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ORIGINAL PAPER

The role of intense pulsed light (IPL) in the treatment of meibomian gland dysfunction (MGD)

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Abstract

Background Meibomian gland dysfunction (MGD) may result in alteration of the tear film, symptoms of eye irritation, and evaporative dry eye disease (DED). Recent studies suggest that intense-pulsed light (IPL) treatments reduce ocular signs and symptoms, through direct/indirect actions on meibomian glands. The aim of this study is to analyse and measure efficacy and safety of IPL treatment in patients affected by MGD.

Methods Between September 2016 and January 2017, eleven patients were enrolled in this univariate study based on a single variable. All patients have undergone two IPL sections with Synchro FT- DEKA MELA, once a month. Ocular Surface Disease Index (OSDI), breakup time (BUT), and Schirmer Test Type I have been evaluated preop, 10 days after every treatment and followed up to 1 year.

Results All patients referred to a relevant improvement of symptoms with two treatments. A reduction of epithelial damage and a modification of glandular function confirmed a statistically significant difference.

Conclusions IPL could be considered as an adjunctive tool in patients suffering from MGD. The high versatility of IPL device allows customized treatment with minimum discomfort and high tolerability.

Level of Evidence: Level IV, therapeutic study.

Keywords Dry eye · Meibomian glands · Intense pulsed light

Introduction

Meibomian gland dysfunction (MGD), as stated in The International Workshop on Meibomian Gland Dysfunction of 2011 [1], is a widespread, chronic alteration of the meibomian glands, which presents with a terminal duct obstruction and qualitative or quantitative changes in the glandular secretion. It may result in abnormal tear film, easy eye irritation, recurrent inflammation, and ocular surface disease [1].

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Two major categories of MGD can be distinguished according to meibomian gland secretion: respectively low-delivery and high-delivery states. The former, also classified as hypo-secretory or obstructive, present different subcategories according to scarring or non-scarring process. The latter shows the release of a large volume of lipid at the eyelid margin that becomes visible on application of pressure onto the tarsus during examination. Aetiology also differs, referring either to primary conditions for which there are no discernible underlying causes [1] or secondary causes. According to patients' symptoms and signs, MGD can be classified as (a) isolated, asymptomatic or symptomatic (scarring/not scarring); (b) related to damaged ocular surface (OSD); (c) related to dry eye disease (DED), and (d) due to other ocular pathologies (f.e. meibomian keratoconjunctivitis).

Skin inflammatory diseases often occur in proximity of the eyelids, and they have been associated with dry eye disease. As a matter of facts, a number of recent studies demonstrated

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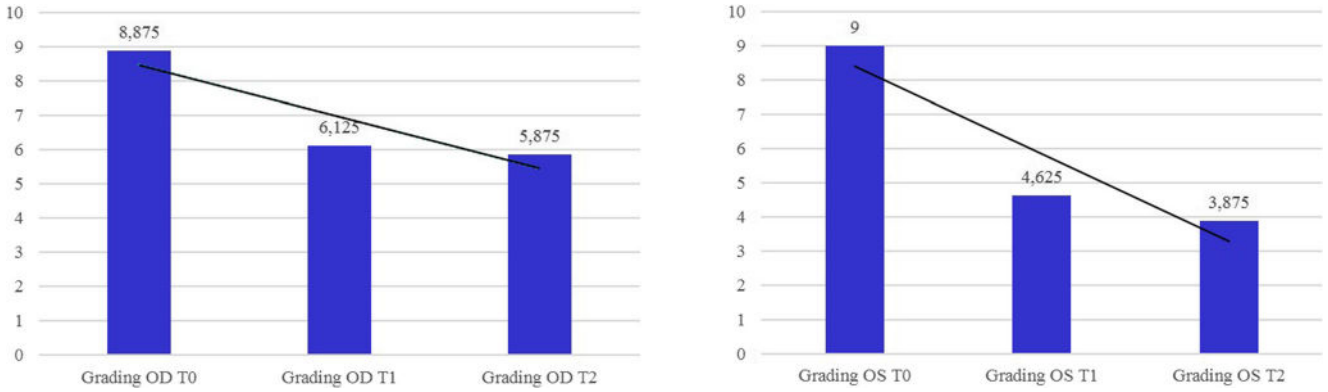

Fig. 1 Reduction of epithelial damage analysed through fluorescein staining (NEI/Industry Schema from 0 to 15) in the right eye (OD) and left eye (OS)

that IPL therapy, reducing signs and symptoms of DED, could be also used in patients suffering from meibomian gland dysfunction [2, 3].

