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Review article

Hot towels: The bedrock of Meibomian gland dysfunction treatment – A review

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ABSTRACT

Background: Meibomian gland dysfunction (MGD) reduces quality-of-life and hinders work productivity of millions of patients, with high direct and indirect societal costs. Thickened meibum obstructs the glands and disrupts ocular surface health. Heating the eyelids to soften and express meibum from the glands can be beneficial. The most accessible method for eyelid warming uses heated, wet towels. However, the efficacy of this treatment is reliant on the methodology, and evidence-based best-practice recommendations are needed.
Purpose: To evaluate the literature on hot towels in MGD treatment and recommend a best-practice protocol for future research and patient treatment.
Methods: Studies were identified through PubMed on the May 28, 2021, with the search terms: *(warm* OR heat* OR thermal* OR towel OR wet towel) AND (meibomian OR MGD OR eyelid OR "dry eye" OR DED)*. All relevant original articles with English full-text were included.
Results: The search yielded 903 results, of which 22 met the inclusion criteria. Across studies, hot towels were found to be effective at reducing ocular symptoms. However, without reheating, the temperature quickly fell below the therapeutic range, which was deemed to be between 40 °C and 47 °C. Towels heated to around 45 °C

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and reheated every-two minutes were most effective at increasing eyelid temperature, comparable or better than several commercially available eyelid warming devices. No adverse effects were reported in the studies.
Conclusion: Hot towel treatment effectively warms the eyelids and reduces ocular symptoms, but must be standardized, and towels reheated to achieve maximum benefit. Future research should assess patient satisfaction with different hot towel treatment methods that reheat or replace the towel at least every-two minutes, to establish which methods yield the greatest compliance. Guidelines or clinical recommendations that do not mention the need for regular reheating during hot towel compress treatment should be updated to include this.

1. Introduction

Meibomian gland dysfunction (MGD) is the most common cause of dry eye disease (DED), affecting several hundred million people worldwide [1]. MGD is hallmarked by increased tear evaporation, hyperosmolarity and symptoms of dry eye, including discomfort, visual disruption, and eyelid tenderness [2]. The healthy eye is protected by the tear film, which provides a physical and immunological barrier against microorganisms, pollutants, and other stressors [3,4]. The tear film is made up of two main layers, the inner mucoaqueous layer and the outer lipid layer (Fig. 1) [5]. The meibomian glands, located in the tarsal plates of the eyelids produce the meibum that makes up the outer lipid layer which stabilizes, reduces the surface tension of, and prevents the evaporation of the aqueous tear fluid [6].

In MGD, the loss of healthy meibum production and function leads to lipid layer deterioration, which causes the tear film to become unstable, resulting in DED [6]. The clinical presentation of MGD is often characterized by altered meibum secretion, meibomian gland dropout, and orifice plugging [2]. Meibum in healthy adults has a transition temperature of around 28 °C [7]. This is low enough to keep the meibum mostly fluid during normal conditions, where the ocular surface and eyelids maintain a temperature of between 33 °C and 36 °C [8–10]. The meibum can then freely flow onto the ocular surface from the main secretory duct where it is stored [6]. In MGD, the increased viscosity, higher melting point of the meibum, and hyper-keratinization of the ductal epithelium together lead to the obstruction of the terminal ducts, which halts the secretion of healthy meibum [11]. Generally, the chemical structure of the meibum from patients suffering from MGD is more ordered than healthy meibum and has a hydrocarbon chain stiffness halfway between olive oil and butter [7]. To achieve the same level of disorder and liquidity as healthy meibum at 36 °C, meibum from patients with MGD requires a temperature of 38.5 °C on average [9]. This may explain the poor meibum secretion observed in this patient group [12–14]. This abnormal secretion in turn leads to glandular atrophy, dropout, and decreased gland function [15]. Excreting this thickened meibum, therefore, plays a vital role in the treatment of MGD [16]. This can be accomplished by delivering localized heat to warm the meibum beyond its melting point and applying pressure to express the softened meibum.

For warming of the eyelids, the application of a warm compress for five to fifteen minutes, followed by brief eyelid hygiene between once and four times daily is often recommended [16]. The most accessible method for warm compress treatment is the use of a wetted and heated towel that is placed over the eyelids to provide direct, moist heat to the eyelids [16]. Despite the long clinical tradition of recommending this treatment to patients, limited research has been performed to standardize this practice. Recently, several studies were published focusing on the ever-increasing number of alternative modalities for eyelid warming. These include commercially available dry-heat eyelid masks, steam-based systems, and in-office treatment systems [17–25]. In these studies, a wide range of hot towel warm compress techniques were used as control groups, with no clear standardization or repeatability [24,26,27]. By critically reviewing the current literature on hot towel compresses in the treatment of MGD, this review aims to establish a best-practice for hot towel treatment and recommend a standard methodology for the application of hot towel treatment as a control in future studies. As hot towel compresses are the most widely available and affordable treatment option, a large number of patients worldwide are reliant on this treatment. Standardization of methodology could both help patients achieve the best possible results from treatment and improve the quality of research on eyelid warming devices, further advancing the field.

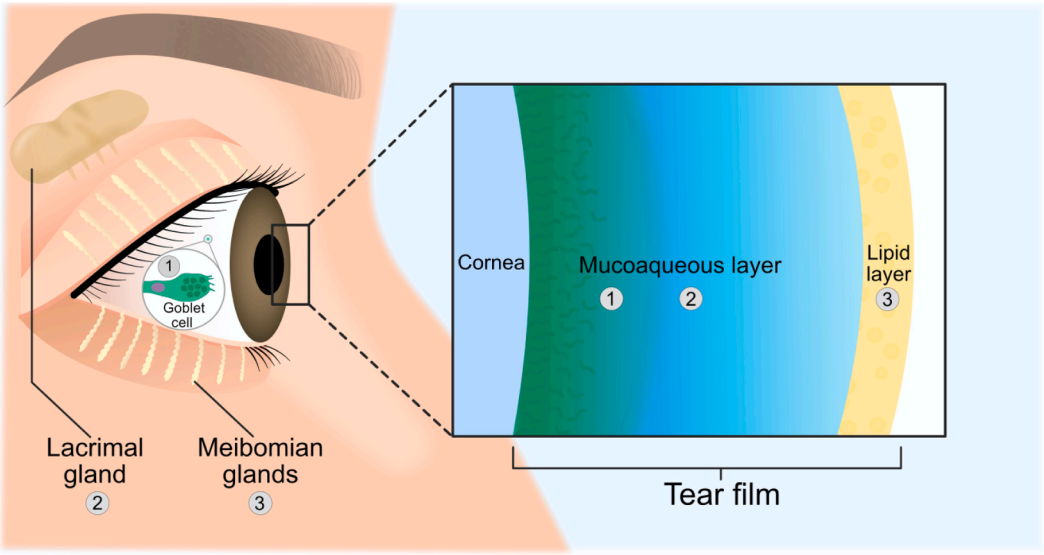

Fig. 1. Schematic drawing of the anterior segment of the eye and ocular adnexa with the overlying tear film. The tear film is made up of two distinct layers, with three major components; mucin (1), aqueous tears (2), and lipids (3) secreted by the goblet cells, lacrimal gland, and meibomian glands, respectively. Illustration by Sara Nøland.

