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Compatibility of phospholipid liposomal spray with silicone hydrogel contact lens wear

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ABSTRACT

Purpose: To assess the effects of two weeks of regular phospholipid liposomal spray application on lipid layer grade, tear film stability, subjective comfort, visual acuity, and lipid deposition in silicone hydrogel contact lens wearers.

Methods: Thirty-one existing contact lens wearers were enrolled and fitted with two week planned replacement silicone hydrogel contact lenses (Acuvue® Oasys®) in a prospective, randomized, paired-eye, investigator-masked trial. A phospholipid liposomal spray (Tears Again®) was applied to one eye (randomized) four times daily for two weeks. LogMAR high contrast visual acuity (VA), low contrast glare acuity (LCGA), non-invasive tear film break-up time (NIBUT), and lipid layer grade (LLG) were measured at baseline and day 14, in both treated and control eyes. Subjective comfort relative to baseline, and spectrofluorophotometric assessment of contact lens surface lipid deposition were also assessed on day 14.

Results: All measurements did not differ at baseline between treated and control eyes. Lipid layer thickness and tear film stability were increased on day 14 in treated eyes (all $p < 0.05$), but not in control eyes (all $p > 0.05$). A greater proportion of participants reported improved comfort in the treated eye relative to the control eye ($p = 0.002$). There were no significant differences in visual acuity or in contact lens surface lipid deposition, between treated and control eyes, on day 14 (all $p > 0.05$).

Conclusion: The phospholipid liposomal spray increased tear film stability, lipid layer thickness and subjective comfort in silicone hydrogel contact lens wearers, without adversely affecting visual acuity or contact lens surface lipid deposition.

1. Introduction

Up to 35% of patients in optometric practice report symptoms of dry eye [1], with contact lens wearers being twice as likely to be symptomatic as non-wearers [2,3]. Discomfort and dryness are considered largely responsible for high contact lens discontinuation rates [4–7], and are believed to contribute towards the lack of growth of the contact lens industry [8]. Contact lens wear can destabilize the structure of the superficial tear lipid layer, increasing the rate of tear film evaporation, and leading to the development of evaporative dry eye symptoms [9–12].

Improving the quality and thickness of the lipid layer can be associated with increased tear film stability [13–15]. Tears Again® (Optima Pharmazeutische GmbH, Germany) is a phospholipid liposomal spray designed for application to the closed eyelids. Liposomes that migrate across the lid margins transport phospholipids into the tear film, to supplement the lipid layer [16–21]. Phospholipid liposomal sprays are currently marketed for use in both contact lens and non-contact lens related dry eye. Previous studies have demonstrated that a single application of the liposomal spray is effective in improving tear film stability and subjective comfort in both soft hydrogel contact lens wearers [16], and non-wearers [17]. Improvements in symptomatology, tear production, lid margin inflammation and lid-parallel conjunctival folds have also been reported in both contact lens wearers [18], and dry eye patients [19–21].

The development and widespread adoption of silicone hydrogel contact lens materials have met the majority of concerns

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associated with conventional HEMA-based hydrogel lenses with regard to oxygen transmission to the cornea [22]. However, the use of siloxane compounds increases lens modulus and reduces wettability, and has the propensity to attract lipids and form deposits [12,22–24]. Despite surface modifications and incorporation of internal wetting components, silicone hydrogel materials remain more hydrophobic than those of conventional hydrogel lenses [25], and greater contact lens lipid deposition has been anecdotally reported [12,26].

The compatibility of phospholipid sprays with silicone hydrogel contact lenses has yet to be established. The aim of this study was to assess the impact of phospholipid liposomal spray application on tear film measurements, vision, comfort, and contact lens surface lipid deposition in silicone hydrogel contact lens wearers.

2. Methods

This prospective, two-week, randomized, paired eye, investigator-masked trial, followed the tenets of the Declaration of Helinski, and received institutional ethics approval. Participants were required to be between 18 and 40 years of age, with no systemic/topical medications/treatments affecting the eye within the month prior to commencement in the trial, no systemic conditions affecting the eye, and no ocular pathology identified by slit lamp examination. All participants were established contact lens wearers (>1 year), to eliminate neophyte effects, with myopic prescriptions ≤ -4.00DS. Participants were also required to have vision correctable to $\geq$6/7.5, to facilitate subtle changes in visual acuity to be tracked during the time course of the study. The McMonnies Dry Eye Questionnaire was administered to grade dry eye severity at baseline.

