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Effect of the Bruder moist heat eye compress on contact lens discomfort in contact lens wearers: An open-label randomized clinical trial

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ABSTRACT

The purpose of this study was to investigate the effect of the Bruder Moist Heat Compress on contact lens (CL) discomfort in subjects with contact lens-related dry eye (CLDE). This was a 4-week, single-center, three-arm, randomized, open-label clinical trial in subjects diagnosed with CLDE using the Contact Lens Dry Eye Questionnaire. Fifty-one CL wearers were randomized to one of three treatment groups: application of the Bruder Compress twice a day, Bruder Compress once a day, or warm washcloth used for ten minutes twice a day without reheating. Subject diaries were monitored for compliance and collected data on daily CL comfort upon awakening and throughout the afternoon. Clinical assessments included tear film break-up time (TBUT), lipid layer thickness (LLT), and meibomian gland evaluation. Statistical tests included a generalized linear model and one-way analysis of variance (ANOVA) to investigate treatment effect on comfortable wear time.

Fifty-one subjects (98% female) completed the study. After treatment, subjects using a washcloth reported more uncomfortable contact lens wear time on average (mean = 5.1 ± 2.8 h) when compared with subjects who had used the Bruder Compress in Group 1 (mean = 2.8 ± 1.6 h) ($p = 0.02$). In the Bruder Compress groups, there was a significant reduction in the blockage of meibomian glands ($p < 0.01$). No significant difference in uncomfortable wear time was found between subjects using the Bruder Compress twice daily versus once daily ($p = 0.48$). Subjects using the Bruder Compress once daily had the highest rate of compliance at 90.2% ($p < 0.01$). No significant improvements were observed in TBUT ($p = 0.76$) or LLT ($p = 0.78$).

The Bruder Moist Heat Compress resulted in a significant improvement in comfortable CL wear time in subjects with CLDE.

1. Introduction

An estimated 40.9 million people in the United States aged 18 or older wear contact lenses [1]. Though newer and healthier contact lens materials have been developed, discomfort remains the top reason for contact lens discontinuation and dropout rates are estimated to be as high as 15.9% in the United States [2]. The International Workshop on Contact Lens Discomfort published in 2013 concluded from a thorough review of the literature that discomfort and dryness are the primary reasons for contact lens intolerance [3]. Indeed, when a contact lens is placed on the eye, the tear film is split into pre- and post-lens tear films. As a result of this disruption from the contact lens, the tear film tends to have an increased rate of evaporation which is accompanied by poor wetting on the surface of the contact lens and inadequate lubrication on the surface of the eye [4,5]. This is further exacerbated if the patient has an already unstable lipid layer due to the presence of meibomian gland dysfunction (MGD) [6,7]. MGD is considered by many to be the leading cause of dry eye disease throughout the world, and is a chronic and progressive condition that can contribute to a poor quality lipid layer and contact lens discomfort [8,9].

Contact lens wearers often report dry eye symptoms and show signs of MGD including gland atrophy, thinned lipid layer, and increased tear film instability [7,10,11]. Korb and Henriquez found evidence of MGD in 36.6% of symptomatic contact lens wearers [9]. Another study by Ong and Larke that enrolled both contact lens wearers and controls found MGD in 30% of the contact lens wearers compared to only 20% of

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controls [12]. Consequently, treatment of MGD may support functioning of the meibomian glands and lead to improvement in patient contact lens comfort. Warm compresses are a commonly prescribed treatment method for applying localized heat to the meibomian glands to improve secretion [13–15]. With good patient compliance, warm compresses have been shown to be an adequate supplemental therapy for MGD as the heat softens meibum in glands allowing for secretion from the gland orifice. A study by Olson et al. demonstrated that a warm compress applied to the eyelids increased tear lipid layer thickness by increasing meibum secretion from the glands [15]. Due to the disruption to the tear film and lipid layer that results from a contact lens on the surface of the eye, it was hypothesized that applying a warm compress to the eyelids to improve functioning of the meibomian glands would result in increased meibum secretion and improve comfortable contact lens wear time. Therefore, the purpose of this study was to assess the potential benefits of using the Bruder Moist Heat Eye Compress (Bruder Healthcare Company; Alpharetta, GA, USA), a warm compress capable of maintaining a stable heat profile, in contact lens wearers with contact lens-related dry eye (CLDE) [16].

2. Methods

This study was a single-center, randomized, open-label, unmasked clinical trial of the effect of the Bruder Moist Heat Compress compared to a warm washcloth in subjects with CLDE. This research was conducted in accordance with the Declaration of Helsinki with Institutional Review Board approval at the University of Alabama at Birmingham. The study was registered at ClinicalTrials.gov under the registry number NCT02848222. Informed consent was obtained from all subjects after explanation of the purpose of the study and the procedures involved before any study procedures were performed.

Subjects were recruited through a recruitment database as well as advertisements and were included if they were at least 18 years of age. In addition, subjects were included in the study if they had a positive diagnosis of CLDE based on their responses to the Contact Lens Dry Eye Questionnaire long form (CLDEQ) [17] and reported at least a two-hour difference between their average overall daily wear time and average comfortable daily wear time of contact lenses. All subjects were required to have self-reported use of soft daily contact lenses at least four days a week for a total average wear time of at least four hours a day. The subject must have been wearing the same type of reusable soft contact lenses, brand, and material for at least 30 days before screening, which were verified by the clinical examiner to ensure that the contact lens fit, material, and disinfecting solution were not the reason for contact lens discomfort. Subjects were excluded if they showed evidence of an ongoing ocular infection, disease, or abnormality requiring the use of prescription ophthalmic medications. Additional exclusion criteria included pregnancy by self-report, uncontrolled systemic disease that could interfere with the study especially those associated with dry eye disease, severe eyelid inflammation, any previous history of refractive or corneal surgery, and initiated or altered dosage of omega-3 dietary supplements 30 days prior to screening. Subjects were also excluded if they had cauterization of the puncta or had temporary and/or permanent punctal plugs. Any overnight wear of contact lenses or usage of daily disposable contact lenses also excluded subjects from participating in the study.