2. Methods

A search was conducted on PubMed on the 28th of May 2021 using the following search terms: *(warm* OR heat* OR thermal* OR towel OR wet towel) AND (meibomian OR MGD OR eyelid OR "dry eye" OR DED)*. All search results were evaluated by a single author, first by title and later by abstract to ensure relevance to the topic and satisfaction of the inclusion criteria. The inclusion criteria for this review were: original, peer-reviewed studies with available English full text that investigated hot towel warm compresses to treat MGD. Only articles clearly describing the use of a towel/cloth-based method of warm compress treatment were included, studies on commercial devices or which did not describe the method of warm compress treatment were excluded. Further, case reports, review articles, and non-peer-reviewed literature were excluded. The methodology is illustrated in Fig. 2.

3. Results

3.1. Overview of existing literature

The search term *(warm* OR heat* OR thermal* OR towel OR wet towel) AND (meibomian OR MGD OR eyelid OR "dry eye" OR DED)* yielded 903 results, spanning from April 1948 to May 2021. Review article and case reports were filtered out, leaving 688 studies to be assessed for relevance by title and abstract. At this step, 623 articles were excluded, leaving 65 full-text articles to be evaluated. Of these, 22 articles were selected for this review based on the content of the full text. A majority of the 43 studies that were excluded in this last step either clearly stated the use of a commercially available eyelid warming device, not hot towels, or failed to provide any information on the type of warm compress used. One article was excluded as the group receiving hot towel treatment was pooled with other treatments and no clinical measures were reported separately for this group [28]. The final 22 articles included in this review were published between April 2003 [29] and September 2020 [30], and were conducted in 10 different countries: (USA [24,29,31–35], Japan [26,36], China [37], Germany [22,38], Singapore [27,39–41], Canada [42,43], Korea [44], Thailand [30], Australia [23], and Ireland [45]). Seven of the included studies used hot, wet towel compresses as the only eyelid warming technique [29,32–35,37,44]. Twelve studies compared the effect of towels to other eyelid warming therapies [22–24,26,27,31,36,38,39,42,43,45]. These therapies included the use of latent moist heat devices [22,26,27,31,38], commercially available eye masks or warm compresses [23,24,31,36,42,43,45], and in-office, vectored thermal pulsation treatment [30,39]. A summary of important characteristics of all included trials is presented in Table 1.

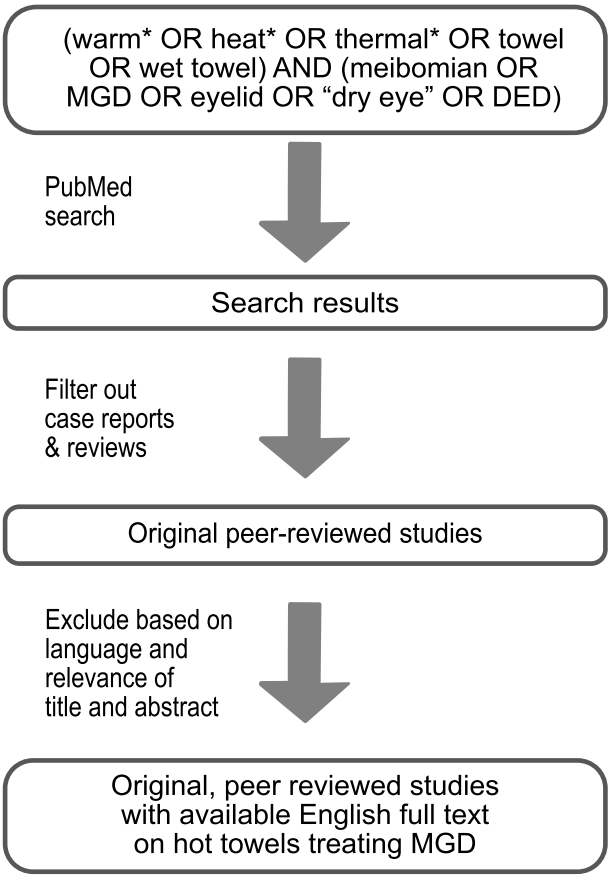

Fig. 2. Flow chart of PubMed search methodology.

3.2. Thermal properties and efficacy of hot towel treatment

Studies varied in the types of towels used, method of heating, and desired temperature. As shown in Table 1, eight studies relied on microwaves to heat the towels [29,31,33–36,42,43], while five used hot water to heat towels to a certain temperature [22,23,26,38,45]. An additional six studies used hot water to heat the towels but did not specify a desired temperature [24,27,32,39–41]. Finally, two studies did not provide details on how towels were heated [30,44], and one study used a hot egg to warm the towels [37].

Several of the included articles investigated the thermal properties of hot towel compresses. Table 2 provides further details on these trials [22,29,31,33,34,37,38,42,43]. Most of these single-visit studies on healthy subjects examined the changes in eyelid temperature with the application of hot towel compress [22,29,31,33,34,37,38,43]. Six of the nine studies examining thermal properties used cotton cloths, folded 3–4 times [22,29,33,34,42,43], while Murakami used microfiber towels in a bundle [31]. The last two studies did not specify the type of towel/cloth [37,38]. One study compared, ex-vivo, the heat retaining properties of different warm compresses, including hot towels [42]. The cotton facecloth was wetted in room-temperature water, folded three times, and heated for 20 s in a microwave oven. This yielded an initial temperature of around 43 °C, but fell below 40 °C after 2 min and the towel had a temperature of less than 30 °C after 10 min [42]. This rapid drop in temperature was also shown when applied to healthy subjects in a subsequent trial [43]. In this trial, Bitton et al. found that when applied over closed eyes, a cotton facecloth similarly folded three times would fall from 39.2 °C to below 35 °C after the first two minutes of application and fall further, to under 30 °C, by the end of the 12 min period [43].

The clinical effect of this rapid fall in temperature in the hot towels that were not reheated was shown in study by Pult et al., investigating the change in outer eyelid temperature with application of either hot towel compresses or Blephasteam [22]. This study found that upon application of the cotton cloth, folded three times, with an initial temperature of 41 °C, the outer eyelid temperature rose to 38 °C within the first minute but then steadily fell each minute after that, ending at 35 °C after ten minutes of application [22]. This shows that when the towels are not reheated, the temperature falls too quickly to provide enough heat for more than a couple of minutes, potentially preventing the heat from diffusing throughout the whole thickness of the eyelid to warm the meibum sufficiently [22].

The cooling rate found in these studies highlights the importance of reheating the towels to provide effective eyelid warming. As most of the heat loss from the towel is due to conduction and convection, Newton's law of cooling can be used to describe the temperature function [46]. Simply stated, this means that the heat transfer from the object to its surroundings is proportional to the difference in temperature between the object and its environment [46]. This explains why a towel heated to 50 °C will have a much greater drop in temperature within the first two minutes than the same towel heated to 40 °C, all else being equal.

