BMC Ophthalmology

RESEARCH

Open Access

Efficacy and safety of the disposable eyelid warming masks in the treatment of dry eye disease due to Meibomian gland dysfunction

Da-Hu Wang[1†], Hua Guo[2†], Wei Xu[3,4*] and Xin-Quan Liu[1*]

Abstract

Background Warm compresses are the routine treatment for Meibomian gland dysfunction (MGD) in daily life, but in order to achieve satisfactory efficacy, the treatment needs to be sustained over a long time, which can have an impact on the patient compliance. A more convenient warm compresses will help improve the patient compliance. Therefore, the purpose of the study is to investigate the efficacy and safety of the disposable eyelid warming masks for treatment of dry eye disease (DED) due to MGD.

Methods This was a randomized, controlled, non-masked, two-center clinical trial. One hundred and forty-four patients were treated by the masks or the hot towel twice daily for 12 weeks. Patients were evaluated at baseline, 4-week and 12-week visits for subjective symptoms, objective signs and safety assessments, including ocular symptom scores, ocular surface disease index (OSDI), tear break-up time (BUT), corneal fluorescein staining (CFS), Schirmer I test (SIT), meibum quality, meibum expressibility, and adverse events (AEs).

Results A totle of 134 patients were followed in the study. The mean age of the masks group (14 males and 52 females) and the hot towel group (20 males and 48 females) was 43.7 ± 13.5 years and 39.5 ± 13.9 years, respectively. At 4-week visit, there were significant statistical differences in ocular symptom scores, OSDI and CFS between two groups ($P < 0.05$). Except for SIT, the treatment group showed a greater improvement in subjective symptoms and objective signs than the control group at 12-week visit. ($P < 0.05$). In addition, 40 AEs occurred in 27 patients (37.5%) in the treatment group, and 34 AEs occurred in 21 patients (29.17%) in the control group. No serious AEs were reported.

Conclusions The masks had a good efficacy and safety in the treatment of DED due to MGD, and might offer an attractive treatment option for some patients.

Trial registration The study was registered at Chinese Clinical Trial Registry (ChiCTR1900025443) on August 26, 2019.

Keywords Eyelid warming masks, Warm compresses, Meibomian gland dysfunction, Dry eye disease, Patient compliance

[†]Da-Hu Wang and Hua Guo contributed equally to this work.

*Correspondence:
Wei Xu
18817598238@163.com
Xin-Quan Liu
drliuxinquan@hotmail.com
Full list of author information is available at the end of the article

Background

Meibomian gland dysfunction (MGD) is a common ocular surface disease, which may result in alteration of the tear film and discomfort [1]. The terminal duct and orifice obstruction and qualitative/quantitative changes in meibum were the main pathogenesis [2]. Several clinic-based patient cohort studies showed that the prevalence of MGD in dry eye subjects was high, with a range of 46.2% to 86% [3–7], especially in the United States and Europe [7]. Therefore, MGD was considered to be the most common form of dry eye disease (DED), although the evidence was not yet sufficient [7–9].

Current modalities of MGD treatment included lid hygiene, warm compresses, forceful expression/mechanical massage, artificial lubricants, topical anti-inflammatory therapy, and systemic and topical antibiotics [10–12]. Eyelid warming/warm compresses was applied to improve and/or restore the function of the meibomian glands by softening or liquefying the secretions in obstructed glands, so as to improve the subjective feeling of ocular dryness. At present, warm compress therapy is a routinely recommended treatment for MGD in clinical practice due to its convenience, high cost performance and good tolerance [10–12].

Many clinical studies had demonstrated that the methods of heat application to the eyelids for the treatment of MGD was safe and effective [13–15]. As to the conventional hot towel, patients usually needed to replace the compresses during the treatment to ensure that the temperature remained constant. Moreover, since MGD was a chronic disease, in order to achieve satisfactory clinical efficacy, the routine treatment needed to be sustained over a long period of time, i.e., the labor intensity increases, which could have an impact on the patient compliance [9, 10]. Therefore, a more convenient method of performing warm compresses would help improve the patient compliance.

In this study, we investigated the short-term clinical efficacy and safety of the commercially disposable heating eye masks for the treatment of DED due to MGD.

Methods

Warm compresses

Disposable heating eye masks

The disposable heating eye masks (18.5 × 8 cm, Shanghai Warmyou Industry Co.,Ltd, Shanghai, China) in the teatment group are composed of a heating layer and an accessory structure (Fig. 1). The heating layer is composed of a heating sheet (containing iron powder, activated carbon, salt and water) and a breathable membrane. The mechanism of heat generation is the oxidation of iron (Fe). The chemical reaction scheme is as follows: $4\ Fe + 3\ O_2 + 6\ H_2O = 4\ Fe(OH)_3$ [15]. Once the reaction begins, the H_2O is heated and evaporates into the surrounding environment. The whole chemical reaction lasts about 20 min, and the mean temperature was about 41℃. It is important to note that the disposable heating eye masks should be quickly taken out of the sealed package before applying warm compresses to the eyelids.