2.1. Study visits

Demographic data, ocular and non-ocular medical history, and concomitant medications were recorded. The Standard Patient Evaluation of Eye Dryness (SPEED), Ocular Surface Disease Index (OSDI), and CLDEQ questionnaires were administered at every visit [17–19]. Habitual high contrast distance logMAR acuity was obtained with habitual contact lenses. Subjects were asked to estimate the average number of hours of comfortable contact lens wear time and the average total hours of contact lens wear per day over the previous two weeks. The LipiView II (TearScience; Morrisville, NC, USA) was used to record the thickness of the tear lipid layer over the contact lenses; both the average and minimum lipid layer thicknesses were recorded [20]. The contact lens fit was assessed for centration, coverage, and movement. An unacceptable contact lens fit was determined if there was corneal exposure in at least one quadrant in either eye, and/or no movement or excessive (>1.0 mm) movement of the contact lens. Clinical judgement was used to determine if the material (i.e. wear of an older or discontinued hydrogel material) or disinfecting solution (i.e. use of saline instead of a multipurpose cleaning solution) was the reason for discomfort. After determination of appropriately fitting lenses, the subjects were then instructed to remove their contact lenses, and slit lamp biomicroscopy and external eye examinations were performed. Meibomian glands in the lower eyelid were assessed for quality of meibum expressed using a meibomian gland evaluator device. [21]. Expression was assessed in five glands per region of the eyelid including temporal, central, and nasal after holding the expresser against the lower eyelid for fifteen seconds. Meibum was scored on a scale from 0 to 3 where 0 indicated clear oil expressed, 1 indicated cloudy oil, 2 indicated toothpaste-like oil, and 3 indicated no secretion from the gland. Sodium fluorescein was instilled in the eyes (0.6 mg embedded strips wetted with saline) for tear film break up and corneal staining on each eye. The average time of three tear film break up measurements was used in the analysis. Staining was graded according to the Efron Scale thirty seconds to 2.5 min after instillation of fluorescein [22]. Lid wiper epitheliopathy was assessed using two instillations of lissamine green based on the method described by Varikooty et al. [23]. Briefly, lissamine green was instilled using two strips wetted and instilled followed by another instillation of two strips separated by one minute [23]. The upper eyelid of each eye was everted and lid wiper staining was graded based on horizontal length and sagittal height of staining three minutes after the second instillation [24]. Corneal topography images were obtained using the Keratograph 5 M (Oculus, Inc.; Arlington, WA, USA) at baseline and Visit 3. Keratometry values obtained from corneal topography were compared within-subjects from baseline to Visit 3 to determine if any corneal warpage had occurred from warm compress application [25].

Eligible subjects were randomized into either Group 1, 2, or 3. Group 1 subjects were required to use the Bruder Moist Heat Compress twice daily (morning and evening) whereas Group 2 subjects used the Bruder Moist Heat Compress once daily in the evening only. Subjects in Group 3 were required to use a warm washcloth twice daily. Subjects in Group 1 and Group 2 were instructed to heat the Bruder Moist Heat Compress in the microwave for twenty seconds until warm to the touch but not scalding hot (per manufacturer's recommendations). Subjects were allowed to increase the amount of time in the microwave in five second intervals depending on microwave wattage until the compress was warm to the touch; however, total microwave time could not exceed thirty seconds. Subjects were instructed to test the temperature of the compress by touching it to the inside wrist and/or cheek. Subjects were told to wait twenty to thirty seconds if the compress felt too hot to the touch and to wait until the temperature was comfortable before applying to closed eyes. The compress was then applied for ten minutes with eyes closed without contact lenses. Subjects in Group 3 were provided with two standard washcloths and instructed to warm the washcloth under hot faucet water for at least twenty-five seconds to ensure thorough soaking and heating of the cloth until warm to the touch. Subjects in Group 3 were told to test the temperature of the compress to the inside wrist and/or cheek, and to wait twenty to thirty seconds before applying if the temperature was too hot. They were told to then squeeze the excess water out of the cloth, fold into thirds, and lay the cloth over closed eyes without contact lenses for ten minutes without reheating. All subjects were instructed to use a cell phone timer to ensure the compress was applied for ten minutes and required to record the start and end time for application of the compress in a diary.

In addition, subjects recorded an Eye Discomfort Assessment in a modified Symptom Assessment in Dry Eye (SANDE) format using a 1-item severity visual analog scale [26,27]. They were instructed to indicate the severity of their eye discomfort upon awakening in the morning and prior to application of the compress. In the evening, subjects recorded severity of eye discomfort throughout the afternoon, prior to application of the compress. Severity was marked by placing a vertical line across a 100 mm horizontal line that ranged from "very mild" to "very severe."

Subjects were scheduled to return for Visit 2 at 15 ± 2 days and then for Visit 3 at 30 ± 2 days post-baseline, respectively. Attempts were made to schedule Visit 2 and Visit 3 at the same time of day as Visit 1 for each subject; however, scheduling efforts focused primarily on keeping subjects within window based on their availability. The primary purpose of Visit 2 was to review diary data and ensure subject compliance. Outcome measures were primarily assessed comparing data collected at Visit 3 to baseline visit. At subsequent visits, in addition to clinical assessments with a slit lamp biomicroscope, concomitant medication usage was updated, and an adverse event query was performed. Diaries were reviewed to monitor that the compress was being applied daily or twice daily; instructions for applying the compress once or twice daily were reiterated to each subject at Visit 2.

