Original Article

The Effect of Meibomian Gland Dysfunction Treatment on Sleep Quality

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Abstract

Purpose: To assess the therapeutic efficacy of a combinational therapy, including conventional treatment and intense pulsed light (IPL) technique on sleep quality of patients with meibomian gland dysfunction (MGD).

Methods: Fifty participants with a clinical diagnosis of MGD were enrolled in this study. Participants underwent three sessions of IPL therapy. There was a 2-week interval between IPL sessions 1 and 2 and 1 month between sessions 2 and 3. Treatment was supplemented with conventional home-based therapy (including lid hygiene, warm compress, eyelid massage, and lid margin scrub) for MGD. Dry eye symptomatology, tear film, and ocular surface parameters were evaluated at baseline (day 0) and days 15, 45, and 75. Sleep quality was assessed before and after the study using Pittsburgh Sleep Quality Index (PSQI).

Results: PSQI components improved significantly at day 75 in comparison with the baseline (all $P < 0.05$). Ocular Surface Disease Index (OSDI) score, noninvasive Keratograph tear break-up time (NIKBUT), fluorescein tear break-up time (FTBUT), meibomian gland expressibility, meibum quality score, and tear osmolarity improved at follow-up visits ($P < 0.05$). Younger patients showed more improvement in NIKBUT, sleep quality, and duration ($P = 0.024$, $P = 0.047$, and $P = 0.008$). Sleep latency decreased with increased NIKBUT and FTBUT and decreased OSDI score ($P = 0.001$, $P = 0.005$, and $P = 0.041$).

Conclusions: The treatment of MGD is effective for improving sleep quality. Younger patients may preferentially benefit from the treatment.

Keywords: Dry eye disease, Intense pulsed light, Meibomian gland dysfunction, Sleep quality, Tear film

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Introduction

Meibomian gland dysfunction (MGD) is one of the most common ocular surface diseases and the main cause of evaporative dry eye disease (DED).[1] Along with its effect on the ocular surface, DED has been reported to impair vision-related quality of life and other aspects of social and psychological functioning.[2] Furthermore, a positive correlation has been found between sleep and mood disorders and DED.[3] Studies show that sleep quality is important in the regulation of circadian and metabolic systems.[4,5] Poor sleep may also have a role in the development of DED. It can affect tear secretion and stability and cause more ocular irritation and dry eye symptoms and may indirectly aggravate mood disorders such as depression and anxiety.[6-8] On the other hand, DED is a long-term status associated with deteriorated quality of life and depression and can influence sleep quality.[6,9-11] MGD is the leading cause of increased tear evaporation rate, tear hyperosmolarity, inflammation, ocular irritation, pain, and foreign body sensation,[1,12] and it seems that it has a potential role in sleep difficulties.

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There is a lack of studies evaluating the effect of MGD and its treatment on the sleep quality of patients. In 2016, Ayaki *et al*. showed an improvement in sleep quality after the topical treatment of DED.[9] They hypothesized that in dry eye, pro-inflammatory status results in ocular irritation and sleep difficulty. According to the revised definition of Tear Film and Ocular Surface Society (TFOS DEWS II) for dry eye, neurosensory abnormalities play etiological roles in DED.[1] In DED, chronic inflammation may affect the corneal pain signal pathways and cause symptomatic pain.[13] Corneal hypersensitivity to temperature variations or mechanical stimulations has been detected in dry eye patients in comparison with healthy participants.[13]

So far, different treatment modalities have been implemented for the treatment of patients with MGD. Conventional topical and home-based therapies include artificial tear supplementation, dietary omega-3 oil supplementation, anti-inflammatory and antibacterial agents, eyelid hygiene and warm compress therapy, meibomian gland expression[14-17] and more recent in-office treatments offering thermal pulsation, intense pulsed light (IPL), and wet chamber latent heat application.[14,18,19] Studies show that IPL can increase mitochondrial activity and wound healing, decrease lid margin bacterial load and Demodex by photocoagulation, improve elastosis, and connective tissue disorganization that occurs with MGD rosacea.[19] However, considering the treatment-refractory nature of MGD and according to the recent report of the American Academy of Ophthalmology, incorporating multiple modality treatments may be more beneficial in achieving higher therapeutic efficacy.[20]

Dry eye treatment may help break the vicious circle of DED and sleep quality. To the best of our knowledge in this study for the first time, we evaluated the effect of a combination of office-based and home-based therapies on the sleep quality of patients with symptomatic MGD.

Methods

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran (ethical code: IR.MUMS.REC.1398.081). Informed consent was obtained from all patients before study enrollment.