A total of 31 eligible participants who provided written informed consent were recruited, exceeding the sample size requirement for the desired study power. The designated outcome measure for determining sample size was tear film lipid layer grade. Power calculations showed that a minimum of 15 participants was required, to detect a clinically significant difference of 1 lipid layer grade, in any of the 4 pairwise comparisons, with 80% power ($\beta = 0.2$) and at a two-sided statistical significance level of 5% ($\alpha = 0.05$). To preserve the overall significance level, a Bonferroni corrected p value (0.0125) was used in the power calculation. This correction accounted for the randomized paired-eye design of the trial, with the SD of normal values being estimated at 1 lipid layer grade [27,28]. Sample size estimates were determined using a uniform non-parametric adjustment, with PASS 2002.

2.1. Materials

Participants were fitted with senofilcon A contact lenses (Acuvue® Oasys®, Johnson & Johnson Vision Care), with either 8.4 or 8.8 mm base curves, according to topographic evaluation (E300 Corneal Topographer, Medmont International). Participants were provided with Opti-Free Replenish multi-purpose solution (Alcon Laboratories), and instructed to perform a 10 s rub and rinse care regimen, before and after each day of contact lens wear. Participants were requested to wear contact lenses for 6–8 h each day during the two-week trial period.

2.2. Intervention

Participants were randomly assigned to apply the liposomal spray to the left or right eye (treated eye). The fellow eye received no intervention (control eye). A 10 ml bottle of liposomal spray (Tears Again®) was provided to each participant, with instructions to apply a single spray onto the closed eyelid from a distance of 10 cm, four times daily during contact lens wear, according to the manufacturer's instructions, for a period of 14 days. A midline nose bridge septum was supplied to each participant, to minimize contamination of the control eye during each spray application. The use of the septum and closed eyelid application of the spray was demonstrated to all participants prior to the commencement of the trial.

2.3. Measurements

The investigator conducting measurements was masked to the treatment status of each eye. All measurements were conducted with contact lenses *in situ*. Six metre LogMAR visual acuity (VA), and 1 m low contrast glare acuity (LCGA; BEGAT, Tawa Holdings New Zealand) were assessed at baseline and on day 14, after 2 weeks of 4 times daily use. Non-invasive tear film break-up time (NIBUT) and lipid layer grade (LLG) were evaluated with the Tearscope Plus™ (Keeler, UK), with and without the fine grid insert, respectively [29]. A mean of three consecutive NIBUT measurements was calculated. LLG grading was based on the Guillon-Keeler grading system: grade 1, open meshwork; grade 2, closed meshwork; grade 3, wave or flow; grade 4, amorphous; grade 5, colored fringes; grade 0, non-visibility of lipid or abnormal colored fringes as they both indicate a non-functional lipid layer less capable of inhibiting evaporation [29–31].

Subjective ocular comfort relative to baseline was assessed on day 14, using a forced-choice, three-point scale for each eye: greater, equal or lesser comfort. On day 14, contact lenses were removed using an aseptic technique, and transferred to a 24-well opaque plate containing 1 ml of distilled water. Plates were analyzed for lipid deposition, with a SpectraMax M2 Microplate Reader spectrofluorophotometer (Molecular Devices), at an excitation wavelength of 360 nm, and an emission wavelength of 440 nm [32]. Values were then normalized to the autofluorescence of unworn lenses.

2.4. Statistics

Statistical analyses were performed using Graph Pad Prism version 6.02 (http://www.graphpad.com). Comparison of continuous variables (VA, LCGA) between and within treatment groups were performed using paired *t*-tests, where normal distribution had been confirmed by the D'Agostino and Pearson test ($p > 0.05$). Non-normally distributed measures (NIBUT) were logarithmically transformed before being assessed by paired *t*-tests. Ordinal data (LLG) were analyzed using Wilcoxon signed-rank test. Categorical data (subjective comfort) were compared using Fisher's exact test and chi-squared test. All tests were two-tailed and $p < 0.05$ was considered significant. All continuous data are presented as mean ± SD, and ordinal data as median (95% CI), unless otherwise stated.

3. Results

Thirty-one participants (21 females, 10 males) with a mean age of 23 ± 4 years (range, 18–33 years) were recruited. Baseline measurements are listed in Table 1. There were no statistically significant differences in pre-treatment measures at baseline between treated and control eyes (all $p > 0.05$). The mean McMonnies score was 6.7 ± 4.9, with only 4 participants (12.9%) displaying scores of $\geq$15.

3.1. Tear film lipid layer grade

After two weeks, LLG was significantly increased from baseline in the treated eyes ($p < 0.001$, Fig. 1), but not in control eyes

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