Factors Influencing the Effectiveness of Intense Pulsed Light for Meibomian Gland Dysfunction

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Abstract

Purpose: To observe the effectiveness of intense pulsed light (IPL) for meibomian gland dysfunction (MGD) and identify its influencing factors.

Methods: Forty-eight eyes of 48 patients with MGD were included. Subjects were followed up 5 times and received IPL during the first three visits. Gender, age, duration of MGD, time of video display terminal usage, and severity of MGD were recorded at baseline. At every visit, Ocular Surface Disease Index (OSDI), eyelid margin abnormality score (EMAS), tear film breakup time (TBUT), Schirmer Ⅰ test (SⅠt) and corneal fluorescein staining (CFS) were recorded. The clinical parameters before and after 3 IPL treatments were compared. Univariate and multivariable logistic regression analyses were performed to explore influencing factors.

Results: Compared with baseline, the TBUT was increased and the CFS score and OSDI were significantly decreased on day 45 and day 120 (all $P < 0.001$). In univariate analysis, among the patients with a younger age (18-39 years), moderate MGD, higher baseline SIt and higher baseline OSDI, the IPL treatment had a higher effective rate ($P = 0.032$, 0.004, 0.024 and 0.014 respectively). The MGD severity was strongly associated with effective IPL, and patients with moderate MGD had an OR of 5.493 compared with the severe MGD patients (OR = 22.454, 95% CI: 2.890-174.436, $P = 0.003$).

Conclusions: IPL effectively improves clinical symptoms and some signs in MGD patients. Age, MGD severity, baseline SIt and baseline OSDI are potential factors that may influence the effectiveness of IPL. MGD severity is an independent influencing factor.

Key Messages

- The advent of intense pulsed light (IPL) provides a novel treatment in patients with Meibomian gland dysfunction (MGD), but the poor clinical efficacy of IPL was reported in some studies and the optimal candidates for IPL treatment remain unclear.
- The patients with a younger age, moderate MGD, higher baseline Schirmer Ⅰ test (SIt) and higher baseline Ocular Surface Disease Index (OSDI) had a higher effective rate of IPL treatment.
- Age, the severity of MGD, and the baseline SIt and OSDI are potential factors that may influence the effectiveness of IPL. And the severity of MGD is an independent influencing factor.

Introduction

Worldwide, meibomian gland dysfunction (MGD) has become a hotspot issue in recent decades that poses serious risks to the quality of people's daily life and work. Epidemiological evidence shows that the prevalence of MGD ranges from 3.5% to almost 70% in various countries[1], and the data reported in Asian countries are generally higher than those reported in Western countries[2]. It is well established that MGD can not only cause ocular surface discomfort related to impaired meibomian gland (MG) function, but also give rise to intractable evaporative dry eye[3]. However, consensus regarding the optimal intervention strategy is lacking. The conventional treatments include lid hygiene, eyelid warming and massage, pharmaceutical-based therapy, and intraductal MG probing[4]. Although the aforementioned therapies reportedly relieve the symptoms of MGD, their efficacy largely depends on patient compliance[5]. Therefore, difficulties and challenges still exist in the treatment of MGD.

In recent years, the advent of intense pulsed light (IPL) has provided a novel treatment for patients with MGD. With regard to MGD, which is mainly characterized by terminal duct obstruction and qualitative or quantitative changes in the meibum[6]. A large amount of lipids accumulates in the ductal system and cannot be smoothly driven toward the orifice at the lid margin to form a tear film lipid layer. Current studies suggest that IPL plays a role in softening the meibum by heat transfer[7] to facilitate MG secretion[8] and improve the meibum quality and meibomian gland expression[9]. Significant improvements in ocular surface symptoms and signs have been found after IPL in many studies[9], but some patients have been reported to experience no obvious improvement after several IPL treatments[10]. Furthermore, the high expense of IPL further limits its wide application in clinical practice. Thus, knowledge of the optimal candidates and ideal number of IPL treatments is crucial for the rational and scientific application of IPL, but thus far, the related situation remains unclear.

Identifying the factors influencing the effectiveness of IPL could provide some experience reference and practice foundation for ophthalmologists. As previously reported, age and the male sex are the most common factors contributing to the prevalence of MGD[11, 12]. Long-term video display terminal (VDT) usage has been reported as a vital factor that has a significant impact on MGD[13]. Given this background, we collected information regarding the demographic characteristics, duration and severity of MGD, and hours of daily VDT of all patients.