The aim of our study is to analyse and measure efficacy and safety of IPL treatment together with eyelid moderate/firm massage and expression of MG secretions in patients affected by MGD.

Material and methods

Eleven patients affected by MGD related to DED of standard age were enrolled in this univariate study based on a single variable, conducted by the Campus Bio-Medico University of Rome (Department of Ophthalmology and Department of Plastic, Reconstructive and Aesthetic Surgery) from September 2016 and January 2017. Inclusion criteria were classic symptoms of DED, meibomian gland dysfunction or mild/moderate posterior blepharitis, BUT < 10 s, age > 18 years, Fitzpatrick skin type I and II, willingness to fulfil the study according to information contained in the protocol.

Other patients were excluded from this study due to age < 18 years or Fitzpatrick skin type > III. Exclusion criteria were also: patients affected by Sjögren or by Stevens–Johnson syndromes, patients in treatment with any drugs that may induce photosensitivity or with methotrexate, systemic cyclosporine and oral corticosteroids.

Dermatologists visited patients in order to determine the skin type according to Fitzpatrick (FPI) classification so to enrol only FPI I to III.

Ophthalmologist examination included:

- A slit lamp microscopic examination to detect obstruction/glandular plugging and telangiectasia;
- Breakup time (BUT) and type I Schirmer test to investigate glandular function;
- Measurement of tear osmolality (Tear Lab);
- Grading score of corneal and conjunctival fluorescein staining (NEI/Industry Schema: analyse 5 corneal regions and 2*3 conjunctival regions, each region is classified with a score from 0 to 3, including the 0.5 value);
- Validated questionnaire for dry eye diagnosis (OSDI, Ocular Surface Disease Index).

International criteria DEWS 2007 [4] were used for the classification of severity of DED signs and symptoms.

All patients received the proper information by the doctors and signed the informed consent. Clinical pictures of the eyes and the periorbital region were taken to compare them with those taken after each laser treatment. All patients underwent two sessions of IPL treatment (Synchro FT- DEKA MELA) with a period inter-treatment of no more than 30 days. IPL

Table 1 Results and statistical significance values of epithelial damage reduction

Grading OS			Pa
Grading 0	-	Grading 1_os	0,0053
	-	Grading 2_os	0,0016
Grading 1	-	Grading 2_os	0,0015
Grading OD			Pa
Grading 0	-	Grading 1_od	0,0114
	-	Grading 2_od	0,0019
Grading 1	-	Grading 2_od	0,0024

Table 2 Results and statistical significance values of increase of BUT

BUT OS			Pa
BUT 0	-	BUT 1_os	0,001
	-	BUT 2_os	0,0004
BUT 1	-	BUT 2_os	0,0556
BUT OD			Pa
BUT 0	-	BUT 1_od	0,0003
	-	BUT 2_od	<0,0001
BUT 1	-	BUT 2_od	0,0413

Table 3 Results and statistical significance values of Schirmer test

Schirmer OS			Pa
Schirmer T0	-	Schirmer T1_os	0,0217
	-	Schirmer T2_os	0,0009
Schirmer T1	-	Schirmer T2_os	0,0113
Schirmer OD			Pa
Schirmer T0	-	Schirmer T1_od	0,4812
	-	Schirmer T2_od	0,0039
Schirmer T1	-	Schirmer T2_od	0,0728

treatment was carried out in the periocular region, 2 mm from the lower eyelid margin. The emitting surface area is above 3 mm distant from the lower eyelid margin, a driver gel is used to help impulse conduction. Proper corneal shields are also wearied to protect the eye.

IPL parameters' setting was substantially the same suggested for rosacea [5], also considering original instructions by Synchro FT- DEKA MELA, a 500 nm filter was preferred, with 10–12 msec double pulses, and a time delay of 20 msec. The average fluence applied was between 14 and 16 J/cm^2.

In patients affected by MGD related to dry eye, the beam of light is headed towards the telangiectasia of the lower eyelid margin. The treatment begins pointing the light from a tragus to the contralateral one before repeating the same action again.

