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Changes by Optical Coherence Tomography after Ocular Moisturization of the Cornea Using Artificial Tears in a Spanish Population

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Abstract

Purpose: The aim of this study was to evaluate the efficacy of three different artificial tears (0.4% hyaluronic acid, a combination of polyethylene glycol 400 4 mg/ml-Propylene glycol 3 mg/ml, and the combination of 5 mg/ml of sodium carboxymethyl cellulose and glycerin) to increase the corneal OCT pachymetry in a group of patients.

Material and methods: 53 patients admitted to the Ophthalmology Unit in Hospital San Juan de Dios, Tenerife, Canary Islands, Spain were analyzed by corneal OCT and the obtained data were compared before and after application of artificial tears. The pachymetry was compared with the instillation of sodium fluorescein and hydrochloride oxybuprocaine prior to the use of the tear and after application of tears.

Results: We observed that pachymetry increased after application of the three different artificial tears mentioned above. No significant differences were observed when the efficacy of the three different artificial tears preparations was compared after statistical analysis.

Conclusions: In this study, the efficacy of the artificial tears to raise pachymetry was demonstrated and also this increase was mainly dependent on the corneal epithelium layer in the patients included in this study.

Keywords: OCT; Artificial; Tears; Changes

Introduction

Corneal Optical Coherence Tomography (OCT) is becoming an essential tool in the control of various corneal pathologies such as keratoconus, penetrating and endothelial keratoplasty and refractive surgeries. The measurement of the cornea thickness or non- contact pachymetry which presents important diagnostic and surgical applications could be used in order to monitor possible corneal edema and endothelial dysfunction [1-4] in the management of ocular hypertension [5-6]. OCT is a non-contact method that performs axial sections of the cornea with very high resolution [7-8]. Moreover, dry eye is a disturbance of the tear film that causes damage to the ocular surface and also ocular discomfort [9]. The tear film is composed of three layers, the innermost is the mucus produced by goblet cells, the middle layer is aqueous itself secreted by the lacrimal glands and the outermost is the oily layer, produced by the Meibomian glands. The oily layer prevents evaporation of the tear and keeps the necessary hydration on the ocular surface.

The natural tear presents proteins, enzymes and immunoglobulins, these substances are essential to fight certain diseases and infections. The tear film which is distributed over the surface epithelium of the conjunctiva and cornea has a thickness of 5 to 30 microns and is comprised of the three layers mentioned above. The lipid layer represents 0.02% of the tear and is a very thin film composed mainly of low-polar lipids, particularly of cholesterol and wax esters, as well as traces of triglycerides, which are at the front of the layer. The rest are lipids with high polarity as glycolipids, free fatty acids, aliphatic alcohols and small amounts of lecithin, which are located in the deep part of the layer. Furthermore, the relationship between corneal thickness measurement by spectral OCT noncontact corneal and ocular moisturization has been recently reported [10]. It has been used to measure parameters such as the inferior tear meniscus, being a non-contact, rapid and reproducible tool [11-14].

The aim of the present study was to demonstrate the changes that occur in the corneal thickness of patients with different ocular surface and also in apparently healthy individuals, comparing three artificial tears commonly available in an ophthalmology consultation. For this purpose, we measured and compared the changes in corneal pachymetry before and after the application of artificial tears.

Material and Methods

Recruitment and clinical assessment

Patients included in this study were admitted to the Ophthalmology Unit of Hospital San Juan de Dios, Tenerife, Canary Islands, Spain. These also signed an informed consent in accordance with the international standards of the Declaration of Helsinki. The study was performed in 53 patients attending an ophthalmology consultation in the hospital mentioned above.

OCT measurement and description of patients

Center corneal thickness was checked before and after treatment and then several seconds after instillation of the artificial tears using OCT. The artificials tears used were 0.4% hyaluronic acid (Aquoral®), combination of 4 mg/ml Polietilenglicol 400-3 mg/ml Propilenglicol (Systane®), and the combination of 5 mg/ml sodium carboxymethylcellulose and glycerin (Optava®). The 3D OCT-2000 Spectral Domain OCT was used for the measurements which is able to take 27.000 images per second. Moreover and in terms of the ability to capture images, it is able to capture the anterior segment in the cornea with defined epithelial layer, Bowman membrane and endothelium. It is also able to perform the measurement of corneal thickness, vertical and horizontal radius, and to establish the distribution of corneal thickness and recognize corneal abnormalities [15]. Furthermore, corneal thickness changes were also correlated with age, sex, ocular surface abnormalities, ocular dryness, seborrheic blepharitis, lacrimal duct obstruction, allergic conjunctivitis or other proper and common ocular surface abnormalities. Prior to measurement of OCT anesthesia was used in 38 of the 53 patients included in this study. Non-parametric statistical analysis for data testing was performed.

