

Assessment of a Cationic Emulsion to Control the Tear Film Evaporation Rate

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Purpose: To investigate the effect of a single application of cationic emulsion in controlling tear film evaporation and improving tear quality and quantity.

Materials a Methods: Twenty male subjects diagnosed with DE were enrolled in the study with an average age of 45.8 ± 6.37 years. The tear film parameters were observed at several time points post-instillation of the cationic emulsion (10, 20, 30, and 60 min). The tear evaporation rate (TER) was measured with a VapoMeter. Noninvasive tear break-up time and meniscus height were assessed using OCULUS Keratograph.

Results: TER decreased by more than 20% at 20, 30, and 60 minutes time points after instillation of single drop of cationic emulsion. Also, a significant improvement in tear film stability was found at all time points following the instillation of cationic emulsion eye drops. The mean tear break-up time increased from 5.55 ± 2.87 to 6.6 ± 4.2 sec at 60 minutes. The maximum increase in tear break-up time occurred at 30 minutes time point. The TMH was also significantly higher post-instillation of oil emulsion eye drops. There was a significant increase in the TMH post-therapy with oil drop at all time points.

Conclusion: The overall study findings of this study illustrate that the single application of a cationic emulsion effectively controls tear film evaporation in patients with mild to moderate DEs. The cationic emulsion efficiently enhanced both the tear film stability and the tear meniscus volume.

Keywords: dry eye, evaporation rate, cationic emulsion, tear stability

Introduction

Dry eye (DE) is a complex multifactorial disease associated with disruption of the tear film's homeostasis, resulting in many changes in the ocular surface. Factors including eyelid and blinking abnormality or tear film deficiencies represent the most common reason for the loss of tear film homeostasis, inducing tear film instability and tear hyperosmolarity.¹ Up to 30% of the global population has reported a combination of symptoms and signs of DE disease. However, based on clinical findings, a prevalence rate of up to 68% has been reported in populations over 40 years old.²

The tear film lipid layer plays a vital role in controlling tear film evaporation and maintaining tear film stability. Korb et al observed the lipid layer after blinking and found that the distribution and increase in lipid secretion are blink-dependent.³ Furthermore, McCulley and Shine suggested that tear lipid has two phases. The outer thick non-polar layer protects from evaporation, whereas the thin inner polar lipid plays an important role in maintaining stability and providing interference with the aqueous layer.⁴

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Numerous therapeutic protocols have been adopted to control tear evaporation by increasing tear film stability. Artificial tears and lubricants are considered one of the most common methods to treat dry the signs and symptoms of DE.⁵ Formulations containing electrolytes, mucomimetic agents, or oil emulsion are significantly helpful in DE management.⁶ However, the main drawback of most of these formulations is their short retention time, as the solution can easily drain via the lacrimal drainage system.⁷

One type of formulation is the oil-in-water emulsion, designed to enhance, and thicken the tear film lipid layer. The first oil-in-water emulsion was combined with an anti-inflammatory agent (cyclosporin).⁸ Then, this ophthalmic emulsion was modified to an over-the-counter oil-in-water-emulsion tear supplement with no anti-inflammatory agents. Different oils such as castor oil, mineral oil, soya bean oil, and phospholipid liposomal have been used to develop oil-in-water emulsions to manage DE signs and symptoms.^{5,9}

The safety and efficacy of oil emulsion artificial tears in managing DE signs and symptoms are well documented. Previous studies have reported a significant improvement in corneal staining, tear stability, and production following the use of oil ophthalmic emulsion.^{10,11} More specifically, it has been reported that a single dose of oil emulsion resulted in a significant increase in tear meniscus height (TMH) up to 30 minutes after instilling the drop.¹¹ Moreover, a clinical trial evaluating the efficacy of an oil-based formula (Castor oil) has shown a significant reduction in the respective signs and symptoms, including tear break-up time, corneal staining, and tear production following the use of the formula for seven days.¹⁰ It has been shown that optical coherence tomography imaging (OCT) has the potential to provide clinicians with a reliable approach to evaluate rapidly the precorneal tear film thinning and adhesive properties of the ocular surface.^{12,13} A previous study evaluated the clearance of tear lipids using OCT imaging has reported a prolonged tear lipid retention time following installation of oil-in-water emulsion.¹⁴

Excessive tear evaporation rate is considered a major cause of DE symptoms, leading to tear hyperosmolarity. Tear hyperosmolarity causes inflammatory processes in epithelial cells. These processes activate the inflammatory cells to generate cytokines and matrix metalloproteinases.¹⁵ The Definition and Classification Subcommittee of the International Workshop on Dry Eye (DEWS) suggested that all forms of DE, either aqueous

deficient DE (ADDE) or evaporative dry eye are evaporative.¹ Therefore, managing and controlling tear film evaporation is vital in treating the signs and symptoms of DE. Although several research studies have been performed on lipid containing artificial tears, no previous studies have investigated the immediate effect of cationic emulsion (oil-based formulation) in controlling tear film evaporation. This study investigated the effect of a single application of cationic emulsion in controlling tear film evaporation and improving tear quality and quantity.