Hot towel

The plain white cotton towels (68 × 34 cm) were used as the compresses applied to the eyelids of each patient in the control group. The towel needed to be replaced after one week of use. The specific operation is as follows: (1) First, heat water up to 45℃ (± 1℃) measured by a thermometer with digital display; (2) Second, fold the compresses in a way of approximately 17 × 8.5 cm and 16 layers thick, then immerse the folded compresses into the heated water; (3) Third, after removing excess water by wringing the towels, place the moist compresses over both eyelids. Finally, in order to achieve an effective warm compress therapy, the hot towel should be replaced every 3 min to ensure that the temperature remained relatively constant.

Study design and participants

This was a randomized, controlled, non-masked, two-center clinical trial, which included follow-up for 12 weeks and consisted of 4-week and 12-week visits. Patients were recruited from the outpatient departments of Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine and Tongji Hospital of Tongji University between August 2019 and December 2021. Consecutive patients were randomized 1:1 to the treatment group (disposable heating eye masks) or the control group (folded hot towel) using the random numerical table. This research was reviewed by an independent ethical review board and conforms with the principles and applicable guidelines for the protection of human subjects in biomedical research. Subsequently, the study was registered at Chinese Clinical Trial Registry (ChiCTR1900025443). Written informed consent was obtained from all patients after explaining the purpose of study. The duration of the study was 3 years.

Inclusion criteria were as follows [10, 12, 16–18]: (1) participants aged ≥ 18 years and ≤ 70 years, (2) complaint of ocular discomfort symptoms—foreign body sensation, dryness, blurred vision, pain, itching, redness, photophobia, lacrimation, excessive blinking, etc., (3) ocular surface disease index (OSDI) scores of 13 points or higher, (4) tear break-up time (BUT) of 5 s or less, (5) Schirmer I testwithout anesthesia of 5 mm or more at 5 min, (6) abnormalities of meibum quality and expressibility, (7) ability to understand and sign informed consent, willingness and ability to cooperate with study requirements,

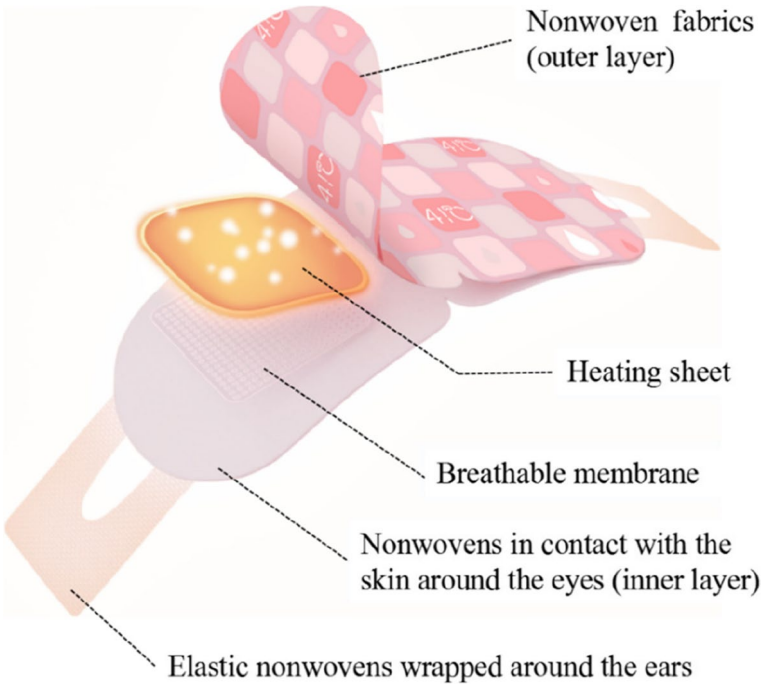

Fig. 1 Schematic diagram of disposable heating eye masks

and (8) agreeing to use a reliable form of contraception in cases of patients with childbearing potential.