After each IPL treatment, eyelid moderate/firm massage and expression of MG secretions were carried out;

local antibiotic cream, betamethasone valerate USP equivalent to 1 mg (0.1%) betamethasone alcohol and gentamicin sulfate USP equivalent to 1 mg (0.1%) of gentamicin base, was applied only once, right after the treatment. Sunscreen (SPF 15–30) has been recommended, and patients have been advised to avoid sunlight exposure for 1–2 weeks after each laser treatment.

Patients were evaluated every 10 days after each IPL treatment, in order to verify and determine changes of tests and related symptoms and take new pictures that can be compared with the previous ones.

Results

Results were analysed with ANOVA test (ANalysis Of VAriance), only p value < 0.05 was considered as statistically significant in order to compare tests of glandular function, grading score according to NEI/Industry Schema and before/after-treatment OSDI questionnaire.

Results were analysed as average value plus or minus the standard deviation unless otherwise stated.

Ophthalmological examination showed a significant improvement of patients' ocular signs and symptoms, without any noteworthy side effect. Each parameter measured in the statistical analysis was analysed at T0 (screening examination), T1 (examination 10 days after the first laser treatment) and T2 (examination 10 days after the second laser treatment).

Results, compared with data collected in the screening examination, can be summarized as follows:

1. A reduction of epithelial damage analysed through fluorescein staining (NEI/Industry Schema from 0 to 15) in the right eye (OD) and the left eye (OS) was observed. Results and statistical significance values are shown in Fig. 1 and Table 1.
2. Measuring the tear film breakup time (BUT) and type I Schirmer test, a modification of glandular function statistically significant (Tables 2 and 3) was registered respectively:

   (1) Increase of BUT (breakup time test) in the right (OD) and left eye (OS) (Fig. 2)
   (2) Increase of results of Schirmer test type I in the right (OD) and left eye (OS)(Fig. 3)

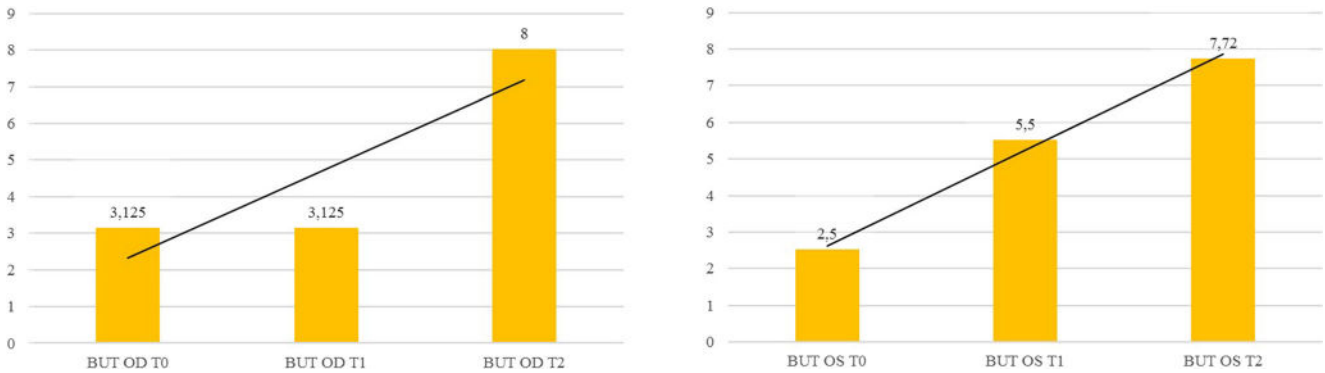

Fig. 2 Modification of tests of glandular function (measurement of the tear film breakup time and type I Schirmer test): increase of BUT (breakup time test) in the right (OD) and left eye (OS)