Here, we conducted a study to observe the effectiveness of IPL treatment in MGD patients and investigate the above-mentioned factors influencing the effectiveness of IPL to provide some evidence regarding the optimal candidates for IPL treatment.

Methods

Patients

In this study, 48 eyes of 48 patients with MGD were enrolled among outpatients of the Ophthalmology Department of Peking Union Medical College Hospital from June 2019 to September 2019. If both eyes met the inclusion criteria and failed the exclusion criteria, the right eye was selected. This study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Peking Union Medical College Hospital. All participants voluntarily signed an informed consent form.

The inclusion criteria were: (1) 18 years old or above; (2) Patients diagnosed with MGD according to previously reported diagnostic criteria, presenting at least two clinical signs: redness or thickening of the lid margin, telangiectasia, reduced or no secretions, poor quality secretions, and meibomian gland capping[14]; (3) Patients volunteered to participate and cooperate for more than 3 months; and (4) Patients was in good physical and mental health.

The exclusion criteria were: (1) dermatosis or skin damage to the eyes and face; (2) history of ocular surgery or trauma; (3) active ocular inflammation, allergy or infection within 3 months, which was not caused by dry eye or MGD; (4) eyelid deformity; (5) use of any other treatment except artificial tears within the past 1 month; (6) Sjögren's syndrome and other systemic diseases; (7) facial skin treatment within the past 3 months; (8) pregnancy or lactation period; and (9) any unpredictable risks of abnormal performance on the ocular surface or treatment area.

Clinical examinations and evaluations

Demographic characteristics and medical history were collected for all subjects, including age, gender, duration of MGD, and time of VDT usage daily. The severity of MGD was estimated by a self-assessment questionnaire to evaluate the symptoms before treatment, as reported in previous studies[15, 16]. The patients were asked to grade the extent of 10 specific symptoms, including dryness, foreign body sensation, ache, burning, tearing, asthenopia, blurry vision, itching, secretions, and photophobia. The score of each symptom ranged from 0 to 10 (0 for none, 10 for severe), and the total score was the sum of each score of the ten symptoms. All eyes were classified into mild, moderate and severe groups before treatment based on the following criteria[16]: mild (total score $\leq$ 30), moderate (30 < total score $\leq$ 60), and severe (total score > 60).

The subjective and objective clinical parameters were recorded in the following order by the same experienced doctor during each visit: Ocular Surface Disease Index (OSDI) questionnaire, eyelid margin abnormality score (EMAS), tear film breakup time (TBUT), Schirmer Ⅰ test (SIt) and corneal fluorescein staining (CFS). These parameters were measured as previously described[17]. In brief, (1) the OSDI score was calculated based on the 12 questions on the OSDI questionnaire according to the following formula: total score = total score of all questions/total number of questions answered × 25[18]. (2) The EMAS was assessed based on obstruction of the MG orifices, irregularity of the lid margin, vascular congestion over the lid margin, and anatomic displacement of the mucocutaneous junction, and the presence of each sign was given one point[19]. (3) The TBUT was evaluated with sodium fluorescein, and the mean value of three measurements was calculated to obtain the best and most accurate results. (4) The SIt was conducted without surface anesthesia. (5) The CFS scores of each quadrant ranged from 0 to 3 (0: no punctate staining; 1: less than half was stained; 2: more than half was stained; and 3: the whole quadrant was stained). The total score was the sum of the four quadrants of the cornea[20].

Treatment procedure

Before the IPL treatment, all enrolled patients were required to cease any topical ophthalmic drugs and treatment for two weeks. After the washout period, the patients underwent 3 sessions of the IPL treatment after clinical examinations and evaluations on day 1, day 15 and day 30. The remaining two follow-up observations were completed on days 45 and 120. During the follow-up period, other treatments were forbidden.

An E-eye light pulse dry eye therapy instrument (E-SWIN, Paris, France) was used in this study. Patients were treated in the sitting position with their eyes covered by goggles. The energy level (energy range 9 J/cm2 ~ 13 J/cm2) was selected based on Fitzpatrick's skin type classification standard[7]. Four flashes were performed under the eyelid skin from the nasal side to the temporal side, and ultrasonic gel was applied to the treatment area.

Definition of effective and ineffective IPL

Efficacy was mainly assessed according to the OSDI. “Effective IPL” was defined as a reduction of 5 or more points in OSDI after 3 sessions of the IPL treatment. “Ineffective IPL” was considered when this condition was not met, as previously described[21].