Method

Twenty male subjects diagnosed with DE were enrolled in the study with an average age of 45.8 ± 6.37 years. Patients were enrolled in the study if they fulfilled the following criteria: Ocular surface disease index (OSDI) score > 13 , noninvasive tear film break-up time < 10 s and < 10 mm in 5 min for Schirmer test. Subjects with a history of ocular surgery, ocular disease or who wear contact lenses were excluded from this study. Patients taking medications that could influence the tear film were also excluded from the study. All procedures were approved by the College of Applied Medical Sciences Ethics Committee, King Saud University, Riyadh, Saudi Arabia. All subjects provided written informed consent. The study was conducted according to the tenets of the Declaration of Helsinki.

Tear Parameters

Tear Evaporation Rate (TER)

The TER was measured with a VapoMeter (Delfin Technologies, Kuopio, Finland) [19]. Initially, two readings were obtained with eyes open, representing the evaporation rate from the ocular surface and the lid skin. Then, second measurement was obtained with eyes closed, and these measurements were subtracted from the open-eye readings. Three measurements were obtained; then, the average value was calculated.

Noninvasive Tear Break-Up Time and Meniscus Height

The OCULUS Keratograph 4 (OCULUS Inc., Wetzlar, Germany) was used to monitor the change in the (NITBUT) and TMH post-instillation. The Keratograph illumination system consists of 200 red LEDs (wavelength 653 nm). It is installed with a Placido disk consisting of 22 rings which project an illuminated ring pattern on the corneal surface.¹⁶ Furthermore, the Keratograph

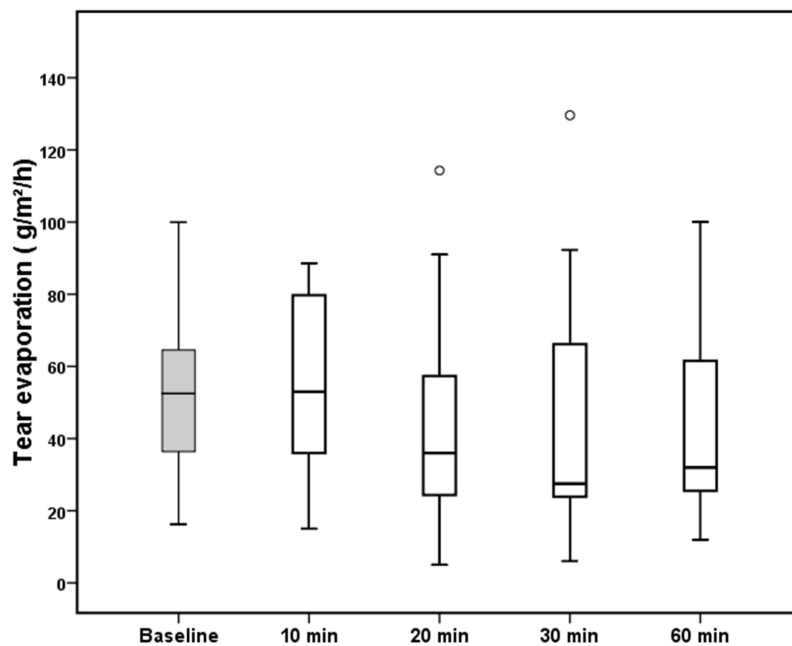


Figure 1 A box plot showing evaporation rate measured at different time points pre and post instillation of cationic emulsion.

illumination system is equipped with software (Tear Film Scan) that can provide automated analysis of the tear break-up time, the meniscus height and other ocular parameters.¹⁶

In order to monitor changes to tear film behavior after instilling tear supplements, the tear film parameters were observed at several time points post-instillation of the cationic oil-based eye drop (10, 20, 30, and 60 min).

Statistical Analysis

Variables were tested for normality using a Kolmogorov–Smirnov test. A repeated measure ANOVA and Tukey’s post-hoc test were applied for normally distributed data while the ordinal and data with non-normal distribution were analysed using Friedman test and post-hoc Wilcoxon rank-sum test.

Results

The mean tear film evaporation rate decreased by more than 20% at 20, 30, and 60 minutes time points after instillation of single drop of cationic emulsion (Figure 1).

