

Increase in Tear Film Lipid Layer Thickness Following Treatment with Warm Compresses in Patients with Meibomian Gland Dysfunction

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Purpose. Warm-compress therapy applied to the skin of the closed eyelids has been recommended as a treatment for meibomian gland dysfunction (MGD). Previous studies have evaluated the effects of warm-compress therapy on tear-film fluorescein break-up time and tear evaporation rate. The purpose of this study was to determine if tear-film lipid layer thickness (TFLLT) was altered following 5, 15, and 30 minutes of warm, moist compress therapy. **Methods.** Twenty patients with a diagnosis of dry eye associated with MGD and a baseline TFLLT of ≤ 90 nm (baseline difference between experimental and control eyes ≤ 25 nm) were studied. The skin of the closed eyelids of one eye of each subject was treated for a total of 30 minutes with a compress saturated with warm ($40.0 \pm 2.0^\circ\text{C}$) water used as a compress; and the skin of the closed eyelids of the contralateral control eye was treated for a total of 30 minutes with a compress saturated with room-temperature ($24.0^\circ\text{C} \pm 1.0^\circ\text{C}$) water used as a compress. The subjects' eyes were randomized into experimental and control eyes. TFLLT was measured at the following time points: 5, 15, and 30 minutes during the 30-minute treatment period, and after 5 minutes following the 30-minute treatment period. **Results.** The mean baseline TFLLT of the experimental eye prior to treatment with a warm, moist compress was 57.8 ± 12.9 (standard error) nm; after 5 minutes of treatment, TFLLT was 105.8 ± 23.7 nm; after 15 minutes of treatment, 117.8 ± 26.4 nm; after 30 minutes of treatment, 121.5 ± 27.1 nm; and after 5 minutes following the 30-minute treatment, 96.0 ± 21.5 nm. The mean baseline TFLLT of the control eye prior to treatment with a room temperature, moist compress was 63.0 ± 14.1 nm; after 5 minutes of treatment, TFLLT was 63.8 ± 14.3 nm; after 15 minutes of treatment, 62.3 ± 13.9 nm; after 30 minutes of treatment, 64.5 ± 14.4 nm; and after 5 minutes following the 30-minute treatment period, 58.5 ± 13.1 nm. Using a paired-data *t*-test, the results demonstrated a significant increase in mean TFLLT in the experimental eye after 5 minutes ($P < 0.001$), 15 minutes ($P < 0.001$), and 30 minutes ($P < 0.001$) of treatment, and after 5 minutes following the 30-minute treatment period ($P < 0.001$) when compared to baseline TFLLT. In comparison, there was no significant increase in TFLLT of the control eye after 5

minutes ($P = 0.79$), 15 minutes ($P = 0.77$), and 30 minutes ($P = 0.81$) of treatment, and after 5 minutes following the 30-minute treatment period ($P = 0.20$) when compared to baseline TFLLT.

Conclusions. Warm, moist compress therapy applied to the skin of the closed eyelids increases TFLLT for subjects with MGD by more than 80%, 5 minutes after initiating treatment and an additional 20% after 15 minutes of treatment. This study supports clinical experience and previous reports on warm, moist compress therapy as an effective treatment for meibomian gland dysfunction.

Key Words: Warm compress treatment—Meibomian gland dysfunction—Tear film lipid layer thickness—Dry eye.

Warm compresses have been recommended as a therapeutic treatment for conditions of the eyelids that include meibomian gland dysfunction (MGD),^{1–5} internal hordeolum (chalazion),^{6,7} external hordeolum,⁸ and blepharoconjunctivitis.⁹ Typically, a hand towel or face cloth is soaked and heated with hot water, excess water is wrung out, and the cloth is then placed over the skin of the closed eyelids for several minutes. This procedure may be repeated several times. Following treatment with warm compresses, lid scrubs are also recommended to scrape debris from the lid margin, which may block the meibomian gland orifices.^{1,3}