Table 1
Overview of included studies.

First author	Year	Study Design	Subjects*	Important Characteristics
Olson MC [29]	2003	Single-visit	20 MGD	Towels were wetted and microwaved to 40 °C. The compress was reheated every 2 min by replacement of the towel. Unheated towels served as controls.
Matsumoto Y [26]	2006	Open-label prospective	10 MGD	Patients were given thermometers and asked to heat water to 60 °C. Towels were warmed in the water and applied while cooling. Used as control group for moist hot air device.
Lam AKC [37]	2007	Single-visit	25 Healthy	Towels were wetted and wrapped around a hot egg. Temperature was between 40 °C and 50 °C. Study included control groups with either unheated egg or hot egg not touching the eye.
Solomon JD [35]	2007	Single-visit	24 DED	Towels were wetted and microwaved to reach 45 °C. Replaced every 2 min. Towel applied to one eye only, control eye was allowed to stay open.
Blackie CA [34]	2008	Single-visit	32 Healthy	Towels were wetted and microwaved to reach 45 °C. Group A had no reheating. In group B and C, the towel was replaced every 2 min, however group C aimed the compress towards the lower lid. All three groups treated only one eye, with the contralateral eye closed.
Pult H [22]	2012	Single-visit	20 Healthy	Towels were warmed in heated water to achieve 41 °C. Not reheated. Control for Blephasteam.
Blackie CA [33]	2013	Single-visit	12 Healthy	Towels were wetted and microwaved to reach 45 °C. Replaced every 2 min. Towel applied to one eye only, the closed, contralateral eye was used as control.
Sim HS [27]	2014	Single-masked RCT	24 MGD	Towels were heated in "warm" water. Patients were encouraged to reheat when "they feel it get cooler". Use of artificial tears and Blephagel was encouraged. Control group for EyeGiene and Blephasteam.
Lam SM [40]	2014	Follow-up study	10 MGD**	Follow-up on sub-population of Sim et al. Clinical performance deemed equivalent to Blephasteam and EyeGiene and tear lipidome analysis conducted on pooled data for all three groups.
Arita R [36]	2015	Open-label, crossover	10 Healthy	Towels were wetted and microwaved on 500 W for 30 *sec*. Not reheated. The study compared single application of hot towels, Azuki no Chikara, Eye Hot R, Hot Eye Mask, and Memoto Este, and 2 weeks use of either hot towels or Azuki no Chikara.
Korb DR [32]	2015	Single-masked RCT	13 LDDE	Towels were warmed in "maximum comfortable" warm water. Patients were encouraged to keep a bowl of warm water and reheat when it began to cool. Control group for combination treatment that did not include lid warming.
Lacroix Z [42]	2015	Single-visit, Ex-vivo	N/A	Towels were warmed in tap water microwaved for 20 *sec* to reach 43 °C. Not reheated. Placed on a Styrofoam board. Compared with MGDRx, The Eye Doctor, MediBeads, Tranquileyes, and Eye-ssential.
Murakami DK [31]	2015	Single-visit	5 Healthy	Towels were wetted, bundled, and microwaved for 1.5 min to reach 47 °C. New towel unbundled and used every 2 min. Compared with MGDRx, MediBeads, Eye-ssential, Tranquileyes XR, EyeGiene, Blephasteam, and rice bag.
Bitton E [43]	2016	Single-visit	12 Healthy	Towels were warmed in tap water that was microwaved for 20 *sec* to reach 39 °C. Not reheated. Compared with MGDRx, The Eye Doctor, MediBeads, Tranquileyes, and Eye-ssential.
Zhao Y [39]	2016	Follow-up study	22 MGD**	Follow-up on sub-population of Sim et al. Used as control group for LipiFlow.
Yeo S [41]	2016	Follow-up study	22 MGD**	Follow-up on sub-population of Sim et al. Assessed tear film evaporation rates at baseline and 12-weeks.
Lee H [44]	2017	Single-group prospective	32 MGD	The patients were instructed to use a 40–45 °C warm towel. Not reheated. Combined with a lid cleanser and weekly in-office meibomian gland squeezing.
Tan J [23]	2018	Single-visit	31 MGD	Towels were warmed in hot water to reach a maximum temperature of 42 °C. Replaced every 2 min. Compared with Bruder compress.
Tichenor AA [24]	2019	Open-label RCT	17 CLDE	Towels were warmed in "hot faucet water". Not reheated. Control for Bruder Compress.
Kremers I [38]	2020	Single-visit	41 Healthy, 31 MGD	Towels were heated in warm water to reach approximately 40 °C.

(*continued on next page*)

Table 1 (*continued*)

First author	Year	Study Design	Subjects*	Important Characteristics
				Replaced every 20 *sec*, 2 min, or 5 min in different groups. Compared with Blephasteam and sauna.
Murphy O [45]	2020	Single-masked RCT	12 MGD	Subjects were instructed to boil 200 ml of water and let it cool in an open bowl for 10 min. This aimed to produce a water temperature of between 39 °C and 50 °C. The towel was heated in the water and reheated every 2 min. Control for MGDRx and OPTASE compresses.
Kasetsuwan N [30]	2020	Single-masked RCT	22 MGD with glaucoma	Participants were provided with a video demonstration. The subjects were instructed to use hot towel compresses for 5 min, then lid massage with baby shampoo. Control for LipiFlow combined with lid hygiene. Desired temperature, method of heating, or reheating schedule not described.

*Subjects receiving hot towels treatment as primary treatment, **Sub-population of Sim et al.
MGD: participants with meibomian gland dysfunction, DED: dry eye disease, CLDE: contact lens associated dry eye, LDDE: lipid deficient dry eye, RCT: randomized control trial.

Therefore, simply having a higher initial temperature of the towel is not sufficient to maintain an adequate temperature over time, and reheating is necessary. This theoretical principle is reflected in the temperature curves shown in Fig. 3 **a)**, which shows the temperatures of cotton towels reported in two studies that did not reheat the towels. Included in the graph is also the temperature range reported in a study where the cotton towel was heated to 40 °C and replaced every-two minutes [29,42,43]. Fig. 3 **b)** and **c)** present the inner and outer eyelid temperatures reported, respectively [31,33,34].

With reheating or replacement of the towels, compresses are capable of producing a more even level of heat over time [29]. A towel warmed to 40 °C and replaced every-two minutes maintained an applied temperature range of between 38 °C and 40 °C for a full 30-minute application [29]. This is a major advantage over the towels that were not reheated, as the ability to provide steady heat over time is important for raising the inner eyelid temperature [34]. However, a limitation of these studies is the use of an already preheated towel to achieve reheating, which might not reflect the clinical setting where reheating of a single towel might be more likely.