2.2. Statistical analyses

2.2.1. Sample size

Sample size was determined to obtain 80% power with a significance level set at $\alpha = 0.05$ and 3 groups, with an effect size of 0.6. Calculations revealed 17 subjects were needed to be enrolled per group.

2.2.2. Endpoints

The primary efficacy endpoint for this study was the mean change from baseline in the duration of subject-reported uncomfortable contact lens daily wear time (hours per day) at Visit 3. The secondary endpoint for this study was the mean change from baseline in uncomfortable contact lens wear time (hours per day) in twice daily application group compared to once daily application group at Visit 3. The tertiary endpoint was the mean change in total meibomian gland score in treatment groups using the Bruder Moist Heat Compress compared to controls in the washcloth group from baseline to Visit 3.

2.2.3. Methods of analysis for endpoints

Descriptive statistics were performed and differences in groups at baseline were analyzed using the Kruskal-Wallis test and the Chi-squared test for categorical variables. Statistical testing of the primary endpoint was performed using a generalized linear model (GLM) with treatment and baseline as main effects while controlling for difference in uncomfortable wear time at baseline and daily hours of contact lens wear time. For the secondary endpoint, a one-way analysis of variance (ANOVA) was used to compare the mean hours of uncomfortable contact lens wear time at Visit 3. Post-hoc comparisons were performed using the Tukey test. For the tertiary endpoint, an exact McNemar's test was used to investigate statistically significant differences in the proportion of meibomian glands scored for meibum quality as zero or one (clear or cloudy) and as two or three (inspissated or obstructed).

To determine the decrease in daily uncomfortable wear time, the hours of uncomfortable wear time at baseline was subtracted from the hours of uncomfortable wear time at Visit 3. The decrease in daily uncomfortable wear time was compared in two scenarios; 1) across all three groups and 2) after combining Groups 1 and 2 to compare the overall decrease in subjects using the Bruder Moist Heat Compress to those using a washcloth. The percent improvement for each subject was calculated from baseline to Visit 3 which was then averaged for each group and compared.

2.2.4. Methods of analysis for clinical and diary data

For the clinical assessments including meibomian gland score, tear film breakup, lipid layer thickness, and questionnaire scores (OSDI and SPEED), a difference score was calculated to compare change from baseline to Visit 3. Only data collected from the right eyes was used in the analysis using the Kruskal-Wallis test [28]. Additional efficacy endpoints from the Eye Discomfort Assessment data captured from subject diaries included daily subject recordings of eye discomfort severity in the mornings, prior to applying a warm compress and in the evenings as an average of eye discomfort experienced throughout the afternoon prior to application of a compress. Data was plotted and fitted with regression lines to investigate changes in recorded eye discomfort from baseline to Visit 3.

All of the statistical analyses were completed in the Statistical Package for Social Science (SPSS) 22 (IBM; Armonk, NY, USA) and GraphPad Prism 7.02 (GraphPad; La Jolla, CA, USA); $p < 0.05$ was considered statistically significant.

3. Results

Sixty subjects were enrolled and randomized in the study; however, fifty-one subjects completed the study and were included in the data analyses. Seven subjects withdrew from the study due to personal issues, one was withdrawn due to poor compliance, and one was lost to follow up. This left seventeen subjects in Group 1 (using the Bruder Moist Heat Compress once a day), seventeen subjects in Group 2 (using the Bruder Moist Heat Compress twice a day), and seventeen subjects in Group 3 (using a warm washcloth twice a day). The demographics for all subjects enrolled are listed in Table 1. The majority of subjects enrolled (98%) were female. There were no statistically significant differences between groups for average age ($p = 0.26$), sex ($p = 0.36$), race ($p = 0.54$), and ethnicity ($p = 0.35$). The contact lens wear parameters and ocular surface characteristics of the study population for each group at baseline are listed in Table 2. While there was not a statistically significant difference in total contact lens wear time and comfortable contact lens wear time across groups at baseline ($p = 0.29$ and $p = 0.15$, respectively), there was a statistically significant difference in uncomfortable contact lens wear time ($p = 0.03$). Post-hoc Tukey analysis indicated a higher average of uncomfortable contact lens wear time in Group 3 (mean = 6.8, SD = 3.4) when compared to Group 1 (mean = 4.2, SD = 1.8) ($p = 0.02$). The only significant difference between ocular surface characteristics of groups at baseline was

Table 1
Demographics of the study population for each group at baseline.

	Group 1 Bruder Compress 2x daily n = 17	Group 2 Bruder Compress 1x daily n = 17	Group 3 Wash cloth 2x daily n = 17	p - value
Demographics				
Mean age (years) ± SD	32 ± 8	32 ± 12	36 ± 11	p = 0.26
Age range (min, max)	(24, 53)	(22, 63)	(19, 57)	
Sex				
Male, n	1	0	0	p = 0.36
Female, n	16	17	17	
Race				
Asian, n	2	1	2	p = 0.54
Native Hawaiian or Pacific Islander, n	0	2	0	
Caucasian, n	10	8	8	
African American, n	5	6	7	
Ethnicity				
Hispanic or Latino, n	0	2	1	p = 0.35
Non-Hispanic or Non-Latino, n	17	15	16	

Table 2
Dry eye and contact lens characteristics of the study population for each group at baseline.