Meibomian gland secretion has a melting point range of 32° to 40°C .¹⁰ As such, the meibomian gland secretion is normally liquid at body temperature (37°C). With meibomian gland inspissation in chronic marginal blepharitis, the melting points of the glandular secretions are elevated,¹¹ and the secretions become stagnant. Samples of meibomian secretions from normal subjects started to melt at 32°C , and in samples from subjects with meibomian gland dysfunction, secretions were found to begin melting at 35°C .¹⁰ Increasing the outflow of lipid from the meibomian glands helps prevent water evaporation from the ocular surface.^{3,11,12} When the tear film lipid layer or the secretory duct system of the meibomian gland is abnormal, as in MGD, water evaporation from the tear film will increase.¹² Moreover, there is a significant positive correlation between evaporative rate and meibomian gland drop out.¹²

Although warm compress therapy has become a standard treatment for MGD, there is no quantitative data on tear film lipid layer thickness (TFLLT) to support this as a primary practice for MGD treatment. The purpose of this study was to investigate whether warm, moist compress therapy would increase TFLLT. To quantify results, baseline TFLLT was compared to TFLLT following periods of controlled warm, moist compress treatment.

This study was supported by a research grant from Ocular Research of Boston, Inc., Boston, MA.

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Accepted January 27, 2003.

DOI: 10.1097/01.ICL.0000060998.20142.8D

TABLE 1. Dry eye questionnaire

Name: _____ Date: _____
 Date of birth: ____ / ____ / ____ Sex: M F

Please check if you have had any of the following symptoms:

Symptoms	Yes	Severity				No
Dryness	0	1	2	3	4	
Grittiness or scratchiness	0	1	2	3	4	
Soreness or irritation	0	1	2	3	4	
Burning or watering	0	1	2	3	4	

Severity:

- 0 = No problems
- 1 = Tolerable—not perfect but not uncomfortable
- 2 = Uncomfortable—irritating but does not interfere with your day
- 3 = Bothersome—irritating and interferes with your day
- 4 = Intolerable—unable to perform your daily tasks

If any of these symptoms are present, please report frequency as sometimes, often or constant.

Symptoms	Sometimes	Often	Constant
Dryness			
Grittiness or scratchiness			
Soreness or irritation			
Burning or watering			

Are your symptoms present today? Yes No

METHODS

Consecutive patients presenting with a principal complaint indicative of ocular dryness were examined until 20 male and female subjects (17 female, 3 male, ranging in age from 26 to 59 years) met the criteria for admission to the study. Subjects included 13 light complected whites, 6 moderate complected whites, and 1 Asian. Subjects were selected using the following criteria: (1) subjective dry eye status determined by a score of 6 or more for dry eye symptoms quantified by a questionnaire (Table 1), modified from a previous questionnaire¹³; (2) meibomian gland obstruction determined by biomicroscopic examination of the eyelid margin¹⁴; (3) baseline TFLLT of ≤ 90 nm (difference between experimental and control eyes ≤ 25 nm), determined by interferometry^{14–17}; (4) fluorescein break-up time (FBUT) of ≤ 10 seconds,^{18–20} determined by the Dry Eye Test (DET)^{21,22}; (5) the Schirmer test, performed with a topical ocular anesthetic,^{15,22} with values of ≤ 10 mm; and (6) no evidence of other ocular pathology.

A questionnaire (Table 1) was used to grade both severity and frequency of four categories of symptoms: dryness; grittiness or scratchiness; soreness or irritation; and burning or watering. Subjects scored the severity of symptoms for each category as: zero for *no problems*, 1 point for *tolerable*, 2 points for *uncomfortable*, 3 points for *bothersome*, and 4 points for *intolerable*. To grade frequency for each category of symptoms experienced subjects were given a score of 1 point for *sometimes*, 2 points for *often*, and 3 points for *constant*. A score of 3 or more for frequency and a score of 3 or more for severity were prerequisites for entrance into the study.

The meibomian gland obstruction criterion for entry into the study was defined by expression of the meibomian glands of the lower eyelid.²³ The central third of the lower eyelid margin was observed with a biomicroscopic magnification $\times 16$ view, and the central 6 meibomian gland orifices were expressed with the examiner’s thumb pressed against the cutaneous surface subjacent to

the lower eyelid margin for 5 seconds to obtain secretion. Meibomian gland obstruction for purposes of meeting the requirements for entry into this study was defined as two or more of the six observed meibomian gland orifices failing to yield any secretion on expression. The quality of the expressed secretion was not considered in the evaluation; the only criterion was whether the gland yielded visible secretion.

