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Artificial Tear Drops Influence on High Order Aberrations in Healthy Eye Subjects

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Authors' contributions

This work was carried out in collaboration among all authors. Author FC designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors CK and AB managed the analyses of the study. Author MA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Purpose: To gain more insight into tear film from a functional standpoint, we investigate artificial tear eye drops effect by assessing its influence on high order aberration in healthy eye subjects using a Shack-Hartmann aberrometer.

Methods: An observational case-control study into which 20 young healthy participants were involved. High order aberrations were measured using Shack-Hartmann technology before; 1 hour and 3 hours after instillation of a 0.3% sodium hyaluronate eye drop.

Main measured outcomes were root mean square of high order aberrations in central 5 mm (HOA 5) and in central 6 mm (HOA 6), spherical aberration, vertical coma, horizontal coma, vertical trefoil, horizontal trefoil.

Results: The HOA 5 mean value was 0.21μ before the instillation of artificial tear eye drops and 0.185μ one hour after instillation with a significant statistical difference ($p=0.01$) and 0.186μ three hours after instillation with no significant statistical difference ($p=0.057$). No significant statistical difference was found for HOA 6 before and after tear eye drops application.

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Vertical coma was the only subset of high order aberrations that was significantly improved from 0.042μ to -0.003μ one hour after tear eye drops application ($p=0.04$). There was no statistical difference for all the other measurements.

Conclusions: Some high order aberrations could arise from the tear film even in a healthy patient. Vertical coma could be used as a tool to point to the integrity of tear film. For wavefront-guided refractive surgery candidates, high order aberrations should be assessed 1 hour after artificial tear drop instillation.

Keywords: Artificial tear eye drops; healthy eye subjects; high order aberrations; vertical coma.

1. INTRODUCTION

The tear film is the first refractive layer of the eye, it has an anterior radius of curvature of 7.8 mm and a refractive index of 1.336 and assuming a refractive power of 43.03 D [1].

To investigate the tear film from a functional standpoint; we elected to perform a study by evaluating its influence on high order aberration in the healthy eye using a Shack-Hartmann aberrometer.

High order aberrations evaluate quality of optical media. In ophthalmology, it is the amount of distortion that a wavefront of light will acquire while through the transparent media of the eye.

Much of the emphasis in the literature was put on studying artificial tear eye drops effects on HOA during the first minutes and up to 15 minutes after instillation in the healthy eye. Through this work, we want to investigate further the effects of hyaluronate sodium-based artificial tear eye drops on HOA changes after the first hour and up until 3 hours after instillation in healthy eyes.

2. MATERIALS AND METHODS

This is a case-control observational study that was conducted following the tenets of the Declaration of Helsinki. The research was approved by our institutional review board and informed consent was obtained from all subjects involved after explanation of the nature and possible consequences of the study. Were excluded all participants with past history of ocular surgery, ocular surface disease, hyperopes or myopes, and those who have been on artificial tear eye drops. All participants had a visual acuity of 20/20 and a refraction between -0.5D and +0.5D with normal slit lamp anterior segment examination and normal biomicroscopic eye fundus evaluation.

20 young healthy participants were involved in this experience by undergoing HOA mensuration

using Shack-Hartmann technology (Zywave II, Bausch and Lomb) before; 1 hour and 3 hours after instillation of a 0.3% sodium hyaluronate eye drop. Main measured outcomes were root mean square of high order aberrations in central 5 mm (HOA 5) and in central 6mm (HOA 6), spherical aberration (SA), vertical coma (VC), horizontal coma (HC), vertical trefoil (VT), horizontal trefoil (HT). Only measurements from the right eyes were taken into consideration. Means of these different parameters were calculated before the instillation of artificial tear eye drops and at 1 and 3 hours after instillation. Means were then compared using student t-test for two dependent means and statistical significance was set at a p-value of 0.05. Statistical calculations were made using the SPSS software version 25.

3. RESULTS

The participants were all training residents in the ophthalmology department of the university hospital Hassan II of Fez; Morocco. There were 20 participants aged 25 to 30 years old (mean age 27 years old), 11 females and 9 males.