	Group 1 Bruder Compress 2x daily n = 17	Group 2 Bruder Compress 1x daily n = 17	Group 3 Washcloth 2x daily n = 17	p - value
Questionnaire Scores, mean ± SD				
SPEED	10.4 ± 4.0	13.1 ± 4.3	11.5 ± 4.8	p = 0.22
OSDI	22.9 ± 11.9	33.8 ± 17.3	27.1 ± 18.4	p = 0.15
CLDEQ	1.1 ± 0.8	1.4 ± 0.7	1.5 ± 0.9	p = 0.36
Contact Lens Wear (CLW)				
Duration of CLW (years)	16.0 ± 6.9	14.5 ± 7.9	13.6 ± 8.8	p = 0.69
Weekly Time of CLW (days)	6.2 ± 1.1	6.4 ± 1.1	6.6 ± 0.9	p = 0.51
Daily Time of CLW (hours)	12.0 ± 2.5	13.5 ± 3.0	12.7 ± 2.9	p = 0.29
Comfortable CLW Time (hours)	7.8 ± 3.0	8.0 ± 3.9	5.9 ± 3.2	p = 0.15
Uncomfortable CLW Time (hours)	4.2 ± 1.8	5.5 ± 2.7	6.8 ± 3.4	p = 0.03
Ocular Surface Characteristics (right eye)				
Lipid Layer Thickness (nanometers)				
Average	57.1 ± 19.2	57.9 ± 21.4	60.3 ± 23.9	p = 0.90
Minimum	46.7 ± 17.5	48.6 ± 21.8	52.2 ± 24.0	p = 0.75
Tear Film Break Up Average (seconds)	7.4 ± 3.8	6.8 ± 2.8	7.6 ± 4.2	p = 0.80
Meibomian Gland Score	36.9 ± 6.9	28.4 ± 11.2	33.7 ± 5.4	p = 0.01

in the average meibomian gland scores between Group 1 (mean = 36.9, SD = 6.9) and Group 2 (mean = 28.4, SD = 11.2) (p = 0.01). Subjects in Group 2 had the highest average rate of compliance (mean = 90.2%, SD = 9.9) when compared to Group 1 (mean = 86.0%, SD = 15.0) and Group 3 (mean = 79.6%, SD = 5.8) (p < 0.01).

3.1. Contact lens wear time and comfort

A one-way ANOVA was used to compare the mean total number of hours of contact lens wear at baseline and Visit 3 across all three groups. No statistically significant differences in total wear time across groups were found at Visit 1 ($F(2,48) = 1.3$, $p = 0.29$) and Visit 3 ($F(2,48) = 0.06$, $p = 0.94$). Uncomfortable hours of contact lens wear time for all subjects was calculated as the difference in total contact lens wear time and comfortable contact lens wear time. When comparing the difference in uncomfortable wear time at Visit 3 between Group 1 and Group 2, there was not a statistically significant difference in those who used the Bruder Moist Heat Compress twice a day (Group 1) versus once a day (Group 2) ($t = -0.72$, $p = 0.48$). Using a GLM and collapsing Groups 1 and 2 to investigate the effect of the Bruder Moist Heat Compress since there were no differences, the uncomfortable contact lens wear time reported at Visit 3 by subjects using the Bruder Moist Heat Compress was compared to those in Group 3 (washcloth). The mean number of hours of uncomfortable lens wear was summarized for those using the Bruder Moist Heat Compress (Groups 1 and 2) and those using the washcloth (Group 3) for each time point. Using a GLM and controlling for the difference in comfortable wear time at baseline and daily hours of contact lens wear time, the ability of the group to predict comfortable wear time after treatment was significant (Wald Chi-Square = 4.2, $p = 0.04$).

A one-way ANOVA was used to compare the mean number of hours of uncomfortable lens wear at Visit 3 across all three groups. At baseline, the average hours of uncomfortable contact lens wear times were 4.2 ± 1.8 for Group 1, 5.5 ± 2.7 for Group 2, and 6.8 ± 3.4 for Group 3. At Visit 3, the average hours of uncomfortable contact lens wear time were 2.8 ± 1.6, 3.3 ± 2.4, and 5.1 ± 2.8 for Groups 1, 2, and 3 respectively. The average decrease in hours of uncomfortable wear time from baseline to Visit 3 was 1.4 ± 1.5 for Group 1, 2.2 ± 3.2 for Group 2, and 1.8 ± 2.5 for Group 3 (Fig. 1). At Visit 3, subjects who had used the warm washcloth had more uncomfortable contact lens wear time on average (mean = 5.1 ± 2.8 h) when compared to subjects who had used the Bruder Moist Heat Compress in Group 1 (mean = 2.8 ± 1.6 h) (p = 0.02) (Table 3). When combining Groups 1 and 2 to determine the average improvement in comfortable wear time in all subjects using the Bruder Moist Heat Compress, the average improvement was 1.8 ± 2.5 h or an 11.6 ± 0.2% increase in comfortable lens wear time.