The pachymetry was compared using Fluotest® (Sodium Fluorescein and hydrochloride oxybuprocaine) prior to the application of the artificial tear and after its instillation. Regarding the patients, 47 of them did not present previous eye surgery and 6 of them previously underwent eye surgery.

Inclusion and exclusion criteria

All patients attending an ophthalmology consultant, some positive for dry eye symptoms were included in this work. Uncooperative patients in performing corneal OCT and patients with active conjunctivitis at the time of examination for another reason than keratoconjunctivitis sicca were excluded from this study.

Statistical analysis

An ANOVA test by ranks of Kruskal-Wallis was used in this study. This is a non- parametric test, but instead of comparing only two means and dependent samples (data before and after the same group of individuals), as in the three previous tables, it compares more than two, three in this case (Δpaq Hial. vs. ΔPaqSyst. vs. ΔPaqOpta.) and for independent samples, the group of individuals that was used before and after each of treatments was not the same as for all other treatments.

Results and Discussion

This study involved 53 patients with mean age of 41.1 years; the average thickness of the cornea prior of the use of artificial tears was 542.52 μm and after artificial tears application was 555.13. Therefore, corneal thickness was increased by 2.27% after using artificial tears.

27 patients used hyaluronic acid (tear 1), 14 patients used the combination of boric acid and polyethylene glycol (tear 2) and 12 patients the combination of carboxymethylcellulose and glycerine (tear 3). Moreover, 29 of 53 eyes included in the study presented abnormalities in the ocular surface including: seborrheic blepharitis (10 eyes), ocular dryness (10), lacrimal duct obstruction (4), ectropion (2), allergic conjunctivitis (1) and pingueculitis (2).

Furthermore, clinical data obtained from the patients included (1) biomicroscopy to measure the tear meniscus revealed that 43 patients presented a meniscus lower than 1 mm and 10 patients greater than 1 mm. (2) Intraocular pressure was 12 mmHg in average. It is also important to mention that 6 patients were contact lens users, 4 patients used topical treatment and 6 patients presented ophthalmic surgical history (two eyes with previous PRK, two eyes radial keratotomy and two eyes with LASIK).

	Valid N	T	Z	p-level
PAQprev (mean=547.77 μm) & PAQpost (mean=559.19 μm)	27	34.50000	3.711862	0.000206

Table 1: Wilcoxon Matched Pairs Mean Comparison Test for dependent samples: before treatment vs. after treatment data. Marked tests are significant at p<0.05000 (HIALURINATO).

The results of tests comparing the central corneal thickness between data before and after the treatment showed that the three tears are associated with significant changes in corneal thickness increased (Figures 1 and 2). However, at least at first glance, it seems that there is a gradient of decreasing effectiveness in this order with regards to the artificial tear used by the patient: tear number 1, tear number 2 and tear number 3 (Tables 1-3). In order to prove this observation statistically (using an ANOVA test by ranks of Kruskal- Wallis as mentioned in material and methods), differences between pachymetry values ΔPaq before and after each treatment (ΔPaq was calculated=Paq.post-Paq.pre) and the mean values ΔPaq of against all differences were compared. This is a non-parametric test, but instead of comparing only two means and for dependent samples (data before and after the same group of individuals), as in the three previous tables, compare more than two, three in this case (Δpaq Hial. vs. ΔPaqSyst. vs. ΔPaqOpta.) and for independent samples, the group of individuals that was used before and after each of treatments was not the same as for all other treatments (Table 4). The obtained results revealed that there were no significant differences between the mean values of ΔPaq from treatment to treatment (p=0.7784>0.05).

