatment evaluations. In addition, the McNemar Change Test was used to compare the proportions of patients having NIBUT of lower than 10 seconds pre-and post-treatment. The alpha value was set at 0.05 for all comparisons.

Results

Seventy-one male and 107 female patients, aged between 28-83 years old (M=35, S.D.=15) with complaints of dry eye symptoms accompanied by clinical signs of MGD were included in the study. Since all parameters obtained for the right eye and left eye were highly correlated in all visits (p-value<0.01), only data from the right eye were analyzed for all outcomes.

The percentage of lower meibomian gland loss and TFSE scores were compared using Repeated-measure ANOVA between pre-and post-treatment visits to determine the effectiveness of the IRPL treatment. Results showed that the percentage of lower meibomian gland loss was significantly decreased post-treatment (M=28.10, S.D.=10.87) compared with pre-treatment (M=30.24, S.D.=11.88) indicating recovery of the meibomian gland, F (1, 177)=4.319, p-value=0.039 (Figure 3).

Similarly, a significant reduction in TFSE score was also found during post-treatment measurement (M=448.16, S.D.=237.75) compared to pre-treatment (M=553.47, S.D.=239.15) indicating improved tear stability after the treatment, F (1, 177)=3.972, p-value=0.048 (Figure 4).

In addition, the percentage of patients having NIBUT of lower than 10 seconds was compared using the McNemar Change Test to determine if the percentage of patients who fall into the dry eye category (NIBUT of lower than 10 seconds) has changed after the treatment. Results showed that the percentage of patients that fell into the dry eye category was significantly lesser during post-treatment measurement (p-value<0.001) (Figure 5).

Discussion

This study investigated the effectiveness of E>Eye intense regulated pulse light (IPL) therapy in treating evaporative dry eye among Southeast Asian patients by comparing the proportion of patients with low non-invasive tear break-up time (NIBUT), tear film stability evaluation score (TFSE) and the percentage of lower meibomian gland loss between pre-and post-treatment. Results showed a reduction in the proportion of patients with low NIBUT, an improvement in TFSE score, and a decrease in the percentage of lower meibomian gland loss post-treatment, suggesting an improvement in clinical signs of evaporative dry eye caused by MGD among Southeast Asian patients.

In agreement with previous studies[20–23], our findings also showed that more patients had improved NIBUT

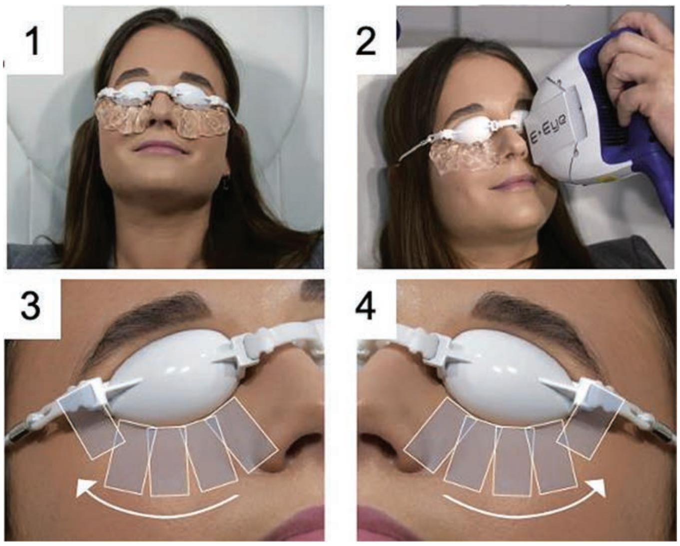


Figure 2 Intense Regulated Pulse Light (IRPL) Therapy. Patient is wearing protective eye mask with the treatment gel applied onto their cheekbone (1) Five flashes of light are applied (2) on the lower lid and temporal part of the right eye (3) and left eye (4)[28]