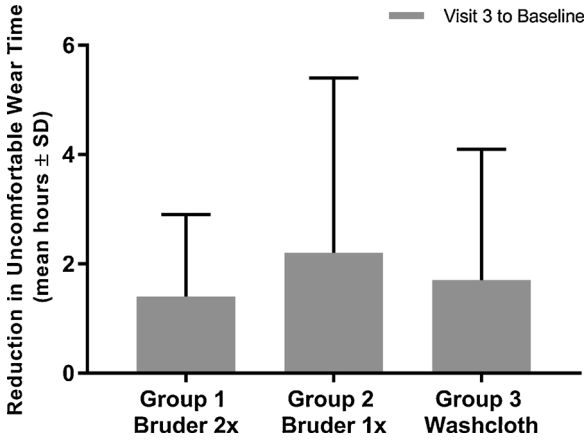

Fig. 1. Reduction in Uncomfortable Wear Time. Total daily contact lens wear time and comfortable contact lens wear time in hours were reported by the subjects at baseline and Visit 3. Uncomfortable wear time in hours was calculated as a difference between total daily wear time and comfortable wear time. The reduction in uncomfortable wear time was calculated as change from baseline at Visit 3 for each treatment group.

Table 3
Effect of treatment on comfortable wear time.

	Uncomfortable Wear Time (hours)		Total Increase in Comfort (hours)
	Baseline (mean ± SD)	Visit 3 (mean ± SD)	
Bruder Compress 2x Daily Group (n = 17)	4.2 ± 1.8	2.8 ± 1.6	1.4
Bruder Compress 1x Daily Group (n = 17)	5.5 ± 2.7	3.3 ± 2.4	2.2
Washcloth Group (n = 17)	6.8 ± 3.4	5.1 ± 2.8	1.7

Comfort was also assessed from daily subject-reported Eye Discomfort level assessments using a diary. Average compliance was calculated for each group based on the expected number of compress application during the 4-week study period. The average compliance for using the Bruder Moist Heat Compress twice daily was 86.0%,

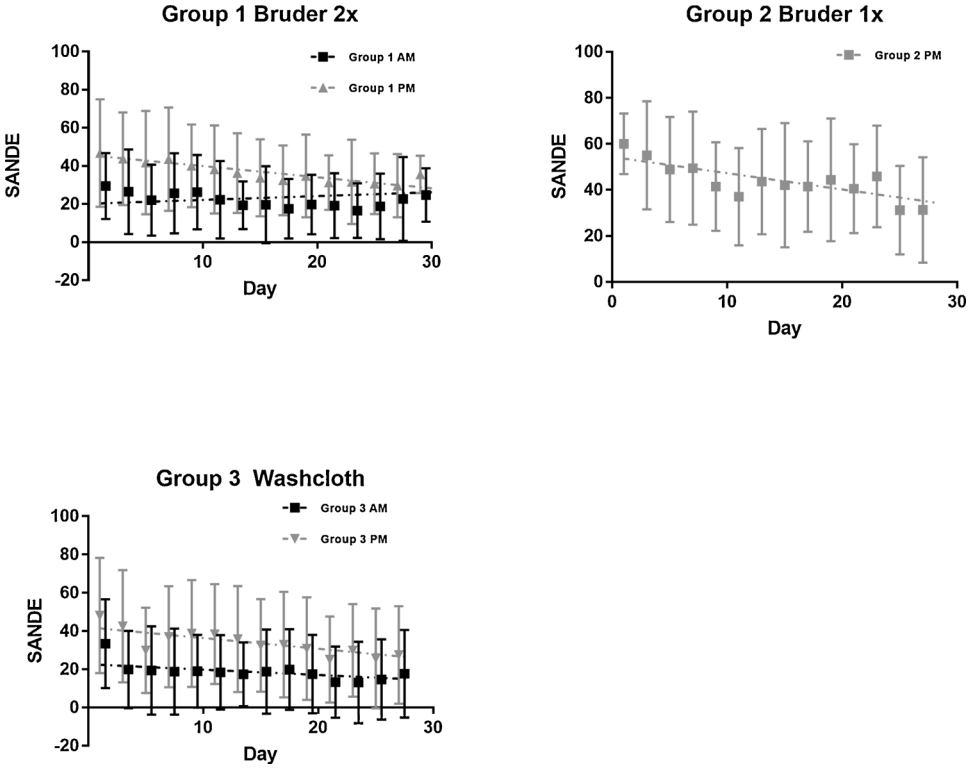

Fig. 2. Subject Diary Data. Subjects recorded a daily eye discomfort assessment using a severity visual analog scale from 0 to 100 mm (SANDE). All subjects were instructed to indicate the severity of eye discomfort throughout the afternoon prior to applying the compress in the evening. Subjects in Groups 1 and 3 also reported on severity of eye discomfort immediately upon awakening prior to application of the compress. Shown here are three graphs representing average SANDE score over the thirty-day time period for each group. Each data point represents the average SANDE score for all subjects in a group at a particular time point with error bars representing the standard deviation for the mean. Linear regression lines (dashed lines in the graphs) were plotted to investigate significant reductions in eye discomfort severity levels reported by subjects.

whereas once daily was 90.2%, and for the warm washcloth twice daily it was 79.6% ($F(2,48) = 4.05$, $p = 0.02$). The diary data for each group showed that for subjects using the Bruder Moist Heat Compress (Groups 1 and 2); there was a trend for a reduction in score over time. The slope of the regression line was statistically different from zero for Group 1 in the afternoon ($F(1,32) = 73.2$, $m = -0.58$, $p < 0.01$) as well as for Group 2 in the afternoon ($F(1,26) = 42.0$, $m = -0.71$, $p < 0.01$) (Fig. 2). For Group 1 morning assessments, the slope of the regression line was not statistically different from zero ($F(1,33) = 3.4$, $m = 0.2$, $p = 0.08$). There was a steeper decline in the Eye Discomfort Assessment scores for subjects using the Bruder Moist Heat Compress compared to those using the washcloth ($p < 0.01$). For those in the washcloth group (Group 3), both the morning ($F(1,26) = 18.4$, $p < 0.01$) and afternoon ($F(1,26) = 61.6$, $p < 0.01$) scores improved slightly (Fig. 2).

