ORIGINAL ARTICLE

Impact of Viscosity Variations in Dual-Polymer Artificial Tears on Corneal Regularity and Aberration

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ABSTRACT

Background: This study was done to explore the possibility of the usage of different viscosities in artificial tears (Systane Ultra and Hydration) in detecting changes in corneal aberration on dry eye patients. **Methods:** 103 diagnosed dry eyes were observed in this study and two different artificial tears with different viscosities were instilled randomly in each eye. Corneal aberration measurement with Fourier index (Spherical aberration (SA), trefoil and coma) was then captured for 10 minutes using CASIA with a 1-minute time interval. Normal saline was instilled before the treatment was given (referred to as baseline). Repeated measure analysis of variance (RM ANOVA) and paired sample t-test were used to evaluate the effects of artificial tears after instillation and comparison between each specific time interval respectively. The P-value of 0.05 was set as the level of significance. **Results:** Corneal aberration with artificial tears was then compared to normal saline and the results showed that there was no significant difference between artificial tears in terms of retention time after 10 minutes (p>0.05) in dry eye participants. Both groups demonstrated significant improvements from baseline and there was a significant difference from baseline (p<0.05). **Conclusion:** Instillation of high viscous artificial tear produce better uniformity of the corneal surface resulting in lower corneal aberration.

Keywords:

Corneal aberration; Systane Ultra, Systane Hydration; Tear retention time

INTRODUCTION

The tear film acts as a protective barrier for the ocular surface, shielding it from mechanical damage and environmental elements to maintain comfort. It is composed of lipid, aqueous, and mucin layers, each component serves specialized roles dictated by its unique composition. The equilibrium and robustness of the tear film hinge upon coordinated processes such as tear generation, evaporation, absorption, and drainage. Disruption of these processes or impairment of the tear film layer can precipitate the onset of dry eye syndrome (Kopacz et al., 2021).

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Dry eye disease (DED) is a multifactorial disorder characterized by symptoms including dry eyes, blurred vision, tear film integrity, and degeneration of the ocular surface. Dryness, grittiness, and burning sensations also increase over time. Other typical symptoms include crusty eyelids, stringy discharge, watery eyes, ocular tiredness, discomfort, and temporary vision loss. According to the Dry Eye Workshop of the Tear Film & Ocular Surface Society (TFOS DEWS II 2017 Report), dry eye is "a multifactorial disease of the ocular surface characterized by a loss of tear film homeostasis, accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles" (Craig et al., 2017). The precorneal tear film plays a critical role in maintaining the optical clarity of the eye. Tear film, which serves as the foremost refractive surface of the eye, deteriorates, it causes irregularities on the optical surface. This breakdown can introduce additional aberrations into the eye's optical system. Several research works support the notion that dry eye conditions lead to heightened irregularity and fluctuation in the tear film, resulting in increased optical aberrations compared to healthy eyes. These changes have been linked to compromised visual acuity and diminished optical quality (Lu et al., 2016; Koh, 2018; Koh et al., 2018).

Corneal wavefront aberrations were found to vary a lot from person to person, and these differences can cause the Zernike aberrations to change over time. Several studies have shown that spherical aberration (SA) changes quickly after blinking, with a significant shift happening about 10 seconds after blinking. This suggests that desiccated tear film can affect the optical quality (Koh et al., 2008; Ferrer-Blasco et al., 2010; Xu et al., 2011). The change in SA could lead to central cornea been evaporated faster than peripheral cornea. Moreover, the corneal surface may shift towards oblate, thus indirectly increasing SA. Previous work had commented that impact of SA on quality of vision is worse than coma and trefoil (Yıldırım et al., 2020). It is an established fact that the usage of artificial tears could increase tears retention time, improving tears stability and reduce corneal irregularities (Che Arif et al., 2020; Che Arif et al., 2021; Che Arif, Hilmi & Kamal, 2023). Currently, there is limited evidence on the impact of instillation of artificial tears on improvement in corneal aberration. Hence, this study aimed to evaluate the changes in aberration on the corneal surface using two dual polymer artificial tears with varied viscosity.