Statistical analysis

The data were analyzed using the statistical software IBM SPSS 19.0 for Windows (SPSS, Chicago, IL). Data normality was verified using the Kolmogorov-Smirnov test. Continuous variables with normal distributions were presented as the mean ± standard deviation, and the nonnormally distributed data were presented as medians (P25, P75). The categorical variables were summarized as the number of cases and percentages (%). To compare the changes in the subjective and objective clinical parameters before and after 3 sessions of the IPL treatment, the paired-sample *t*-test and paired-sample nonparametric Wilcoxon test were used. A Chi-square test was conducted to compare the categorical data between effective IPL and ineffective IPL, and the continuous data were examined using an independent-samples *t*-test or Mann-Whitney *U* test. In the multivariable logistic regression model, variables with $P < 0.05$ in the univariate analysis were included to identify the independent influencing factors. A *P*-value less than 0.05 (two-sided) was considered statistically significant.

Results

Baseline characteristics

Forty-eight eyes from 48 patients were investigated in this study, and their detailed characteristics are shown in Table 1.

Table 1
Baseline characteristics

Characteristics	Number of patients (%)
Gender	
Male	14 (29.2)
Female	34 (70.8)
Age (years)	
18–39	24 (50.0)
40 and above	24 (50.0)
Duration of MGD (months)	
<3	24 (50.0)
3-<6	14 (29.2)
≥6	10 (20.8)
Time of VDT usage (hours/day)	
0-<4	16 (33.3)
≥4	32 (66.7)
Severity of MGD	
Mild	6 (12.5)
Moderate	24 (50.0)
Severe	18 (37.5)

MGD: meibomian gland dysfunction; VDT: video display terminal.

Comparison of the subjective and objective clinical parameters before and after three sessions of the IPL treatments

The statistical analysis revealed that the TBUT on day 45 and day 120 was significantly increased compared to that at baseline (all $P < 0.001$). The CFS scores were significantly decreased on day 45 and day 120 compared to those at baseline (all $P < 0.001$). A significant decrease in the OSDI scores was found on day 45 and day 120 compared with baseline (all $P < 0.001$). In addition, the SIt values on day 45 and day 120 were greater than those at baseline, and the EMAS on day 45 and day 120 were lower than those at baseline, but no statistically significant differences were found (Table 2).

Table 2
Comparison of the subjective and objective clinical parameters before and after three sessions of IPL treatments

Parameters	Day 1 (baseline)	Day 45	Day 120
TBUT [b] (s)	2.00 (1.00, 2.00)	3.00 (3.00, 4.00)*	3.00 (3.00, 4.00)*
SIt [b] (mm/5 min)	6.50 (2.00, 12.00)	8.00 (6.00, 11.00)	6.00 (5.00, 11.50)
CFS [b] (score)	2.00 (1.00, 4.00)	0.00 (0.00, 1.00)*	0.00 (0.00, 1.00)*
OSDI [a] (score)	41.55 ± 19.04	29.84 ± 18.46*	28.76 ± 18.46*
EMAS [b] (score)	2.00 (2.00, 2.00)	2.00 (2.00, 2.00)	2.00 (2.00, 2.00)

TBUT: tear film breakup time; SIt: Schirmer I test; CFS: corneal fluorescent staining; OSDI: Ocular Surface Disease Index; EMAS: eyelid margin abnormality score; *: $P < 0.05$ compared to baseline. [a]: Normally distributed data are presented as the mean ± standard deviation; statistical analysis was performed with a paired-samples t-test; [b]: Nonnormally distributed data are presented as the median (P25, P75); a paired-sample nonparametric Wilcoxon test was used for the comparison.

Comparison of the effective and ineffective IPL treatment outcomes

As shown in Table 3, the effective rate of the IPL treatment in the patients aged 18–39 years (62.5%) was significantly higher than that in the patients aged 40 years or older with statistical significance (P = 0.032). The effective rate of IPL in the patients with moderate MGD (65.6%) was significantly higher than that in the patients with mild or severe MGD (P = 0.004). The baseline SIt and baseline OSDI of the patients with an effective IPL outcome were significantly higher than those in the patients with an ineffective IPL outcome (P = 0.024). The other parameters, including gender, duration of MGD, time of VDT usage, baseline TBUT, baseline CFS, and baseline EMAS, did not significantly differ between the two outcome patient groups (all $P > 0.05$).

Table 3
Comparison of the effective IPL group and ineffective IPL group according to different characteristics.