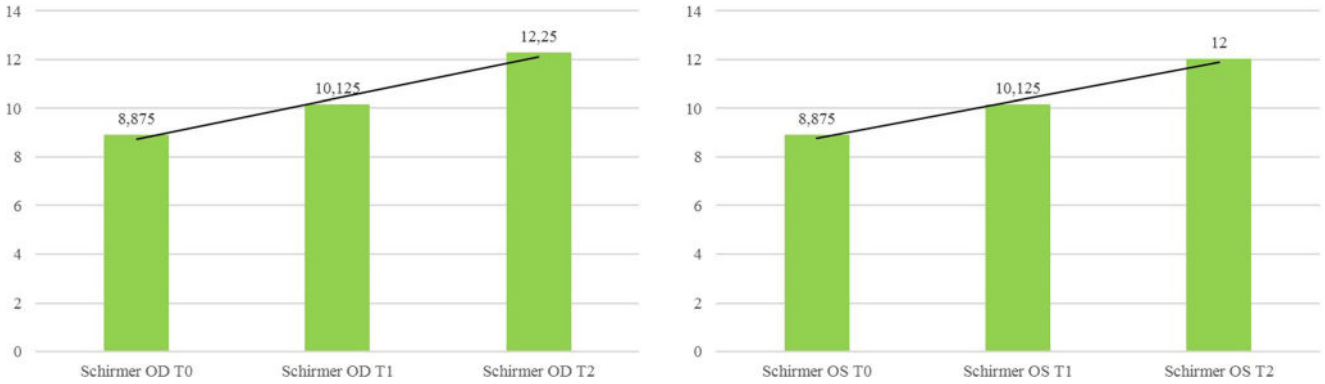

Fig. 3 Increase of results of Schirmer test type I in the right (OD) and left eye (OS)

3. Tear osmolality seemed to be reduced in both right (OD) and left eye (OS) (Fig. 4), but this trend was not statistically significant
4. Modification of symptoms measurement through OSDI questionnaires is shown in Fig. 5 even if results were not statistically significant as confirmed by Table 4.

We also observed a reduction of ocular signs (glandular obstruction, periocular telangiectasia, glandular plugging and capping, thickness of eyelid margin, expression of glandular secretion) and symptoms like burning sensation, photophobia (light sensitivity), foreign body sensation and hyperaemia.

General microscopic appearance showed a significant reduction of ocular inflammation and a convincing improvement of quality and quantity of glandular secretion together with an enhancement of glandular expression and fluidization of meibum.

Discussion

Meibomian gland dysfunction (MGD) related to dry eye disease (DED) is a common ophthalmic disorder that is not curable. Treatments may improve symptoms, but they are not able to achieve a permanent resolution. Anti-inflammatory creams or eye drops followed by massage, serum tears, eye side shields and systemic cholinergic agents are the most popular prescriptions, but they should be applied continuatively. [6].

As confirmed by several trials IPL definitively improves rosacea as well as ocular symptoms related to MGD. [7–9]. Patients suffering from rosacea usually present with cutaneous abnormal blood vessels that are responsible for cytokines and other inflammatory agents release. [10]. Obstruction of meibomian glands also occurs due to increased epithelial turnover. IPL, decreasing blood vessels by a selective thrombolysis and softening the meibum through glands' heating, promises safe advantages to treat refractory MGD symptoms.

The analysis of epithelial damage measured with NEI/Industry Schema grading score confirmed a linear trend of improvement between T0 examination (screening), after the first laser treatment (T1) and after the second laser treatment (T2), with a p value < 0.05 statistically significant. A relevant reduction of dry eye symptoms such as burning sensation, photophobia (light sensitivity), and foreign body