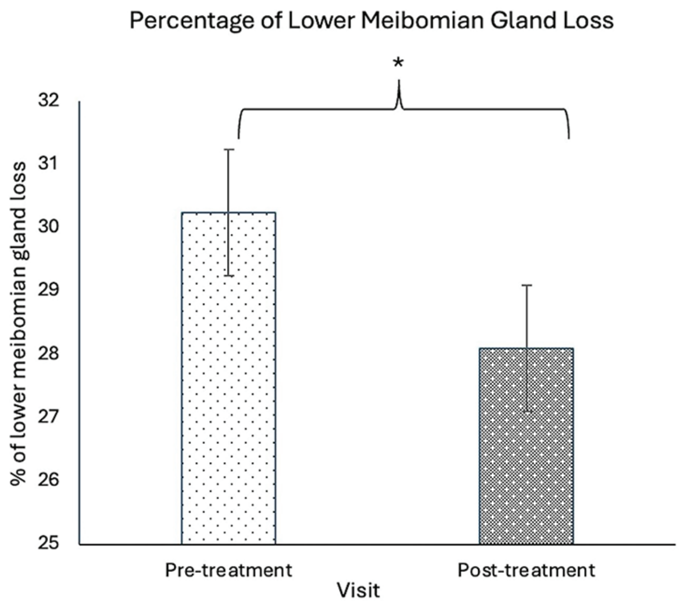


Figure 3 Percentage of lower meibomian gland loss in pre and post-treatment measurements. The asterisk indicates a significant difference, while error bars indicate standard error

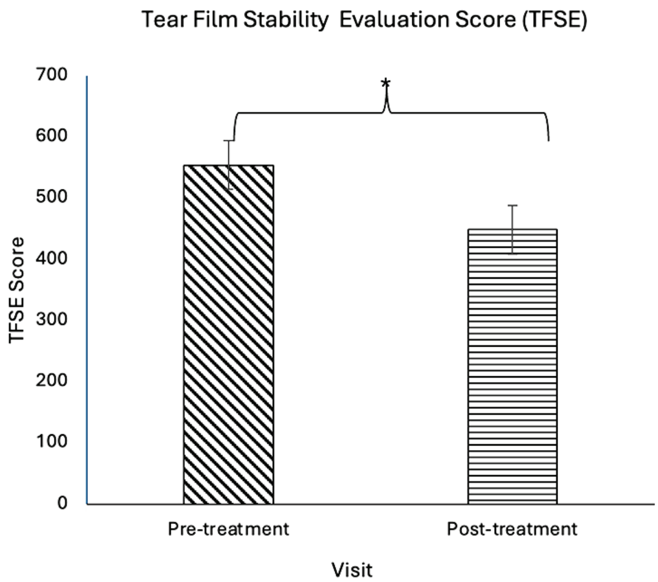
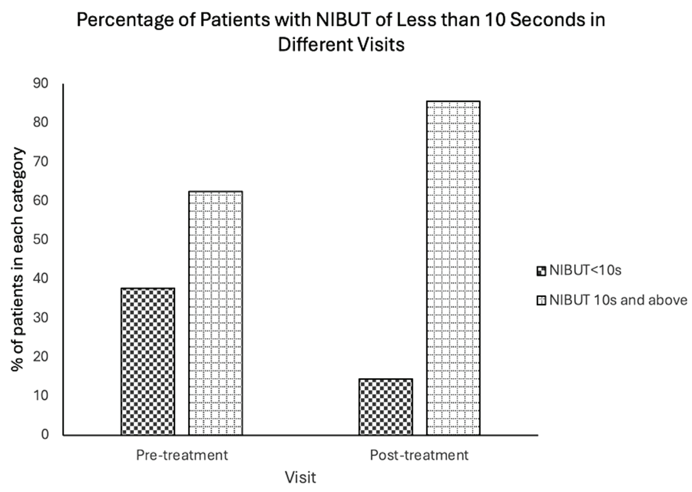


Figure 4 Tear Film Stability Evaluation (TFSE) score in pre and post-treatment measurements. The asterisk indicates a significant difference, while error bars indicate standard error