Key exclusion criteria were as follows: (1) had active ocular allergies; (2) ocular infection/inflammation; (3) conjunctivochalasis; (4) entropion and trichiasis; (5) history of chalazion or hordeolum within the past 3 months; (6) worn contact lens within the past 3 months; (7) had ocular surgery within the past 3 months; (8) meibomian gland loss area $\geq$ 33% of the total area in each eyelid [19]; (9) use of vectored thermal pulsation system (Lipiflow®) or intense pulsed light (IPL) or isotretinoin (accutane) within the past 6 months; (10) had autoimmune disease requiring systemic treatment; (11) was unwilling or unable to discontinue the following medications during the study or during a 14-day washout period before the start of the study: systemic or ocular antibiotics, systemic or ocular steroids, anticholinergics, systemic or ocular antihistamines, ocular nonsteroidal antiinflammatory preparations, ocular vasoconstrictors, and investigational drugs; (12) patients participating in the clinical trial within 3 months; (13) was pregnant or lactating women.

Intervention

The basic treatment of both groups included lid hygiene twice a day and 0.1% sodium hyaluronate eye drops (5 mL:5 mg, Zhuhai Federal Pharmaceutical Limited by Share Ltd, Zhuhai, China) 4 to 6 times a day for 12 weeks [18]. The treatment and control groups were separately treated by the disposable heating eye masks and the folded hot towel twice daily for 12 min each time [13].

In clinical practice, no matter how severe the consequences, there is no assurance that all patients will follow professional medical advice. Warm compresses were time-consuming and labour intensive and might lead to subjective compliance problems in some patients. Considering that inadequate compliance might be a significant contributor to the poor therapeutic effect for MGD patients. To enhance the patient compliance, a text alert three times a week and a telephone interview once a week were conducted in both groups, and the measurement records of the thermometer in the control group were checked in time. It should be emphasized that the compliances of warm compresses were calculated in both groups through the record forms filled out by patients.

Clinical assessments

Referring to our previous articles [18, 20], all patients were required to fill out the subjective symptom and OSDI questionnaires (a scale from 0 to 100, with higher scores indicative of greater symptom severity), and underwent the slit-lamp biomicroscopy examinations as well as clinical tests, including BUT [the average time of three measurements with the sterile sodium fluorescein strips (Tianjin Jinming New Technology Development Co Ltd, Tianjin, China)], corneal fluorescein staining (CFS), Schirmer test without anesthesia [SIT, measured

by a sterile Schirmer strip (Tianjin Jinming New Technology Development Co Ltd)], and meibum expressibility and quality [10, 17, 18, 20, 21]. For consistency, the measurements and evaluations of the parameters were performed by two experienced ophthalmologists (D.-H. W. and W. X.), who were well trained on the protocol for the examinations at the beginning of the study.

Among, a subjective symptom questionnaire graded 7 symptoms (dryness, foreign body sensation, burning sensation, eyestrain, photophobia, itching, and blurred vision) as absent, mild, moderate, or severe. Each symptom was weighted from 0 to 3 depending on severity, giving each patient a maximum possible total score of 21 [18]. After BUT measurements, Fluorescein staining of 4 areas of the cornea (inferior, superior, nasal, and temporal) was rated by the investigator according to the scale (grade 0 [no punctate staining] to grade 3 [confluent patches, filaments, or ulcer]); the total CFS score for each eye was the sum of the individual scores (maximum, 12) [17, 18]. The meibum quality grade scale was evaluated in 8 glands of the lower eyelid on a scale of 0 to 3 for each gland (0, clear; 1, cloudy; 2, cloudy with debris; and 3, thick, like toothpaste) [10, 17, 18]. The meibum expressibility grade scale was evaluated in 5 glands in the lower eyelid, and each scored from 0 to 3 (0, all glands expressible; 1, 3 to 4 glands expressible; 2, 1 to 2 glands expressible; and 3, no glands expressible) [10, 17, 18].

Sample size calculation

The primary effectiveness endpoints were defined as change from baseline to 12 weeks for Ocular Surface Disease Index (OSDI) scores and tear film breakup time (BUT). Secondary effectiveness endpoints included meibum expressibility and quality, and corneal fluorescein staining (CFS) scores. Referring to the existing literatures on the treatment of DED due to MGD [14–16], the sample size was calculated through two independent samples T-test of the mean values of BUT and OSDI scores. Assume that the Type I error rate (α) was 0.05, the Type II error rate (β) was 0.2, and sample allocation ratio was 1. Then, according to the actual situation—loss of follow-up visit, the sample size needed to be increased by a certain proportion (approximately 20%). Finally, the sample size of the treatment group was 72, and the sample size of the control group was 72.

Safety assessments

Ocular safety was assessed at 4-week and 12-week visits by examining best corrected visual acuity (BCVA), intraocular pressure (IOP), eyelids, conjunctiva, cornea, anterior chamber, and lens. At the same time, patients were also questioned for adverse events.