Fifty symptomatic patients with a clinical diagnosis of moderate-to-severe MGD with dry eye were recruited to participate in the study.[12] Eligible participants for the treatment of MGD in this study were patients who did not receive any dry eye treatment for at least 1 month before the study and were required to be aged 18 or older.[14,21] They showed at least one of the following findings: reporting symptoms of ocular surface discomfort such as grittiness, dryness, irritation, itching, and pain and had an Ocular Surface Disease Index (OSDI) score ≥13; fluorescein tear break-up time (FTBUT) <10 s, fluorescein staining of the ocular surface, and clinical signs of MGD (MG capping and drop out, lid margin redness, telangiectasia, and irregularity).[18] Patients presenting with active ocular infection or disease other than dry eye, a history of ophthalmic surgery, any systemic disease including diabetes and autoimmune disease, or use of systemic, photosensitizing, or ocular medications except unpreserved lubricants 1 month before and during the study, eyelid disorders affecting blinking, any diagnosed sleep disorder, mood disorders, and taking sleep medications and antidepressants, and contact lens use within 3 months of or during the study were excluded.

A validated Persian translation of the Pittsburgh sleep quality index (PSQI) questionnaire was used for the subjective assessment of sleep quality of the participants before and after the MGD treatment.[22] PSQI questionnaire consists of 7 components including sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medications, and daytime dysfunction. The total score ranged from 0 to 21, and a sum of >5.50 is indicative of poor sleep.[5,22]

All participants received three sessions of intense regulated pulsed light (IRPL) therapy (E > Eye, E-SWIN, Paris, France) at days 0, 15, and 45, and five sequential, overlapping IRPL flashes were applied to the inferior and temporal periocular area. The E > Eye device produces a wavelength from 580 to 1200 nm. The red-light spectrum (580–1200 nm) delivered by this device can potentially penetrate deeper into the skin and target the underlying sebaceous glands.[19]

Pulse intensity was adjusted according to the Fitzpatrick skin type classification of participants and ranged from 11.4 to 13 J/cm^2.[18] A wavelength range of 500–600 nm was used. All IPL treatments were performed by a trained clinician. Protective eye goggles were used for both clinician and the patients. Furthermore, conventional treatment for MGD including artificial tears (Artelac; Bausch and Lomb, Rochester, NY, USA) four times a day, lid margin hygiene (Eyesol Ophthalmic Cleansing Shampoo, Livar Co., Iran) once a day, ophthalmic gel (Liposic, Bausch and Lomb, Rochester, NY, USA) once a day before sleep, and azithromycin 0.5% eye drops once a day (for 1 month) were prescribed for all patients. Cleansing and massage of the lid margins were followed by warm compress application with a warm, dry, and clean heated bag on closed eyes for 5 min. Twice a day, a written instruction was given to the participants to show how and when they should perform the procedures.

Ocular surface parameters were evaluated at day 0 and after 15, 45, and 75 days. Ocular surface symptomatology was assessed using a validated Persian translation of the OSDI questionnaire.[23] Tear meniscus height (TMH), noninvasive Keratograph tear break-up time (NIKBUT), limbal and bulbar hyperemia (0–4), and upper and lower lid meibography score (0–3)[24] were evaluated using a multifunctional topographer (Keratograph 5M, Oculus Optikgeräte GmbH, Wetzlar, Germany). TMH and NIKBUT values were recorded in triplicate and averaged. Tear volume measurements were performed by tear film meniscometry using SM tube strips (Echo Electricity, Fukushima, Japan). Tear osmolarity was

assessed using the TearLab osmometer (Tear lab, CA, USA).[25] Changes in meibomian gland expressibility, fluorescein corneal staining, and lid margin telangiectasia were also reported in each session.

All data analyses were performed using SPSS statistical software (IBM SPSS, Version 23, NY, USA). Data collected from the right eyes of participants were considered for statistical analysis. Categorical data were analyzed using χ^2 test. Ocular surface changes during study follow-ups were evaluated using one-way repeated measures analysis of variance. A paired *t*-test was used for before-after treatment comparisons. McNemar's test was conducted to compare proportions between groups. Pearson test was used to verify the correlation between parameters. $P < 0.05$ was considered as statistically significant.

Results

A total of fifty participants with a mean age ± standard deviation (SD) of 44 years ± 16 (range, 18–74 years) were enrolled in the study. Eighteen patients (36.0%) were males, and 32 patients (64.0%) were females. Mean time ± SD of the first MGD diagnosis was 16.72 months ± 15.82 (range, 3–72 months).