The HOA 5 mean value was 0.21μ before the instillation of artificial tear eye drops and 0.185μ one hour after instillation with a significant statistical difference ($p=0.01$) and 0.186μ three hours after instillation with no significant statistical difference ($p=0.057$) (Table 1).

The HOA 6 mean value was 0.339μ before instillation and 0.306μ one hour after instillation and 0.326μ three hours after instillation with no significant statistical difference with $p=0.12$ and $p=0.50$ respectively (Table 1).

As for vertical coma; mean value before instillation was 0.042μ and -0.003μ one hour after instillation with a significant statistical difference ($p=0.04$) and become 0.034μ three hours after instillation with no significant statistical difference ($p=0.73$) (Table 2) (Figs. 1 and 2).

Table 1. Total high order aberrations (μ) in 5 mm and 6 mm before and after instillation of artificial tear eyedrops at 1 and 3 hours

Case	HOA 5 *	HOA 5 1H †	HOA 5 3H ‡	HOA 6 §	HOA 6 1H ¶	HOA 6 3H #
1	0.25	0.22	0.18	0.61	0.38	0.36
2	0.19	0.07	0.05	0.42	0.17	0.28
3	0.16	0.15	0.23	0.24	0.28	0.27
4	0.18	0.19	0.16	0.29	0.35	0.29
5	0.46	0.34	0.35	0.62	0.5	0.52
6	0.21	0.15	0.14	0.33	0.26	0.26
7	0.17	0.11	0.18	0.25	0.18	0.22
8	0.21	0.22	0.17	0.3	0.41	0.35
9	0.17	0.21	0.15	0.23	0.24	0.23
10	0.22	0.17	0.3	0.28	0.26	0.41
11	0.26	0.18	0.16	0.36	0.3	0.31
12	0.17	0.14	0.09	0.19	0.22	0.14
13	0.16	0.08	0.09	0.36	0.25	0.27
14	0.23	0.22	0.25	0.3	0.23	0.32
15	0.17	0.19	0.17	0.27	0.21	0.3
16	0.1	0.16	0.15	0.21	0.3	0.26
17	0.22	0.23	0.25	0.42	0.41	0.42
18	0.28	0.23	0.27	0.39	0.4	0.48
19	0.25	0.26	0.25	0.43	0.45	0.44
20	0.22	0.19	0.13	0.29	0.32	0.39
Means (P)	0.21	0.185 (0.01)	0.186 (0.057)	0.339	0.306 (0.12)	0.326 (0.5)

*: HOA in central 5mm before instillation; †: HOA in central 5 mm 1 hour after instillation.; ‡: HOA in central 5mm 3 hours after instillation.; §: HOA in central 6mm before instillation; ¶: HOA in central 6mm 1 hour after instillation; #: HOA in central 6 mm 3 hours after instillation

Table 2. Vertical and horizontal coma root mean square values before and after instillation of artificial eye teardrops at 1 hour and 3 hours

Case	VC *	VC 1H †	VC 3H ‡	HC §	HC 1H ¶	HC 3H #
1	0.27	0.1	0.2	0.16	0.16	0.11
2	0.34	0.11	0.21	-0.04	-0.03	-0.03
3	-0.02	-0.05	0.02	0.05	0.05	0.11
4	-0.23	-0.25	-0.18	-0.14	-0.13	-0.11
5	0.42	0.2	0.28	-0.23	-0.11	-0.19
6	0.02	0.04	0.01	-0.24	-0.17	-0.16
7	0.03	-0.03	0.06	-0.002	0	-0.01
8	-0.14	-0.27	-0.16	0.05	-0.06	-0.02
9	0.02	-0.06	0.01	0.03	0.07	0.05
10	-0.13	-0.15	-0.34	0.02	0.06	0.05
11	0.24	0.16	0.19	-0.02	0.01	-0.1
12	-0.14	-0.001	-0.01	-0.08	-0.15	-0.03
13	-0.31	-0.19	-0.01	-0.05	-0.03	-0.02
14	0.3	0.29	0.25	0.08	0.08	0.1
15	0.05	0.02	0.04	0.16	-0.05	-0.05
16	0.05	0.04	0.06	0.04	0.09	0.08
17	-0.11	-0.15	-0.14	-0.24	-0.09	-0.1
18	0.32	0.26	0.33	-0.06	-0.05	-0.17
19	-0.06	-0.06	-0.05	0.23	0.22	0.19
20	-0.08	-0.07	-0.09	0.07	0.16	0.18
Means (P)	0.042	-0.003 (0.04)	0.034 (0.73)	-0.0106	0.0015 (0.49)	-0.006 (0.8)