The importance of reheating on eyelid temperature was demonstrated in several studies [31,33,34,38]. In 2008, Blackie et al., compared three different regimens of eyelid warming, one without reheating and two groups where the cotton towels were replaced every-two minutes [34]. All three groups started with a towel with an initial temperature of 45 °C [34]. The group without reheating reached peak inner eyelid temperature after only four minutes, and this subsequently fell for the duration of application [34]. In the two groups where the towels were reheated every-two minutes, the inner eyelid reached 40 °C within 6 min and plateaued at this temperature for the remainder of the 30 min [34]. The same was shown for the outer eyelid temperature in a later trial by the same authors, where the outer eyelid temperature plateaued quickly and remained virtually unchanged during application [33]. They also found that the central corneal temperature increased at a slower rate and did not exceed 40 °C [33].

A reheating and replacement interval of two minutes was found to be adequate for maintaining therapeutic heat [34]. A towel heated to 45 °C dropped by 2.3 °C after two minutes, remaining within therapeutic range [34]. Furthermore, a towel warmed to 40 °C increased eyelid temperature by 1.4 °C if changed every 5 min, 2.0 °C if changed every 2 min, and 3.2 °C if changed every 20 s in healthy subjects [38]. In patients with MGD, the results were 1.4 °C when reheated every 5 min and 2.7 °C when reheated every 2 min [38]. No adverse effects related to heating or thermal injuries were noted in any of the studies.

Collectively, these findings indicate that reheating of the towel every 2 min is essential in providing safe, effective, and practical heating of the eyelid.

3.3. Efficacy of hot towel therapy over time

Eleven articles described eight studies with follow-up on patients

Table 2
Temperature profiles of application methods.

First author	Description	Temp	Reheating	Duration	Temperature profile
Olson MC [29]	Cotton cloth, folded four times.	40 °C	Every 2 min	30 min	Initial cloth temperature was 40 °C. The temperature fell quickly, but due to replacement of the towel, the applied compresses were above 38 °C for the duration of treatment.
Blackie CA [34]	Cotton cloth, folded four times.	45 °C	A: NO B: Every 2 min C: Every 2 min	A: 15 min B: 30 min C: 30 min	Maximum inner eyelid temperature in A was 38.8 °C, B was 40.4 °C, and C was 40.8 °C. Both B and C achieved 40 °C within the first 6 min, and remained above 40 °C for the duration of treatment.
Blackie CA [33]	Cotton cloth, folded four times.	45 °C	Every 2 min	30 min	The outer eyelid temperature rose to 42.2 °C after 6 min and was maintained above 40 °C for the duration of the treatment. The cornea reached a maximum temperature of 39.4 °C after 8 min, but never exceeded 40 °C.
Murakami DK [31]	Microfiber towels, folded and bundled	47 °C	Every 2 min	10 min	The inner lower eyelid temperature rose to about 40 °C. The bundle method gave a consistent and distributed temperature of about 40 °C at both the inner and outer eyelid surfaces.
Kremers I [38]	Unspecified towel/cloth	40 °C	Every 20 *sec*, 2 min or 5 min	10 min	Eyelid temperature increase was 3.2 °C when reheated every 20 s, 2.0 °C every 2 min, and 1.4 °C every 5 min, in healthy subjects. In patients with MGD, the increase was 2.7 °C when reheated every 2 min and 1.4 °C every 5 min.
Lam AKC [37]	Wet cloth	40–50 °C	NO	5 min	Raised eyelid temperature 3 °C within first minute, remained above 36 °C until the end of application.
Pult H [22]	Cotton cloth, folded three times	41 °C	NO	10 min	Raised eyelid temperature to 38.2 °C within first minute, then temperature dropped at a rate of 0.44 °C/min.
Bitton E [43]	Cotton facecloth, folded to three layers.	39.2 °C	NO	12 min	Initial cloth temperature was 39.2 °C. The temperature fell about 4 °C within the first two minutes, and ended at 29.2 °C.
Lacroix Z [42]	Cotton facecloth, folded to three layers.	43 °C	NO	12 min	The cloth remained above 40 °C for two min, then had a cooling rate of about −1°C/min over the next ten min.

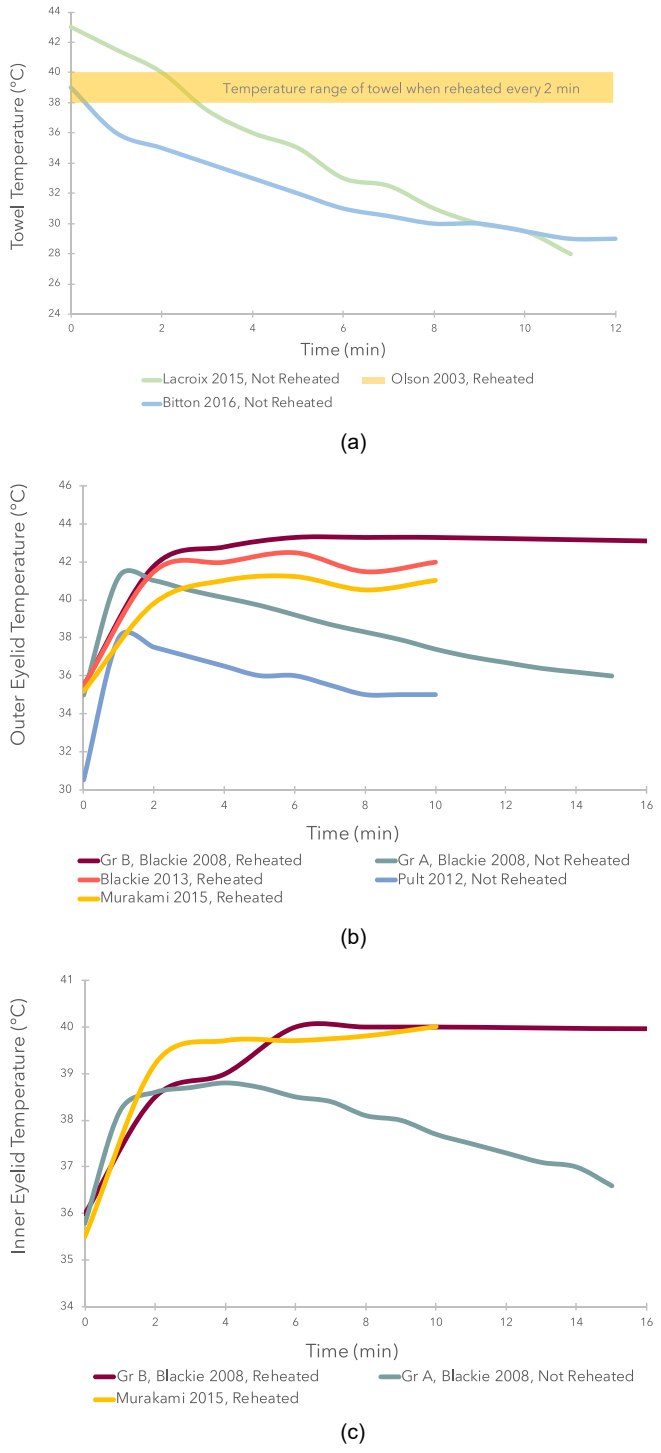

Fig. 3. Temperatures over time, interpolated from listed studies. The three graphs show the temperature of **a)** the physical towel used for treatment **b)** the outer eyelid, and **c)** the inner eyelid in studies with or without reheating of the compress during application. In the study by Olson et al. **(a)**, towels were replaced every-two minutes with new preheated towels, thus the range represents the temperature range of the applied towels reported in the trial, not the temperature of any individual towel. For the studies labeled reheated, towels were replaced every-two minutes with either new preheated towels, or by applying a new towel from the bundle, effectively reheating the applied compress.