At day 0, 41 patients (82.0%) and at the end of the study, 29 patients (58.0%) were poor sleepers. Although in comparison with good sleepers, poor sleepers showed more improvement in OSDI score (27.85 vs. 20.11), NITBUT (5.78 s vs. 5.58 s), meibomian gland expressibility (0.83 vs. 0.55), the two groups were not significantly different in improvement of tear film parameters during the study (all, $P > 0.05$).

The total PSQI score decreased significantly from 8.32 ± 3.55 to 6.42 ± 3.53 ($P < 0.001$). At day 75, sleep quality, latency, duration, and efficiency improved significantly in comparison with the beginning of the study (day 0) (all, $P < 0.05$) [Table 1]. Furthermore, sleep disturbances and daytime dysfunction decreased significantly ($P < 0.001$).

Improvement of sleep components was not significantly different between men and women (all, $P > 0.05$). Participants with lower age showed more improvement in sleep quality and duration ($P = 0.047$ and $P = 0.008$).

OSDI symptomatology score, NIKBUT, FTBUT, bulbar and limbal hyperemia, MG expressibility, meibum quality score, and tear osmolarity improved significantly from day 0 to day 75 (all, $P < 0.05$) [Table 2].

Adjusting for age, sleep latency, and quality improved in correlation with improvement in MG expressibility ($P = 0.001$, $P = 0.022$). Furthermore, sleep latency improved with increased NIKBUT and FTBUT ($P = 0.001$, $P = 0.005$). Decreased OSDI symptomatology score was significantly correlated with improved sleep latency after treatment ($P = 0.041$).

Table 1: Sleep quality measures at follow-up visits

	Day 0	Day 75	*P*
Sleep quality	1.52±0.89	1.24±0.87	<0.001
Sleep latency	1.56±0.91	1.36±0.80	0.001
Sleep duration	1.12±0.72	1.04±0.75	0.044
Sleep efficiency	1.02±0.82	0.70±0.81	<0.001
Sleep disturbance	1.32±0.65	0.82±0.56	<0.001
Sleep medication	-	-	-
Daytime dysfunction	1.78±0.81	1.26±0.98	<0.001
Total score	8.32±3.55	6.42±3.53	<0.001

Discussion

DED and its common subtype, MGD, are multifactorial conditions that cause various ocular symptoms and visual disturbances affecting patients' productivity, work ability, and quality of life.[10,26] DED impairs quality of vision and affects the social, physical, and psychological well-being of the patients.[5] On the other hand, the association of sleep disorders and DED has been confirmed in previous studies.[3,5] Poor sleep quality is prevalent among patients with dry eye in comparison with controls. The prevalence of sleep disorders in patients with DED has been reported from 15.3% to 64.3%.[27] Sleep quality may be affected by sleep latency, duration, and disturbances and result in changes in daytime functionality.

In this study, it was speculated that the IPL therapy of MGD may be beneficial for the sleep quality of the patients.

Temporary adverse effects have been reported for the IPL (cheek swelling, conjunctival cyst, floaters, blistering, hair loss at brow and forehead, light sensitivity, and facial redness), which usually resolve without treatment within 1 week.[28] In this study, the IRPL treatment was performed on the lower lid, and no adverse effect or complication was observed.

Interestingly at the beginning of the study, 82.0% of the patients were poor sleepers. At the final visit, although the mean PSQI total score was still in the abnormal range, a significant improvement was observed in all PSQI components.

Studies show that during sleep, patients with DED may have more inflammatory processes.[29] Although research to assess the specific effect of MGD on sleep quality is yet to be conducted, it is an inflammatory condition that may be associated with neurosensory abnormalities[1] and may have even more effects on sleep quality during sleep. No direct connection is still proposed between DED and sleep disorders. However, there is a direct association between sleep disorders and mood disorders including depression and between depression and DED. According to a hypothesis by Ayaki *et al*., along with depression as a possible causality in sleep disorders, pain may affect sleep quality in patients with DED.[29] In MGD, the accumulation of microorganisms and inflammatory molecules during sleep may increase sleep difficulty. According to previous reports, sleep quality improves after topical treatment of DED.[9]

The therapeutic efficacy of IPL in MGD treatment has been investigated in previous studies.[30-32] Although its exact