	Valid N	T	Z	p-level
PAQprev (mean=530.93 μm) & PAQpost (mean=542.93 μm)	14	1.500000	2.941742	0.003264

Table 2: Wilcoxon Matched Pairs Mean Comparison Test for dependent samples: before treatment vs. after treatment data. Marked tests are significant at p <0.05000 (lágrima 2).

	Valid N	T	Z	p-level
PAQprev (mean=551.75 μm) & PAQpost (mean=567.08 μm)	12	7.000000	2.510287	0.012064

Table 3: Wilcoxon Matched Pairs Mean Comparison Test for dependent samples: before treatment vs. after treatment data. Marked tests are significant at p <0.05000 (lágrima 3).
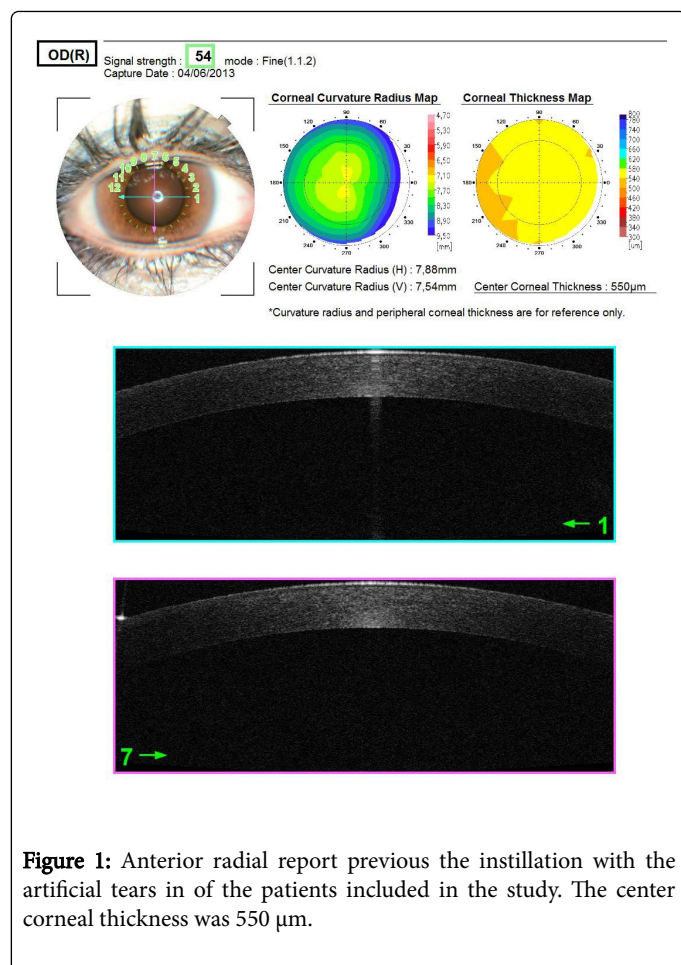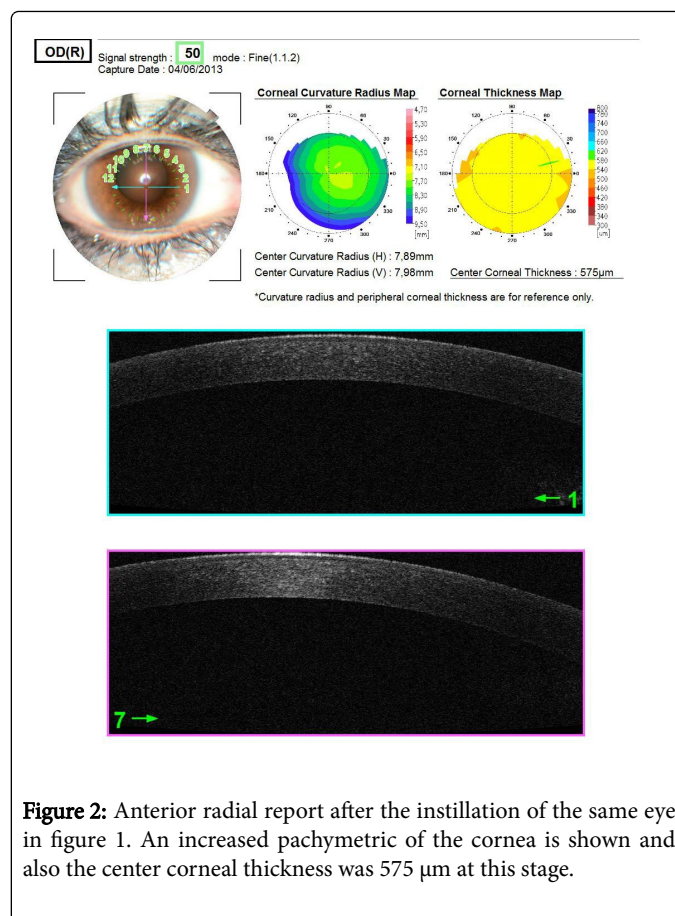
Figure 1: Anterior radial report previous the instillation with the artificial tears in of the patients included in the study. The center corneal thickness was 550 μm.
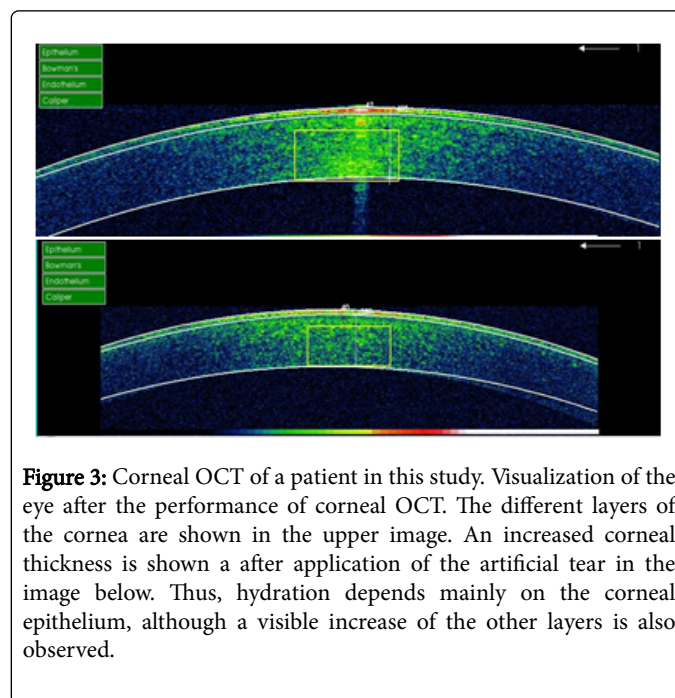