MATERIALS AND METHODS

This study was conducted at IIUM Optometry Clinic, Kuliyyah of Allied Health Sciences, IIUM Kuantan, Pahang. During the study, a total of 103 eyes were recruited in this prospective study. All participants were briefed and informed about all procedures and their consent obtained prior to data acquisition. in accordance was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the institution ethical board (IREC 2023-KAHS/DOVS2). All procedures were conducted in the same examination room, with temperature and humidity kept constant at 20°C-24°C (Carracedo et al., 2019) and 40%-50%, respectively (Torkildsen et al., 2017). Both participant and optometrist conducting the procedures were blinded to the ophthalmic solutions used at each visit. Inclusion criteria set for this study include university students aged 20-26 years old, scotopic pupil size ≤ 6 .5 mm (Md Rejab et al., 2023), having one or more of the following symptoms present: dry eyes, burning, foreign body sensation, blurred vision, and other associated symptoms of dry eye (Yildirim et al., 2021), tear breakup time (TBUT) for each eye was ≤ 6 seconds (Stein et al., 2006), and OSDI score > 13 (Paugh et al., 2008; Che Arif et al., 2023). Participants will be excluded from the study if there is presence of ocular surface abnormalities or diseases such as superficial punctate keratitis, recurrent pterygium, corneal opacity or irregularity (Hilmi et al., 2020; Jais et al., 2021). Participants that are regularly wearing contact lens and currently using artificial tears also were excluded (Hilmi et al., 2019). A condition in which corneal topography could not provide reproducible measurement due to obstruction of the central cornea by pterygium were also excluded. (Che Azemin et al., 2016; Mohd Radzi et al., 2019; Yildrim et al., 2020).

Three ophthalmic solutions were used in this study, which were two dual-polymers artificial tears; Systane® hydration (SH) (Alcon Laboratories Inc, Fort Worth, TX, USA) and Systane® Ultra (SU) (Alcon Laboratories Inc, Fort Worth, TX, USA), and one control solution; Opticare Normal saline solution (Excel Pharmaceutical Sdn. Bhd., Selangor, Malaysia). The viscosity of SH and SU were 26.70 cP and 12.40 cP respectively, based on our previous work (Che Arif et al., 2020). Research randomizer software (https://www.randomizer.org/) was used to randomise the sequence of solutions to be used at each visit, and the sequence and ophthalmic drops was masked from the observer.

TBUT was observed on each participant. A fluorescein strip was applied to the inferior fornix as the participant looked upward. Then, the participant was required to blink several times to ensure that the dye was evenly distributed throughout the cornea. The time required under cobalt blue light until the first black spot appears on the corneal surface is considered break-up time (Abdullah, Ithnin & Hilmi, 2019). The test was performed using a video camera mounted on digital high-definition slit-lamp biomicroscopy (Model SL 990, SLB Mega Digital Vision HR, Costruzione Strumenti Oftalmici, Italy). Measurements of TBUT were done three times, and the average of the results were used for analysis. Anterior segment imaging was done with a swept-source ocular coherence tomography (SS-OCT) (CASIA-2; Tomey Corporation, Nagoya, Japan), which utilise 1,310 nm laser wavelength and a speed of 30,000 A-scans per second. In this study, Zernike polynomials are used to describe wavefront aberrations of the cornea or lens from an ideal spherical shape, which result in refractive errors. Then, from Zernike analysis, it is transformed into a three-dimensional model of the anterior cornea. The loaded ray tracking program was used to compute corneal aberration. The built-in software automatically calculates the anterior corneal surface's 3rd, 4th, and

5th aberrations, SA (Z4, 0), trefoil (Z3, −3), and coma (Z3, −1), using Zernike polynomials translated from corneal data (Lu et al., 2016).

Prior to corneal aberration measurements with CASIA, each participant was instilled with Opticare Normal saline solution (Excel Pharmaceutical Sdn. Bhd., Selangor, Malaysia) in both eyes and instructed to blink several times. The corneal aberrations measurement will be taken immediately following the blink to prevent tear evaporation. This test was performed in a normal lit room and the participant was required to focus on the illuminated target. The first measurement taken was referred to as the baseline. Following the saline application, the first artificial tear was instilled, and the corneal aberration result was captured immediately one minute after the instillation of the artificial tear and after 10 minutes (Montés-Micó, Cáliz & Alió, 2004; Lee et al., 2024). After that, a few drops of saline were instilled for washout period which was set at 60 minutes to avoid the cross-over effect of the previous artificial tears which could affect the aberration reading (Markoulli et al., 2018). All data were analysed using IBM SPSS Statistics for Windows, Version 20 (IBM Corp., Armonk, N.Y., USA). Normality of all the data was assessed using Shapiro-Wik test.

