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Pelin Özyol, Erhan Özyol & Aylin Karalezli

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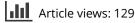
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#### ORIGINAL ARTICLE

## Evaluation of Visual Field Test Parameters after Artificial Tear Administration in Patients with Glaucoma and Dry Eye

Pelin Özyol, Erhan Özyol, and Aylin Karalezli

Department of Ophthalmology, Muğla Sıtkı Koçman University Faculty of Medicine, Muğla, Turkey

#### ABSTRACT

*Purpose*: To examine the effect of a single dose of artificial tear administration on automated visual field (VF) testing in patients with glaucoma and dry eye syndrome. *Material and Methods*: A total of 35 patients with primary open-angle glaucoma experienced in VF testing with symptoms of dry eye were enrolled in this study. At the first visit, standard VF testing was performed. At the second and third visits with an interval of one week, while the left eyes served as control, one drop of artificial tear was administered to each patient's right eye, and then VF testing was performed again. The reliability parameters, VF indices, number of depressed points at probability levels of pattern deviation plots, and test times were compared between visits. *Results*: No significant difference was observed in any VF testing parameters of control eyes (P>0.05). In artificial tear administered eyes, significant improvement was observed in test duration, mean deviation, and the number of depressed points at probability levels (P<0.5%, P<1%, P<2%) of pattern deviation plots (P<0.05). The post-hoc test revealed that artificial tear administration elicited an improvement in test duration, mean deviation, and the number of depressed points at probability levels (P<0.5%, P<1%, P<2%) of pattern deviation plots from first visit to second and third visits (P<0.01, for all comparisons). The intraclass correlation coefficient for the three VF test indices was found to be between 0.735 and 0.85 (P<0.001, for all). *Discussion*: A single dose of artificial tear administration immediately before VF testing seems to improve test results and decrease test time.

Keywords: Antiglaucomatous medication, artificial tear, dry eye, glaucoma, visual field testing

#### INTRODUCTION

Chronic use of topical antiglaucomatous medication has been associated with an increased prevalence of ocular surface disease in glaucoma patients treated for a lifetime.-<sup>1,2</sup> Ocular surface side-effects of antiglaucomatous drugs are caused by either the drug itself or by preservatives.<sup>3</sup> In particular, preservatives of antiglaucomatous medication decrease tear production and goblet cell density,<sup>3,4-7</sup> which induces impairment of tear film stability. The use of artificial tears in patients with dry eye has been associated with improving visual acuity,<sup>8-10</sup> contrast sensitivity,<sup>8,11</sup> corneal topographical measurements,<sup>12-15</sup> glare disability,-<sup>8</sup> and wavefront aberrations<sup>16</sup> in several studies.

Automated perimetry is widely used to assess functional glaucomatous loss and is a standard procedure in the management of glaucoma. The results of automated perimetry can be influenced by many factors, such as pupil size,<sup>17</sup> media opacities,<sup>18</sup> learning effect,<sup>19,20</sup> fatigue,<sup>21</sup> and tear film stability.<sup>9</sup>

The purpose of this study was to evaluate the effect of a single dose of artificial tear administration on automated perimetry global indices, reliability parameters, and the number of depressed points at probability levels (P<5%, P<2%, P<1%, and P<0.5%) of pattern deviation plots in patients with glaucoma and dry eye syndrome.

#### **METHODS**

Thirty-five patients with diagnosis of primary openangle glaucoma and dry eye under antiglaucomatous medication who had long-term follow-up with at least two or more standard visual fields and best-corrected

Received 25 March 2016; accepted 8 September 2016; published online 25 November 2016 Correspondence: Pelin Özyol, Muğla Sıtkı Koçman Üniversitesi, Tıp Fakültesi Göz Hastalıkları, 48000 Menteşe, Muğla, Turkey. E-mail: pelingesoglu@yahoo.com.tr

visual acuity of 20/40 or better were enrolled in this study. The tenets of the Declaration of Helsinki were followed throughout the study. Informed consent was obtained from all patients, and the study was carried out with approval from the institutional review board.

Exclusion criteria were artificial eye drop usage, visual acuity <20/40, mean deviation value >-7.0 in visual field tests, any history of ocular trauma, intraocular surgery or refractive corneal procedures, and contact lens wear.

The diagnosis of dry eye was made on the basis of the presence of symptoms of dry eye (feeling of burning, dryness, and foreign body sensation in the eye), Schirmer test results of less than 5 mm in five minutes with topical 0.5% proparacaine hydrocloride anaesthesia, and tear break-up time (BUT) of less than 10 seconds.