Statistical analysis

According to CFS, only the more severe eye was included in this study. If the data of both eyes were the same, the data of right eyes were included. The data of clinical tests were presented as the mean ± standard deviations (SD). The Shapiro–Wilk (S-W) test was used to calculate the normality of the ocular symptom scores, OSDI, BUT, CFS, SIT, meibum quality, and meibum expressibility at baseline, at 4-week, and 12-week visits. The statistical analyses were performed with Student's t test and nonparametric test. The description of the classification indicators uses the number of cases and percentages of each category. $P < 0.05$ was considered significant. All analyses were performed with SAS (version 9.0, SAS Institute Inc., Cary, NC, USA).

Results

A total of 144 patients were enrolled in this study, and 134 patients completed the study (93.1%), as shown in Fig. 2. The mean age of 66 subjects (14 males and 52 females) in the eye masks group and 68 subjects (20 males and 48 females) in the hot towel group was 43.7 ± 13.5 years and 39.5 ± 13.9 years, respectively. The detailed demographic characteristics were presented in Table 1.

At 4-week and 12-week visits, the two groups had varying degrees of improvement in ocular symptom scores, OSDI, BUT, CFS, meibum quality and meibum expressibility compared with the baseline ($P < 0.05$). At 4-week visit, there were significant statistical differences in ocular symptom scores, OSDI and CFS between two groups ($P < 0.05$). At 12-week visit, except for SIT, the eye masks group showed a greater improvement in subjective symptoms and objective signs than the hot towel group ($P < 0.05$). The detailed clinical parameters of the study were presented in Table 2.

Patients were treated with warm compresses twice daily for 12 weeks, with an overall compliance rate of 88.6% (9824/11088) in the eye masks group and 81.5% (9311/11424) in the hot towel group. Forty adverse events occurred in 27 patients (37.5%) in the treatment group, and 34 adverse events occurred in 21 patients (29.17%) in the control group. Among, ocular AEs that might be related to warm compresses in both groups included dryness, eyelid edema, blurred vision, itching or eye pruritus, chemosis, conjunctival congestion, foreign body sensation, irritation, lacrimation or tearing, and subconjunctival hemorrhage (Table 3). Furthermore, there was no significant impact on BCVA, IOP and lens in both groups. During the 3-month study, no serious adverse events were reported.

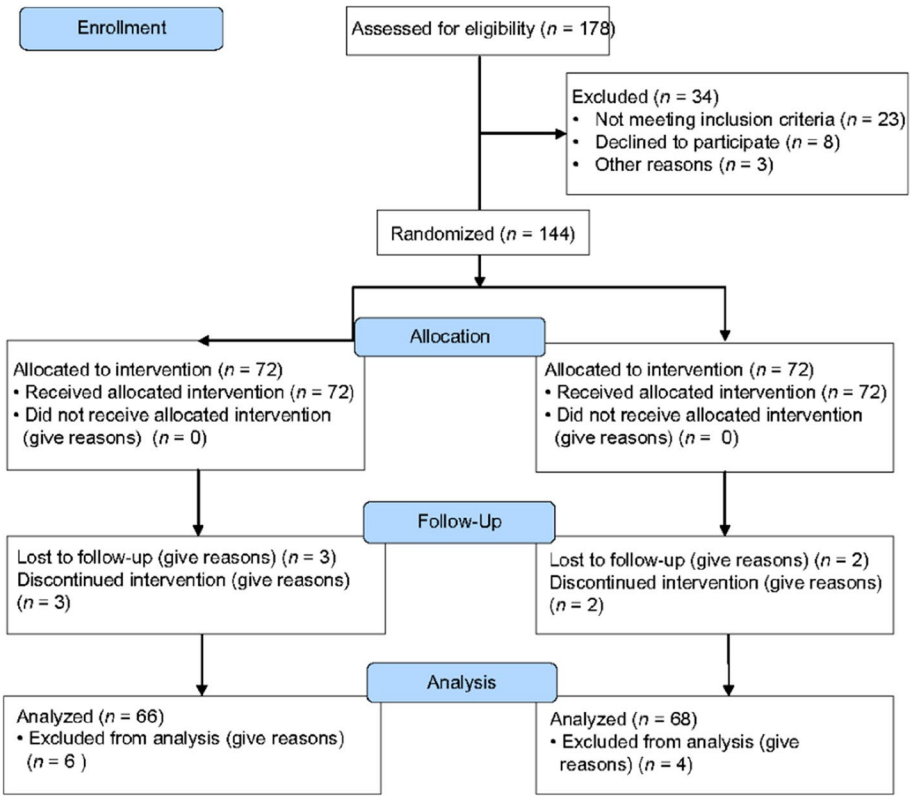

Fig. 2 Flowchart to indicate the disposition of subjects from screening to study completion