undergoing hot towel compress treatment [24,26,27,30,32,36,39–41,44,45]. The subjects undergoing hot towel treatment in Zhao et al. [39], Yeo et al. [41], and Lam et al. [40] are the same subjects as Sim et al. [27]. Important outcomes of the initial studies are summarized in Table 3. In many of these studies, hot towel compresses were used as controls to other treatments, and the application method was not well-described [24,26,27,30,32,36,39,45]. This lack of a well-described method presents a limitation of these studies. Follow-up time varied between two weeks [26,36] and six months [30]. Across studies, the most frequently used treatment regime consisted of twice-daily, ten-minute treatment with a warm cotton towel that was either reheated when cooled, or not reheated. Most studies offered only a subjective description of the towel preparation and application method, such as the temperature of the towel being "warm" [24,27,32,36,39] and for the reheating; "rewarm it once it cools" [39]. Only three trials provided information on the desired temperature, with one using a 60 °C hot towel that was not reheated [26], one using 40–45 °C and no reheating [44], and one study using towels of between 39 and 50 °C that were reheated every-two minutes [45]. One study provided the participants with video instruction to standardize the hot towel compress treatment [30]. However, beyond the application time being 5 min, no further information regarding technique was provided. An additional limitation was that three of the seven comparative studies were open label [24,26,36], and one of the studies assessing treatment over time did not include a control group [44].

Subjective symptoms of dry eye and ocular irritation were measured in seven of the eight studies with follow-up [24,26,27,30,32,44,45]. Symptom scores improved in all eight from baseline compared to the last follow-up for those receiving hot towel compresses. One study used three separate measures of symptoms: the Ocular Surface Disease Index (OSDI) and Standard Patient Evaluation of Eye Dryness (SPEED) at baseline and follow-up, and a daily assessment of dry eye severity using a visual analog scale (VAS) [24]. The authors noted improvement in the daily symptom burden using VAS, while OSDI and SPEED scores were not significantly different from baseline at follow-up [24]. Korb et al. used both the Standard Patient Evaluation of Eye Dryness (SPEED) and the OSDI questionnaire and found significant improvements in both scores at the 1-, 2-, and 3-month follow-ups [32]. Three other trials also found a significant improvement in OSDI over time [30,44,45]. Taken together, these findings show a clear improvement in subjective symptoms over time with hot towel compresses.

Seven out of the eight studies with a follow-up period reported tear film breakup time (TBUT) measures [24,26,27,30,36,44,45]. Only the study with the largest sample receiving hot towel compresses noted improvement in TBUT [44]. The other six studies did not find significant change in TBUT upon application of hot towels [24,26,27,30,36,45]. In these six studies, hot towel compresses were used as the control intervention for other eyelid warming devices, either commercially available or under development [24,26,27,30,36,45].

Other clinical measures of MGD were reported in a subset of trials. Corneal fluorescein staining was reported in four of the studies with follow-up [26,30,44,45]. Corneal fluorescein staining scores improved in two of these trials [44,45]. The remaining two studies showed no significant change in corneal fluorescein staining scores [26,30]. Another clinical parameter measured in four of the longitudinal studies was lipid layer thickness [24,26,30,44]. Only one of these trials noted a change from baseline, with an improvement in lipid layer thickness after long-term hot towel treatment [30]. Further clinical measurements such as Schirmer I and meibomian gland scores and gradings were also reported in a smaller number of trials. None of the four studies measuring Schirmer I found any change from baseline at follow-up [27,30,36,45]. Five studies examined different aspects of meibomian gland scoring or meibum excretion [24,30,32,44,45]. Korb et al. explored the number of meibomian glands yielding liquid secretion and found no significant increase in the group receiving warm compress treatment [32]. Three studies reported improvement in both meibum quality and expressibility

Table 3
Studies assessing treatment over time.

First author	Study Design	Description	Reheat	Frequency	Symptoms	TBUT	CFS	LLT	Sch. I	VA	MG Score	Other Outcomes
Matsumoto Y [26]	Open-label prospective	60 °C 10 min	NO	2x/day for 2 w	↑	—	—	—	N.D	N.D	N.D	Rose Bengal scores did not change.
Sim HS [27]	Single-masked RCT	"Warm" 10 min	When cooled	2x/day for 3 mo	↑	—	N.D	N.D	—	—	N.D	Number of plugged MGs did not change.
Korb DR [32]	Single-masked RCT	"Maximum comfortable" 8 min	When cooled	1x/day for 3 mo	↑[1]/↑[2]	N.D	N.D	N.D	N.D	—	—	Itching and eye rubbing improved.
Arita R [36]	Open-label, crossover	"Warm" 5 min	NO	2x/day for 2 w	N.D	—	N.D	N.D	—	N.D	N.D	TBUT improved only after single-application.
Lee H [44]	Single-group prospective	40–45 °C 5 min	NO	2x/day for 4 w	↑[1]	↑	↑	—	N.D	N.D	↑	Lid margin abnormalities and MGD stage improved.
Tichenor AA [24]	Open-label RCT	"Warm" 10 min	NO	2x/day for 1 mo	—[1,2]/↑[3]	—	N.D	—	N.D	—	—	Uncomfortable CL wear time was reduced. 80 % were compliant with twice-daily hot towels.
Murphy O [45]	Single-masked RCT	39–50 °C 10 min	Every 2 min	2x/day for 2 w, then 1x/day for 6 w	↑[1]	—	↑	N.D	—	N.D	↑	78 % were compliant with treatment.
Kasetsuwan N [30]	Single-masked RCT	5 min	Not described	2x/day for 6 mo	↑[1]	—	—	↑	—	N.D	↑	12.5 % of total population was compliant with treatment at least once per day, 64.5 % conducted eyelid warming at least 5 days/week, on average.

N.D: Not described, TBUT: Tear film breakup time, CFS: Cornea fluorescein staining, LLT: Lipid layer thickness, Sch. I: Schirmer I, VA: Visual acuity, MG: Meibomian gland, RCT: Randomized clinical trial.
↑: Significant improvement, —: No significant change.
[1] : Ocular Surface Disease Index (OSDI),
[2] : Standard Patient Evaluation of Eye Dryness (SPEED),
[3] : Visual Analog Scale (VAS) for ocular severity.

[30,44,45]. Tichenor et al., however, found no significant difference in meibomian gland score [24].

Across studies, although differing methods and study populations, hot towel compress treatment was consistently shown to effectively reduce symptoms of MGD, but the effect on clinical signs of MGD was more varied.