At the first visit, standard visual field testing was performed by a trained technician with a Humphrey Field Analyzer (HFA) II 740 (Carl Zeiss Meditec Inc., Dublin, CA, USA) using a Swedish Interactive Threshold Algorithm (SITA; Carl Zeiss Meditec, Inc.) strategy and 24-2 program. To be considered reliable, a test had to have false-positive and false-negative responses less than 15% and fixation losses less than 15%. Then, patients were asked to continue their antiglaucomatous medication and called for control visual field testings.

At the second and third visits with an interval of one week, one drop of artificial tear (Systane, Alcon Inc., Fort Worth, TX, USA) was instilled into the inferior conjunctival sac of each patient's right eye. The left eye of each patient served as control. Patients were instructed to blink several times. At 15 min after the administration, visual field testing was performed again, as previously described.

The reliability parameters (false-positive and falsenegative errors), visual field indices (mean deviation (MD), pattern standard deviation (PSD), number of depressed points at probability levels (P < 5%, P < 2%, P < 1%, and P < 0.5%) of pattern deviation plots and test time were obtained from the results of each test session for each eye.

Data analysis was performed by SPSS v 20.0 software package. A one-way repeated-measures analysis of variance (ANOVA) was conducted to determine whether there were significant differences in the parameters obtained from visual field testing at the first, second, and third visits. A post-hoc (Tukey) test was performed to determine a significant difference between any two visits. Test-retest variability of the three visual field test parameters was assessed using an intraclass correlation coefficient (ICC) test. The level of significance was set at P < 0.05.

#### RESULTS

The mean age of patients was  $65.9 \pm 7.6$  (range, 51–79) years. The mean duration of glaucoma was  $8.6 \pm 5.3$ 

(range, 2–15) years. Nineteen of the patients were female and 16 were male. Patients used the same glaucoma medication for both eyes. Fourteen patients (40%) were under prostaglandine analogue monotherapy, 13 (37.1%) were under prostaglandine analogue/ $\beta$  blocker fixed combination therapy, and 8 (22.9%) were under dorzolamide/ $\beta$  blocker fixed combination therapy for both eyes. There were no statistical differences in BUT scores (5.7 ± 1.9 *vs* 5.4 ± 2.1, *P*=0.769) and Schirmer I values (3.2 ± 1.1 *vs* 3.5 ± 1.6, *P*=0.816) between right and left eyes of patients under glaucoma medication.

The reliability parameters (fixation losses, falsepositive and false-negative errors), visual field indices (MD and PSD), test duration, and changes in the number of depressed points at different probability levels in pattern deviation plots are given in Table 1. No significant difference was observed in any visual field testing parameters of control eyes (P>0.05). In artificial tear administered eyes, there was no difference in values of PSD, fixation losses, false-positive errors, and false-negative errors between the visits. However, significant improvement was observed in test duration, MD, and the number of depressed points at probability levels less than 0.5%, less than 1%, and less than 2% in pattern deviation plots (P<0.05). The post-hoc test revealed that artificial tear administration elicited an improvement in test duration (P<0.001 for both visits), MD (P=0.0012 and P=0.0010), and the number of depressed points at probability levels less than 0.5% (P=0.0036 and P=0.0018), less than 1% (P=0.001, for both visits), and less than 2% (P=0.001, for both visits) in pattern deviation plots from first visit to second and third visits. There was no significant difference in those between the second and third visits (P>0.05).

The ICC values and 95% confidence intervals of visual test indices are listed in Table 2. The overall ICC for the three visual field test indices of all patients was found to be between 0.735 and 0.85 (P<0.001, for all).

#### DISCUSSION

To evaluate visual field test parameters properly is important in terms of changes in glaucoma treatment decisions. Therefore, factors that may alter the visual field analysis results incorrectly need to be corrected. Long-term use of antiglaucoma drugs has been associated with toxic as well as inflammatory changes of the ocular surface.<sup>4,5</sup> Preservatives in antiglaucoma drugs have a detergent effect on the precorneal lipid layer, resulting in decreased corneal tear film stability and increased evaporation.<sup>3</sup> Previous studies have shown that visual field test parameters are adversely influenced by corneal surface irregularities.<sup>9,22,23</sup>

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TABLE 1.

