Contact Lens and Anterior Eye xxx (xxxx) xxx

Contents lists available at ScienceDirect

Contact Lens and Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Changes in visual quality with soft contact lenses after the instillation of hyaluronic acid eye drops

Carlos Carpena-Torres, Cristina Pastrana, Candela Rodríguez-Pomar, María Serramito, Laura Batres, Gonzalo Carracedo *

Ocupharm Research Group, Department of Optometry and Vision, Faculty of Optics and Optometry, Complutense University of Madrid, Madrid, Spain

ARTICLE INFO

Keywords:
Eye drops
Visual quality
Contact lens
Hyaluronic acid

ABSTRACT

Purpose: To evaluate the changes in visual function and anterior surface aberrations during soft contact lens (SCL) wear after the instillation of hyaluronic acid (HA) eye drops with different viscosity.
Methods: A prospective, randomized, and participant-masked study was performed. Twenty healthy participants (25.4 ± 2.6 years) were evaluated. Hydrogel (Ocufilcon D) and silicone-hydrogel (Somofilcon A) SCL were randomly assigned to both eyes of the same participant. Visual function in terms of high- and low-contrast corrected distance visual acuity (CDVA) and anterior contact lens surface aberrations (RMS HOA) were measured before and after the instillation, at different times, of different eye drops: saline (control) and 0.1%, 0.2%, and 0.3% HA.
Results: Compared with the saline solution, during hydrogel SCL wear, there was an improvement ($P < 0.05$) in high-contrast CDVA after 3 and 10 min with 0.1% HA, and after 5 and 20 min with 0.2% HA. During silicone-hydrogel SCL wear, there was a deterioration ($P < 0.05$) in high-contrast CDVA after 1 and 30 min with 0.3% HA. Additionally, during silicone-hydrogel SCL wear, there was also a deterioration ($P < 0.05$) in low-contrast CDVA after 5 and 20 min with 0.3% HA. In terms of RMS HOA, there were no clinically relevant changes with both SCL.
Conclusions: The instillation of HA eye drops could have a different effect on visual quality depending on their concentration of HA, the contact lens material, its surface ionicity, or other physicochemical properties that should be studied in future studies.

1. Introduction

Hyaluronic acid (HA) is a natural polysaccharide which is mainly present in the connective tissue of vertebrates [1]. It is a versatile biomolecule with many applications in biomedicine due to its ability to act as a lubricant agent, its viscoelastic properties and water holding capacity [2]. Eye drops with viscous agents are used for the treatment of dry eye due to their capability of regenerating the ocular surface damage [3,4]. For this reason, HA is incorporated to eye drops not only for dry eye treatment but also for relieving ocular dryness symptoms associated with environmental factors. HA eye drops demonstrated their efficacy by improving dry eye signs and symptoms for concentrations between 0.1% and 0.3% [5–9].

In the contact lens field, new materials incorporating HA into their structure have been developed to enhance their wettability and water retention [10–12]. The aim of enhancing these parameters is to improve comfort during contact lens wear [13]. Despite these materials not yet being available on the market, viscous eye drops are used to manage contact lens discomfort [14–17], including HA eye drops [18].

The tear film plays a crucial role in the optical and visual quality of the eye. For this reason, patients with tear film instability show loss of optical quality [19,20]. Some authors suggested that long-term instillation of HA eye drops could improve the optical quality of dry eye patients [21,22]. After a single instillation, Vandermeer et al. [23] found an improvement in optical quality with 0.1% HA, while Lekhanont et al. [24] did not find changes with 0.18% HA. In healthy subjects, the most viscous eye drops (0.3% HA) could decrease optical quality immediately after their instillation [25,26]. During soft contact lens wear, Lee et al. [27] reported a reduction of both visual and optical quality immediately after a single instillation of 0.3% HA.

* Corresponding author at: Departamento de Optometría y Visión, Facultad de Óptica y Optometría, Universidad Complutense de Madrid, C/ Arcos de Jalón 118, 28037 Madrid, Spain.
E-mail address: jgcarrac@ucm.es (G. Carracedo).

https://doi.org/10.1016/j.clae.2021.101471
Received 18 July 2020; Received in revised form 26 March 2021; Accepted 22 May 2021

Because it is known that viscosity of eye drops is directly proportional to their residence time over the ocular surface [28], higher concentrations of HA could produce changes in both visual and optical quality for a longer period. Due to the different properties between hydrogel and silicone-hydrogel polymers, these visual and optical changes could also depend on contact lens material.

Based on the premises of the previous paragraph, the purpose of the current study was to evaluate the changes in visual function and anterior surface aberrations during soft contact lens wear after the instillation of HA eye drops with different viscosity.

2. Methods

2.1. Design of the study

A prospective, randomized, and participant-masked study was performed in compliance with good clinical practice guidelines, institutional review board regulations and following the tenets of the Declaration of Helsinki, actualized in 2013 [29].

Twenty healthy and neophyte participants without symptoms of ocular dryness were involved in the study. The average age of the participants was 25.4 ± 2.6 years, ranging from 23 to 32 years. Inclusion criteria were aged between 18 and 35 years, understanding the informed consent and being aware of the indications and possible risks of wearing soft contact lenses. Exclusion criteria were high-contrast corrected distance visual acuity (CDVA) inferior to 20/20 (superior to 0.00 logMAR), any contra-indication to wear soft contact lenses, any ocular pathology and the use of systemic or ocular drugs that could affect the results.

All participants were voluntarily included in the study after signing the written informed consent where the procedure of the study and complications associated with soft contact lens wear were explained. Participants were free to leave the study at any time. All trials were performed at the University Clinic of Optometry of the Complutense University of Madrid (Madrid, Spain).