Baseline TFLLT was measured using a custom designed specular reflection microscope system and known interference colors of the lipid layer to determine thickness values for the TFLLT, using methods standard in our laboratory.^{14–16} Assigned values of lipid layer thickness were given to specific observed colors based on previous methods.^{14–16}

The tear film FBUT as measured by the DET method^{21,22} was performed three times in each eye. The mean test score was obtained, and values less than 10 seconds met this criterion for entrance into the study. Using methods standard in our clinic and described previously, the Schirmer test was performed in each eye using a topical anesthetic (0.5% proparacaine hydrochloride ophthalmic solution) to prevent reflex tearing.^{15,22} To ensure anesthetic effect, a second drop was instilled after 2 minutes. Excess moisture was wicked with a sterile gauze pad before the Schirmer tear test strips (IOLAB Pharmaceuticals, Claremont, CA) were inserted for the 5 minutes testing period.^{15,22} Measurements of less than 10 mm were required for entrance into the study.

Identical white cotton napkins (50 cm \times 50 cm) were used as compresses applied to the eyelids of each eye. The compresses were saturated with tap water at room temperature ($24.0 \pm 1.0^\circ\text{C}$). Excess water was removed by wringing both cloths with equal pressure; then one compress was heated ($40.0 \pm 2.0^\circ\text{C}$) using a Compact series MW200U microwave (Samsung, Ridgefield Park, NJ). Temperature was determined using a Traceable Big-Digit Hygrometer/Thermometer (Control Company, Friendswood, TX). Left and right eyes were randomized into experimental and control eyes. The compresses were folded in a manner such that they measured approximately 12.5 cm by 12.5 cm and 16 layers thick. Subjects were instructed to place the warm, moist compress over the experimental eye to completely cover the cutaneous surface of the closed eyelids. The room-temperature moist compress was placed over the control eye in an identical manner. Each subject was instructed not to squeeze their closed eyelids and to hold the compresses in place with gentle pressure to minimize the effect of lid closure on the TFLLT.¹⁶

Two new compresses, one heated ($40.0 \pm 2.0^\circ\text{C}$) and the other at room temperature ($24.0 \pm 1.0^\circ\text{C}$), were provided to the subjects every 2 minutes throughout the 30-minute period to ensure maintenance of the constant temperature in each compress covering the eyelids and periocular skin. After 5 minutes, the compresses were removed from the closed eyelids, and the TFLLT was immediately measured and recorded using procedures standard in our laboratory.^{14–16} During the TFLLT measurements, subjects were instructed to blink normally while gazing at a fixation target. The time the compresses were removed from the eyelids did not exceed 60 seconds. After the TFLLT was measured, eyelids were again closed and new compresses were immediately replaced. The TFLLT was remeasured after 15 and 30 minutes of treatment with compresses. The TFLLT was again measured 5 minutes after the compress treatment was terminated.

Data were analyzed for significance at all time points using the paired-data *t*-test to compare each TFLLT measurement to base-

TABLE 2. Questionnaire, FBUT, and Schirmer test data for study participants

Mean questionnaire points ± SD (standard deviation) ^a		Mean FBUT (sec) ± SD ^b	Mean Schirmer test values (mm) ± SD ^c
Severity	Frequency		
4.8 ± 2.1	4.7 ± 1.6	4.9 ± 2.1	6.1 ± 2.2

A score of 3 or more for severity and a score of 3 or more for frequency were prerequisites for entrance into the study.

FBUT (fluorescein break-up time) of ≤ 10 sec using the Dry Eye Test method^{21,22} was required for study entrance criteria.

Schirmer test, with anesthetic,^{15,22} of ≤ 10 mm was required for study entrance criteria.

line after each time interval. A level of $P < 0.01$ was accepted as statistically significant.