*: vertical coma before artificial tear eyedrops instillation.; †: vertical coma 1 hour after artificial tear eyedrops instillation; ‡: vertical coma 3 hour after artificial tear eyedrops instillation; §: Horizontal coma before artificial tear eyedrops instillation; ¶: Horizontal coma 1 hour after artificial tear eyedrops instillation; #: Horizontal coma 3 hour after artificial tear eyedrops instillation

Table 3. Vertical and horizontal trefoil root mean square values before and after instillation of artificial eye teardrops at 1 hour and 3 hours

Case	HT *	HT 1H †	HT 3H ‡	VT §	VT 1H ¶	VT 3H #
1	0.11	0.12	0.12	0.27	-0.02	-0.01
2	-0.12	-0.07	-0.13	-0.02	-0.002	-0.01
3	-0.16	-0.23	-0.2	0.08	0.1	0.11
4	-0.04	-0.002	-0.01	0.03	0.01	-0.03
5	0.22	0.18	0.28	0.28	0.14	0.19
6	0.15	0.1	0.07	0.05	0.04	0.04
7	-0.18	-0.11	-0.12	-0.12	0.001	-0.06
8	0.06	0.08	0.12	0.17	0.17	0.14
9	0.04	-0.02	0.04	0.13	0.11	0.1
10	0.14	0.06	0.11	0.09	0.14	0.13
11	-0.14	-0.11	-0.11	-0.07	-0.01	-0.08
12	0.002	0.04	0.06	0.01	-0.11	-0.06
13	-0.01	-0.01	-0.05	0.08	0.15	0.03
14	-0.02	-0.02	-0.08	0.08	0.08	0.08
15	-0.17	-0.16	-0.2	0.16	0.08	0.19
16	0.05	0.17	0.03	-0.11	-0.13	-0.15
17	0.08	0.01	-0.03	0.06	0.003	0.02
18	0.17	0.19	0.19	-0.02	-0.02	-0.1
19	-0.21	-0.25	-0.25	-0.28	-0.27	-0.28
20	-0.16	-0.13	-0.15	0.16	0.16	0.23
Means (P)	-0.0094	-0.008 (0.91)	-0.015 (0.58)	0.0515	0.0311 (0.31)	0.024 (0.11)

*: Horizontal trefoil before artificial tear eyedrops instillation; †: Horizontal trefoil 1 hour after artificial tear eyedrops instillation; ‡: Horizontal trefoil 3 hour after artificial tear eyedrops instillation; §: vertical trefoil before artificial tear eyedrops instillation; ¶: vertical trefoil 1 hour after artificial tear eyedrops instillation; #: vertical trefoil 3 hour after artificial tear eyedrops instillation

Table 4. Spherical aberrations root means square values before and after instillation of artificial eye teardrops at 1 hour and 3 hours

Case	SA *	SA 1H †	SA 3H ‡
1	-0.23	-0.24	-0.24
2	0.15	0.08	0.1
3	-0.06	-0.03	-0.04
4	0.04	0.13	0.09
5	0.03	0.05	0.02
6	0.09	0.15	0.16
7	-0.05	-0.09	-0.13
8	-0.19	-0.23	-0.23
9	-0.08	-0.15	-0.18
10	-0.16	-0.1	0.001
11	0.18	-0.04	0.14
12	0.01	0.09	0.04
13	-0.05	0.01	0.003
14	0.01	0.01	-0.01
15	-0.05	-0.03	-0.03
16	-0.15	-0.13	-0.16
17	-0.31	-0.35	-0.35
18	-0.1	-0.21	-0.21
19	-0.04	-0.08	-0.08
20	-0.12	-0.17	-0.16
Means (P)	-0.054	-0.066 (0.45)	0.063 (0.5)

