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The effect of ageing on the ocular surface parameters

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1. Introduction

Ageing is a biological process that lead to a decline of biological functions and remains as the major risk factor for most of the prevalent diseases of developed countries [1]. In fact, the global population of older people is projected to be more than double its current amount by 2050, reaching nearly 2.1 billion as reported by United Nations. Nowadays, advancing age already has a profound impact on the economic, political and social processes [2]. Most components of the ocular surface experience age-related changes that might impact on the ocular surface equilibrium. Several ocular surface age-related changes have been reported in the literature such as [3] reduction in lacrimal secretion and changes on its composition [4]; reduction in functional meibomian glands and changes in lipid secretions [5]; the composition and amount of the tear film changes [6] and the conjunctival development of conjunctivochalasis [7]. Furthermore, the corneal sensitivity is reduced, epithelial and endothelial basement membranes increase its thickness, the number of keratocytes decrease [8] and there is an increased loss of corneal endothelial cells [9]. The incidence and prevalence of ocular diseases as age-related maculopathy, liquefaction of the vitreous, glaucoma, vascular occlusive diseases, cataract and dry eye increase significantly with age [10,11].

Currently, between 5 and 50% of people suffer from dry eye disease (DED) around the world [12]. This condition was recently re-defined by the *Tear Film and Ocular Surface Society* (TFOS) as *"multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles"* [13]. According to recent epidemiological studies, the prevalence of DED increases significantly and shows a linear association with age [12]. Moreover, it has been observed that the escalating prevalence of DED signs shows a greater increase than for a diagnosis based on symptoms. Regarding prevalence by sex, women with increased age show a higher DED prevalence than males, though there is considerable variability [12]. In fact, Guillon et al. [14] found higher tear film evaporation in older patients suggesting that it may be a significant contributing factor to DED in that population. Additionally, they found higher evaporation in women than in men in the 45 and over age group. It could explain the higher prevalence of DED complaints in the older women population [14].

Decades of knowledge about DED has been collected within the new DEWS II report [15] that confirm the great impact of this multifactorial disease on the ocular surface and on the lifestyle of the people who suffer from it, mostly from aged 40 when the presbyopia arises [12,16]. From these epidemiological data and considering that the most prevalence condition related with ageing is presbyopia [16], there are many patients worldwide in which both presbyopia and DED co-exist. Currently, multifocal contact lenses (MCLs) [17,18] and multifocal intraocular lenses (IOLs) [19] are both well-established and an effective way to compensate the presbyopia, reducing spectacle dependency. The ocular surface changes related to ageing may adversely affect the optical quality of the eye and could have a detrimental effect on the success of these treatments. For example, in the case of IOL implantation, optimal pre-surgical ocular conditions are required in order to avoid risks such as severe DED, inaccurate IOL power estimation [20] and ocular discomfort after IOL [21]. Despite the fact that most of the research studies conducted until now have demonstrated that MCLs provide good visual quality results [17,22–27], the prescription rate

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[28,29]) is low. Although many factors could be behind this low adherence, it should be noted that the CLs materials are the same as monofocal CLs.

For this reason, the main aim of this study is to assess the effect of ageing on the ocular surface parameters that would affect the MCLs fitting and even the IOL implants in this population.

2. Material and methods

2.1. Patients

This study was reviewed and approved by the Ethics Committee of San Carlos University Hospital (Madrid) and all the procedures followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from all included participants after explanation of the purpose and possible consequences of the study. Exclusion criteria was: age < 18 years, participant unable to complete the questionnaire or understand the procedures or contact lens wore in the past 24 h before the study. A total of 110 participants were included, and were divided into three age groups: group A (61 participants; < 42 years), group B (24 participants; 42–65 years) and group C (24 participants; > 65years). This classification by age was done according the effect of the ocular surface changes may have on several optical corrections for presbyopia. The first group is composed by young adults (< 42 years) who do not experience presbyopia yet or begin to experience early symptoms. The second group is composed by presbyopes (42–65) who are eligible for MCLs wear and the third group are advanced presbyopes (> 65 years) presenting smaller pupils size, lens alterations and who could be benefited by IOL implantation instead of MCLs.

2.2. Clinical signs and symptoms assessment

2.2.1. Symptomatology assessment

During the clinical examination, patients were required to complete five of the most common Dry Eye Questionnaires used in the clinical setting: The Ocular-surface-disease-index (OSDI) [30], Mcmonnies (MQ) [31], the standard patient evaluation of eye dryness (SPEED) [32], the Symptom Assessment in Dry Eye (SANDE) [33] and the Dry Eye Questionnaire (DEQ-5; short version) [34].