Both eyes of participants were evaluated, one eye wearing hydrogel contact lens (Ocufilcon D) and another wearing silicone-hydrogel contact lens (Somofilcon A), randomly. Visual function in terms of high- and low-contrast corrected distance visual acuity (CDVA) and anterior contact lens surface aberrations were measured before (baseline) and after (1, 3, 5, 10, 20 and 30 min) the instillation of different eye drops: saline solution (control) and 0.1%, 0.2%, and 0.3% HA. The saline solution was selected as a negative control because it has relatively low viscosity in comparison with the other eye drops using in this study (cP = 1), while the HA eye drops had a viscosity directly related to their concentration (Table 2). Additionally, the saline solution was selected rather than a non-treated control as the instillation of eye drops could affect the rate of blinking, the contact lens hydration, or other parameters affecting the visual quality.

The solutions studied were instilled randomly on four different days, firstly in one eye, and after 2 h in the contralateral eye, one solution being evaluated per day. The participants wore the first contact lens for 30 min. Then, once that the first eye drop was instilled, the measurements were done for another 30 min. After the last measurement, this contact lens was removed and the contralateral eye was evaluated after 1 h. Prior to contact lens insertion, the healthy state of the ocular surface was evaluated with a slit-lamp VX75 (Luneau Technology; Chartres, France). A commercial 2% fluorescein sodium (Alcon Cusi; Barcelona, Spain) was used for this evaluation and, after finishing, the ocular surface was washed with saline solution. The order of the trials was: anterior contact lens surface aberrometry, high-contrast CDVA, and low-contrast CDVA.

2.2. Soft contact lenses

Two daily disponsable soft contact lenses were used in the study. Hydrogel (Ocufilcon D) contact lens had a spherical design on both surfaces, while the silicone-hydrogel (Somofilcon A) contact lens had a spherical design on the posterior surface and aspherical design on the anterior surface. Their characteristics are detailed in Table 1.

Additionally, all the soft contact lenses were equilibrated for 24 h in a preservative free saline solution (Avizor; Madrid, Spain) to avoid comfort bias from the preservative solution of the packaging.

2.3. Hyaluronic acid eye drops

Considering that viscosity depends on the molecular weight of HA, three eye drops with different concentrations of HA (0.1%, 0.2%, and 0.3%) and the same molecular weight were used. All the eye drops had the same composition, except their concentration of both HA and buffers to adjust the pH. The osmolarity of each eye drop was different depending on its HA concentration. Additionally, saline solution was used as control. Their characteristics are detailed in Table 2.

All the eye drops were provided by the same manufacturer (Avizor). They are commercially available and approved for use in contact lens wearers. The eye drops were provided inside their commercial packaging. With a micropipette, 35 μL of each eye drop was instilled on four different visits, evaluating one eye drop per visit in random order. The participants did not know which eye drop was instilled during each visit.

2.4. Visual function

Visual function was measured in terms of high- and low-contrast CDVA under photopic conditions. These measurements were performed with a trial frame incorporating the usual refraction of the participants, where an overcorrection of +0.50 D was added to compensate for the refractive power of the contact lenses (Table 1). High-contrast CDVA (100%) and low-contrast CDVA (10%) were measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) chart of the VX24 chart display (Luneau Technology) placed at 4 m. Both parameters were analyzed using logarithmic units.

2.5. Anterior contact lens surface aberrometry

Anterior contact lens surface aberrations were measured using the dynamic-area videokeratoscopy Medmont E300 (Medmont International Pty Ltd; Victoria, Australia), which incorporates a Placido rings system. A dynamic corneal topography was performed for 10 s (2 frames per second) after two consecutive blinks. Participants were not allowed to blink during the 10 s of the measurement. Data 2 s after blinking were analyzed to evaluate the aberrations at the same point in all the participants, once that tear film is distributed over the contact lens surface.

Zernike coefficients of 3rd and 4th order were considered for the analysis, selecting a 6 mm pupil size diameter for this analysis. Root means square (RMS) of high-order aberrations (HOA) was calculated by the following expression:

Table 1
Characteristics of the soft contact lenses used in the study.

PARAMETER	SOFT CONTACT LENSES	
Material	Hydrogel	Silicone-hydrogel
Material (USAN)	Ocufilcon D	Somofilcon A
Commercial name	Biomedics 1 day Extra	Clarity 1 day
Laboratory	CooperVision (Lake Forest, CA, USA)	
FDA group	Group IV	Group II
Ionicity	Ionic	Nonionic
Dk/t (at -3.00D)	27	86
Water content (%)	55	56
Base curve (mm)	8.6	8.6
Diameter (mm)	14.2	14.1
Power (D)	−0.50	−0.50

USAN: United States Adopted Names; FDA: Food and Drug Administration.

Table 2
Characteristics of the eye drops used in the study.

PARAMETER	SALINE	0.1%	0.2%	0.3%
Main component	NaCl 0.9%	HA 0.1%	HA 0.2%	HA 0.3%
pH	7.0 – 7.2	7.0 – 7.4	7.0 – 7.4	7.0 – 7.4
Osmolality (mmol/kg)	295 – 305	280 – 320	160 – 220	160 – 220
Viscosity (cP)	1	4 – 8	10 – 20	50 – 52

HA: hyaluronic acid. NaCl: sodium chloride.

$$RMS\ HOA = \sum_{i=6}^{i=14} \sqrt{(Z_i)^2}$$

where Zi was the Zernike coefficients of 3rd and 4th order, expressed according to the pyramidal criteria of the American National Standards Institute (ANSI) [30].

2.6. Statistical analysis

Sample size calculations were performed with the statistical software Granmo 6.0 (Institut Municipal d'Investigació Mèdica; Barcelona, Spain), considering both high- and low-contrast CDVA as the main variables. An alpha risk of 0.05 and a beta risk of 0.2 in a two-sided test was accepted. Twenty eyes were necessary for the first group and 20 for the second one to recognize as statistically significant a difference greater than or equal to 0.04 logMAR. The common standard deviation was assumed to be 0.06 logMAR. The dropout rate was assumed to be 0.1 (10%).

