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Long-term effects of intense pulsed light treatment on the ocular surface in patients with rosacea-associated meibomian gland dysfunction

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ABSTRACT

Purpose: We aimed to determine the long-term effects of intense pulsed light (IPL) treatment in rosacea-associated meibomian gland dysfunction (MGD).

Methods: We enrolled 17 rosacea subjects with moderate and severe MGD who underwent four IPL sessions at 3-week intervals and were followed up for 12 months. The subjects underwent clinical examinations at baseline (first IPL) and at 3 (second), 6 (third), 9 (fourth), and 12 weeks, as well as 6 and 12 months, after baseline. Ocular surface parameters, including the Ocular Surface Disease Index (OSDI), tear break-up time (TBUT), staining score, and noninvasive Keratograph tear break-up time (NIKBUT), as well as meibomian gland parameters, including the lid margin vascularity and meibum expressibility and quality, were evaluated.

Results: All ocular surface and meibomian gland parameters for all subjects exhibited significant changes from baseline to the final examination (Friedman, $P < 0.050$ for all). In particular, improvements in the lower lid margin vascularity, meibum expressibility and quality, and ocular symptoms persisted up to the final examination (Wilcoxon, $P < 0.050$ for all). However, the improvements of TBUT, staining score, and NIKBUT after IPL were not maintained at 6 and 12 months after baseline.

Conclusions: In rosacea-associated MGD, four IPL treatments at 3-week intervals can improve long-term lid parameters and ocular symptoms without adverse effects.

1. Introduction

Rosacea is a chronic cutaneous disorder characterized by persistent erythema, telangiectasis, papules, and pustules, which primarily occur in the convexities of the central face [1,2]. Approximately 30–50% of patients with rosacea present with a broad spectrum of ocular findings [2]; the most common ocular sign is meibomian gland dysfunction (MGD), observed in several previous studies [3–5]. MGD in ocular rosacea is characterized by telangiectasia and erythema of the lid margin and qualitative and/or quantitative changes in the meibum, including turbid meibum and plugging of the gland orifices [2,4,5].

Ocular rosacea is usually associated with ocular surface inflammation [6–8]. Inflammatory processes can cause ocular surface epithelial damage and low tear secretion in rosacea-associated MGD, compared with normal controls [6–8]. Therefore, control of ocular surface inflammation is important in the treatment of ocular rosacea [2]. Generally, treatments for rosacea-associated MGD include the use of lubricants and maintenance of lid hygiene in the initial stages, similar to treatment for MGD not associated with rosacea. However, rosacea-associated MGD patients have a frequent need for systemic antibiotics or topical anti-inflammatory drugs [2].

Dysregulation of the vasomotor response is suggested as a mechanism for the erythema or telangiectasia in patients with cutaneous rosacea; it causes abnormal vasodilation and inflammatory mediator release [9–11]. Accordingly, some studies have reported that intense pulsed light (IPL) therapy targets these vascular components and decreases facial erythema and telangiectasia in patients with rosacea [1,12–14]. With the use of filters, light of approximately 500 nm can selectively coagulate and close the abnormal blood vessels in the skin, resulting in reduced inflammation [15,16].

Since Toyos reported the effects of IPL on ocular symptoms in facial rosacea patients [17], several studies have included IPL treatment for MGD and demonstrated its therapeutic potential [15,18–24]. These studies showed clinical improvements in tear film abnormality and symptoms due to MGD after IPL treatments. Recently, one study [24] demonstrated a reduction in tear inflammatory markers, as well as corresponding clinical improvements. These findings proved a possible mechanism of IPL effects on MGD.

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To the best of our knowledge, there have been no studies regarding the long-term effects of IPL treatment; previous studies [15,18–24] focused on patients with dry eye disease with MGD, regardless of rosacea. Therefore, we evaluated the long-term effects of four IPL treatments with 3-week intervals, specifically in moderate or severe rosacea-associated MGD patients.

2. Materials and methods

2.1. Subjects

The protocol for this prospective study was written in accordance with the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Inha University Hospital, Incheon, South Korea (IRB no. 2016-05-010).

From November 2015 to July 2016, study subjects were recruited from among patients visiting the dry eye clinic of Inha University Hospital. Subjects with moderate or severe MGD who fulfilled the diagnostic criteria for rosacea, or who were previously diagnosed with rosacea, were included. The grade of MGD was determined through assessment of meibomian gland parameters: abnormal lid margin vascularity, meibum expressibility, and meibum secretion [25,26]. Moderate or severe MGD was defined as follows: abnormal lid margin vascularity (grade ≥ 2), moderately or severely altered expressibility (grade ≥ 2), and secretion quality (grade ≥ 8) [25,26]. In accordance with the National Rosacea Society guidelines for rosacea [1], eligible subjects had any one of these primary features: transient erythema, persistent erythema, papules/pustules, and telangiectasia. Some subjects also had secondary features, such as phymatous changes. When necessary, we consulted a dermatologist for diagnosis and classification of rosacea. Informed consent was obtained from all eligible subjects after explanation of the purpose and possible consequences of the study.