3.2. Ocular surface characteristics

To investigate changes in ocular surface characteristics over time, difference scores were calculated by subtracting Visit 3 scores from baseline scores. The meibomian gland grading scores for the meibomian glands in the lower eyelid of the right eye were added for a total meibomian gland score. A higher score was indicative of more gland obstruction or expressing cloudy or toothpaste-like meibum. The average improvement in meibomian gland score for the Bruder Moist Heat Compress 2x daily group was 5.7 ± 10.8 whereas it was only 1.2 ± 7.5 in the washcloth group ($p = 0.27$) (Table 4), which was not statistically significant. To investigate improvement in individual meibomian gland meibum quality scores, the percentage of glands scored as a zero or one and as a two or three was examined across groups before and after treatment. The percentage of glands scored as zero or one at baseline was 21.2%, 40.8%, and 30.2% for Groups 1, 2, and 3 respectively. After treatment, the percentage of glands scored zero or one increased to 35.7%, 47.5%, and 31.0% respectively for Groups 1, 2, and 3 (Fig. 3A). The percentage of glands scored as two or three at baseline was 78.8%, 59.2%, and 69.8% for Groups 1, 2, and 3 respectively. After treatment, the percentage of glands scored as two or three was 64.3%, 52.5%, and 69.0% for Groups 1, 2, and 3 respectively (Fig. 3B). An exact McNemar's test determined that there was a statistically significant difference in the proportion of glands scored as zero or one before and after treatment for subjects in Group 1 and 2 ($p < 0.01$). There was not a statistically significant difference in the proportion of glands scored as zero or one before and after treatment for Group 3 ($p = 0.50$).

As shown in Table 4, there were no statistically significant changes in tear film breakup time, lipid layer thickness average and minimum, SPEED, and OSDI scores ($p = 0.76$, $p = 0.78$, $p = 0.32$, $p = 0.26$, $p = 0.20$ respectively). While not statistically significant when looking at each of the groups, there was a clinically significant trend in reduction of symptom scores on the SPEED and OSDI questionnaires (Table 4). However, overall for all subjects that completed the study, the average SPEED score improved from baseline (mean = 11.7, SD = 4.4) to Visit 3 (mean = 7.6, SD = 5.2) which was statistically and clinically significant ($p < 0.01$). Similarly, average OSDI score improved from baseline (mean = 28.0, SD = 16.4) to Visit 3 (mean = 16.7, SD = 13.6) which was also statistically and clinically significant ($p < 0.01$).

3.3. Safety

There were no clinically significant changes from baseline observed in logMAR habitual visual acuity measurements nor any statistically significant changes in corneal topography measurements from baseline to the final visit. There were no adverse events related to the device that were encountered throughout the study.

4. Discussion

Due to the disruption that occurs to the tear film and lipid layer during contact lens wear, it was hypothesized that a warm compress applied to the eyelids could facilitate lipid secretion, stabilize the tear film, and be effective in treating contact lens dry eye and discomfort.

Table 4
Effects of treatment on ocular surface characteristics and questionnaire scores.

	Bruder Compress 2x Daily	Bruder Compress 1x Daily	Washcloth Group	p - value
Difference Parameter Baseline to Visit 3, mean ± SD				
Difference in Meibomian Gland Score	−5.7 ± 10.8	−1.0 ± 9.6	−1.2 ± 7.5	p = 0.27
Difference in Tear Film Breakup (seconds)	0.05 ± 4.0	−0.2 ± 2.7	−0.9 ± 4.3	p = 0.76
Difference in Lipid Layer Thickness Average (nanometers)	1.1 ± 18.6	1.4 ± 21.7	−3.3 ± 23.0	p = 0.78
Difference in Lipid Layer Thickness Minimum (nanometers)	0.2 ± 14.4	−0.8 ± 17.3	−8.3 ± 19.8	p = 0.32
Difference in SPEED Questionnaire Score	−3.7 ± 2.7	−5.6 ± 6.5	−2.8 ± 5.4	p = 0.26
Difference in OSDI Questionnaire Score	−8.9 ± 8.3	−16.3 ± 17.7	−8.5 ± 14.5	p = 0.20
Difference in CLDEQ Score	−0.2 ± 0.7	−0.5 ± 0.8	−0.2 ± 1.2	p = 0.57

Note: negative mean value indicates reduction in score from baseline to final visit SPEED = Standardized Patient Evaluation of Eye Dryness; OSDI = Ocular Surface Disease Index; CLDEQ = Contact Lens Dry Eye Questionnaire.