Statistical analysis was performed using the SPSS Statistics 23 software (IBM; Chicago, Illinois, USA). The normality of the distribution of each variable was assessed using the Shapiro-Wilk test. Once that normal distribution was confirmed, the one-way analysis of variance (ANOVA) for related samples with Bonferroni correction was performed to compare the changes from baseline between the saline solution (control) and the HA eye drops (0.1%, 0.2%, and 0.3%). Additionally, the same test was carried out to compare the baseline and the other measurements (1, 3, 5, 10, 20, and 30 min) for each eye drop. A statistical significance of 95% ($P < 0.05$) was established.

3. Results

3.1. High-contrast visual acuity

Table 3 summarizes the values of high-contrast CDVA. The saline solution decreased this visual acuity 10 and 20 min after its instillation ($P < 0.05$), reaching three letters of worsening when participants wore the hydrogel contact lens. However, this visual acuity remained stable during the silicone-hydrogel contact lens wear. In the case of HA eye drops, there were no statistically significant changes with both hydrogel and silicone-hydrogel contact lenses ($P \geq 0.05$).

Fig. 1 shows the changes in high-contrast CDVA with both hydrogel and silicone-hydrogel contact lenses where statistically significant differences between saline solution (control) and the different HA eye drops are highlighted. During the hydrogel contact lens wear, there was a statistically significant improvement ($P < 0.05$) of this visual acuity after 3 and 10 min with 0.1% HA, and after 5 and 20 min with 0.2% HA, compared with saline solution. Conversely, with the silicone-hydrogel contact lens, there was a deterioration of high-contrast CDVA ($P < 0.05$) after 1 and 30 min with 0.3%, compared with saline solution.

With 0.1% HA, the percentage of participants who improved their high-contrast CDVA compared with the saline solution during the hydrogel contact lens wear were 70% (after 1 and 3 min), 75% (5 min),

Table 3
Comparison of both high- and low-contrast corrected distance visual acuity (CDVA) values before (baseline) and after the instillation of the different eye drops: saline solution (control) and 0.1%, 0.2%, and 0.3% hyaluronic acid. Values are shown in logMAR units as mean ± SD. *P < 0.05, one-way ANOVA for related samples, pairwise comparison with Bonferroni correction (comparison with baseline).

VARIABLE	LENS	EYE DROP	TIME AFTER INSTILLATION						
			Baseline	1 min	3 min	5 min	10 min	20 min	30 min
High-contrast CDVA	**Hydrogel**	**Saline**	−0.24 ± 0.05	−0.22 ± 0.06	−0.22 ± 0.04	−0.21 ± 0.05	−0.20 ± 0.07	−0.18 ± 0.08	−0.23 ± 0.07
			P-value	1.000	0.972	0.184	0.018*	0.018*	1.000
		0.1%	−0.20 ± 0.04	−0.22 ± 0.05	−0.22 ± 0.04	−0.21 ± 0.06	−0.22 ± 0.06	−0.20 ± 0.06	−0.23 ± 0.03
			P-value	1.000	0.214	1.000	1.000	1.000	0.113
		0.2%	−0.21 ± 0.05	−0.19 ± 0.05	−0.21 ± 0.04	−0.21 ± 0.05	−0.21 ± 0.05	−0.22 ± 0.06	−0.22 ± 0.06
			P-value	1.000	1.000	1.000	1.000	1.000	1.000
		0.3%	−0.21 ± 0.07	−0.18 ± 0.06	−0.21 ± 0.08	−0.19 ± 0.08	−0.21 ± 0.06	−0.22 ± 0.05	−0.22 ± 0.07
			P-value	1.000	1.000	1.000	1.000	1.000	1.000
	Silicone-hydrogel	**Saline**	−0.18 ± 0.06	−0.21 ± 0.08	−0.19 ± 0.07	−0.17 ± 0.11	−0.16 ± 0.07	−0.16 ± 0.09	−0.21 ± 0.06
			P-value	1.000	1.000	1.000	1.000	1.000	0.284
		0.1%	−0.18 ± 0.08	−0.18 ± 0.05	−0.19 ± 0.05	−0.22 ± 0.06	−0.16 ± 0.07	−0.17 ± 0.10	−0.14 ± 0.10
			P-value	1.000	1.000	1.000	1.000	1.000	1.000
		0.2%	−0.22 ± 0.05	−0.19 ± 0.06	−0.19 ± 0.07	−0.20 ± 0.06	−0.20 ± 0.09	−0.21 ± 0.07	−0.22 ± 0.06
			P-value	0.942	1.000	1.000	1.000	1.000	1.000
		0.3%	−0.22 ± 0.06	−0.16 ± 0.08	−0.16 ± 0.07	−0.18 ± 0.05	−0.20 ± 0.05	−0.17 ± 0.07	−0.19 ± 0.07
			P-value	0.184	0.284	1.000	1.000	0.707	1.000
Low-contrast CDVA	**Hydrogel**	**Saline**	0.05 ± 0.10	0.07 ± 0.07	0.07 ± 0.09	0.08 ± 0.07	0.08 ± 0.08	0.10 ± 0.08	0.09 ± 0.06
			P-value	1.000	1.000	1.000	1.000	1.000	1.000
		0.1%	0.09 ± 0.04	0.08 ± 0.06	0.08 ± 0.08	0.06 ± 0.07	0.06 ± 0.07	0.11 ± 0.08	0.07 ± 0.06
			P-value	1.000	1.000	1.000	1.000	1.000	1.000
		0.2%	0.09 ± 0.07	0.10 ± 0.08	0.10 ± 0.04	0.07 ± 0.06	0.10 ± 0.08	0.09 ± 0.07	0.05 ± 0.11
			P-value	1.000	1.000	1.000	1.000	1.000	0.142
		0.3%	0.08 ± 0.08	0.10 ± 0.09	0.14 ± 0.09	0.12 ± 0.10	0.07 ± 0.13	0.02 ± 0.09	0.07 ± 0.10
			P-value	1.000	0.567	0.990	1.000	0.788	1.000
	Silicone-hydrogel	**Saline**	0.14 ± 0.09	0.09 ± 0.10	0.13 ± 0.09	0.08 ± 0.10	0.12 ± 0.06	0.11 ± 0.08	0.10 ± 0.06
			P-value	0.144	1.000	0.020*	1.000	1.000	0.689
		0.1%	0.10 ± 0.11	0.08 ± 0.04	0.10 ± 0.07	0.11 ± 0.06	0.12 ± 0.05	0.13 ± 0.12	0.15 ± 0.10
			P-value	1.000	1.000	1.000	1.000	1.000	1.000
		0.2%	0.13 ± 0.09	0.14 ± 0.07	0.08 ± 0.07	0.09 ± 0.09	0.10 ± 0.07	0.09 ± 0.09	0.12 ± 0.07
			P-value	1.000	0.639	1.000	1.000	1.000	1.000
		0.3%	0.08 ± 0.05	0.12 ± 0.14	0.13 ± 0.09	0.11 ± 0.08	0.13 ± 0.07	0.12 ± 0.09	0.09 ± 0.07
			P-value	1.000	0.297	1.000	0.524	0.435	1.000