However, this reduction was not statistically significant. The mean tear film dropped from 40.88 ± 37.14 at baseline to 28.88 ± 16.90 g/m²/h after 60 minutes (Table 1).

Tear film stability improved significantly from baseline to 20, 30, and 60 minutes time points following the instillation of cationic emulsion eye drops ($p = 0.03$). The mean tear break-up time increased from 5.55 ± 2.87 to 6.6 ± 4.2 sec at 60 minutes (Figure 2). The maximum increase in tear break-up time occurred at 30 minutes time point, with an average value of 7.57 ± 3.94 sec ($p = 0.01$) (Table 1). Figure 2 demonstrates the changes in tear break-up time measured at different time points before and after instillation of cationic emulsion eye drops.

The TMH was significantly higher post-instillation of cationic emulsion eye drops ($p = 0.004$). There was a significant increase in the TMH post-therapy with cationic emulsion at all time points (10, 20, 30 and 60 minutes) compared to the values obtained at baseline ($p = 0.01$, $p = 0.007$, $p = 0.018$ and $p = 0.05$, respectively) (Figure 2). The maximum increase in TMH was recorded at time

Table 1 Mean and Standard Deviation of the Tear Evaporation Rate (g/M²/h) Tear Break-Up Time (Sec) and Meniscus Height (Mm) Measured Before and at Different Time Points After Instillation of Cationic Emulsion

	Baseline	10 Minutes	20 Minutes	30 Minutes	60 Minutes
Tear evaporation	40.89 ± 37.14	39.15 ± 24.79	32.27 ± 19.62	29.76 ± 18.21	28.81 ± 16.81
Tear break-up time	5.88 ± 2.87	4.94 ± 2.06	7.38 ± 3.93	7.57 ± 3.06	6.67 ± 4.22
Tear meniscus height	0.148 ± 0.0186	0.169 ± 0.0216	0.185 ± 0.0179	0.163 ± 0.0169	0.161 ± 0.021

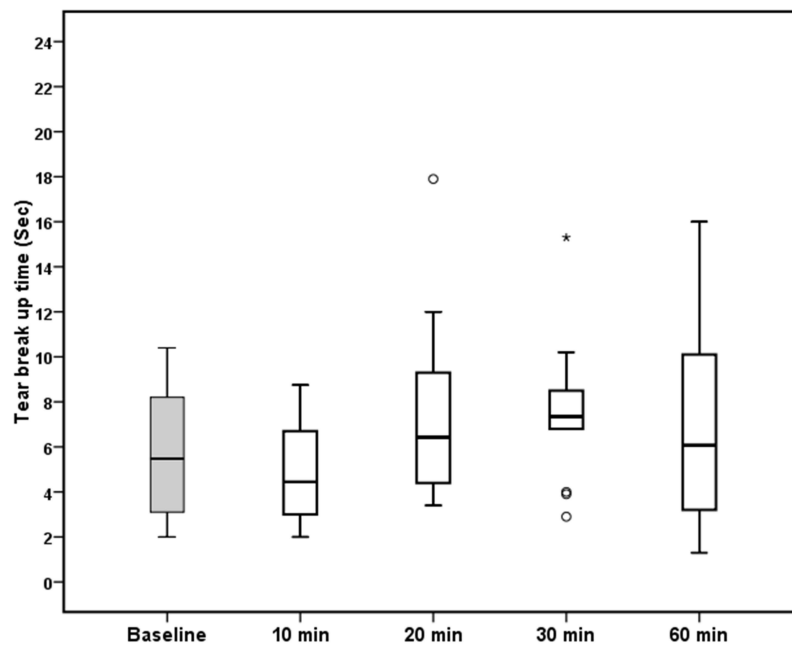


Figure 2 A box plot showing tear break up time measured at different time points pre and post instillation of cationic emulsion.

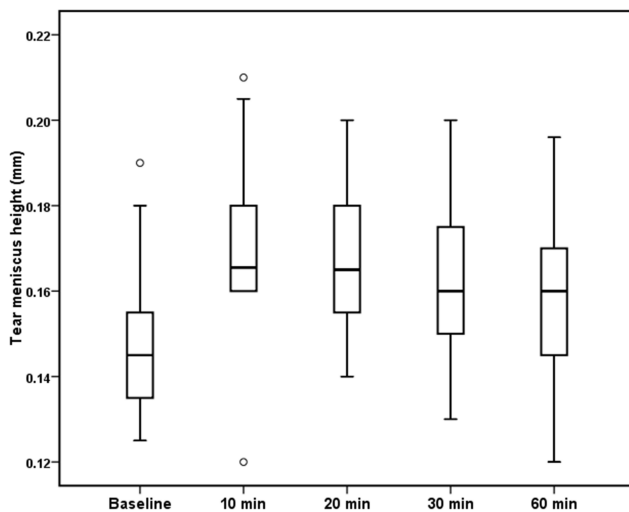


Figure 3 A box plot showing tear meniscus height measured at different time points pre and post instillation of cationic emulsion.

points 10 and 30 minutes. The mean TMH increased from 0.15 at baseline to 0.17 and 0.19 mm at time points 10 and 30 after, respectively, following the instillation of eye drops (Figure 3).