*: spherical aberrations before instillation of artificial tear eyedrops; †: spherical aberrations 1 hour after instillation of artificial tear eyedrops; ‡: spherical aberrations 3 hours after instillation of artificial tear eyedrops

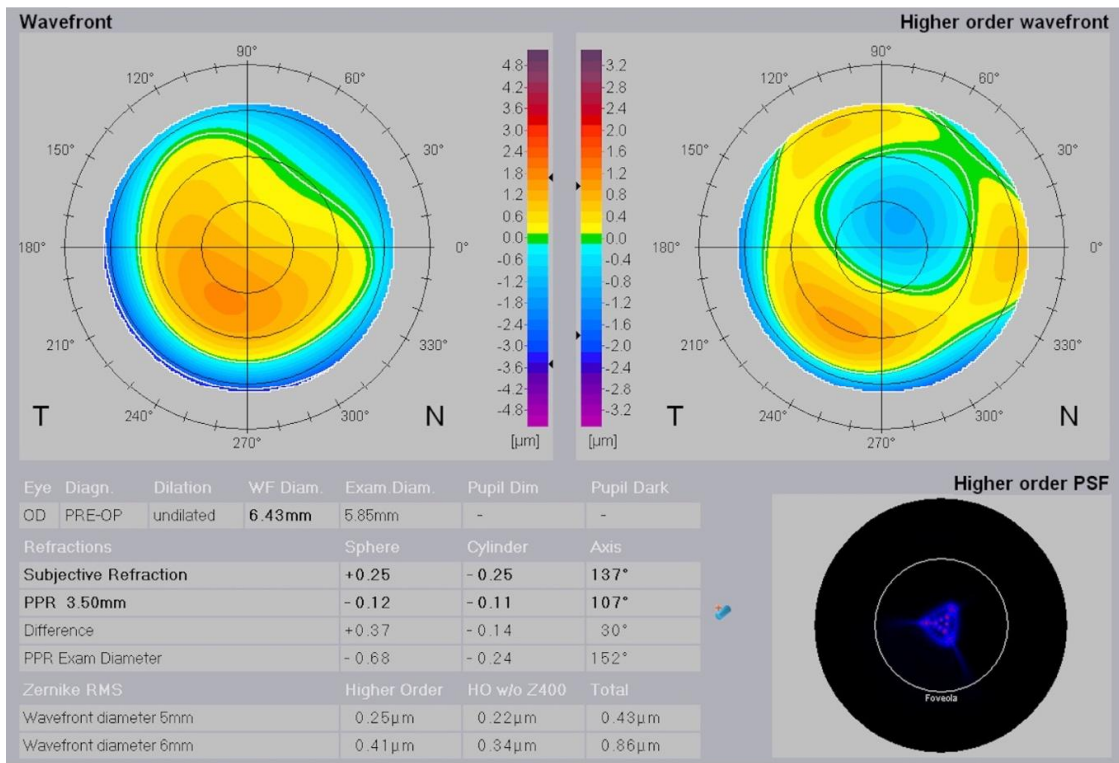


Fig. 1. Example of total high order aberrations before artificial tear eye drops instillation