Parameters	**Effective IPL (n = 32)**	**Ineffective IPL (n = 16)**	***P* value**
Gender			1.000[c]
Male	9 (28.1)	5 (31.3)	
Female	23 (71.9)	11 (68.7)	
Age (years)			**0.032**[c]
18–39	20 (62.5)	4 (25.0)	
40 and above	12 (37.5)	12 (75.0)	
Duration of MGD (months)			0.504[c]
<3	16 (50.0)	8 (50.0)	
3-<6	8 (25.0)	6 (37.5)	
≥6	8 (25.0)	2 (12.5)	
Time of VDT usage (hours/day)			0.665[c]
0-<4	10 (31.3)	6 (37.5)	
≥4	22 (68.7)	10 (62.5)	
Severity of MGD			**0.004**[c]
Mild	4 (12.5)	2 (12.5)	
Moderate	21 (65.6)	3 (18.7)	
Severe	7 (21.9)	11 (68.8)	
Baseline TBUT (s)	1.50 (1.00, 2.00)	2.00 (1.00, 2.00)	0.592[d]
Baseline SIt (mm/5 min)	9.50 (4.00, 13.00)	4.00 (2.00, 7.75)	**0.024**[d]
Baseline CFS (score)	2.00 (1.00, 4.00)	2.00 (1.00, 3.00)	0.548[d]

IPL: intense pulsed light; MGD: meibomian gland dysfunction; VDT: video display terminal; [c]: statistical analysis was performed with chi-square tests; [d]: Nonnormally distributed data are presented as the median (P25, P75); statistical analysis was performed with a Mann-Whitney U test; [e]: Normally distributed data are presented as the mean ± standard deviation; statistical analysis was performed with an independent-samples t-test; Bold values indicate $P < 0.05$, and the difference is statistically significant.

Parameters	Effective IPL (n = 32)	Ineffective IPL (n = 16)	*P* value
Baseline OSDI (score)	43.37 ± 21.39	37.91 ± 13.00	**0.014**[e]
Baseline EMAS (score)	2.00 (2.00, 2.00)	2.00 (1.25, 2.00)	0.639[d]

IPL: intense pulsed light; MGD: meibomian gland dysfunction; VDT: video display terminal; [c]: statistical analysis was performed with chi-square tests; [d]: Nonnormally distributed data are presented as the median (P25, P75); statistical analysis was performed with a Mann-Whitney U test; [e]: Normally distributed data are presented as the mean ± standard deviation; statistical analysis was performed with an independent-samples t-test; Bold values indicate $P < 0.05$, and the difference is statistically significant.

Independent influencing factors of IPL effectiveness

After adjusting for age, severity of MGD, baseline SIt and baseline OSDI, the multivariable logistic regression models showed that the severity of MGD was significantly associated with effective IPL. Compared with severe MGD, the odds ratio of effective IPL in the patients with moderate MGD was 22.454 (95% CI: 2.890 ~ 174.436, *P* = 0.003) (Table 4).

Table 4
Multivariable logistic regression analysis of the factors associated with effective IPL

Parameter		β value	SE value	OR (95% CI)	*P* value
Age (years)	18–39	1.306	0.943	3.692 (0.581 ~ 23.458)	0.166
	40 and above	0	—	1.000	—
Severity of MGD	Mild	1.209	1.113	3.351 (0.379 ~ 29.664)	0.277
	Moderate	3.111	1.046	22.454 (2.890 ~ 174.436)	0.003
	Severe	0	—	1.000	—
Baseline SIt (mm/5 min)		0.095	0.081	1.100 (0.939 ~ 1.288)	0.240
Baseline OSDI (score)		0.034	0.025	1.034 (0.985 ~ 1.086)	0.172

SE: Standard error; OR: odds ratio; CI: confidence interval; MGD: meibomian gland dysfunction.

Discussion

In the present study, the effectiveness of IPL for MGD was confirmed, and factors that influence the efficacy of IPL were also explored. After IPL treatment, the TBUT, CFS scores and OSDI had a better performance than before. To take it a step further, we observed a significant association between an effective IPL treatment outcome and a younger age (18–39 years), moderate MGD, higher baseline SIt, and higher baseline OSDI. The severity of MGD attained statistical significance in both our univariate and multivariable logistic regression analyses.

Our results demonstrated that IPL treatment improved TBUT and resulted in reduced CFS scores and OSDI. Postoperative and preoperative data suggested that the beneficial effects of IPL could be sustained for at least three months. This finding indicated that IPL helped stabilize the tear film and improved ocular surface damage and symptoms of MGD[22]. However, there was no significant change in the SIt values after the treatment. The reason might be that MGD is a major cause of evaporative dry eye, whose main manifestation is a significant change in the tear quality rather than the tear amount[17, 23]. The EMAS did not respond ideally to IPL, and this result was similar to previous results reported by Karaca EE et al[24].