2.2.2. Tear film osmolarity

Tear film osmolarity (TFO) was measured using the TearLab Osmolarity System (TearLab Corp, San Diego, CA, USA) in both eyes of each participant according to the manufacturer's instructions. It was conducted before other measurements in order to avoid reflex tearing or the instillation of any dye that could affect the results. One measurement per eye was performed but only the right eye (OD) and the difference between both eyes (intereye variability) of each patient were included in the analysis.

2.2.3. Keratograph 5M

All the participants underwent imaging with the Keratograph 5M (K5M; Oculus GmbH, Wetzlar, Germany) equipped with a modified tear film scanning function. Three measurements of the tear meniscus height (TMHk), first break-up of the tear film (NIKBUT first), the average time of all tear film breakup incidents (NIKBUTavg), bulbar redness (BR) and limbal redness (LR) were obtained automatically by Oculus K5M software according to the manufacturer's instructions. The average of the measurements from OD of each participant was used for the statistical analysis. The meibography was performed using the K5M infrared camera system. Meibomian gland (MG) dropout of the upper and lower eyelid was graded subjectively by the examiner using the meiboscore (grade 0, no gland loss; grade 1, area of gland loss < 33% of the total gland area; grade 2, area of gland loss 33%–67%; and grade 3, area of gland loss > 67%) [35]. The meiboscore for each eyelid was summed to give a total score of 0–6.

2.2.4. Ocular surface examination and lid margin Assessment/MG grading

Slit-lamp examination of the cornea, conjunctiva and eyelids (from the OD of each participant) was performed under diffuse illumination using ×10–×16 magnification. Before the fluorescein instillation, lid abnormalities and meibomian gland grading were observed and scored according to Foulks/Bron scoring [36] as recommended by the Diagnosis Subcommittee from International Workshop on Meibomian Gland Dysfunction [37]. The lid margin and MGs features used for the statistical analysis were as follows: the eyelid margin thickness was assessed on a scale from 1 to 5: 1–2 = thin; 3 = normal; 4–5 = thick. The meibum quality from the central 8 MGs of the lower eyelid was assessed on a scale from 0 to 3: 0 = clear meibum readily expressed; 1 = cloudy meibum expressed with mild pressure; 2 = cloudy meibum expressed with more than moderate pressure; 3 = meibum could not be expressed even with strong pressure. The number of functional MGs was assessed on a scale from 0 to 3: 0= > 5 glands expressible; 1 = 3–4 glands expressible; 2 = 1–2 glands expressible; 3 = no glands expressible. Lid wiper epitheliopathy (LWE) of the upper and lower lid was assessed using a combination of fluorescein and lissamine green (Korb Protocol B). The higher of the final fluorescein or lissamine green staining were used as LWE severity grade (0 = absent, 1 = mild, 2 = moderate and 3 = severe) [38].

Corneal integrity was assessed by instilling fluorescein dye and after that corneal staining was graded using the Oxford scoring scheme [39]. The tear film breakup time (BUT) was measured three times with a stopwatch and averaged for analysis. Furthermore, bulbar conjunctival integrity was assessed using lissamine green and graded using the Oxford scoring scheme.

2.2.5. Tear film volume

Schirmer's test was performed with topical anaesthesia (Colirio Anestésico Doble®, Alcon Laboratories, Spain) as the final test performed in the examination. Before starting, one drop of topical anaesthesia was instilled on the conjunctival lower fornix of the OD, 5 min prior to the test. Afterwards, the Schirmer strip (35-mm Whatman filter paper; Tiedra Laboratories, Spain) was placed in the lower conjunctival sac at the junction of the lateral and middle thirds (avoiding touching the cornea) and the length of wetting was recorded after 5 min. The participants were seated at rest and their eyes closed during the test.

2.2.6. Study protocol

As shown in Fig. 1, automated measurements and clinical examination were performed in the following order to minimize the effect of the previous measurement: TFO by the TearLab System; TMHk, BR, LR, NIKBUT-first, NIKBUTavg, by K5 M; ocular surface examination and MGD grading, ocular surface staining using fluorescein, TBUT, conjunctival staining using lissamine green dye by slit lamp; meibography by the K5M and Schirmer test with topical anaesthesia. A 5-min interval between each test was established, and all tests were performed in the same order. All the measurements were performed by the same examiner.

2.3. Data analysis

Statistical analysis was performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, USA). Normality of the data distribution was tested using the Kolmogorov–Smirnov test. ANOVA test and Kruskal–Wallis test were used for comparisons between age groups. When statistically significant differences were found, post hoc tests were performed for multiple comparisons (Duncan's Test for ANOVA and Bonferroni for Kruskal- Wallis). T-student and Wilcoxon Two-Samples test were used for comparisons between gender groups. Correlations among variables were assessed through Pearson and Spearman coefficients. The correlations were considered strong