3.4. Safety assessment and adverse effects

In two of the studies without extended follow-up, there was a significant drop in visual acuity and increased in subjective blur immediately after hot towel compress treatment [22,35]. Solomon et al. also noted the presence of a Fischer-Schweitzer polygonal reflex in patients after a 30-minute hot-towel treatment and linked this to the reduced visual acuity [35]. This phenomenon consists of a honey-comb pattern on the cornea and commonly occurs after rubbing [47]. Another study found that the pressing force negatively affected the corneal topography, when the hot towel was wrapped around an egg to increase the heat capacity [37]. One study by Blackie et al. also raised the issue of elevated corneal temperature as a possible adverse outcome, as 30 min of 45 °C hot towel increased the central corneal temperature to near 40 °C, the level they deemed to be the safe upper limit [33]. Due to these findings, three of the studies with a follow-up period included measures of visual acuity, with one of these also measuring corneal topography [24,27,32]. All three studies found visual acuity to remain unchanged at all timepoints throughout the trials [24,27,32]. Tichenor et al. also found no warpage or change in corneal topography at any timepoint [24].

Compliance with hot towel compress treatment over time was reported in three studies [24,30,45]. These studies demonstrated varying compliance, with more than 70 % of subjects complying with treatment in two studies [24,45], but only 12.5 % conducted hot towel treatment once daily and 64.5 % at least 5 days per week in another study [30]. None of the studies reported any form of thermal injuries or patient complaints about the towels being too hot.

In summation, the adverse effects noted in the trials without follow-up, were not found in the studies with follow-up. Long-term treatment with hot towels therefore appears safe as long as the towels are not heated beyond safe limits or applied with excessive force.

3.5. Comparative studies and outcomes

The single-visit studies that did not reheat the wet towels found that the heat retention and eyelid warming effect of hot towels were inferior to the commercially available alternatives [22,42,43]. However, when reheated, hot towels showed equivalent, or better, heating abilities than commercial options [31,38]. Murakami et al. found that of the eight devices tested (the bundle method, EyeGiene, MediBeads, Eye-ssential, MGDRx Eyebag, a rice bag, Tranquileyes XR, and Blephasteam), the bundle method of hot towel treatment was the only method capable of heating the eyelids above 40 °C. Moreover, the bundle method provided consistent heat to both the outer and inner eyelid surface [31]. In short, the bundle method consists of wrapping five or six wetted and folded microfiber towels in a bundle and microwaving the bundle in a covered dish for about 1.5 min. The temperature of the outer towel should then be measured, with the targeted temperature being 47 °C, as described elsewhere [31]. It is important to note, however, that the temperature should not exceed 48–49 °C and the patient should be advised to wait before application if the towels are too hot. Although not described in the original publication, a simple way to test if the towels are too hot, is to touch them against the inside of the wrist to ensure that this does not provoke pain. The outer towel is then peeled off the bundle and applied for two min while the remaining towels in the bundle are left in the covered dish. Every-two minutes, the applied towel is placed aside and the next towel in the bundle is peeled off and applied, giving a total duration of application around ten to twelve minutes [31]. This procedure is illustrated in Fig. 4.

Towels warmed to 40 °C and changed every 20 s gave the same level of eyelid warming as one session of Blephasteam; however, when

changed only every 2 or 5 min, they were significantly cooler [38]. A 10-minute sauna at 85 °C was found to increase eyelid temperature similarly to applying hot towels [38].

Four prospective studies used hot towel treatment without reheating as comparators for other eyelid warming treatments [24,26,30,36]. Kasetsuwan et al. found no difference in any measured parameter between the group allocated to six months of twice-daily hot towel compress treatment only and the group receiving a single LipiFlow treatment in addition to twice-daily hot towel compress treatment for six months [30]. Another study found no difference between hot towels and the Bruder Moist Heat Compress in ocular surface parameters nor improvement in symptoms from contact lens wear [24]. Although there were no statistical comparisons between groups, two prospective studies found significant improvements from baseline in the groups receiving experimental treatment that was not observed in those receiving hot towel treatment [26,36].

Four studies used hot towels that were reheated as controls to other MGD treatments [23,27,32,45]. Three of them found no difference in clinical signs between the experimental treatment group and the hot towel control group [23,27,45]. Korb et al. found that the number of meibomian glands yielding liquid secretion increased significantly more in the combination treatment group using lid wipes, eye drops, and omega-3 supplements than in the group receiving hot towels [32]. Two studies found no difference between groups when comparing hot towels to other treatments using symptom scores as outcome variable [32,45]. Sim et al. found no difference between groups in any parameter at the primary assessment point after one month [27]. However, after three months, the group receiving Blephasteam was more likely to have experienced an improvement in frequency and severity of symptoms, compared to the hot towel group, but there was no difference noted between EyeGiene and hot towels [27,32,45].

Despite differing initial temperatures and study designs, a majority of studies found hot towels to be mostly equivalent to other eyelid warming therapies in both heating capability and clinical effect, if following a protocol which included reheating or replacement of the towels.

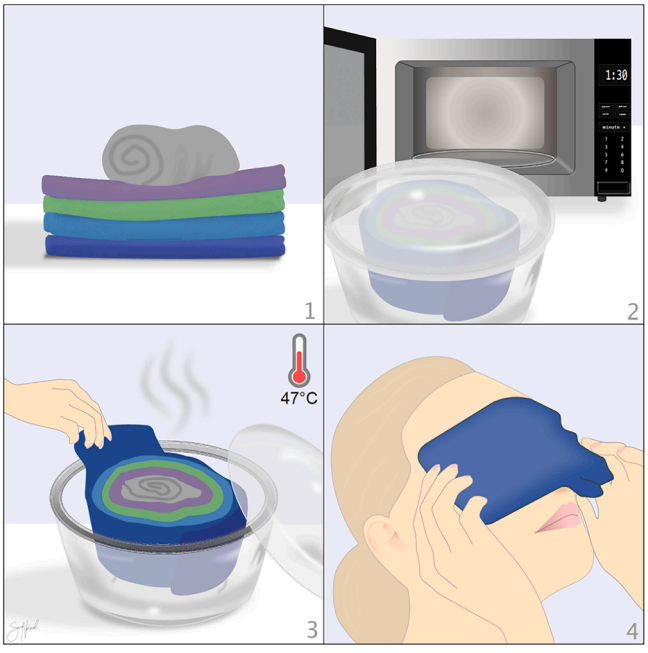

Fig. 4. Illustration showing the bundle method, described by Murakami et al. [31], an application method for hot towel treatment shown effective at raising eyelid temperature. **1)** A standard bundle consists of five or six folded towels that are then bundled together; **2)** the bundle of towels is placed in a covered glass dish and heated in the microwave; **3)** the towels are used one at a time. The outer towel is peeled off and applied, while the rest of the towels remain in the covered dish. Every-two minutes, the used towel is placed aside and a new towel is taken from the bundle **4)** the towel should be placed over closed eyes with minimal pressure. Illustration by Sara Nøland.

