



The Effect of Artificial Tear Preparations with Three Different Ingredients on Contrast Sensitivity in Patients with Dry Eye Syndrome

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ABSTRACT

This study was conducted to investigate the effects of Artificial Tear Preparations (ATP) with three different ingredients on contrast sensitivity in patients with dry eye syndrome. Contrast sensitivity measurements were obtained before and 5, 15, 30, 60, and 90 minutes after administering three different ATPs, containing dextran 70, hydroxypropyl methylcellulose (ATP-1), polyvinyl alcohol-povidone (ATP-2) and carbomer (ATP-3) to one eye of 20 patients with dry eye syndrome, who had been divided to three groups. Contrast sensitivity measurements were obtained at 1.5, 3, 6, 12, and 18 spatial frequencies (cpd). Compared with the baseline measurements, ATP-1 provided a significant increase of 1.5 and 3 cpd at the 15th minute, 12 cpd at the 60th minute, and 18 cpd at the 30th minute, ATP-2 significantly increased contrast sensitivity compared with the baseline at the 15th, 30th, 60th, and 90th minute measurements, recorded as 1.5, 3, 12, and 18 cpd, and ATP-3 provided significant increases of 18 cpd at 60th and 90th minute measurements compared with the baseline. In conclusion, while ATP-2 increased the majority of contrast sensitivity measurements both at early, mid, and late terms, the ATP-1 and ATP-3 were found to be effective on mid-term and late-term contrast sensitivity measurements, respectively.

KEY WORDS

Artificial Tear Preparations; Contrast Sensitivity; Dry Eye Syndromes

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INTRODUCTION

The International Dry Eye Workshop (DEWS) defined dry eye syndrome as "a multifactorial disease of the tears and ocular surface that results in discomfort, visual impairment, and tear layer instability, with a potential to cause damage on the ocular surface". The syndrome is accompanied by increased osmolarity of the tear layer and inflammation of the ocular surface [1]. While the

prevalence of dry eye syndrome has been reported as 9% among the population aged between 40 and 65 years old, after the age of 65, this rate is increased up to 15% [2]. Irrespective of the cause, patients with dry eye syndrome frequently have complaints of 'dryness,' 'sensation of a foreign body,' 'burning' and 'irritated' eyes, and 'blurred vision.' Chronic dry eye leads to



changes in ocular surface, consequently resulting in a lower visual quality and a decrease in vision-related quality of life [3]. Studies have demonstrated that dry eye syndrome may cause a decrease in contrast sensitivity before there is a decrease in visual acuity. Patients complain of blurred and insufficient vision, even when they have full visual acuity. This finding has been demonstrated by measuring contrast sensitivity in healthy individuals and patients with dry eye syndrome [4]. Artificial Tear Preparations (ATP), which are administered to patients with dry eyes to reduce symptoms as well as to relieve them, also result in an improvement of contrast sensitivity. The endurance time of ATPs vary, depending on their ingredients [5]. The differences between the endurance times of artificial tears cause them to be effective on contrast sensitivity at different spatial frequencies. A number of studies have reported that in addition to the relief provided for the patient, the use of artificial tears also increases contrast sensitivity [6]. The present study was designed to evaluate the effects of ATPs with three different ingredients on contrast sensitivity in patients with dry eye syndrome. For this purpose, contrast sensitivity measurements were obtained between 5 and 90 minutes, after the administration of ATPs.

MATERIALS and METHODS

This study was carried out in accordance with the principles of the Helsinki Declaration. All patients provided written informed consent for their participation in the study. In total, 60 females with dry eye syndrome, whose Schirmer 2 test result was lower than 5 mm, were included in the study. The patients were randomly divided to three groups and one of their eyes was administered one of the three different ATPs, containing dextran 70, hydroxypropyl methylcellulose (ATP-1), polyvinyl alcohol-povidone (ATP-2) and carbomer (ATP-3). The other eye of each patient was considered as the control eye. Patients, who used contact lenses, had undergone refractive surgery, used any kind of eye drop in the previous two weeks, had any additional eye disorder (pterygium, etc.), had cataract, and were unable to answer the questions, were excluded from the study. The visual acuity of each patient, corrected or uncorrected, was at the level of 10/10 in the Snellen chart. Patients refractions were between +0.50 and -0.50 spherical equivalent. The Functional Acuity Contrast Test (FACT) (Stereo Optical) was used for spatial contrast sensitivity assessment at a three-meter distance and