Furthermore, we compared the characteristics of the effective and ineffective IPL treatment outcomes. The analysis implied that after three sessions of the IPL treatment, the outcomes were divergent among patients with different age, different severity of MGD, different baseline SIt or different baseline OSDI. As age increased, the occurrence rate of effective IPL decreased. A recent retrospective study showed a similar view and reported that a younger age was associated with greater benefits of IPL[25]. The results might be explained as follows. First, the decrease in the ability to synthesize estrogen in senior patients could affect the quantity and quality of lipid secretion from the MG[11], resulting in tear film instability and ocular surface inflammatory reactions[26]. Second, regarding histology, with increasing age, the acinar basement membrane becomes thicker[26], while the MG density and diameter decrease[27, 28]. In addition, it has been found that older people have fewer acinar cells, which eventually becomes acinar atrophy, solidification and even scarring[29]. Thus, it is possible that elderly MGD patients are more difficult to treat.

In our univariate analysis, higher baseline SIt and baseline OSDI also displayed a higher effective rate of IPL treatment. Thus. the patients with higher amounts of tear and more severe symptoms were more likely to benefit from the IPL treatment. Previous studies have found that IPL significantly improves the thickness of the tear film lipid layer[30]. Patients with high baseline SIT had better secretion function in the main lacrimal gland; thus, it is reasonable to presume that the amount of aqueous layer in patients with high baseline SIt was mainly reduced by evaporation, but the secretion function was less affected. The lipid layer repair by IPL can better protect the aqueous layer to reduce the evaporation of tear, thus achieving a better therapeutic effect. Additionally, IPL regulates the secretion of pro-inflammatory and anti-inflammatory molecules[31]. Their levels were closely related to pain, tear instability, tear production and ocular surface integrity[32]. Through this mechanism, IPL was helpful for patients with high baseline OSDI to repair ocular surface damage[33]. The above research results provided some references for selecting patients and communicating with patients about their prognosis before IPL treatment in the clinic. However, these factors could not be used as prognostic factors independently.

Based on our multivariable logistic regression model, severity of MGD was an independent influencing factor. The effective rate of IPL in the moderate MGD group (65.6%) was the highest among all groups. Moderate MGD was associated with increased odds of effective IPL in our analysis. The results indicated that effective IPL in moderate MGD patients was 22.454 times as high as that in severe MGD patients. Vegunta et al. [10] reported that pronounced gland dropout or atrophy contributed to failed IPL treatment. Similarly, Tang Y et al. [25] proposed that the extent of meibomian gland dropout may be a key factor in the outcome of IPL treatment. Therefore, we inferred that more serious and unrecoverable damage to the physiological structure and function of the MG in patients with severe MGD was a possible reason for this result in our study[34].

An unexpected finding was that there was no significant association between mild MGD and effective IPL when severe MGD was used as the reference group in the multivariable logistic regression analysis. According to published studies, improvements in the OSDI after IPL are negatively correlated with the baseline MG expression, i.e., the higher the baseline MG expression capacity, the smaller the improvement in OSDI[35]. Therefore, we speculated that the MG expression capacity in patients with mild MGD was better than that in those with severe MGD, resulting in smaller improvements in OSDI in patients with mild MGD after IPL. Furthermore, the main efficacy evaluation in this study was based on improvement in OSDI. Consequently, we did not observe any association between mild MGD and effective IPL.

To the best of our knowledge, the optimal candidates for IPL have not been identified. This study represents the first prospective research to perform a statistical analysis of the factors influencing the effectiveness of IPL treatment until now[36]. Nevertheless, the sample size of our study was relatively small. Some factors are difficult to control, such as patients' lifestyle, hormone levels, mood, and environment, which may affect the therapeutic effect of IPL treatment [37, 38]. Large-sample multicenter studies are expected to further confirm these results in the future.

In conclusion, IPL can effectively improve the clinical symptoms and some signs in patients with MGD, and the beneficial effects can be maintained for at least three months. Age, the severity of MGD, and the baseline SIt and OSDI are potential factors that may influence the effectiveness of IPL. The severity of MGD is an independent influencing factor.

Declarations

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Compliance with ethical standards

Conflicts of interest: The authors declare that they have no conflicts of interest.

Ethical approval: All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the institutional research committee and the 1964 Helsinki declaration and its later amendments. This study was approved by the Institutional Review Board of Peking Union Medical College Hospital.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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