4. Discussion

Across the included studies, several different methods for hot towel treatment were found. There was no clear standardization or best-practice. Many studies did not report the initial temperatures used [24,27,30,32,36,39], and one study advised starting with water at 60 °C [26], which is well above safe limits for prolonged skin contact [48]. It is, therefore, necessary to establish a best practice to promote patient safety and effective treatment. When performed correctly, hot towels have been shown to effectively raise eyelid temperature [31] and alleviate dry eye symptoms [24,26,27,30,32,44,45]. To achieve therapeutic levels of eyelid warming, the towel must maintain a sustained temperature greater than 40 °C [31] but should not exceed 48 °C to avoid thermal injury [48]. A best-practice treatment regime should therefore provide the patients with detailed instructions on proper hot towel use. This regimen should strive towards achieving an initial temperature between 42 °C and 47 °C and should ensure reheating or change of towel every-two minutes in order to achieve a sustained temperature above 40 °C for the duration of treatment while still remaining practical. Thus, patient-aimed information should emphasize the necessity of reheating every-two minutes, before the compress feels cool, and explain that this is likely more important than a higher initial temperature. This might both improve patient safety and compliance and improve the chance of effective treatment even when exact temperatures are not measured, but instead instructions such as “warm, but not painful” are given and the patient is asked to check the tolerability against the inside of their wrists.

4.1. Limitations and future directions

As this review focused on the efficacy of hot towel warm compresses only and not warm compresses in general, some articles describing the use of warm compresses without stating the type of compress had to be excluded. Additionally, only full-text English articles were included.

The included studies have some limitations. First, some of the studies were sponsored by the manufacturers of products that the hot towels were tested against, introducing a potential conflict of interest [24,32]. Second, the sample sizes across studies were relatively small, with the largest including only 32 MGD patients receiving hot towel compress treatment [44]. Third, a major limitation in several of the prospective studies was the lack of a detailed description of patient information and treatment regime. Only three of the prospective studies provided information on the targeted temperature for the towels, and two of these did not encourage the patients to reheat the towels [26,44,45]. Moreover, measuring patient compliance with treatment is in general difficult to assess, and is made more challenging by the lack of transparency around patient instructions given in these studies. Fourth, most of the included studies had relatively short follow-up times. The longest follow-up reported was six months [30] and the shortest two weeks [26,36]. As MGD is a chronic disease requiring long-term treatment, it is important to study the long-term effects and compliance with treatment in future trials. Fifth, of the eight studies assessing treatment over time, only four were single-blinded RCTs [27,30,32,45], with the remaining being either open-label studies [24,26,36], or without a control group [44]. None of the included studies were double-blinded RCTs. Furthermore, differences in the materials used and towel characteristics, as described in 3.2, could impact the thermal properties of the compress. Thus, this presents a limitation of this review as this makes comparison across studies more challenging.

Finally, the frequency of treatment applications was not standardized across studies. Future treatments investigating patient outcomes and compliance with different lengths and numbers of sessions per day

are warranted. Furthermore, reheating of the towel before it falls below therapeutic temperatures appears to be essential to the clinical effect of hot towel treatment. Studies should investigate patient engagement and current home solutions to minimize the gap during application when reheating or changing of the towel is necessary. As a result, replacing phrasings such as "reheat the compress when cold," common in a clinical setting, with "reheat the compress every-two minutes" may improve compliance and patient outcomes by preventing the hot towel compress from dropping below the therapeutic range before the compress is reheated.

Heating the towel with warm tap water could make the heating process easier for patients and enhance compliance. However, this requires that these temperatures are within both therapeutic and safe limits. To prevent scalding injuries the Consumer Product Safety Commission and several US states recommend that the maximal temperature of tap water in US houses does not exceed 120°F (48.9 °C) [49]. A recent study, however, found that the maximum temperature of tap water exceeded the recommended temperature in 41 % of cases, most often in houses with gas water heaters [50]. Using maximally hot tap water to warm the towel could thus result in temperatures above safe limits if the temperature is not measured before application. As it is unlikely that all patients will check the temperature of the towel with a thermometer before application, studies trying to standardize methods to achieve a temperature of approximately 45 °C are warranted. Methods that could be investigated are the use of different ratios of boiled and cold water or known volumes of water heated at a fixed wattage for a certain amount of time in the microwave. Despite this, the general advice should always be to measure the temperature with a thermometer before application and to test the compress against the inside of the wrist before applying to the eyelids. Importantly, as reheating every-two minutes appears to be essential to a successful outcome, future studies should assess the efficacy of a protocol emphasizing this as an objective measure, but with more simple/subjective instructions regarding the heat of the towels, with the aim of improving patient compliance. For example, simple to follow instructions, such as using tap water which is "tolerably hot, but not painful," as measured against the inside of the wrist, to wet and heat the towel, applying the towel for two minutes before reheating the towel and again checking for tolerability against the wrist, may improve compliance. Such a method, that requires only a means of keeping time may provide improved outcomes compared to more labor-intensive methods due to increased therapeutic heat throughout the process.

4.2. Compliance and safety

Compliance was shown to be moderately high even with relatively complex protocols [45]. Murphy et al. instructed patients to boil 200 ml of water and let it cool for 10 min before heating the towel in it and then reheating every 2 min, for 10 min [45]. Even with this somewhat cumbersome method, compliance was noted to be above 75 % [45]. This is promising for compliance to simpler techniques, such as using a larger volume of hot tap water and measuring with a thermometer or the bundle method [31]. It is likely that compliance among patients not enrolled in clinical trials will be substantially lower, as education and frequent contact with healthcare personnel during these trials is known to promote overall medical compliance [51]. A study looking at compliance with lid hygiene treatment in patients with lid margin disease found that 55 % of all patients and 74 % of symptomatic patients reported being compliant with the six-week treatment [52]. In contrast, in the study with the longest follow-up, six months, 64.5 % of participants conducted hot towel treatment and eyelid hygiene at least five days per week but only 12.5 % performing the treatment every day, as instructed [30]. As the bundle method was better at providing therapeutic levels of heat than the commercially-available, specialized eyelid warmers it was tested against [31], the resulting improvement in patient motivation and compliance is likely to improve patient outcomes. Overall, compliance with medical procedures for chronic diseases is estimated to be around 50 % and a key element to raise adherence with treatment is motivation and belief in the efficacy of treatment [53]. It is therefore important that physicians highlight the benefits of the prescribed treatment and provide clear information on how it is performed and the expected timeframe for improvement. It is often estimated that on average patients remember only half of what they are told during a consultation. Thus, providing a written description of how to perform the prescribed at-home treatment is essential [54]. Furthermore, as compresses may fall below therapeutic range if not reheated, even with higher initial temperatures, patient instructions should make this clear and advise reheating every-two minutes; simple instructions should convey the temperature can be checked subjectively against the inside of the wrist to be "warm, but not painful.".

Future studies should aim to assess the usability and compliance of different methods of hot towel compress techniques that includes regular reheating of the towels to ensure good safety and compliance also within an at-home setting. Ultimately, the optimal method for at-home hot towel treatment is the one a patient is most likely to adhere to, as long as it also incorporates the regular reheating of the towel throughout the treatment.

As several of the studies exposed the skin to heat for up to 30 min at a time, even at lower temperatures, scalding could be a risk [48]. At 50 °C the skin can burn within minutes, while at 45 °C the necessary exposure time is estimated to be several hours [48]. It is, therefore, of the utmost importance patients comply with the described treatment regime, especially ensuring that the temperature and duration of application is within safe limits.