Table 1 Demographic data for all participants

	Hot towel	Eye masks	*P* value
Number of subjects	68	66	NA
Age, years			
Mean ± SD	39.5 ± 13.9	43.7 ± 13.5	0.08
Median	35.5	43.0	NA
Minimum, maximum	22, 67	23, 70	NA
Gender, *n* (%)			
Male	20 (29.4)	14 (21.2)	0.28
Female	48 (70.6)	52 (78.8)	

NA not applicable

Discussion

MGD is a common disease in ophthalmology, which is closely associated with evaporative dry eye [8]. A systematic review and meta-analysis showed that the global prevalence of MGD was 35.9% [22]. According to several population-based cross-sectional studies, the prevalence of MGD and DED in Japan was 32.9% and 33.4%, respectively, with a coexistence rate of 12.9% [23]. The prevalence of MGD and DED in the United States were 21.2% and 8.1%, respectively [24]. The prevalence of MGD and DED among people over 40 years of age in Russia was 52.6% and 35.3%, respectively [25]. In addition, with the widespread use of video display terminals in daily work and life, the prevalence of MGD in video display terminals workers is high (74.3%) [26], and it plays an important role in the severity of DED [27].

Obstructive MGD is characterized by the abnormal gland structure and lipid changes in the meibomian glands [1]. Clinically, warm compresses is a routine recommended treatment for MGD [10–12]. But so far, the temperature and time required to melt the secretions in the meibomian gland ducts have been unclear [11]. Several studies had shown that the melting point of meibomian gland lipids ranged from 30℃ to 45℃ [28–31], which partly reflected that the lipids were a highly complex mixture [32]. McCulley et al. [33] suggested that the lipids with different compositions had different melting points, and MGD could make lipids shift to higher melting points, resulting in stagnant and poor dynamic tear films. In addition, Murakami et al. [13] believed that heating a single meibomian gland to a temperature of 40℃ might be the best treatment. It should be pointed out here that 40℃ referred to the temperature of the conjunctiva and meibomian glands, not the temperature on the contact surface of the device or eyelid skin.

Table 2 Ocular symptom scores, OSDI, BUT, CFS, SIT, meibum quality and meibum expressibility at each visit for both groups

Clinical parameters	Treatment	Severity score (mean ± SD)		
		Baseline	4 weeks	12 weeks
Ocular symptom scores	Hot towel	7.85 ± 2.81	6.22 ± 2.51*	5.28 ± 2.37*
	Eye masks	8.86 ± 3.18	4.79 ± 2.37*△	2.91 ± 2.09*△
OSDI	Hot towel	25.89 ± 13.34	21.63 ± 13.51*	19.24 ± 11.55*
	Eye masks	27.03 ± 13.71	13.31 ± 9.53*△	6.28 ± 5.51*△
BUT (seconds)	Hot towel	2.90 ± 1.71	3.22 ± 2.01*	3.24 ± 2.36*
	Eye masks	2.67 ± 1.69	3.73 ± 2.19*	5.02 ± 3.03*△
CFS	Hot towel	1.94 ± 3.09	1.76 ± 2.33*	1.35 ± 2.51*
	Eye masks	1.76 ± 2.41	0.82 ± 1.79*△	0.45 ± 1.34*△
SIT (mm)	Hot towel	10.26 ± 9.34	9.01 ± 7.25	9.37 ± 7.06
	Eye masks	11.26 ± 9.02	11.24 ± 8.32	12.52 ± 8.83
Meibum quality	Hot towel	9.37 ± 6.20	8.47 ± 5.29*	8.07 ± 5.35*
	Eye masks	10.35 ± 5.69	8.88 ± 4.29*	5.97 ± 4.24*△
Meibum expressibility	Hot towel	1.24 ± 0.69	0.90 ± 0.72*	0.62 ± 0.60*
	Eye masks	1.24 ± 0.79	0.86 ± 0.68*	0.27 ± 0.48*△

OSDI ocular surface disease index, *BUT* tear break-up time, *CFS* corneal fluorescein staining, *SIT* Schirmer test without anesthesia

* Compared with before treatment, $P < 0.05$

△ compared with the control group, $P < 0.05$

Table 3 Frequent of the adverse events(AEs) that might be related to warm compresses in both groups

	Hot towel ($n = 68$), n (%)	Eye masks ($n = 66$), n (%)
Dryness	2 (2.94%)	1 (1.52%)
Eyelid edema	2 (2.94%)	3 (4.55%)
Blurred vision	3 (4.41%)	2 (3.03%)
Itching	0	3 (4.55%)
Chemosis	0	1 (1.52%)
Conjunctival congestion	1 (1.47%)	2 (3.03%)
Foreign body sensation	1 (1.47%)	0
Irritation	0	2 (3.03%)
Lacrimation	1 (1.47%)	0
Subconjunctival hemorrhage	1 (1.47%)	0