illumination of 25 foot-Lamberts, as normal office illumination or luminance of 85 cd/m². To maintain test accuracy, the light meter (Stereo Optical) of FACT was used for standardization of lighting conditions. Characteristics of FACT and the test method have already been described by Onal et al. and the current research followed the same procedure during contrast sensitivity measurement of the study subjects [7]. Data were kept at 95% confidence interval during the statistical analyses. Normally distributed data were compared between groups by using parametric tests, while the corresponding non-parametric tests were used to compare non-normally distributed data. Friedman and Kruskal-Wallis tests were used to compare dependent and independent variables, respectively. A P Value of < 0.05 was considered statistically significant.

RESULTS

In total, 60 females with dry eye syndrome were included in the study and mean age of the study group was 58.65 ± 5.11 years. The mean age and Schirmer 2 test scores were not significantly different between the three groups (P > 0.05) (Table 1). Table 2 shows the mean contrast sensitivity measurements and Standard Deviations (SD) of the three groups and the control group, recorded at the baseline and at the 5th, 15th, 30th, 60th, and 90th minute, at spatial frequencies of 1.5, 3, 6, 12, and 18 spatial frequencies (cpd).

While the measurements recorded in the control group were not significantly different compared to the baseline at neither spatial frequency, the changes in contrast sensitivity caused by ATP-1, ATP-2, and ATP-3 at different time points are shown in Table 2. ATP-1 significantly increased contrast sensitivity to 1.5 and 3 cpd at the 15th minute, to 12 cpd at the 60th minute, and to 18 cpd at the 30th minute, compared to baseline. ATP-2 significantly increased contrast sensitivity to 1.5, 3, 12, and 18 cpd at the 15th, 30th, 60th and 90th minute measurements, compared to baseline. ATP-3 was found to significantly increase contrast sensitivity to 18 cpd at 60th and 90th minute measurements, compared to baseline. Comparison of the three different ATPs demonstrated that ATP-2 caused an overall increase at 15th, 30th, 60th and 90th minute measurements, while ATP-1 increased contrast sensitivity at 15th, 30th, and 60th minute measurements for only certain frequencies. Similarly, ATP-3 increased contrast sensitivity at the 60th and 90th minute measurements only for certain frequencies.



Table 1: Mean Age and Schirmer Scores of Patients

| | ATP-1 (n = 20) | ATP-2 (n = 20) | ATP-3 (n = 20) | P-value |
|-----------------------------|----------------|----------------|----------------|----------|
| Age (Years ± SD) | 58.16 ± 5.22 | 57.65 ± 7.05 | 59.17 ± 2.56 | P > 0.05 |
| Schirmer 2 test (mean ± SD) | 4.8 ± 0.2 mm | 4.6 ± 0.4 mm | 4.7 ± 0.1 mm | P > 0.05 |

ATP: artificial tear preparations; n: number; SD: standard deviation; mm: millimeter.

Table 2: Mean Contrast Sensitivity Measurements of Patients at Baseline and at the 5th, 15th, 30th, 60th and 90th Minute with Spatial Frequencies of 1.5, 3, 6, 12 and 18