Not all patients are suited for hot towel compress treatment. In addition to those with DED stemming from sources other than MGD or people with disabilities that make the treatment challenging, the reduced cornea thickness and strength seen with keratoconus could be a contraindication against warm compress treatment in general [33]. It has also been suggested that glaucoma and axial myopia might be contraindications against the eyelid massage often conducted following warm compress treatment [33].

When using a 45 °C hot towel reheated every-two minutes, Blackie et al. found that the inner eyelid reached over 95 % of the maximal warming within 6 min [34]. This indicated that the heat had been conducted throughout the thickness of the eyelid, transferring to the meibomian glands and warming any stagnant meibum. These findings reveal that a treatment duration of 6–8 min is likely sufficient to achieve effective full-thickness eyelid warming. Ensuring that patients are specifically instructed that the temperature of towel should lie in the range between 40 °C and 45 °C, but not exceed 48 °C, and that the treatment duration should not be longer than 10 min would substantially reduce the risk of thermal injury. Furthermore, several studies found that the temperature of the eyelids returned to baseline within few minutes after ceasing eyelid warming, regardless of the device or method used [33,34,36,38]. It is thus important to commence eyelid massage immediately after the end of eyelid warming, while the temperature of the meibum is still elevated.

4.3. Standardizing methodology for the use of hot towels in treatment and future research

Without a clear protocol for patients that includes a clear target temperature and reheating at regular intervals, efficacy and compliance with treatment is likely to be far lower than desired. Lacroix et al. highlight the inadequacy of only advising the patients to use "warm compresses for 10 min, twice daily" without explicit instruction to reheat or replace the towels. The study found that a towel heated to 43 °C had fallen to below 35 °C after 5 min [42]. In essence, this means that for the last 5 min of the 10-minute treatment, the patients were using an "eyelid cooling device," not an eyelid warming device [42]. To prevent this, it is essential that physicians provide their patients suffering from MGD with a detailed oral and written description,

preferably in conjunction with a video demonstration, of the recommended treatment to increase confidence in and compliance with treatment [53]. This description should either be using the bundle method [31], or another user-friendly hot towel methodology that clearly describes a desired temperature of between 40 °C and 45 °C with reheating every-two minutes [29,33,34,38,45]. This can easily be achieved using a bowl filled with one liter of water at the desired temperature and two towels that alternate between being applied and submerged in the warm water. The bundle method may be better for use in a controlled clinical or research setting, while at home using a bowl of water might be best. Furthermore, as the eyelid temperature drops rapidly following application of all eyelid warming treatments, eyelid massaging should be performed immediately [38]. Three minutes after the end of application, both inner and outer eyelid temperature had fallen to around 38 °C, from about 40 °C and 42 °C, respectively, immediately after application [34]. Therefore, to make the most of the softening of the meibum from the warming treatment, massaging should be performed as close to the end of the application of heat as possible.

As compliance with at-home treatments is often a challenge, especially with more complicated procedures, simple instructions should be preferred when possible. As there were clear differences between the studies reheating at least every-two minutes and those that did not reheat the towels, the most important message for patients is likely the need for regular reheating. Further, reheating based on a timed interval and not when the hot towel compress subjectively feels cool may ensure the compress maintains therapeutic temperature throughout the application period. Thus, patient-oriented instructions would likely benefit from a greater emphasis on the importance of reheating every-two minutes rather than the exact initial temperature, as long as safety is maintained.

5. Conclusion

Hot towel compress treatment is effective at raising the eyelid temperature to therapeutic ranges when conducted in accordance with best practice. Ideally, this method entails an initial temperature of 45 °C, reheating the towel every-two minutes, and applying the towel for six to ten minutes in total. However, as reheating of the compress before it cooled appeared to be key, the strict adherence to an exact protocol for heating the towels might not be necessary, as long as safety is preserved, and towels are reheated at least every-two minutes. Thus, patient-oriented instructions should include instructions to reheat the compress before it cools substantially, at least every-two minutes. Patient motivation is here essential, as the best at-home hot towel treatment is likely the one that a patient can adhere to, as long as it also incorporates regular reheating of the towel throughout the session. When performed over time, hot towel treatment improves dry eye symptom scores and select clinical measures, often on par with more costly MGD treatment devices. Hot towel treatment without reheating at least every-two minutes is not sufficiently effective. Clinicians both when advising patients and for future studies using hot towels as control groups should provide patients with clear oral and written instructions that specify the desired temperature and reheating schedule in line with best practice.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: **Morten Schjerven Magno:** Nothing to disclose. **Jonatan Olafsson:** Nothing to disclose. **Marie Beining:** Nothing to disclose. **Emily Moschowits:** Nothing to disclose. **Neil Lagali:** Nothing to disclose. **James S. Wolffsohn** is the Chief Scientific Officer of the International Myopia Institute, on the Executive of the Tear Film and Ocular Surface Society and Academic Chair to the BCLA. Honoraria for consultancy received from AtiaVision, Bausch and Lomb, Alcon, CooperVision, Johnson and Johnson Vision, Nevakar, Novartis and Thea Pharmaceutical. He has also received research funding from Alcon, Allergan, Johnson and Johnson Vision, Novartis, M2C Therapeutics, Rayner, and Thea Pharmaceuticals. He is a founder and shareholder in Aston Vision Sciences, Eyoto and Wolffsohn Research ltd. **Jennifer P. Craig** is founder of the Ocular Surface Laboratory at the University of Auckland, New Zealand which in the last three years has delivered talks for and/or received financial support for research and education in the area of dry eye and ocular surface disease from Alcon, Azura Ophthalmics, E-Swin, Johnson & Johnson Vision, Laboratoires Théa, Manuka Health NZ, Novartis, Resono Ophthalmic, and Topcon. **Jelle Vehof** has received financial support for talks and education in the area of dry eye and ocular surface disease from Santen. Tramedico, Théa Pharma and Horus Pharma, and is consultant for Santen and Tramedico. Vehof is the Dutch Global Ambassador for Tear Film and Ocular Surface Society (TFOS). **Darlene A. Dartt:** Nothing to disclose. **Tor Paaske Utheim** is co-founder and co-owner of The Norwegian dry eye clinic and the Clinic of eye health, Oslo, Norway, which delivers talks for and/or receives financial support from the following: ABIGO, Alcon, Allergan, AMWO, Bausch&Lomb, Bayer, European school for advanced studies in ophthalmology, InnZ Medical, Medilens Nordic, Medistim, Novartis, Santen, Specsavers, Shire Pharmaceuticals and Thea Laboratories. He has served on the global scientific advisory board for Novartis and Alcon as well as the European advisory board for Shire Pharmaceuticals. Utheim is the Norwegian Global Ambassador for Tear Film and Ocular Surface Society (TFOS), a Board Member of the International Ocular Surface Society, a Consultant at the Norwegian Association for the Blind and Partially Sighted, and the Editor-in-Chief of Oftalmolog, an eye journal distributed to all eye doctors in the Nordic region since 1980.

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