NIBUT=non-invasive break-up time

Figure 5 Percentage of patients with NIBUT of less than 10 seconds before and after the treatment

following the treatment, suggesting that the tear layer can sustain longer on the ocular surface. With a temporary local thermal effect generated by IRPL, the outflow of meibum can be improved, therefore enhancing the quality of meibum secretion that forms the outer oily layer of the tears[18]. As the secretion of the oily layer of the tears improves, evaporation of the tears reduces, resulting in better stability of the tears on the corneal surface. In addition, improved stability of the tears was also reflected in the reduction of TFSE score post-treatment. The score indicates micro-movement of the tears in 10 seconds, with a higher score indicating lesser tear stability on the cornea. This non-invasive objective scoring provides a more accurate judgment of tear film stability compared to TBUT. Similar to NIBUT, TFSE was improved post-treatment following restoration of the meibomian gland function, therefore improving the oily layer of the tears and tear stability.

Apart from improvement in tear stability, results showed that IRPL also helps to restore meibomian glands. Patients with MGD may have fewer meibomian glands causing an insufficient oily layer of the tears. With a larger sample, our results support those found by Yin et al.[22] where the percentage of lower meibomian gland loss has reduced following the treatment, in contrast to no changes reported by Vigo et al.[21]. Without a control group, we could not determine whether this effect is exclusive to only IRPL or may apply to other treatments as well. Nevertheless, this retrospective finding does provide additional evidence to support the potential benefit of IRPL in restoring meibomian glands, as the patients received no other treatment apart from IRPL during the course of the treatment.

The mechanism of how IRPL works to restore the percentage of meibomian glands is not well understood. In the dermatology field, advancement in technology has led to the use of a low-energy, narrow-band light to rejuvenate the skin cells, termed photomodulation. Photomodulation of the cells occurs via stimulation of the mitochondrial activities, hence promoting wound healing and recovery of the cells[29]. Although the pathogenesis of MGD remains elusive, it has been widely accepted that the epithelial hyper-keratinization of the ducts may lead to obstruction of the meibum flow and secondary damage to the gland, causing meibomian gland loss[6,30]. Adapting a similar concept from the use of photomodulation on skin rejuvenation, IRPL treatment has been speculated to induce a similar photomodulation effect that helps improve meibomian glands' microstructure by stimulating the acinar cells' activity[22]. Treating the condition at the cellular level offers a longer-lasting impact on the condition compared to other treatments, with a potential benefit of up to six to twelve months effect. However, since this study only involves clinical data, a histological study is needed to prove the improvement of meibomian glands at the cellular level.

A limitation of this study is its retrospective nature, which has resulted in limited information about the patients. One important set of data that is missing due to data corruption involves the upper meibomian glands loss before and after the treatment. Therefore, it remains unknown whether the upper meibomian gland benefits from the treatment similar to the lower glands. Additionally, the anterior and posterior eye parameters of each patient were not recorded during the pre-treatment assessment, leading to limited information on the characteristics of the patients' eyes that respond well to the treatment. Moreover, since the post-treatment data were measured at day 45 of the treatment, we were unable to determine the long-term effectiveness of the treatment. However, the findings reported do indicate promising benefits of IRPL advocating the use of this treatment as an adjunct to existing treatment among the Southeast Asian population. In addition, the effectiveness of the therapy reported in this study is only confined to dry eye patients with signs of MGD and may not apply to other types of dry eye.

Conclusion

E>Eye IRPL was found to improve NIBUT and TFSE, as well as promoting recovery of the lower meibomian gland loss in patients with MGD. These suggest that after three consecutive treatments, IRPL is also effective in restoring meibomian gland function and improving dry eye conditions in MGD patients in Southeast Asia. In conclusion, IRPL is recommended as an adjunct treatment for EDE caused by MGD, providing longer-lasting relief of the condition.

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Conflict of interest

There are no potential conflicts of interest to declare.

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