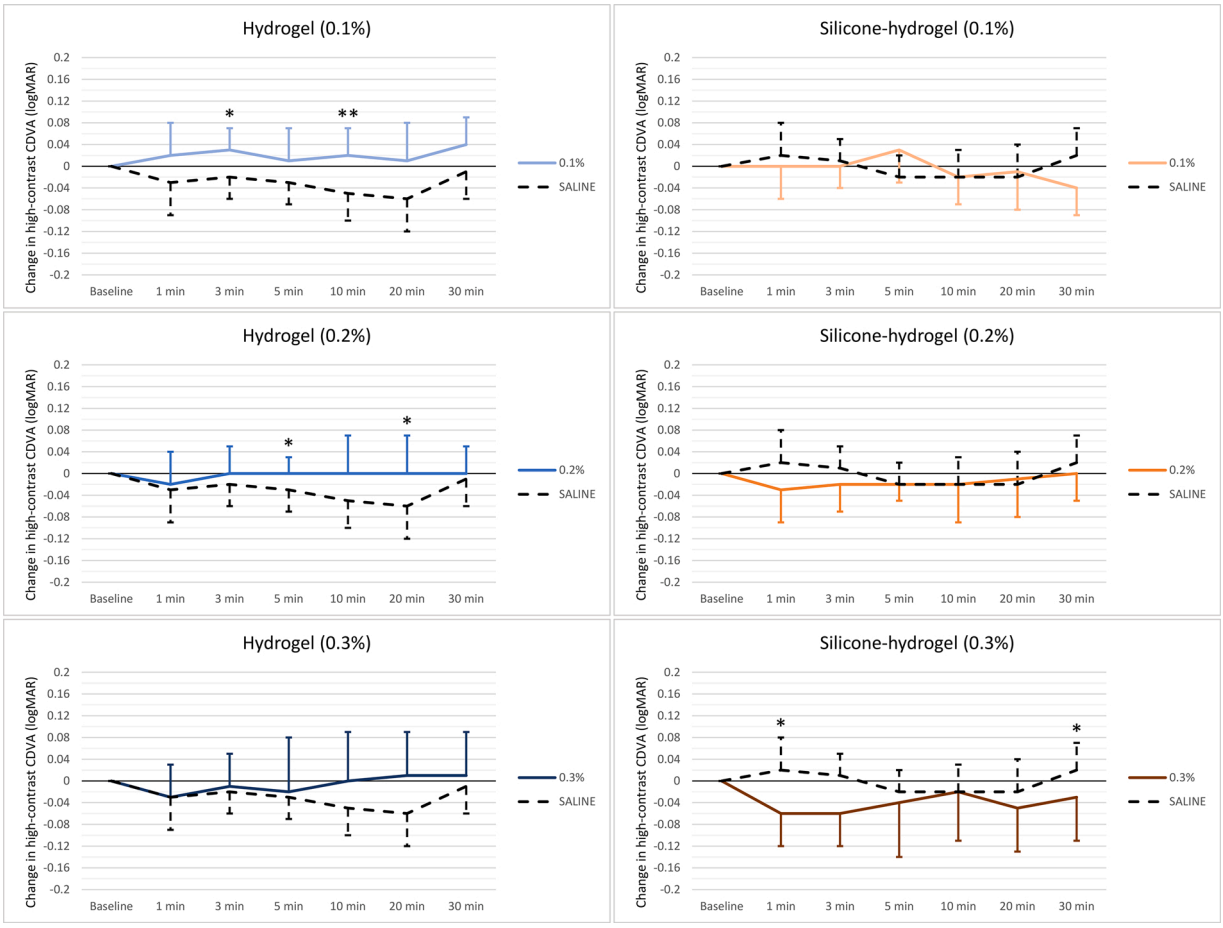

Fig. 1. Change in high-contrast corrected distance visual acuity (CDVA) with both hydrogel and silicone-hydrogel contact lenses after the instillation of saline solution (control) and 0.1%, 0.2%, and 0.3% hyaluronic acid eye drops. Positive and negative values represent an improvement or deterioration respectively, compared with baseline. *P < 0.05, **P < 0.01, one-way ANOVA for related samples, pairwise comparison with Bonferroni correction between hyaluronic acid and control at each point.

85% (10 min), 65% (20 min), and again 70% (30 min). With 0.2% HA, these percentages were 65% (after 1, 3, 5, 10, and 20 min) and 55% (30 min).