| | ATP-1 (n = 20) | ATP -2 (n = 20) | ATP -3 (n = 20) | Control (n = 60) |
|-----------------|----------------|-----------------|-----------------|------------------|
| Baseline | | | | |
| 1.5 sf | 20.80 ± 2.931 | 15.10 ± 4.327 | 15.00 ± 2.865 | 19.43 ± 3.968 |
| 3 sf | 46.35 ± 5.575 | 38.85 ± 5.641 | 36.50 ± 5.063 | 43.10 ± 4.919 |
| 6 sf | 57.20 ± 2.966 | 53.95 ± 2.544 | 49.30 ± 4.508 | 53.90 ± 3.463 |
| 12 sf | 21.15 ± 3.014 | 24.00 ± 3.309 | 30.10 ± 1.774 | 26.65 ± 4.468 |
| 18 sf | 7.95 ± 0.826 | 9.70 ± 1.342 | 10.65 ± 1.565 | 9.50 ± 1.408 |
| 5. min. | | | | |
| 1.5 sf | 24.65 ± 3.631 | 15.10 ± 3.144 | 13.70 ± 2.922 | 18.23 ± 3.127 |
| 3 sf | 45.25 ± 8.503 | 39.60 ± 4.083 | 35.30 ± 5.814 | 42.90 ± 5.001 |
| 6 sf | 58.25 ± 2.447 | 54.00 ± 3.179 | 44.30 ± 6.997 | 52.70 ± 4.244 |
| 12 sf | 21.70 ± 1.867 | 26.10 ± 4.876 | 28.60 ± 1.957 | 28.57 ± 3.610 |
| 18 sf | 8.45 ± 0.510 | 10.70 ± 2.849 | 9.50 ± 1.433 | 10.50 ± 2.004 |
| 15. min. | | | | |
| 1.5 sf | 33.20 ± 4.225* | 23.60 ± 4.795* | 14.90 ± 3.007 | 20.00 ± 3.701 |
| 3 sf | 61.90 ± 2.553* | 53.90 ± 8.117* | 36.60 ± 5.951 | 43.00 ± 4.207 |
| 6 sf | 60.60 ± 0.940 | 62.80 ± 3.861 | 46.80 ± 6.437 | 54.00 ± 4.419 |
| 12 sf | 23.00 ± 1.717 | 34.65 ± 1.814* | 29.90 ± 2.713 | 26.75 ± 3.564 |
| 18 sf | 11.25 ± 2.633 | 15.90 ± 3.810* | 11.40 ± 2.521 | 10.60 ± 1.440 |
| 30 min. | | | | |
| 1.5 sf | 26.20 ± 1.399 | 21.80 ± 4.584* | 15.60 ± 3.218 | 19.97 ± 4.636 |
| 3 sf | 48.65 ± 3.717 | 57.30 ± 5.814* | 36.50 ± 5.463 | 42.80 ± 4.153 |
| 6 sf | 55.60 ± 3.119 | 59.05 ± 3.410 | 47.70 ± 5.814 | 55.20 ± 3.019 |
| 12 sf | 23.10 ± 3.754 | 35.85 ± 3.133* | 31.10 ± 2.864 | 29.40 ± 3.441 |
| 18 sf | 17.80 ± 4.299* | 17.30 ± 3.063* | 11.35 ± 2.498 | 11.60 ± 0.807 |
| 60.min. | | | | |
| 1.5 sf | 23.20 ± 5.167 | 24.20 ± 3.302* | 20.40 ± 4.185 | 20.03 ± 2.718 |
| 3 sf | 45.75 ± 11.097 | 55.10 ± 4.128* | 46.75 ± 5.893 | 40.70 ± 1.598 |
| 6 sf | 59.30 ± 4.079 | 59.10 ± 5.600 | 54.40 ± 4.967 | 53.20 ± 3.277 |
| 12 sf | 35.75 ± 7.786* | 31.90 ± 2.713* | 35.30 ± 2.536 | 29.30 ± 3.946 |
| 18 sf | 12.40 ± 1.273 | 15.00 ± 1.026* | 15.20 ± 1.642* | 11.60 ± 1.509 |
| 90.min. | | | | |
| 1.5 sf | 24.65 ± 7.322 | 19.80 ± 2.238* | 19.30 ± 3.686 | 20.00 ± 3.719 |
| 3 sf | 56.00 ± 0.973 | 54.30 ± 5.667* | 45.50 ± 6.894 | 41.30 ± 3.010 |
| 6 sf | 62.35 ± 2.159 | 57.30 ± 4.601 | 53.20 ± 5.406 | 53.30 ± 1.942 |
| 12 sf | 26.80 ± 1.989 | 32.70 ± 5.401* | 33.10 ± 1.021 | 28.35 ± 3.763 |
| 18 sf | 10.10 ± 1.071 | 15.40 ± 1.957* | 14.00 ± 1.717* | 11.90 ± 1.189 |

ATP: Artificial Tear Preparations; SD: Standard Deviation; min: Minute; sf: Spatial Frequency

*: P < 0.05

Data in table are presented as mean ± SD.