Figure 2: Anterior radial report after the instillation of the same eye in figure 1. An increased pachymetric of the cornea is shown and also the center corneal thickness was 575 μm at this stage.

	Code per group	Valid N	Sum of Ranks
Tear 1 (Mean ΔPaq= +11.40 μm)	101	27	728.5000
Tear 2 (Mean ΔPaq= +12 μm)	103	14	350.5000
Tear 3 (Mean ΔPaq= +15 μm)	102	12	352.0000

Table 4: Kruskal-Wallis ANOVA by Ranks; Dependent variable: ΔPaq Independent (grouping) variable: Tipo de lag. Kruskal-Wallis test: H (2, N=53)=0.5010691 p=0.7784.

In conclusion, the main finding of this work was the observation of an increased pachymetry after the application of ocular hydration drops in all corneal layers, but particularly in the corneal epithelium (Figure 3). No significant differences between the three analyzed tears were found, although more studies are needed in the future to compare corneal OCT and increased corneal thickness [16-17], to prove if there is a higher potential between each other, to understand the pathophysiology of the ocular surface and to predict what is the artificial tear fits most to each patient in particular.

Figure 3: Corneal OCT of a patient in this study. Visualization of the eye after the performance of corneal OCT. The different layers of the cornea are shown in the upper image. An increased corneal thickness is shown a after application of the artificial tear in the image below. Thus, hydration depends mainly on the corneal epithelium, although a visible increase of the other layers is also observed.

Nevertheless, the use of artificial tears seems to be useful to prevent long-term problems of the ocular surface by what is shown in studies to date. Corneal OCT could be a useful tool for the study of patients with dry eye as it was proven in this study that it was effective in

detecting changes that occur after the hydration of the cornea. OCT could also provide a non-invasive *in vivo* evaluation of the epithelial thickness of the ocular surface [18]. Finally, OCT induced changes after ocular moisturization could be a factor to be considered in the future when adjusting intraocular pressure measurements as an increase of pachymetry could cause an overestimation of ocular pressure.

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