With 0.3% HA, the percentage of participants who suffered a deterioration in this visual acuity compared with the saline solution with the silicone-hydrogel contact lens were 75% (after 1 min), 55% (3 min), 45% (5 and 10 min), 55% (20 min), and 75% (30 min)

3.2. Low-contrast visual acuity

Table 3 summarizes the values of low-contrast CDVA. With all the eye drops, this visual acuity remained stable with both hydrogel and silicone-hydrogel contact lenses. The only exception was a statistical improvement (P < 0.05) with saline solution 5 min after its instillation during the silicone-hydrogel contact lens wear.

Fig. 2 shows the changes in low-contrast CDVA with both hydrogel and silicone-hydrogel contact lenses where statistically significant differences between saline solution (control) and the different HA eye drops are highlighted. With the silicone-hydrogel contact lens, there was a statistically significant deterioration (P < 0.05) of this visual acuity after 5 and 20 min with 0.3% HA, compared with saline solution. There were no statistical differences (P ≥ 0.05) during the hydrogel contact lens wear.

With 0.3% HA, during the silicone-hydrogel contact lens wear, the percentage of participants who suffered a deterioration in this visual acuity compared with the saline solution were 65% (after 1 min), 75% (3 and 5 min), 65% (10 min), 85% (20 min), and again 65% (30 min).

3.3. Anterior contact lens surface aberrometry

RMS HOA was also evaluated (Table 4). When comparing baseline and the different times after instillation, none of the eye drops produced statistically significant changes (P ≥ 0.05) with either hydrogel or silicone-hydrogel contact lenses.

The statistical comparison between changes from baseline of the saline solution (control) and the different HA eye drops showed that, during the hydrogel contact lens wear, there was only a deterioration of RMA HOA (P < 0.05) after 1 min with both 0.2% HA and 0.3% HA. With the silicone hydrogel contact lens, this deterioration (P < 0.05) only affected 3 min after 0.1% HA instillation.

4. Discussion

Despite the fact that the effect of viscous eye drops in comfort during soft contact lens wear is well known [14–18], the effect of their viscosity in visual and optical quality is still unclear. Some authors studied the effect of viscous eye drops on visual and optical quality, but they did not evaluate this effect over their residence time on the ocular surface [17, 27].

The current study evaluated the influence of the viscosity of HA eye drops in both visual and optical quality with two specific soft contact lenses. To this end, 0.1%, 0.2%, and 0.3% HA eye drops were instilled over contact lenses of hydrogel (Ocufilcon D) and silicone-hydrogel (Somofilcon A). It found that the instillation of HA improved visual quality with the hydrogel contact lens, but it was deteriorated with the