The differences in all variables pre- and post-instillation (Baseline vs. 1 min, Baseline vs. 5 min, Baseline vs. 10 min) were examined using paired sample T-test. Repeated measure analysis of variance (RM ANOVA) and paired sample t-test was used to determine the differences in spherical aberration (SA), trefoil and coma between groups at specific time intervals. The significance level was set at P <0.05.

Table 1: Descriptive analysis for spherical aberration (SA), trefoil and coma

Artificial tear	Time interval (Min)	Aberration			P-value	
		SA (mean ± SD)(μm)	Trefoil (mean ± SD)(μm)	Coma (mean ± SD)(μm)	RM-ANOVA	Paired T-Test
Systane® hydration	Baseline	0.36 ± 0.56	0.18 ± 0.44	0.37 ± 0.24		
	one-minute	0.14 ± 0.34	0.08 ± 0.12	0.17 ± 0.12	< 0.001 for all aberration	*P = 0.55
	10-minute	0.27 ± 0.24	0.12 ± 0.23	0.33 ± 0.14		
Systane® Ultra	Baseline	0.35 ± 0.46	0.17 ± 0.36	0.36 ± 0.16		
	one-minute	0.18 ± 0.32	0.12 ± 0.45	0.19 ± 0.23	< 0.001 for all aberration	*P = 0.63
	10-minute	0.29 ± 0.14	0.15 ± 0.25	0.28 ± 0.14		

Mean ± SD: Mean and standard deviation
Min: Minutes
RM-ANOVA: Repeated measure analysis of variance
*Paired T-test: comparison between baseline and 10-minutes

RESULTS

Based on Shapiro-Wilk test, all data were normally distributed. Based on descriptive analysis, for SH group at baseline the mean and standard deviation (mean ± SD) for spherical aberration (SA), trefoil and coma were 0.36 ± 0.56, 0.18 ± 0.44 and 0.37 ± 0.24 respectively. At one-minute post-instillation, we found steep reduction in all parameters with 0.14 ± 0.34, 0.08 ± 0.12 and 0.17 ±0.12 respectively. At 10-minutes post instillation, there was slight increment with 0.27 ± 0.24, 0.12 ± 0.23 and 0.33 ± 0.14 respectively compared to one-minute interval. For SU group, at baseline the mean ± SD for spherical aberration (SA), trefoil and coma were 0.35 ± 0.46, 0.17 ± 0.36 and 0.36 ± 0.16 respectively. At one-minute post-instillation, we found steep reduction in all parameters with 0.18 ± 0.32, 0.12 ± 0.45 and 0.19 ± 0.23 respectively.

At 10-minutes post instillation, there were slight increment with 0.29 ± 0.14, 0.15 ± 0.25 and 0.28 ± 0.14 respectively compared to one-minute interval. The descriptive analysis is summarised in Table 1 below.

For SH group, RM-ANOVA findings revealed statistically significant changes in SA, trefoil and coma between baseline and 10 minutes observation period. Post hoc comparisons using the Tukey HSD test indicated that SA, trefoil and coma between baseline, one-minute and 10-minutes time interval was significantly different.

However, this study found no significant difference (Paired T-test, P = 0.55). Likewise for SU group, RM-ANOVA findings revealed statistically significant changes in SA, trefoil and coma between baseline and 10 minutes observation period. Post hoc comparisons using the Tukey HSD test indicated that SA, trefoil and coma between baseline, one-minute and 10-minutes time interval was significantly different (all P < 0.001). However, this study found no significant difference (Paired T-test, P = 0.63) between baseline and at 10-minutes instillation. The RM-ANOVA and post hoc findings were summarised in Table 1.