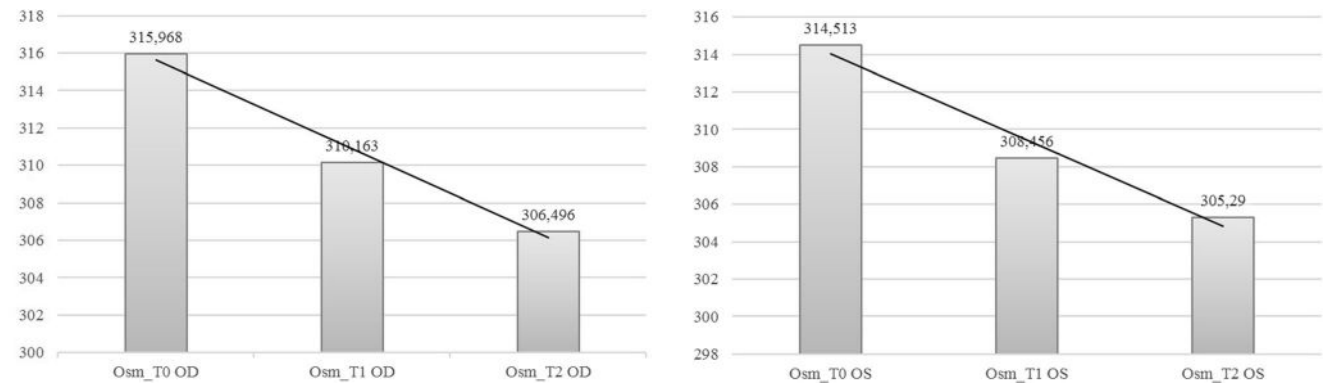

Fig. 4 Reduction of tear osmolarity in of the right (OD) and left eye (OS)

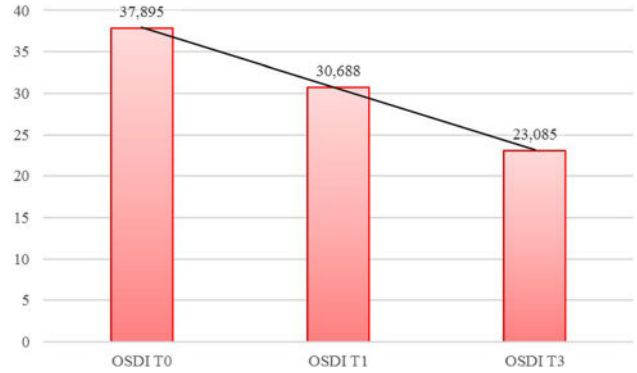

Fig. 5 Modification of symptoms measurement through OSDI questionnaires

sensation as well as a regression of eyelid telangiectasia was registered in all patients.

As far as it concerns glandular function, we also observed a changing of quality and quantity of meibum secreted, and a linear trend of improvement between T0 examination (screening), after the first laser treatment (T1) and after the second laser treatment (T2). All values were statistically significant with a p value < 0.05 for both the BUT and the Schirmer type I test in the right (OD) and left (OS) eye.

In our experience, this change in the sebum facilitates its manual drainage, since the very first IPL sections. Finally, the measurement of tear osmolality value (through Tear Lab device) showed no statistically significant variation, as values of both right (OD) and left (OS) eye were more or less constant over the study. However, the OSDI score' analysis shows a statistical significance modification of ocular symptoms between the baseline value at the beginning of the study (OSDI T0) and the second laser treatment ($p = 0.002$) confirming the overall improvement of patients' quality of life.

Despite the small group of patients, the significant improvements we have registered in all patients, just with two sections, should encourage in offering this method as an alternative option to standard medical treatments. We did not observe any side effect or local/systemic intolerance; however, since this pathology has a chronic relapsing course, a long-lasting follow-up is necessary in order to analyse the effect of this treatment.

Table 4 Results and statistical significance values of tear osmolarity values (OSDI)

OSDI score			Pa
OSDI T0	-	OSDI T1	0,068
	-	OSDI T2	0,036
OSDI T1	-	OSDI T2	0,061

Even if IPL effects may be not long lasting, the method is simple, without relevant collateral effects and sections can be offered on demand.

Conclusion

This study confirms that IPL achieves statistically significant improvements in the relief of clinical ocular signs and symptoms of patients affected by MGD related to DED, even after few treatments.

The high versatility of IPL device allows doctors to set customized treatment according to patient's characteristics in order to guarantee maximum efficacy and tolerability.

Further studies may lead to a better understanding of the mechanism of function and may help the diffusion of IPL technology introducing proper treatment protocols.

Compliance with ethical standards

Conflict of interest Stefania Tenna, Piergiorgio Turco, Beniamino Brunetti, Antonio Di Zazzo, Jacopo Macchi, Stefano Bonini and Paolo Persichetti declare that they have no conflict of interest

Ethical approval The Campus Bio Medico University Ethics Committee gave formal approval to this study in May 2016. All procedures performed in studies were in accordance with the ethical standard of 1964 Helsinki Declaration. All authors have contributed equally to the scientific work.

Informed consent Informed consent was obtained from all patients to undergo the treatments. Informed consent for publication is not applicable as no identifying photographs or information have been included.

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