Discussion

The purpose of this study was to evaluate the efficiency of a single dose of cationic emulsion drop in controlling tear film evaporation and improving tear film stability. A panel of tear film measures were carried out to observe tear film

parameters before and after instillation of cationic emulsion eye drops at different time points. Improvement in DE signs and symptoms has been previously reported following the application of cationic emulsion eye lubricants.¹⁷

Different tear film supplements containing various ingredients have been developed to control the signs and symptoms of DE. However, these tear film supplements are not meant to treat DE syndrome, and thus they can relieve DE signs and symptoms and help to restore the normal homeostatic state of the ocular surface.¹⁸ In addition, these formulations play a role in improving turnover, stability, and evaporation rate of the tear film and inhibiting the inflammatory changes in ocular tissue.^{19,20}

In the present study, a cationic emulsion was used. Nanotechnologies are currently used to improve the retention and bio adhesive properties of ophthalmic solutions. A novel technology exploits the fact that the ocular surface, including the corneal and conjunctival tissues, is negatively charged. Therefore, the bio adhesive properties and retention time can be improved by using positively charged ophthalmic solutions.^{17,21} The efficacy of this relatively new technology in extending the ocular solution retention time is well documented.²¹ However, according to the TFOS DEWS II management and therapy report, the long-term safety of Cationic-based formulation needs to be assessed due to the reported alterations of the corneal stroma and corneal

epitheliopathy.⁶ This affect could be caused by its preservative cetalkonium chloride or due to the fact that the prolonged bioavailability of Cationic formulation may affect the epithelial cells migration onto stromal areas of erosions that result in corneal epitheliopathy.²²

This study shows that a single drop of cationic emulsion results in a noticeable reduction in tear film evaporation following the application of a cationic emulsion. More specifically, a 20 and 30% decrease in tear film evaporation was found at 20 and 60 minute time points post-instillation, respectively. This is consistent with the findings of a previous study that reported a reduction of more than 50% in tear evaporation following the use of oil emulsion for 30 days. Another study has reported that a single dose of oil-in-water emulsion can result in significant tear film evaporation.²³ This is unsurprising because the oil emulsion formulations are prepared to replenish the tear film lipid layer that plays an important role in improving tear film stability and controlling tear evaporation.

In addition, there was a significant improvement in tear film stability post-instillation of a single oil emulsion drop. An increase in tear break-up time by up to 1.7 seconds (22%) occurred after a single dose. It has been previously demonstrated that the use of oil-based lubricants resulted in a 40% increase in the tear break-up time in patients with mild to moderate DE symptoms.²⁴ A recent study found that the tear break-up time increased significantly when using oil-based lubricants for 35 days.²⁵ The authors suggested that the oil lubricant formulations containing polar phospholipids can improve the interference between the lubricant components and the non-polar lipid and aqueous layer.²⁵

Lipid layer of tear film play plays an important role in controlling tear film evaporation and improving tear stability. Studies have suggested that tear lipids, containing proteins that interact with meibomian lipids, form a thin polar phase that maintains a stable spread of lipids over the aqueous layer.²⁶ In addition, nanoemulsion ocular solutions could increase the lipid layer thickness at 10 minutes post-instillation of the emulsion.²⁷ A recent study investigating tear lipid thickness using the tear film interferometry method found that the tear lipid thickness increased significantly with lipid tear supplements.²⁸ Therefore, this increase in lipid layer thickness may explain the reduction in tear film evaporation rate and improved tear film stability.

The overall study findings of this study illustrate that the single application of a cationic emulsion effectively

controls tear film evaporation in patients with mild to moderate DEs. The cationic emulsion efficiently enhanced both the tear film stability and the tear meniscus volume. These outcomes suggest that improving tear lipids spread and stability with cationic emulsions can help patients maintain a healthy and stable tear film and thus restore the normal homeostatic state of the ocular surface.

Acknowledgments

The author extends his appreciation to the College of Applied Medical Sciences Research Center and the Deanship of Scientific Research at King Saud University, for funding this research.

Disclosure

The author reports no conflicts of interest in this work.

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