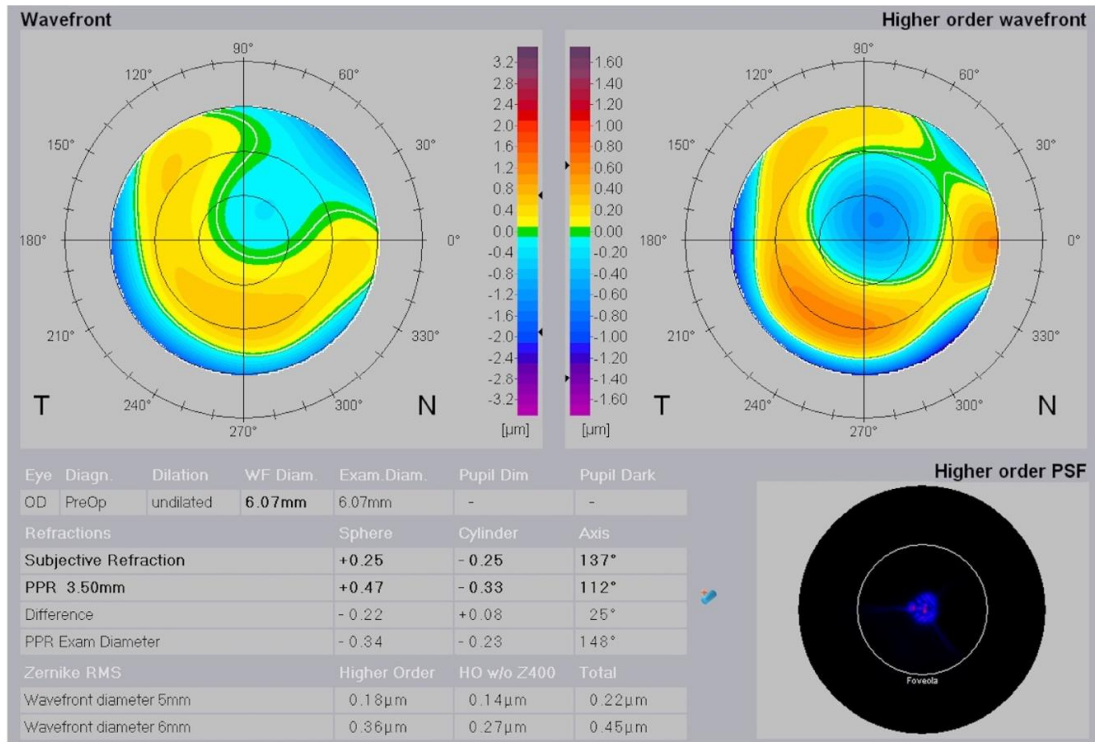


Fig. 2. The same example as in Fig. 1, high order aberrations 3 hours after instillation of artificial tear eye drops. Point spread function (PSF) and high order aberrations are reduced comparatively to initial values

For horizontal coma, it was -0.0106μ before instillation and become 0.0015μ after 1 hour and -0.006μ after 3 hours with no significant statistical difference with $p=0.49$ and $p=0.80$ respectively (Table 2).

For horizontal trefoil mean value; it was -0.0094μ before instillation and becomes -0.0081μ after 1 hour and -0.0155μ after 3 hours with no significant statistical difference ($p=0.91$ and $p=0.58$ respectively) (Table 3).

For vertical trefoil mean value it was 0.0515μ before instillation and become 0.0311μ after 1 hour and 0.024μ after 3 hours with no significant statistical difference ($p=0.31$ and $p=0.11$ respectively) (Table 3).

For spherical aberrations, the mean value was -0.054μ before instillation and -0.066μ after 1 hour, -0.063μ after 3 hours with no significant statistical difference ($p=0.45$ and $p=0.51$ respectively) (Table 4).

4. DISCUSSION

The tear film plays an important role in the quality of vision. Many factors related to tear film had been reported to influence HOA. Thus; in normal eyes and during the first seconds after a blink, there is an increase in high order aberrations caused by the initially irregular tear film [1]. On the other hand; measuring HOA before and after tear film break up shows an increase of HOA by 1.23 to 1.44 folds [2]. Also; the height of tear meniscus height had been reported to correlate positively with HOA [3]. For all of these reasons, we elected to investigate tear film in healthy eyes by measuring HOA; a technique that has already been used as a tool to investigate indirectly the integrity of tear film such as measuring tear film break up time by monitoring high order aberrations changes [4]. Besides; in the literature, most of the studies were carried out to explore HOA alteration effects of lubricants up to 15 minutes in healthy eyes and up to 2 hours in dry eye patients. Thus; we decided to extend further the timing of measurement up to 3 hours in healthy eyes. Our study is the first to show an improvement of HOA RMS in the central 5 mm at 1 hour after instillation of 0.3% hyaluronate sodium tear eye drops in healthy eyes with statistical significance; although, this improvement lacked statistical significance at 3 hours measurements. The other improvement was seen in a vertical coma after 1 hour of instillation, which is maybe the element that