The application of warm compresses with or without moisture, had been extensively studied in the treatment of MGD [13–15, 34–40]. Murakami et al. [13] tested 8 forms of contact and non-contact warm compress methods (dry, wet/moist and chemically activated dry heat), and found the efficacy of the compresses with moisture was better than that of the compresses using dry heat, which might be related to the different physical properties of heat transfer. Conversely, Arita et al. [40] suggested that the repeated eyelid warming with non-moist devices was more effective than that with warm-moist devices in improving the tear film function. The likely explanation for this discrepancy was that the rapid evaporative cooling of oculur surface after the wet heating treatment limited the efficacy of the heating devices. Based on the mentioned above, compared with dry heat treatment, the heating effect of moist warm compresses on the eyelids is still controversial. In addition, the novel eyelid warming treatments are also used in clinical practice, such as the vectored thermal pulsation system (42.5℃) and Activa mask (42℃) [41, 42].

In this study, our results showed that the disposable eyelid warming masks could be effective and the overall improvement of symptoms could be due to significant improvement of the function of the meibomian glands, which was consistent with the previous studies [15, 34, 38]. Reheating the compresses every 3 min to maintain the therapeutic levels of heat was time consuming and tedious in the hot towel group, which might result in poor compliance. At this time, the efficacy of the treatment was often hampered. In addition, the discrepancies in the ocular surface temperature between two groups might contribute to different outcomes, which might partly explain the poor efficacy of the hot towel group compared with the eye masks group.

Although warm compresses are convenient for patients with diverse economic capability in daily life, the compliance with warm compress therapy is a long-existing problem for the treatment of MGD [10, 11]. So far, there are few relevant published literatures. In this trial, referring to the data on the compliance with warm compress therapy for 12 weeks, we believed that it was very difficult

to urge patients to keep conducting warm compresses to maintain long-term control of symptoms. Therefore, in order to improve the patient compliance, it is necessary to develop or invent a warm compress device which can maintain long-time efficiency after a single or short-term treatment. The vectored thermal pulsation system seems to provide a good reference for future research [43].

It should be noted that we didn't measure the ocular temperature before and after warm compresses in this pilot study. Nevertheless, both groups raised the ocular temperatures to the levels of treatment, demonstrating the potential to provide the symptomatic relief in patients with lower disease severity. Referring to previously published literatures [13, 15, 39, 44], the external eyelid temperature after using the disposable eyelid warming masks for 2–5 min ranged from 38.6℃ to 40.3℃, which was lower than that (40.4℃ to 41.4℃) after using the warming towel for 4–6 min. However, a randomized, controlled trial demonstrated that the effect of the disposable eyelid warming masks was similar to that of the warm towel, which was inconsistent with our study [45]. A possible explanation was that different products, and the severity of symptoms and signs of MGD at baseline might affect the results of the study [45]. Moreover, although many studies had demonstrated the efficacy of the disposable eyelid warming masks in treating MGD [13, 15, 39, 44, 45], there were a lack of relevant data in China. Therefore, in order to increase the integrity of the global data, we conducted this study, although new information or additional benefit exceed the current methods of heating eye masks was insufficient compared to other similar products previously studied.

Generally, the disposable eyelid warming masks were safe and effective, with mild ocular AEs and no SAES, which was similar to the previous reports [45, 46]. Furthermore, despite positive outcomes, there were some limitations in this prospective clinical trial, including the following aspects: 1) Care should be taken to avoid the thermal damage after warm compresses. Fortunately, the pain response is a safeguard to avoid thermal damage to the eyelid skin. 2) To facilitate the study, we excluded patients with moderate to severe meibomian gland dropout, which might diminish the relevance of this article. 3) Additionally, the thickness of tear lipid layer before and after warm compresses was not investigated. Further studies are warranted to provide more information.

Conclusions

Our study suggested that the disposable eyelid warming masks had a good efficacy and safety in the treatment of DED due to MGD, and might offer an attractive treatment option for some patients.

Abbreviations

MGD	Meibomian gland dysfunction
DED	Dry eye disease
OSDI	Ocular surface disease index
BUT	Tear break-up time
CFS	Corneal fluorescein staining
SIT	Schirmer I test
AEs	Adverse events
BCVA	Best corrected visual acuity
IOP	Intraocular pressure

Acknowledgements

We thank Xiao-Hui Tang for her help in language editing.

Authors' contributions

D.-H. W. and W. X.: Conceptualization, data curation, formal analysis, methodology, funding acquisition, writing—original draft, writing—review & editing. H. G.: writing—original draft. X.-Q. L.: Conceptualization, investigation, methodology, resources, project administration, writing—review & editing. All authors reviewed the manuscript.