The exclusion criteria were as follows: age < 20 years; a history of other ocular surgeries or ocular injury within 6 months before the study; presence of ocular diseases, such as infection or allergy; a history of contact lens use or glaucoma medication; contraindication to light therapy; and the presence of tattoos or pigmented lesions in the treatment area.

2.2. Treatment procedure

This prospective case series study was conducted for 12 months in all 17 subjects with rosacea-associated MGD who underwent four IPL treatment sessions at 3-week intervals and were followed up for the entire study period (Fig. 1). IPL treatment was administered on both eyes by using the M22™ Optima™ IPL (Lumenis, Yokneam, Israel), following the technique described by Toyos et al. [18] A 590-nm expert filter and pulse intensity of 11 J/cm^2 were used. Four separate treatment sessions were conducted at 3-week intervals, during which IPL was applied to four periocular areas from the nasal to temporal side below each lower lid, as in a previous report [19]. Following IPL application, the meibomian glands were expressed by using a cotton-tip applicator placed on the inside of the eyelid and the clinician's fingers positioned on the outside of the eyelid; this was performed at multiple sites of the lower lid. All procedures were performed by one of the authors (J.W.J). The subjects were instructed to continue the use of artificial tears and lid hygiene, as they had before participating in this study. They did not use other topical or systemic agents that could affect the ocular surface, from 1 month before the start of the study to the final follow-up.

2.3. Clinical assessments

The subjects were clinically evaluated at baseline (just before the first IPL treatment); 3 (before the second session), 6 (before the third session), 9 (before the 4th session), and 12 weeks after baseline; and 6 and 12 months after baseline. The first four evaluations were conducted just before IPL treatment. Each patient was followed up for a total 12 months from baseline. Data for analysis was obtained from the right eye unless right eye was excluded from the study, in which case ($n = 2$) data were collected from the left eye.

All measurements were sequentially performed as follows (Fig. 1). The tear film was assessed using the "TF-Scan, noninvasive Keratograph break-up time (NIKBUT)" mode of the Keratograph® 5 M (K5 M; Oculus, Optikgerate, Germany). The subjects were asked to completely blink two times and keep their eyes open for as long as possible. Irregularities in the image indicated instability or break-up of the tear film. At the same time, a video was recorded. The device provided a representation of the tear film break-up over time, and we selected the first break-up time (NIKBUT-first), in accordance with a previously described method [27,28]. Subjective symptoms were graded on a numerical scale from 0 to 4, according to the validated 12-item Ocular Surface Disease Index (OSDI) questionnaire. The total OSDI score was calculated using the following formula: OSDI = (sum of scores for all questions answered $\times$ 100)/(total number of answered questions $\times$ 4). The total score ranges from 0 to 100 [29]. The fluorescein tear break-up time (TBUT) was measured by applying a single fluorescein strip (Haag-Streit, Koeniz, Switzerland) moistened after instilling a drop of normal saline to the inferior palpebral conjunctiva. The mean time in three attempts was recorded. On the basis of the fluorescein staining pattern noted on slit-lamp biomicroscopy, ocular surface staining was graded from 0 to 3 according to the National Eye Institute (NEI)/Industry Workshop scale of 0–33 [30]. Schirmer's test I was performed only at baseline, without

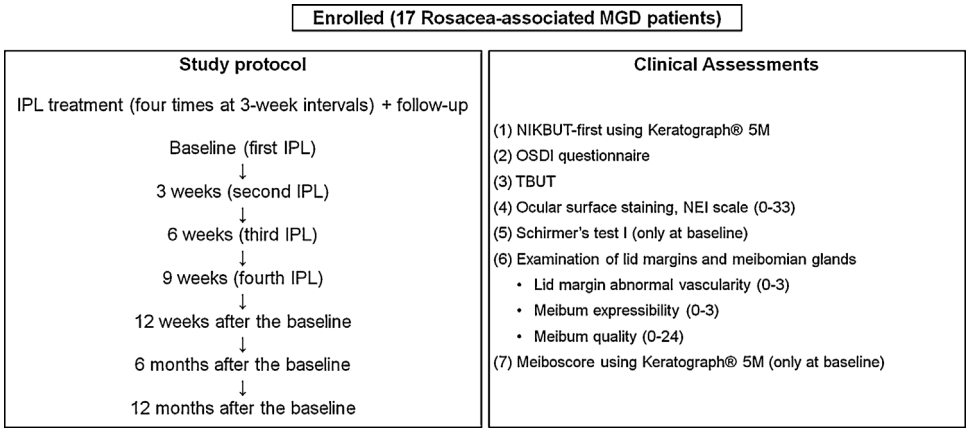

Fig. 1. Study flowchart showing the process and protocols.
MGD, meibomian gland dysfunction; IPL, intense pulsed light; NIKBUT, noninvasive Keratograph® tear break-up time; OSDI, ocular surface disease index.