accounts for overall HOA improvement. For all the other studied parameters there were no statistical differences either at 1 hour or 3 hours measurements.

The effect of artificial tear eye drops on high order aberrations depends on the timing of measurement and the viscosity of the used medication. In a study comparing 0.3% sodium hyaluronate; 2% rebamipide and 3% diquafosol artificial tear drops in dry eyes, there was a significant increase of HOAs 1 minute after instillation with recovering to the baseline values thereafter; while the 0.3% sodium hyaluronate had the most significant effect to worsen HOA 1 minute after instillation [5]. In another study by Berger et al.; they measured HOA during the first 60 seconds after instillation of two artificial tear drops (a non-preserved sodium carboxymethylcellulose 0.25% baes eyedrop and more viscous artificial tear eye drops of polyethylene glycol 400 0.4%) in healthy eyes; they found significantly increased HOA after tear eye drops instillation and more important in the more viscous product [6]. Hiraoka et al. [7] in a study comparing two antiglaucoma eye drops medications, a suspension, and a gel; the authors found an increase in HOA up to 5 minutes for gel and up to 2 minutes for suspension, with a return to basal values at 15 minutes after instillation. For Montés-Micó et al, [8] when comparing the effect of instillation of tear eye drops in the setting of dry eye; they found a reduction by a factor of 2 to 3 times of HOA immediately and up to 10 minutes after instillation of an artificial teardrop made of sodium hyaluronate at 0.18%. Using the same molecule; sodium hyaluronate (0.18%) in dry eye patients, Lekhanont et al. [9] found an improvement of spherical aberrations one minute after instillation with a return to baseline value up to 2 hours after instillation. On the contrary to that; Tung et al. [10] using five types of artificial teardrops in dry eye patients, the authors found an increase of HOA in the first five minutes with a return to baseline value at 20- and 40-minutes measurements.

In a study comparing lipid-based eye drops and hyaluronate eye drops in dry eye patients; Lipid-containing artificial tears were superior to sodium hyaluronate-containing drops in terms of improving HOA in patients with Meibomian gland dysfunction [11].

Long term effects with respect to HOA of daily use of three artificial tear eye drops containing

Rebamipide; 0.5% carboxymethylcellulose sodium and diquafosol respectively in dry eye patients were evaluated in three separate studies. They all found improvement of HOA after 2 to 4 weeks treatment duration [12-14].

All of the previous studies show the tight link between HOA and the tear film. Thus; and taking into consideration the results in our study, we recommend that HOAs should be carefully assessed in refractive surgery candidates even in cases with no obvious signs of dry eye; to avoid prescribing abusively wavefront-guided refractive surgery.

We believe in the light of the results of our study, that many patients with increased HOA with no evident clinical or physical sign of dry eye disease could be ruled out of wavefront-guided refractive surgery if the measurement were performed after teardrop installation may be because of an infra-clinical quality or quantity disturbance of tear film.

5. CONCLUSIONS

Artificial tear drops could improve the optical quality of the eye even in healthy eye patients. This means that some of HOA could have as origin the tear film even in the absence of evident signs of dry eye. Thus; it may be wise to not include this subset of patients in the routine wavefront-guided refractive surgery by performing HOA assessment 1 hour after artificial tear drop instillation of refractive surgery candidates.

CONSENT AND ETHICAL APPROVAL

The research was approved by our institutional review board and informed consent was obtained from all subjects involved after explanation of the nature and possible consequences of the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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