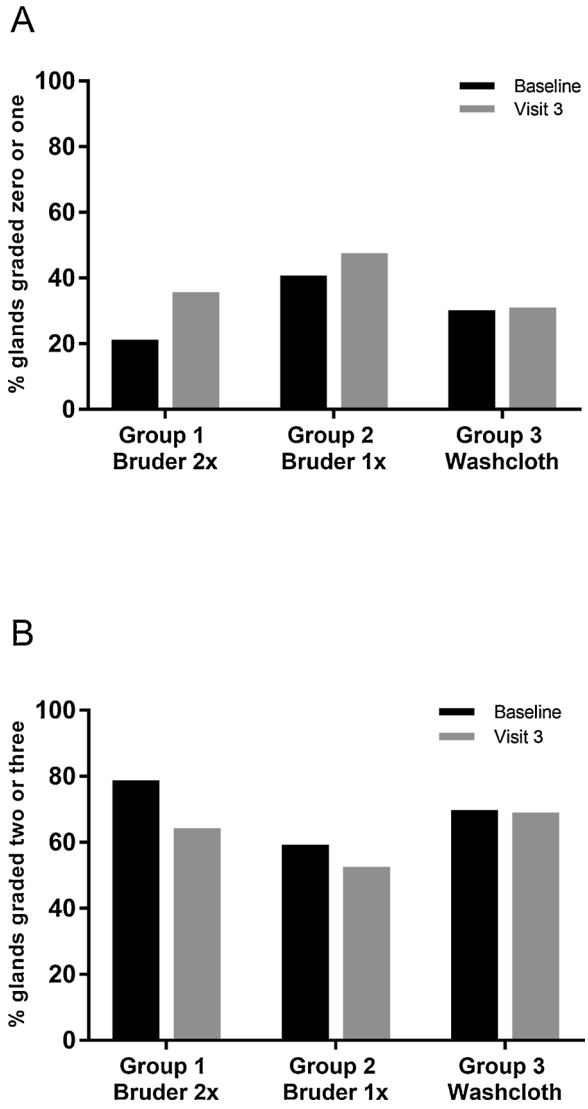

Fig. 3. Meibum Quality Scores. Percentage of all fifteen glands evaluated in the lower lid for meibum quality that were graded as clear or cloudy liquid (grade 0 or 1) or as inspissated or obstructed (grade 2 or 3). (A) Percentage of glands graded 0 or 1 per group before and after treatment. (B) Percentage of glands graded 2 or 3 per group before and after treatment.

This study investigated whether application of a commercially available moist heat compress, the Bruder Moist Heat Eye Compress, led to improvement in comfortable contact lens wear time in subjects classified as having contact lens dry eye. The results show an average improvement in daily comfortable wear time of 1.8 h in subjects who used a Bruder Moist Heat Compress either once or twice daily over a one-month period. There was not a statistically significant difference between subjects who applied the Bruder Moist Heat Compress once or twice daily. While on average, there was a clinically significant improvement in meibomian gland score in subjects who applied the Bruder Moist Heat Compress twice daily, the differences were not statistically significant across groups and when compared to subjects who used a warm wet washcloth. There was a significant improvement in the number of glands secreting clear/cloudy meibum (grade zero or one) indicating the MGs shifted from a greater degree of blockage (grade two or three) to a lesser degree in the Bruder Moist Heat Compress groups. This was not observed in subjects applying a warm washcloth.

Warm compresses are a mainstay clinical therapy for MGD [15]. The goal of this therapy is to apply heat to the eyelids to melt the altered meibum lipids and improve secretion from the glands. The optimum heat to achieve therapeutic effectiveness is around 104 °F or greater than 40 °C [29]. The challenge in applying heat to the eyelids is to ensure an effective level of heat is being applied without causing thermal injury to the ocular surface [25]. A variety of warming methods exist including using a warm wet washcloth, heated rice bag, or a commercially made compress such as a beaded mask that have varying levels of effectiveness [30]. Previous studies have shown the Bruder Moist Heat Compress capable of warming the eyelids to the therapeutic temperature required [30]. Moreover, due to its design, the Bruder Moist Heat Compress maintains a high level of heat throughout a ten-minute application period whereas the warm washcloth loses heat rapidly and needs reheating every two minutes during treatment [16,29]. This likely reduces patient compliance with the warm washcloth due to its laborious nature. This study utilized a daily diary, and subjects were instructed to record the start and end time for application of the compress. As expected, subjects randomized to apply a warm wet washcloth to the eyelids had the lowest compliance rate (79.6%) whereas those applying the Bruder Moist Heat Compress once daily had the highest compliance rate (90.2%).

Contact lens discomfort is most frequently reported to occur towards the end of the day, during the late afternoon and evening [31–33]. In this study, all subjects used a SANDE severity scale to record daily eye discomfort experienced throughout the afternoon. Those who applied a compress twice daily also reported on eye discomfort immediately upon awakening. While the average eye discomfort severity in the afternoon decreased for all subjects, this decline was greatest for subjects who applied the Bruder Moist Heat Compress once a day. Subjects in this group had higher compliance for application of the compress which may contribute to this effect.

The results of this study did not show a statistically significant improvement in meibomian gland score, fluorescein tear film breakup time, or tear film lipid layer thickness over the contact lens. While there are studies in the literature that have investigated the effect of warm compress treatment on these parameters in subjects with MGD, there are a lack of longitudinal studies in contact lens wearers classified as having contact lens related dry eye investigating these parameters

[34–37]. A study by Arita et al. evaluated the effects of eyelid warming in ten patients with obstructive MGD. Subjects applied a warming compress twice daily for five minutes and results showed a statistically significant increase in tear film break up time [34]. Another study by Turnbull et al. investigated tear film quality of three different therapies for MGD including warm compress in patients with meibomian gland dropout [35]. They noted an improvement in non-invasive tear break up time but no statistically significant improvements. Subjects in the current study were not enrolled based on the absence or presence of MGD. In addition, the majority of these studies had subjects applying warm compresses in office with ocular surface parameters measured by examiners immediately after ten minutes of application. Since subjects were scheduled throughout the day in this study, the gap in time between application of the warm compress and the study visit may explain the lack of statistically significant improvements in ocular surface parameters. Moreover, average baseline clinical parameters of all subjects in this study including lipid layer thickness over the contact lens (mean = 58.4, SD = 21.2 nm), tear film break up (mean = 7.3, SD = 3.6 s), and meibomian gland score (mean = 32.9, SD = 8.8) were not indicative of severe ocular surface disease, which may explain the lack of statistically significant improvement [38–41].