DISCUSSION

The present study investigated the effects of three different ATPs on contrast sensitivity in patients with dry eye syndrome. These three different preparations were compared with each other, as well as the control eyes of the same patient, to which no tear drop had been administered. Measurements were obtained between 5 and 90 minutes after administering ATPs, with the aim of investigating the short-term effects of ATPs on contrast sensitivity. Previous studies have suggested that ATPs may negatively affect contrast sensitivity immediately after administration, yet this may improve after a certain time period [6, 8-10]. Objective findings obtained in the present study demonstrated that artificial tears had positive effects on contrast sensitivity in the short-term. The improvement in the 3 cpd range of contrast sensitivity may be limited change of visual performance. High spatial frequencies closely influence reading capabilities and finer resolution tasks [11]. However, low to middle spatial frequencies could improve facial recognition capability [12]. At 3 cpd, which is the medium spatial frequency corresponding to the highest contrast sensitivity in healthy eyes, ATP-2 provided significant increases in the measurements obtained at the 15th, 30th, 60th, and 90th minute. ATP-1 contains dextran 70 and hydroxypropyl methylcellulose, and has moderate viscosity, therefore, it causes a marked improvement in contrast sensitivity at certain spatial frequencies at the 15th, 30th and 60th minute. ATP-2, which contains polyvinylpyrrolidone and has a higher viscosity, improved contrast sensitivity at all spatial frequencies in the measurements obtained at the 15th, 30th, 60th, and 90th minute.

ATP-3, which contains carbomer, has a higher density and therefore decreases contrast sensitivity, five minutes after use; however, contrast sensitivity returned to baseline levels at the 15th and 30th minute measurements and was found to be increased at the measurements obtained at the 60th and 90th minute. Carbomers are synthetic polymers that are found as active ingredients in several topical agents commonly used by patients with dry eye syndrome. They are hydrophilic polymer-based substances with a high molecular weight, and they have similar pH and osmolarity as natural tears [13]. These characteristics allow them to form a long-lasting, transparent, lubricated, and wet film layer on the eye surface. As carbomer has a high molecular weight, it cannot be absorbed through the eyes or be accumulated in eye tissue [14]. In a multi-center, randomized, placebo-controlled study, it was demonstrated that carbomer was

safe and more effective than the placebo, in terms of improving subjective and objective symptoms of moderate to advanced dry eye syndrome [15]. In a prospective study conducted by Xiao Q et al. to compare the clinical efficacy of artificial tears containing 0.4% carbomer and 1% carboxymethyl cellulose in patients with dry eye syndrome, carbomer gel was found to remain on the cornea for a longer period and be more effective than carboxymethyl cellulose [16]. In another randomized double-blind study conducted by Johnson et al., the efficacy of 3% carbomer and 0.18% sodium hyaluronate on dry eyes was compared and both agents were found to decrease symptom severity, while they did not have long-term effects on Tear Breakup Time (TBUT) [17]. Therefore, artificial tear drops increase optic quality by forming a more lubricated and smoother layer on the cornea surface and they eventually improve contrast sensitivity. The duration of contact with cornea and endurance time of ATPs vary according to their ingredients, and these factors determine which ATP improves contrast sensitivity at a given spatial frequency and time interval. Particularly, in patients with dry eye syndrome that causes disruption of ocular surface, recovery of the ocular surface gains significance for increasing contrast sensitivity [18]. Patients with dry eye syndrome complain of decreased visual quality even if they have full visual acuity. This is because contrast sensitivity is already lost before visual acuity starts to decrease. ATPs used at this stage increase visual quality of the patients, while providing relief of symptoms, such as burning, stinging, soreness, irritation and gritty, and itchy sensations experienced by the patients [19]. Having a cross sectional study design, measurement of only contrast sensitivity, as one of vision quality measures, and lack of evaluation of ATPs long term effects on quality of vision could be considered as limitations of the current study. Moreover, contrast sensitivity, as a psychophysical test, is not constant. Therefore, for better evaluation of shorter term effects of ATPs on dry eyes, more constant measures of visual optics, such as dynamic wavefront aberrometry, are recommended [20].

CONCLUSION

ATPs provide both symptom relief in patients with dry eye syndrome, and increase visual quality by increasing contrast sensitivity, depending on their ingredient content. Future studies with larger sample sizes and additional measures of tear residence time and dynamic aberrometry may be helpful for characterization of better visual benefits of artificial tears in the short-term.

**DISCLOSURE**

Ethical issues have been completely observed by the authors. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published. No conflict of interest has been presented.

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