DISCUSSION

In this study, we compared the different viscosities of artificial tears and evaluated their effects on the corneal aberration measurement. Our findings showed that both artificial tears produced reduction in corneal aberration at post one-minute instillation and increased slightly at 10-minutes towards baseline. However, the decrement at one-minute post-instillation showed high viscosity artificial tear produce more reduction compared to medium viscosity artificial tears. This findings in agreement (Röggla et al., 2021). And at 10-minutes, both artificial tears showed an increase of corneal aberration compared to one-minute post-instillation, however it was still lower than baseline. Thus, our study showed that higher viscosity artificial tears provide additional benefits while improving the corneal regularity and last longer on the ocular surface, as previously reported (Pavlopoulos, Horn & Feldman, 1995; Liu & Pflugfelder, 1999; Huang et al., 2002; Wolffsohn et al., 2023).

Although the usage of artificial tears seems to improve the corneal regularity, it is with to note the impact on the quality of vision. Improvement of corneal aberration with the usage of artificial tears should be prudently examined. It needs to be looked upon from the perspective of just-noticeable differences (JND) for each corneal aberration parameter. For SH group, reduction of SA, trefoil and coma between baseline and one-minute interval were 0.22 µm, 0.1 µm and 0.2 µm respectively. Meanwhile for SU group, reduction for SA, trefoil and coma between baseline and one-minute interval were slightly smaller than SH group with 0.17 µm, 0.05 µm and 0.17 µm respectively. Even though the magnitude changes in all parameters were statistically significant (All P < 0.05), we postulate that these differences were clinically insignificant. This could happen due to these changes being lesser or just approximately reaching the JND for each aberration. Numerous works had suggested the JND for each aberration are varies with SA approximately 0.15 to 0.25 diopters (D), trefoil in ranges of 0.10 to 0.15 microns and coma at approximately 0.10 microns (He et al., 1998; Oshika et al., 1999; Thibos et al., 2002; Applegate et al., 2003; Marsack, Thibos & Applegate, 2004; Jungnickel et al., 2013). These indicate that the impact of aberration on visual quality varies depending on the types and magnitude of each aberration. Thus, these could suggest the reason why not all patients reported visual disturbance or discomfort due to aberration.

With advancement in artificial tears formulation, high viscous are no longer being used for overnight treatment purposes as it would induce temporary blurred vision. Lievens et al. (2019) reported no differences between high and mid-viscosity eye drops with regards to immediate experiences such as "no blurring or visual interference" upon application and "clear and comfortable vision" within days. Recent study has postulated that the differences in initial eye comfort and visual interference shortly after application could be due to presence of lubricant in its formulation (Weisenberger, Fogt & Swingle Fogt, 2021). In general, the high viscosity lubricant eye drop was well tolerated and proved effective in alleviating signs and symptoms of dry eyes (Saad & Brings, 2023). Previous studies have demonstrated that viscosity plays a crucial role in maintaining tears on the surface of the eye (Paugh et al., 2008; Che Arif et al., 2020; Kaido & Arita, 2024). Similarly, the findings of this study indicate that both types of artificial tears exhibit shear-thinning behaviour, in which viscosity is higher under low shear stress and vice versa. This suggests that higher viscosity may enhance the effectiveness of artificial tears in maintaining moisture on the ocular surface during periods of minimal shear, such as when the eye is open, thereby reducing evaporation rates (Che Arif et al., 2020). However, in lower viscosity, at higher shear rates, such as during blinking, it may improve ocular comfort and minimise ocular surface friction (Aragona et al., 2019).

There are several limitations which are worth noting. We only recruited participants with mild dry eyes based on the signs and symptoms from OSDI and TBUT measurements. Thus, for future research, it is suggested to include moderate to severe dry eye participants to evaluate if there are any significant differences in corneal aberration. This study only focuses on the observation and measurement of corneal aberration right after artificial tears application. The long-term effects of usage of these artificial tears, alongside multiple instillations, also need further investigation. The selection of age as participant should cover a wider range. This is because tear production tends to diminish as age increases, thus posed higher risk of getting dry eye in older patients. It is suggested that different levels of severity and types of dry eyes with additional factors such as with and without using artificial tears can be included for further research.

CONCLUSION

Instillation of high viscous artificial tear produces better uniformity of the corneal surface resulting in lower corneal aberration.

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