Glaucoma with dry eye

		Right eyes				Left eyes (control)	ontrol)	
	The first visit (without artificial tear)	The first visit (without artificial The second visit (with artificial The third visit (with artificial tear) tear) tear)	The third visit (with artificial tear)	<i>P</i> value*	The first visit	The second visit	The third visit	<i>P</i> value*
Fixation losses (%) False-positive errors	$1.50 \pm 2.83$ $2.17 \pm 1.91$	$1.31 \pm 2.74$ $1.70 \pm 2.46$	$1.34 \pm 1.97$ $1.77 \pm 2.21$	0.672 0.098	$1.65 \pm 2.7$ $3.12 \pm 3.7$	$1.74 \pm 3.81$ $3.0 \pm 2.95$	$1.64 \pm 3.1$ $3.16 \pm 3.3$	0.457 0.312
(%) False-negative errors	$3.73 \pm 2.38$	$2.91 \pm 1.84$	$3.05 \pm 3.3$	0.11	$4.0 \pm 4.9$	$3.65 \pm 3.9$	$3.86 \pm 4.01$	0.706
( 70) Test duration (min) Mean deviation	$4.80 \pm 0.98$ -4.79 + 4.12	$4.19 \pm 1.17$ -4.25 + 4.32	$4.11 \pm 1.05 \\ -4.17 + 3.96$	< 0.001	$5.43 \pm 1.4$ -4.2 + 3.5	$5.27 \pm 1.1$ -3.9 + 4.1	$5.32 \pm 1.9$ -4.07 + 3.4	0.517
Pattern standard deviation	$3.54 \pm 2.70$	$3.31 \pm 2.53$	$3.36 \pm 2.97$	0.106	$3.71 \pm 3.5$	$3.4 \pm 3.9$	$3.53 \pm 2.97$	0.745
Number of depressed points $P < 0.5\%$	oints $4.21 \pm 5.64$	$2.73 \pm 3.53$	2.58 ± 2.84	0.022	$3.71 \pm 4.5$	3.52 ± 4.1	$3.69 \pm 3.83$	0.640
P < 1%	$3.30 \pm 1.81$	$1.92 \pm 1.30$	$1.98 \pm 1.43$	0.016	$2.9 \pm 1.1$	$3.03 \pm 1.4$	$2.85 \pm 1.44$	0.685
P < 2% P < 5%	$3.86 \pm 2.57$ $5.13 \pm 4.50$	$2.40 \pm 2.27$ $4.98 \pm 4.02$	$2.48 \pm 2.19$ $4.85 \pm 4.55$	0.001 0.72	$3.1 \pm 2.7$ $4.3 \pm 3.9$	$3.0 \pm 1.9$ $4.51 \pm 4.8$	$2.97 \pm 2.3$ $4.38 \pm 4.11$	0.77 0.873
*Repeated measures of ANOVA.	of ANOVA.							

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Visual field indices	Intraclass correlation coefficient	95% confidence interval	P value
Fixation losses	0.834	0.768-0.95	< 0.001
False-positive errors	0.79	0.659–0.84	< 0.001
False-negative errors	0.735	0.64–0.796	< 0.001
Test duration	0.762	0.702-0.814	< 0.001
Mean deviation	0.74	0.606-0.895	< 0.001
Pattern standard deviation	0.85	0.715-0.920	< 0.001

TABLE 2. Intraclass correlation coefficient values of visual field test parameters.

In the present study, all patients were on preservative-containing glaucoma medication and had ocular surface disease. We assessed the effect of a single dose of artificial tear administration before visual field testing on visual field test parameters of those patients. Our results revealed that administration of a single dose of artificial tear resulted in significant improvements in MD values, the number of depressed points in probability scores (P<0.5%, P<1%, and P<2%), and test duration. The improvement in visual field test parameters could be associated with more regular ocular surface that may contribute to increased patient comfort and improved visual function during visual field testing.

In the literature, the use of artificial tears was associated with improvements in visual acuity, contrast sensitivity, and corneal surface regularity indices that could contribute visual field analysis results.<sup>8-11,14</sup> Few studies have evaluated the effect of artificial tear treatment on visual field testing. Rieger et al.9 showed a significant improvement in macular thresholds on a 10-2 central visual field test after tear replacement. Yenice et al.<sup>22</sup> reported significant improvement in visual field test indices, reliability parameters, and the number of depressed points on a 30-2 full-threshold program in patients with primary openangle glaucoma and dry eye after treatment of artificial tear solution for one week. Guzey et al.23 showed an improvement in FASTPAC test indices, test duration, and the number of depressed points in pattern deviation plots after lubricating eye drop treatment for eight weeks. Similarly, Kocabeyoglu et al.<sup>24</sup> reported a decrease in testing time and an improvement in test results on visual field test using SITA strategy and 24-2 program after one week of treatment using a lubricating eye drop. In the current study, improvement in test parameters and test duration on a visual field test carried out at two different visits was elicited after a single dose of artificial tear administration.

In this study, learning effect could be discussed. However, all patients included in this study had experience in visual field testing that was verified by reproducibility of the three visual field tests that was excellent, with ICC values of between 0.735 and 0.85. Automated perimetry testing results depend on the reliability of the patient's response. The differentiation of true progression between any two consecutive visual field examinations is important. Thus, factors that can be changed should be eliminated. Based on the current study results, it is recommended that, before visual field examination, at least one drop of artificial tear should be administered in eyes under antiglaucomatous medication with ocular surface disease to avoid any unnecessary intervention because of misleading progression of the visual field.

#### **DECLARATION OF INTEREST**

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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