RESULTS

Scoring of prerequisite criteria determined subjects' entry into the study (Table 2). Baseline TFLLT, TFLLT after 5 minutes, 15 minutes, and 30 minutes treatment, and TFLLT 5 minutes following the 30-minute treatment period were determined for both experimental and control eyes (Table 3). The mean baseline TFLLT of the experimental eye prior to treatment with a warm, moist compress was 57.8 ± 12.9 (standard error) nm; after 5 minutes of treatment, TFLLT was 105.8 ± 23.7 nm; after 15 minutes of treatment, 117.8 ± 26.4 nm; after 30 minutes of treatment, 121.5 ± 27.1 nm; and after 5 minutes following the 30-minute treatment, 96.0 ± 21.5 nm (Table 3). The mean baseline TFLLT of the control eye prior to treatment with a room-temperature, moist compress was 63.0 ± 14.1 nm; after 5 minutes of treatment, TFLLT was 63.8 ± 14.3 nm; after 15 minutes of treatment, 62.3 ± 13.9 nm; after 30 minutes of treatment, 64.5 ± 14.4 nm; and after 5 minutes following the 30-minute treatment period, 58.5 ± 13.1 nm (Table 3). There was a significant increase in mean TFLLT compared to baseline mean TFLLT after 5 minutes ($P < 0.001$), 15 minutes ($P < 0.001$), 30 minutes ($P < 0.001$) in the experimental eye and 5 minutes following the 30-minute treatment period ($P < 0.001$). In comparison, following the completion of the 30-minute control treatment, there was no significant increase in TFLLT when compared to baseline TFLLT after 5 minutes ($P = 0.79$), 15 minutes ($P = 0.77$), 30 minutes ($P = 0.81$) and after 5 minutes following the 30-minute treatment period ($P = 0.20$).

In summary, mean TFLLT after 5 minutes of treatment with warm, moist compress therapy increased more than 80% from mean baseline TFLLT ($P < 0.001$). After 15 minutes of treatment, mean TFLLT increased only an additional 20% compared to 5 minutes of treatment ($P = 0.1$); and again, after 30 minutes of treatment there was no significant change compared to 15 minutes of treatment ($P = 0.46$). Five minutes after the 30-minute treatment,

the mean TFLLT decreased 26%. In three of the 20 subjects, following warm, moist compress therapy there was no significant increase from baseline TFLLT compared to their contralateral control eye.

DISCUSSION

Meibomian glands secrete lipids to form the lipid layer of the tear film.^{3,24} The major functions of the lipid layer purportedly are to provide a barrier to skin-surface lipid invading the tear film, to prevent tear spillage from the lid margin, to act as an ocular lubricant, and to control water evaporation from the ocular surface.^{3,11,24} When the lipid layer is abnormal, or absent because of abnormal or inspissated meibomian glands,^{3,25} some or all of these functions are compromised, which in turn leads to discomfort and possible dry eye condition. When the tear film lipid layer or the secretory system of the meibomian gland is abnormal, as in MGD, water evaporation from the ocular surface will increase.¹² This response has been observed in the relationship between evaporative keratoconjunctivitis sicca and low or abnormal meibomian phospholipid secretions.^{26,27} Further, it has been demonstrated in the rabbit model that when meibomian gland orifices were obstructed, tear film osmolarity increased²⁸ and TFLLT decreased.²⁹

Secretion from abnormal meibomian glands has been found to have a higher melting point than normal meibomian oil^{10,11}; therefore, abnormal secretions become stagnant along the lid margin. When the temperature surrounding the ocular surface is raised, abnormal meibomian lipids can melt and form the lipid layer of the tear film.¹¹ Therefore, in this study, we attempted to increase the temperature of the meibomian secretion above the normal temperature of the naked eye in order to achieve a temperature range high enough to melt the abnormal lipids in subjects with MGD. Mean ocular surface temperatures from normal subjects have been reported as $31.94 \pm 0.54^\circ\text{C}$, whereas mean ocular surface temperatures from dry eye subjects have been reported as 32.38 ± 0.69 degree C.³⁰

In the subjects studied, the TFLLT in the experimental eye with eyelids covered with a warm ($40.0 \pm 2.0^\circ\text{C}$), moist compress increased significantly more than the control eye covered with a moist compress at room-temperature ($24.0 \pm 1.0^\circ\text{C}$). As such, one can speculate that plugs principally composed of lipid¹ that obstruct the meibomian gland ostia are melted, allowing outflow of meibomian gland excrete. For those three subjects whose TFLLT did not improve from this therapy, the lack of improvement is most likely caused by plugs in their ostia that cannot be melted, meibomian gland dropout, or meibomian gland atrophy.