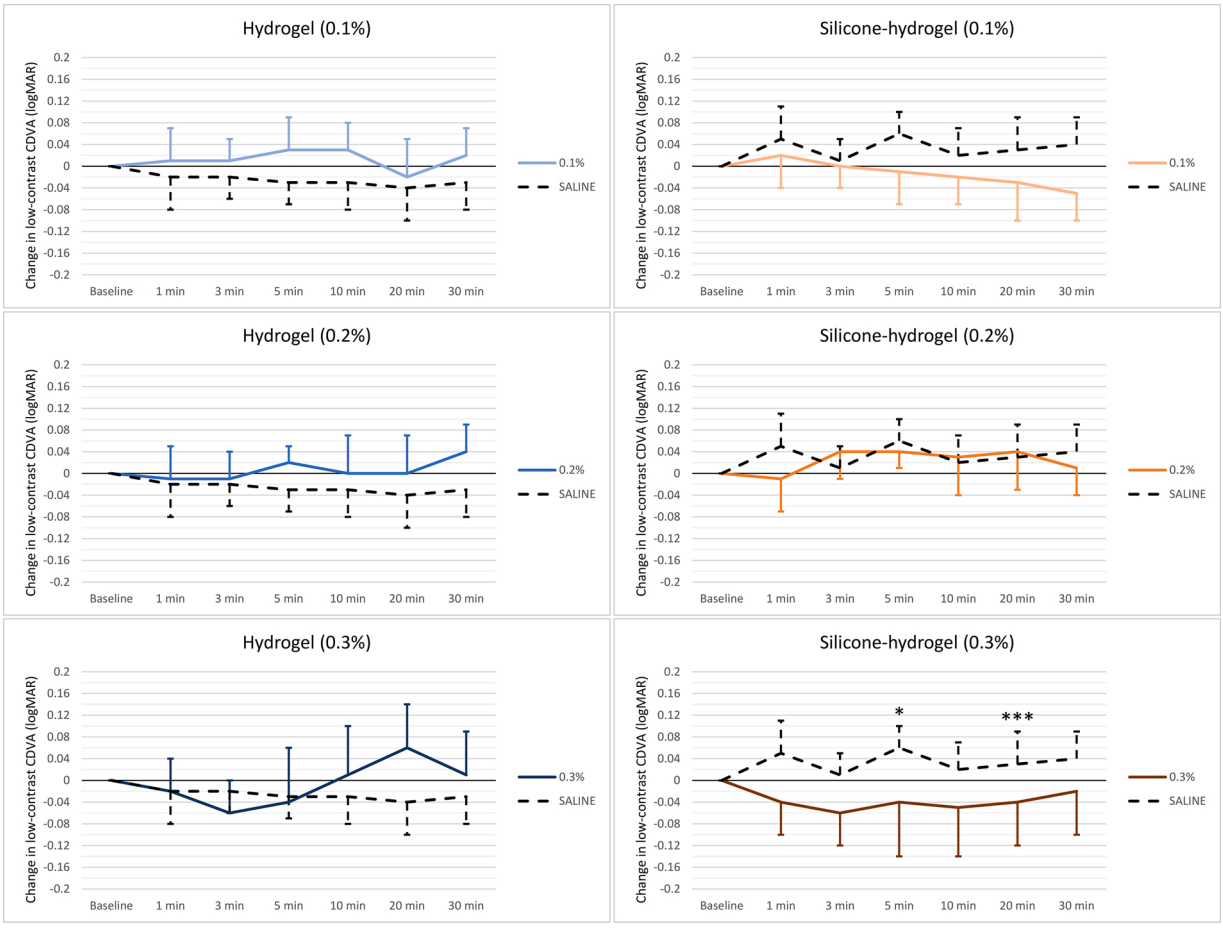

Fig. 2. Change in low-contrast corrected distance visual acuity (CDVA) with both hydrogel and silicone-hydrogel contact lenses after the instillation of saline solution (control) and 0.1%, 0.2%, and 0.3% hyaluronic acid eye drops. Positive and negative values represent an improvement or deterioration respectively, compared with baseline. *P < 0.05, ***P < 0.001, one-way ANOVA for related samples, pairwise comparison with Bonferroni correction between hyaluronic acid and control at each point.

Table 4
Comparison of root mean square of high-order aberrations (RMS HOA) values before (baseline) and after the instillation of the different eye drops: saline solution (control) and 0.1%, 0.2%, and 0.3% hyaluronic acid. Values are shown in microns as mean ± SD. *P < 0.05, one-way ANOVA for related samples, pairwise comparison with Bonferroni correction (comparison with baseline).

LENS	EYE DROP	TIME AFTER INSTILLATION						
		Baseline	1 min	3 min	5 min	10 min	20 min	30 min
Hydrogel	**Saline**	0.994 ± 0.552	0.819 ± 0.349	0.793 ± 0.205	0.805 ± 0.176	0.803 ± 0.264	0.822 ± 0.244	0.752 ± 0.179
		P-value	0.312	0.745	1.000	0.405	0.584	0.520
	0.1%	0.741 ± 0.219	0.717 ± 0.202	0.727 ± 0.168	0.705 ± 0.189	0.735 ± 0.196	0.722 ± 0.173	0.711 ± 0.164
		P-value	1.000	1.000	1.000	1.000	1.000	1.000
	0.2%	0.765 ± 0.166	1.241 ± 0.897	0.792 ± 0.207	0.846 ± 0.295	0.850 ± 0.326	0.727 ± 0.155	0.765 ± 0.166
		P-value	0.630	1.000	1.000	1.000	0.052	1.000
	0.3%	0.892 ± 0.354	0.971 ± 0.365	0.890 ± 0.252	0.885 ± 0.351	1.217 ± 1.371	0.703 ± 0.169	0.796 ± 0.231
		P-value	1.000	1.000	1.000	1.000	1.000	1.000
Silicone-hydrogel	**Saline**	0.762 ± 0.238	0.780 ± 0.221	0.685 ± 0.175	0.702 ± 0.208	0.734 ± 0.182	0.703 ± 0.151	0.680 ± 0.213
		P-value	1.000	1.000	1.000	1.000	1.000	1.000
	0.1%	0.767 ± 0.193	0.853 ± 0.500	0.828 ± 0.262	0.793 ± 0.260	0.965 ± 0.713	0.767 ± 0.237	0.769 ± 0.268
		P-value	1.000	0.504	1.000	1.000	1.000	1.000
	0.2%	0.833 ± 0.418	0.885 ± 0.277	0.768 ± 0.161	0.742 ± 0.257	0.764 ± 0.206	0.977 ± 0.692	0.663 ± 0.157
		P-value	1.000	1.000	1.000	1.000	1.000	1.000
	0.3%	0.946 ± 0.612	0.965 ± 0.480	0.910 ± 0.255	0.857 ± 0.280	0.784 ± 0.253	0.785 ± 0.200	0.809 ± 0.396
		P-value	1.000	1.000	1.000	1.000	1.000	1.000

silicone-hydrogel contact lens, compared with the instillation of saline solution (control). Conversely, HA eye drops instillation deteriorated optical quality with both hydrogel and silicone-hydrogel contact lenses, compared with the instillation of saline solution.

In terms of visual quality, both contact lenses (hydrogel and silicone-hydrogel) showed completely different results. Firstly, the analysis is focused on the hydrogel (Ocufilcon D) contact lens (see Fig. 1). These results suggest that HA eye drops with low (0.1%) and mid (0.2%) viscosities could improve visual quality, specifically high-contrast CDVA, compared to the instilled saline solution. Additionally, the low viscosity

(0.1%) showed an improvement for a shorter time compared to the mid viscosity (0.2%). Nevertheless, it is not clear if the improvement in high-contrast CDVA would be directly related to the viscosity and residence time of the HA eye drops since the higher viscosity (0.3%) did not show changes [28].

Secondly, the analysis is focused on the silicone-hydrogel (Somofilcon A) contact lens (see Fig. 2). According to these results, it is suggested that only the HA eye drops with high viscosity (0.3%) would decrease the visual quality after its instillation. If both high- and low-contrast CDVA are analyzed together, it is observed a deterioration of visual quality after the instillation of 0.3% HA for 30 min, except after 3 and 10 min.

Concerning other studies, only Lee et al. [27] evaluated the visual quality after the instillation of HA eye drops during silicone-hydrogel (Senofilcon A) contact lens wear. They measured high-contrast CDVA before and immediately after a single instillation of 0.1% HA and 0.3% HA eye drops. They found a deterioration of 4 letters (0.08 logMAR) with the 0.3% HA. In accordance with their results, the current study showed a deterioration of 3 letters (0.06 logMAR) for the first minute after the instillation of 0.3% HA during silicone-hydrogel (Somofilcon A) contact lens wear (see Fig. 1). However, the low-contrast CDVA results of the current study showed that this deterioration of visual quality could affect at least 20 min (see Fig. 2). No other studies evaluating the visual function during contact lens wear after the instillation of other viscous eye drops were found in the scientific literature.