Funding

This work was supported by the Shanghai Municipal Health Commission (grant no. 20194Y0246), and the Young Talent Program of Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine (grant no. RC-2020-01-08).

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study followed the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, and was registered at Chinese Clinical Trial Registry (ChiCTR1900025443). Written informed consent was obtained from all patients after explaining the purpose of study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Ophthalmology, Longhua Hospital Affiliated to Shanghai University of Traditional Chinese Medicine, No.725 South Wanping Road, Xuhui District, Shanghai 200032, China. [2]Department of Ophthalmology, Shanghai East Hospital, School of Medicine, Tongji University, Shanghai, China. [3]Department of Ophthalmology, Tongji Hospital of Tongji University, Shanghai, China. [4]Shanghai Eye Disease Prevention and Treatment Center, Shanghai, China.

Received: 7 April 2024 Accepted: 16 August 2024
Published online: 26 August 2024

References

1. Nelson JD, Shimazaki J, Benitez-del-Castillo JM, et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52:1930–7.
2. Knop E, Knop N, Millar T, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011;52:1938–78.
3. Lekhanont K, Rojanaporn D, Chuck RS, et al. Prevalence of dry eye in Bangkok. Thailand Cornea. 2006;25:1162–7.

4. Lin PY, Tsai SY, Cheng CY, et al. Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. Ophthalmology. 2003;110:1096–101.
5. Han SB, Hyon JY, Woo SJ, et al. Prevalence of dry eye disease in an elderly Korean population. Arch Ophthalmol. 2011;129:633–8.
6. Jie Y, Xu L, Wu YY, et al. Prevalence of dry eye among adult Chinese in the Beijing Eye Study. Eye. 2009;23:688–93.
7. Lemp MA, Crews LA, Bron AJ, et al. Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. Cornea. 2012;31:472–8.
8. Nichols KK. The international workshop on meibomian gland dysfunction: introduction. Invest Ophthalmol Vis Sci. 2011;52:1917–21.
9. Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II epidemiology report. Ocul Surf. 2017;15:334–65.
10. Geerling G, Tauber J, Baudouin C, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011;52:2050–64.
11. Jones L, Downie LE, Korb D, et al. TFOS DEWS II management and therapy report. Ocul Surf. 2017;15:575–628.
12. Asia Dry Eye Association China Branch, Ocular Surface and Tear Disease Group of Ophthalmology Specialized Committee of the Cross-Strait Medical Exchange Association. Chinese expert consensus on the diagnosis and treatment of meibomian gland dysfunction. Chin J Ophthalmol. 2017;53:657–61. https://doi.org/10.3760/cma.j.issn.0412-4081.2017.09.005. Chinese.
13. Murakami DK, Blackie CA, Korb DR. All warm compresses are not equally efficacious. Optom Vis Sci. 2015;92:e327-33.
14. Goto E, Monden Y, Takano Y, et al. Treatment of non-inflamed obstructive meibomian gland dysfunction by an infrared warm compression device. Br J Ophthalmol. 2002;86:1403–7.
15. Mori A, Shimazaki J, Shimmura S, et al. Disposable eyelid-warming device for the treatment of meibomian gland dysfunction. Jpn J Ophthalmol. 2003;47:578–86.
16. Wolffsohn JS, Arita R, Chalmers R, et al. TFOS DEWS II diagnostic methodology report. Ocul Surf. 2017;15:539–74.
17. Corneal Group of Ophthalmology Branch of the Chinese Medical Association. Chinese expert consensus on the diagnosis and treatment of dry eye disease. Chin J Ophthalmol. 2013;49:73–5. https://doi.org/10.3760/cma.j.issn.0412-4081.2013.020. Chinese.
18. Wang DH, Liu XQ, Hao XJ, et al. Effect of the meibomian gland squeezer for treatment of meibomian gland dysfunction. Cornea. 2018;37:1270–8.
19. Arita R, Itoh K, Inoue K, et al. Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. Ophthalmology. 2008;115:911–5.
20. Zhu HY, Liu XQ, Yuan YZ, et al. Measurement of the lid margin thickness in meibomian gland dysfunction with vernier micrometer. Ophthalmol Ther. 2022;11:177–86.
21. Schiffman RM, Christianson MD, Jacobsen G, et al. Reliability and validity of the ocular surface disease index. Arch Ophthalmol. 2000;118:615–21.
22. Hassanzadeh S, Varmaghani M, Zarei-Ghanavati S, et al. Global prevalence of meibomian gland dysfunction: a systematic review and meta-analysis. Ocul Immunol Inflamm. 2021;29(1):66–75.