In a similar study, Goto et al.⁵ studied the effect of 5 minutes of warm compression on tear stability in patients with MGD, demonstrating a decrease in tear evaporation rate and orifice obstruction, and an increase in FBUT. Paugh et al.² reported that after 2 weeks of both warm compress treatment and eyelid scrubs there

TABLE 3. Tear film lipid layer thickness with warm compress versus room-temperature compress at time intervals

	TFLLT (nm) ± S.E.				
	Baseline	After 5 min treatment	After 15 min treatment	After 30 min treatment	after 5 min post-treatment
Warm Compress	57.8 ± 12.9	105.8 ± 23.7	117.8 ± 26.4	121.5 ± 27.1	96.0 ± 21.5
Room-temp Compress	63.0 ± 14.1	63.8 ± 14.3	62.3 ± 13.9	64.5 ± 14.4	58.5 ± 13.1

TFLLT, mean tear film lipid layer thickness; SE, standard error; warm compress, therapy with warm, moist compresses at $40^\circ\text{C} \pm 2.0^\circ\text{C}$; room-temp compress, therapy with moist compress at room temperature, $24^\circ\text{C} \pm 1.0^\circ\text{C}$.

was a significant mean increase in tear film FBUT of 4 seconds in treated eyes compared to mean increase in tear film FBUT of 0.2 seconds in control eyes. However, the relative contributions to the increase of FBUT resulting from warm compresses and lid scrubs were not part of the study. And, although it was recently reported that FBUT is directly related to TFLLT,¹⁵ the present study demonstrates that 5 minutes of warm, moist compress therapy increases TFLLT, and continues for 15 minutes, with a lesser increase after 30 minutes (Table 3).

The temperature of the warm, moist compresses decreased over the 2-minute time intervals. However, the compresses still maintained a temperature of $\geq 38^{\circ}\text{C}$ at the end of each 2-minute period, at which time both the heated and room-temperature compresses were changed. If the time interval had been greater than 2 minutes, the temperature of the warm compresses could have fallen below 38°C , a level thought not to be therapeutically effective in improving meibomian gland function. Moreover, the temperature in the superficial layers of the compress exposed to the humidity and temperature-controlled environment of the study room decreased more rapidly than the inner layers of the multilayered compresses. The folded (multilayered) configuration of the compress increased its capacity to maintain its temperature. Other methods reported for heating the warm compress to maintain warm temperatures for longer periods include using a hard boiled egg,⁶ a Re-Heater⁶ (Re-Heater, Inc, Lomita, CA), or an infrared heater⁴ that use dry heat rather than the moist heat described in the present study. Since moist heat is commonly recommended,^{1,2,5} moist rather than dry compresses were used in the present study. Among possible reasons for moist compresses being recommended over dry compresses is that a moist compress creates a more uniform contact with the surface of the skin and more efficiently transmits the heat to the periocular skin. Also, because dry heat will desiccate the skin, moist heat functions as a humectant and will help maintain the hydration status of the delicate periocular skin.

In conclusion, warm, moist compresses applied to the closed eyelids increases TFLLT for subjects with TFLLT ≤ 90 nm, the apparent result of increasing lipid secretion. Thickening the tear film lipid layer appears to be the reason for the increase in FBUT that has been reported following warm moist, compress therapy.^{2,5} This may be especially important in patients who wear contact lenses because blinking may be inhibited,³¹⁻³³ and there is often incomplete eyelid closure, which has been observed to increase meibomian gland inspissation¹⁴ and MGD.²³ Thus, this therapy can provide an effective method to improve and maintain the function of meibomian glands in contact lens wearers, ultimately improving oil secretion, thereby improving contact lens wearing tolerance. This study supports both the universal use and previous reports of warm, moist compress therapy of the eyelids as an effective treatment for dry eye states and meibomian gland dysfunction.

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