In terms of optical quality, the results of both contact lenses of the current study were also completely different from each other. With the hydrogel (Ocufilcon D) contact lens, mid (0.2%) and high (0.3%) viscosities of HA showed a deterioration of RMS HOA during the first minute after being instilled in comparison with the saline solution. However, the magnitude of these differences was around 0.200 μm (except for two abnormal values), which seems to be an insufficient value to produce clinically relevant changes in vision [31]. With the silicone-hydrogel (Somofilcon A) contact lens, only the lower viscosity of HA (0.1%) showed a deterioration of RMS HOA, 3 min after its instillation, in comparison with the saline solution. As before, this difference was not considered clinically relevant since it was around 0.100 μm.

Lee et al. [27] studied the effect of 0.1% and 0.3% HA eye drops in anterior contact lens surface aberrations during silicone-hydrogel (Senofilcon A) contact lens wear. They found a deterioration in these aberrations immediately after a single instillation of the 0.3% HA, which agrees with their high-contrast CDVA results. On the other hand, Asharlous et al. [17] evaluated the effect of a viscous eye drop containing 0.1% povidone in total aberrations during silicone-hydrogel (Lotrafilcon A) contact lens wear. They did not show differences 1 h after its instillation, probably due to the low viscosity of this eye drop or because its residence time was inferior to 1 h. In dry eye patients and healthy subjects, other authors evaluated the effect of different HA eye drops in ocular aberrations [21–26]. Nevertheless, their results should not be extrapolated to soft contact lens wear.

In the current study, the changes in visual quality were not in agreement with the changes in optical quality. Different factors could explain this fact. First, aberrations were measured over the anterior surface of the soft contact lenses, without considering the internal ocular optics. Secondly, visual acuity was measured under physiological pupil size, while the aberrations were analyzed for a pupil size diameter of 6 mm. Finally, visual acuity was a dynamic measurement while the participants were blinking, and aberrations were analyzed two seconds after blinking.

These differences between visual and optical quality also affected both hydrogel and silicone-hydrogel contact lenses, but in different ways. This fact could be explained by considering that the hydrogel polymer was ionic, while the silicone-hydrogel polymer was nonionic (see Table 1), which could be interacting with the HA differently. It is known that physicochemical properties of contact lenses such as their composition, water content, or ionicity affect the retention time of topical formulations into the matrix of hydrogel [32,33].

The main limitation of this study was that only two materials (Ocufilcon D and Somofilcon A) were evaluated. Thus, the implications of these results should not be extrapolated to other polymers. In terms of statistical analysis, the use of the Bonferroni correction increased type II error (false negative) due to it decreases the statistical power compared with the Student's *t*-test. This fact could be masking some statistical differences that could have been solved by increasing the sample size. The number of participants should have been increased by establishing a lower beta and/or alfa risks for the sample size calculation. On the other hand, the differences found in the baseline between the different eye drops (see Table 3) could be biasing some results, especially overestimating the improvement or deterioration obtained by the different HA eye drops compared with the saline solution. This bias could be partially associated with environmental factors since the eye drops were evaluated on different days and could have been minimized by increasing the sample size. Regarding the results of the optical quality, they would have been more consistent if a wavefront aberrometer had been used since it provides the optical quality of the whole eye, not only the tear film. Another limitation of this optical quality analysis was that only a single measurement was done, which could introduce random results since the type of blink may affect the tear film distribution and, hence, the assessment of aberrations. Finally, the results of this study might differ from those of an older symptomatic population, likely with a compromised tear film.

In conclusion, the instillation of 0.1% and 0.2% HA could improve the visual quality with the Ocufilcon D contact lens. Conversely, the instillation of 0.3% could deteriorate the visual quality with the Somofilcon A contact lens. In this sense, the instillation of hyaluronic acid eye drops could have a different effect on visual quality depending on their concentration of HA, the contact lens material, its surface ionicity, or other physicochemical properties that should be studied in future studies. Nevertheless, future studies should confirm the findings of the present study.

Declaration of Competing Interest

No author has a financial or proprietary interest in any material or method mentioned.

References

[1] Prehm P. Release of hyaluronate from eukaryotic cells. Biochem J 1990;267(1):185–9.
[2] Salwowska NM, Bebenek KA, Zadlo DA, Wcislo-Dziadecka DL. Physiochemical properties and application of hyaluronic acid: a systematic review. J Cosmet Dermatol 2016;15(4):520–6.
[3] Wegener AR, Meyer LM, Schonfeld CL. Effect of viscous agents on corneal density in dry eye disease. J Ocul Pharmacol Ther 2015;31(8):504–8.
[4] Jones L, Downie LE, Korb D, Benitez-Del-Castillo JM, Dana R, Deng SX, et al. TFOS DEWS II management and therapy report. Ocul Surf 2017;15(3):575–628.
[5] Takamura E, Tsubota K, Watanabe H, Ohashi Y. A randomised, double-masked comparison study of diquafosol versus sodium hyaluronate ophthalmic solutions in dry eye patients. Br J Ophthalmol 2012;96(10):1310–5.
[6] Baudouin C, Cochener B, Pisella PJ, Girard B, Pouliquen P, Cooper H, et al. Randomized, phase III study comparing osmoprotective carboxymethylcellulose with sodium hyaluronate in dry eye disease. Eur J Ophthalmol 2012;22(5):751–61.
[7] Park Y, Song JS, Choi CY, Yoon KC, Lee HK, Kim HS. A Randomized Multicenter Study Comparing 0.1%, 0.15%, and 0.3% Sodium Hyaluronate with 0.05% Cyclosporine in the Treatment of Dry Eye. J Ocul Pharmacol Ther 2017;33(2):66–72.
[8] Pinto-Fraga J, Lopez-de la Rosa A, Blazquez Arauzo F, et al. Efficacy and safety of 0.2% hyaluronic acid in the management of dry eye disease. Eye Contact Lens 2017;43(1):57–63.
[9] Lopez-de la Rosa A, Pinto-Fraga J, Blazquez Arauzo F, et al. Safety and efficacy of an artificial tear containing 0.3% hyaluronic acid in the management of moderate-to-Severe dry eye disease. Eye Contact Lens 2017;43(6):383–8.
[10] Singh A, Li P, Beachley V, McDonnell P, Elisseeff JH. A hyaluronic acid-binding contact lens with enhanced water retention. Cont Lens Anterior Eye 2015;38(2):79–84.
[11] Deng X, Korogiannaki M, Rastegari B, Zhang J, Chen M, Fu Q, et al. Click" chemistry-tethered hyaluronic acid-based contact Lens coatings improve Lens