At baseline, there was a statistically significant difference in uncomfortable contact lens wear time and meibomian gland score. This occurred despite subject randomization. Subjects in Group 3 had statistically higher daily uncomfortable contact lens wear time although there were no differences in daily contact lens wear time or comfortable contact lens wear time. Subjects in Group 1 had a statistically higher meibomian gland score compared to subjects in Group 2. The analysis is not expected to be impacted since the GLM controlled for differences at baseline.

Despite a lack of statistically significant improvement in total meibomian gland score evaluating meibum quality, there was a significant increase in the number of glands scored as zero or one (clear or cloudy liquid) and decrease in the number of glands scored as two or three (inspissated or obstructed) in subjects using the Bruder Moist Heat Compress. Clinical improvement in MG quality and quantity of secretions remains a challenge due to the grading systems used and the lack in ability to determine whether a grade 3 is a stable yet currently inactive gland or if it is an obstructed or absent gland. Therefore, it may be prudent to evaluate the proportion of glands scored as secreting clear or cloudy meibum before and after a treatment, instead of analyzing the total meibomian gland meibum quality score as it may mask any treatment effects.

One potential limitation of this study is the lack of investigator masking. However, both the primary and secondary outcome variables are subject-reported and thus not influenced by investigator bias. Subject masking to treatment was not feasible as the Bruder Moist Heat Compress was compared to the typical clinical recommendation of a warm washcloth. Furthermore, tertiary outcome variable, meibomian gland expression, was assessed by the meibomian gland evaluator (MGE). The MGE is one of the most standardized clinical evaluation of meibomian gland function at the slit lamp available [21,42]. A strict protocol was enforced to deliver a steady pressure for a consistent duration. Thus, even though investigators weren't masked, the strict protocol eliminates concern of investigator bias for this tertiary outcome variable.

Another limitation of this study is the lack of washcloth reheating and variations in household water temperatures used to heat the washcloth. Murakami et al. reported in 2015 that compresses were given to subjects when they were 47 °C [30]. The heating instructions for the Bruder Compress in the Murakami study were consistent with instructions provided to subjects in this study. The United States Consumer Product Safety Commission recommends a tap water heat setting of 49 °C, which is consistent with an article by Levesque et al. to avoid water scalds [43,44]. Clinical guidelines are vague with respect to a protocol for heating a washcloth and simply instruct the patient to "soak the cloth in hot water." The heating procedure for the washcloth in this study was formulated to simulate what is typically done in clinical care. Patients may or may not be instructed to reheat the washcloth in a clinical setting; that is, reheating is not something routinely recommended nor accomplished. In addition, if the washcloth had been reheated in this study, additional variables would be introduced. For example, instead of having a compress that is hottest initially and slowly dissipates (as is the case with both the Bruder Moist Heat Compress and washcloth), reheating would have introduced a temporal variability in heat that could have confounded the results. Additionally, it would have resulted in non-continuous application of heat (while the washcloth was being reheated). Therefore, the results of the study based on this heating procedure provides the most clinical relevance and what can be expected if patients are simply instructed to use a warm washcloth for relief of discomfort.

While the cause of contact lens dry eye varies in patients and is contributed to by many factors, all contact lenses when placed on the eye cause some disruption to the tear film [7,45,46]. Therefore, in patients who have symptoms of CLDE, stabilizing the tear film through application of a warm compress could be a viable first step in treatment prior to contact lens refitting. Treatment with a warm compress, like with the Bruder Moist Heat Compress, in these patients may reduce the contact lens dropout rate and have a significant impact on a patient's quality of life while wearing lenses by increasing comfortable wear time of two hours as demonstrated in this study. A similar magnitude of effect was shown by Hom in contact lens wearers experiencing contact lens intolerance; after five weeks of cyclosporine therapy, subjects experienced an average increase in contact lens wear time of 1.9 h per day although there was no distinction made between total wear time and comfortable wear time [47]. Another study by Nichols et al. enrolled fifty contact lens wearers with dry eye as determined by the CLDEQ and observed improvement in comfortable contact lens wear time after one month of treatment with azithromycin ophthalmic solution dosed twice daily [48]. They reported an improvement in comfortable contact lens wear time of at least two hours [48]. While a vectored thermal pulsation treatment in soft contact lens wearers with MGD may improve comfort by up to four hours a day, as observed by Blackie et al. [49], the results of the current study demonstrate that daily application of heat alone with a Bruder Moist Heat Compress may improve comfortable contact lens wear time in lens wearers who may or may not have poorly expressing meibomian glands. While the results here show slightly higher comfortable wear time when the compress was applied twice daily, the difference was not statistically significant and so improvement in wear time may be seen even when the compress is only applied once daily. Although this study could be improved by masking of examiners, the subjective reported improvement in comfortable contact lens wear time through application of the Bruder Moist Heat Eye Compress is a significant finding.

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Declaration of Competing Interest

Alcon (JJN-research, JJN-consultant), Bruder Healthcare (research;

KKN & PMK-consultant), Allergan (KKN-consultant, KKN-research), Kala pharmaceuticals (KKN-research, KKN-consultant), Olympic Ophthalmics (JJN-consultant), Shire (JJN, KKN-consultant), Johnson and Johnson Vision Care (JJN-research), Sun Pharmaceuticals (KKN-consultant), ScienceBased Health (KKN-consultant), Oyster Point (KKN-consultant), Sight Sciences (KKN-consultant), Silk Technologies (KKN-consultant), Topivert (KKN-consultant), TearSolutions (KKN-research), Tearfilm Innovations (KKN-stock/other equity).

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