23. Arita R, Mizoguchi T, Kawashima M, et al. Meibomian gland dysfunction and dry eye are similar but different based on a population-based study: the Hirado-Takushima study in Japan. Am J Ophthalmol. 2019;207:410–8.
24. McCann P, Abraham AG, Mukhopadhyay A, et al. Prevalence and Incidence of dry eye and meibomian gland dysfunction in the United States: a systematic review and meta-analysis. JAMA Ophthalmol. 2022;140(12):1181–92.
25. Bikbov MM, Gilmanshin TR, Zainullin RM, et al. Prevalence and associations of dry eye disease and meibomian gland dysfunction in the ural eye and medical study. Sci Rep. 2022;12(1):18849.
26. Fenga C, Aragona P, Cacciola A, et al. Meibomian gland dysfunction and ocular discomfort in video display terminal workers. Eye (Lond). 2008;22:91–5.
27. Wu H, Wang Y, Dong N, et al. Meibomian gland dysfunction determines the severity of the dry eye conditions in visual display terminal workers. PLoS One. 2014;9:e105575.
28. Nicolaides N. Skin lipids. II. Lipid class composition of samples from various species and anatomical sites. J Am Oil Chem Soc. 1965;42:691–702.
29. Brown SI, Dervichian DG. Hydrodynamics of blinking. In vitro study of the interaction of the superficial oily layer and the tears. Arch Ophthalmol. 1969;82:541–7.
30. Tiffany JM. Refractive index of meibomian and other lipids. Curr Eye Res. 1986;5:887–9.
31. Ong BL, Larke JR. Meibomian gland dysfunction: some clinical, biochemical and physical observations. Ophthalmic Physiol Opt. 1990;10:144–8.
32. Green-Church KB, Butovich I, Willcox M, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on tear film lipids and lipid-protein interactions in health and disease. Invest Ophthalmol Vis Sci. 2011;52:1979–93.
33. McCulley JP, Shine WE. Meibomian secretions in chronic blepharitis. Adv Exp Med Biol. 1998;438:319–26.
34. Ishida R, Matsumoto Y, Onguchi T, et al. Tear film with "Orgahexa EyeMasks" in patients with meibomian gland dysfunction. Optom Vis Sci. 2008;85:684–91.
35. Matsumoto Y, Dogru M, Goto E, et al. Efficacy of a new warm moist air device on tear functions of patients with simple meibomian gland dysfunction. Cornea. 2006;25:644–50.
36. Mitra M, Menon GJ, Casini A, et al. Tear film lipid layer thickness and ocular comfort after meibomian therapy via latent heat with a novel device in normal subjects. Eye (Lond). 2005;19:657–60.
37. Pult H, Riede-Pult BH, Purslow C. A comparison of an eyelid-warming device to traditional compress therapy. Optom Vis Sci. 2012;89:E1035–41.
38. Bilkhu PS, Naroo SA, Wolffsohn JS. Randomised masked clinical trial of the MGDRx EyeBag for the treatment of meibomian gland dysfunction-related evaporative dry eye. Br J Ophthalmol. 2014;98:1707–11.
39. Wang MT, Gokul A, Craig JP. Temperature profiles of patient-applied eyelid warming therapies. Cont Lens Anterior Eye. 2015;38:430–4.
40. Arita R, Morishige N, Shirakawa R, et al. Effects of eyelid warming devices on tear film parameters in normal subjects and patients with meibomian gland dysfunction. Ocul Surf. 2015;13:321–30.
41. Pang SP, Chen YT, Tam KW, et al. Efficacy of vectored thermal pulsation and warm compress treatments in meibomian gland dysfunction: a meta-analysis of randomized controlled trials. Cornea. 2019;38:690–7.
42. Vigo L, Pellegrini M, D'Angelo S, et al. Effects of serial sessions of activa mask for the treatment of meibomian gland dysfunction. Ophthalmol Ther. 2023;12:209–16.
43. Hu J, Zhu S, Liu X. Efficacy and safety of a vectored thermal pulsation system (Lipiflow®) in the treatment of meibomian gland dysfunction: a systematic review and meta-analysis. Graefes Arch Clin Exp Ophthalmol. 2022;260:25–39.
44. Wang MT, Jaitley Z, Lord SM, et al. Comparison of self-applied heat therapy for meibomian gland dysfunction. Optom Vis Sci. 2015;92:e321-6.
45. Sim HS, Petznick A, Barbier S, et al. A randomized, controlled treatment trial of eyelid-warming therapies in meibomian gland dysfunction. Ophthalmol Ther. 2014;3:37–48.
46. Gupta PK, Holland EJ, Hovanesian J, et al. TearCare for the treatment of meibomian gland dysfunction in adult patients with dry eye disease: a masked randomized controlled trial. Cornea. 2022;41:417–26.

Publisher's Note