Table 2: Tear film and ocular surface measures in follow-up visits

	Day 0	Day 15	Day 45	Day 75	*P*
OSDI score	41.28±18.23	29.60±16.29	21.12±13.27	14.82±11.62	<0.001
TMH (mm)	0.22±0.06	0.21±0.05	0.21±0.04	0.22±0.05	0.196
NIKBUT (s)	6.48±2.64	8.53±3.05	10.41±3.92	12.22±4.39	<0.001
FTBUT (s)	5.44±2.29	7.18±3.15	8.34±3.53	9.96±3.57	<0.001
Bulbar hyperemia (0-4)	1.08±0.53	1.02±0.51	0.88±0.59	0.60±0.53	<0.001
Limbal hyperemia (0-4)	0.90±0.54	0.82±0.56	0.70±0.54	0.50±0.54	<0.001
Tear volume (mm/5 s)	4.90±1.46	4.94±1.22	5.06±1.20	5.16±1.13	0.218
Meiboscore (upper lid) (0-3)	1.36±0.66	1.36±0.66	1.36±0.66	1.36±0.66	1.000
Meiboscore (lower lid) (0-3)	1.26±0.56	1.26±0.56	1.26±0.56	1.26±0.56	1.000
MG expressibility	4.10±1.50	4.26±1.50	4.58±1.53	4.68±1.59	<0.001
Meibum quality score (0-3)	1.76±0.66	1.44±0.54	1.14±0.53	0.88±0.59	<0.001
Tear osmolarity (mOsm/L)	309.3±11.86	-	-	300.48±14.19	<0.001

Abnormal range definition: OSDI score >13, FTBUT <10 s, Tear osmolarity ≥308 mOsm/L, Tear volume: Absorbed tears, <5 mm in 5 s. MG expressibility was recorded for the central 8 glands in the lower lid following the application of firm digital pressure.[12] OSDI: Ocular surface disease index, TMH: Tear meniscus height, NIKBUT: Noninvasive Keratograph break-up time, FTBUT: Fluorescein tear break-up time, MG: Meibomian gland

mechanism is still not fully understood, it has been proposed that it can improve tear hemostasis by its anti-inflammatory effect, lowering the load of microorganisms in the lid margin, liquefying the meibum, and improving its quality and expressibility.[19,20,33] The supplementary role of the conventional home-based therapy may increase the therapeutic efficacy of MGD treatment.[17] A thickened lipid layer inhibits tear evaporation, resulting in a more stable tear film, less interaction between lid viper area and ocular surface, decreased inflammation, pain, and ocular discomfort. More feelings of relief and less distressed by symptoms may have a positive effect on patients' mood and sleep quality.[9] On the other hand, pain relief and ocular comfort may directly cause fewer sleep disturbances and enhance sleep quality in patients with MGD.

In this work, a significant improvement in symptomatology and ocular surface parameters including tear osmolarity, TBUT, ocular hyperemia, meibum quality, and expressibility was found 1 month after the last IPL treatment session. The improved tear film stability was associated with improvement in MGD symptoms and sleep quality components. Improved sleep latency and quality were in correlation with the improvement of ocular surface parameters.

More improvement in sleep quality and ocular surface parameters was found in younger patients. Because of the better status of the immune system, less complex ocular surface and lid margin structure, and potentially more functional meibomian glands, younger patients may preferentially benefit more from MGD treatment.[34] Higher therapeutic efficacy of MGD management in younger patients may result in more improvement in sleep quality. In older age, sleep disorders are more prevalent and associated with various factors which may have an effect on the efficacy of DED treatment on sleep quality.

Age, baseline OSDI, and MGD severity are potential factors that may influence the effects of the treatment. Some factors such as patients' lifestyle, hormone levels, mood, and environment, which may affect the therapeutic effect of IPL treatment, are difficult to control. For instance, increased exercise and higher estrogen levels were associated with improved tear quantity during the ovulation phase.[35] On the other hand, sleep deprivation reduces androgen levels parasympathetic activity. It makes high levels of stress hormones and reduces tear secretion and lacrimal system function.[36,37]

This study has several limitations. A larger sample size comparing the results with a control group and using other dry eye diagnostic tests such as Schirmer's test and other therapeutic options may increase the reliability of the results.

The treatment of MGD may break the vicious circle of dry eye, sleep disorder, and mood disorders. Objective assessment of sleep quality in sleep clinics, along with an evaluation of potential psychological factors, and comparing the results with control groups and incorporating effective diagnostic techniques for dry eye may be beneficial to assess the efficacy of DED treatment on other aspects of an individual's well-being. Furthermore, large-sample multicenter studies are expected to confirm these results in future studies.

In conclusion, IPL therapy in combination with supplementary conventional home-based therapy may be beneficial for the sleep quality of patients with moderate-to-severe MGD.

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Conflicts of interest
There are no conflicts of interest.

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