wettability and lower protein adsorption. ACS Appl Mater Interfaces 2016;8(34):22064–73.
[12] Korogiannaki M, Zhang J, Sheardown H. Surface modification of model hydrogel contact lenses with hyaluronic acid via thiol-ene "click" chemistry for enhancing surface characteristics. J Biomater Appl 2017;32(4):446–62.
[13] Jones L, Brennan NA, Gonzalez-Meijome J, Lally J, et al. The TFOS International Workshop on Contact Lens discomfort: report of the contact lens materials, design, and care subcommittee. Invest Ophthalmol Vis Sci 2013;54(11):Tfos37–70.
[14] Guillon M, Maissa C, Pouliquen P, Delval L. Effect of povidone 2% preservative-free eyedrops on contact lens wearers with computer visual syndrome: pilot study. Eye Contact Lens 2004;30(1):34–9.
[15] Subbaraman LN, Bayer S, Glasier MA, Lorentz H, Senchyna M, Jones L. Rewetting drops containing surface active agents improve the clinical performance of silicone hydrogel contact lenses. Optom Vis Sci 2006;83(3):143–51.
[16] McDonald M, Schachet JL, Lievens CW, Kern JR. Systane(R) ultra lubricant eye drops for treatment of contact lens-related dryness. Eye Contact Lens 2014;40(2):106–10.
[17] Asharlous A, Mirzajani A, Jafarzadehpur E, KhabazKhoob M, Ostadimoghaddam H. Objective and subjective assessing efficacy of a lubricating drop in eyes wearing silicone hydrogel contact lenses. J Curr Ophthalmol 2016;28(2):69–74.
[18] Carracedo G, Villa-Collar C, Martin-Gil A, Serramito M, Santamaria L. Comparison Between Viscous Teardrops and Saline Solution to Fill Orthokeratology Contact Lenses Before Overnight Wear. Eye Contact Lens 2018;44(Suppl 1):S307–s311.
[19] Montes-Mico R, Caliz A, Alio JL. Wavefront analysis of higher order aberrations in dry eye patients. J Refract Surg 2004;20(3):243–7.
[20] Montes-Mico R, Alio JL, Charman WN. Dynamic changes in the tear film in dry eyes. Invest Ophthalmol Vis Sci 2005;46(5):1615–9.
[21] Lu N, Lin F, Huang Z, He Q, Han W. Changes of Corneal Wavefront Aberrations in Dry Eye Patients after Treatment with Artificial Lubricant Drops. J Ophthalmol 2016;2016:1342056.
[22] Mihaltz K, Faschinger EM, Vecsei-Marlovits PV. Effects of Lipid- Versus Sodium Hyaluronate-Containing Eye Drops on Optical Quality and Ocular Surface Parameters as a Function of the Meibomian Gland Dropout Rate. Cornea 2018;37(7):886–92.
[23] Vandermeer G, Chamy Y, Pisella PJ. Comparison of objective optical quality measured by double-pass aberrometry in patients with moderate dry eye: Normal saline vs. artificial tears: A pilot study. J Fr Ophtalmol 2018;41(2):e51–7.
[24] Lekhanont K, Chuckpaiwong V, Vongthongsri A, Sangiampornpanit T. Effects of sodium hyaluronate on wavefront aberrations in dry eye patients. Optom Vis Sci 2014;91(1):39–46.
[25] Koh S, Maeda N, Ikeda C, Takai Y, Fujimoto H, Oie Y, et al. Effect of instillation of eyedrops for dry eye on optical quality. Invest Ophthalmol Vis Sci 2013;54(7):4927–33.
[26] Montani G, Murphy PJ, Patel S. Immediate effect of a tear enhancer and meibomian gland expression on the corneal surface and whole eye higher order aberrations. J Optom 2018;11(4):223–31.
[27] Lee JS, Park JM, Cho HK, Kim SJ, Huh HD, Park YM. Influence of Sodium Hyaluronate Concentration on Corneal Aberrations in Soft Contact Lens Wearers. Korean J Ophthalmol 2018;32(2):89–94.
[28] Carracedo G, Pastrana C, Serramito M, Rodriguez-Pomar C. Evaluation of tear meniscus by optical coherence tomography after different sodium hyaluronate eyedrops instillation. Acta Ophthalmol 2019;97(2):e162–9.
[29] World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama 2013;310(20):2191–4.
[30] McAlinden C, McCartney M, Moore J. Mathematics of Zernike polynomials: a review. Clin Exp Ophthalmol 2011;39(8):820–7.
[31] Villegas EA, Alcon E, Artal P. Optical quality of the eye in subjects with normal and excellent visual acuity. Invest Ophthalmol Vis Sci 2008;49(10):4688–96.
[32] Dominguez-Godinez CO, Martin-Gil A, Carracedo G, Guzman-Aranguez A, et al. In vitro and in vivo delivery of the secretagogue diadenosine tetraphosphate from conventional and silicone hydrogel soft contact lenses. J Optom 2013;6(4):205–11.
[33] Dominguez-Godinez C, Carracedo G, Pintor J. Diquafosol Delivery from Silicone Hydrogel Contact Lenses: Improved Effect on Tear Secretion. J Ocul Pharmacol Ther 2018;34(1-2):170–6.