CORNEAL HYSTERESIS, A GLAUCOMA RISK FACTOR INDEPENDENT OF THE INTRAOCULAR PRESSURE

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Recent studies have shown a relationship between corneal hysteresis (CH) and intraocular pressure (IOP) revealing that a low CH associated to a high IOP represents a risk factor in glaucoma patients or suspects. CH has also been correlated to glaucoma severity and visual field defects. At this point, we have to ask ourselves if the low value of CH is related to the high IOP that reflects on the corneal biomechanical properties or is secondary to the glaucomatous damage and corneal hysteresis represents an independent risk factor in glaucoma. In this study we tried to eliminate the IOP factor and to identify whether CH changes in primary open angle glaucoma (POAG), ocular hypertension (OH) or normal eyes when we examine them at the same values of the IOP. Many authors have studied corneal biomechanical properties, but there are no other study that separates IOP and CH showing that corneal biomechanical properties have an independent role in glaucoma patients regardless of the IOP.

1. INTRODUCTION

Glaucoma is the leading cause of irreversible blindness in the world and is characterized by progressive retinal ganglion cell loss that determines optic nerve head changes and visual field defects, affecting quality of life [1–3]. Many authors have tried to investigate and find ways to lower its progression. The most important risk factor is raised intraocular pressure (IOP). Starting with different IOP measurements and trying to make it as accurate as it could get, ophthalmologists began to take into consideration all factors that could influence these values (central corneal thickness (CCT), corneal shape and rigidity along with axial length of the eye) [4, 5]. Today we know that corneal response to IOP variations is important in a glaucomatous patient and in recent years many studies have focused on corneal biomechanical properties (corneal hysteresis (CH) and corneal resistance factor (CRF)) and their relationship to glaucoma [3, 6–10].

2. CORNEAL PROPERTIES

Cornea represents an anatomical structure with an elliptical shape, with a vertical diameter of 10,6 mm and horizontal 11,7 mm. It’s radius of curvature are 7,7–7,8 mm anteriorly and 6,8–6,9 posteriorly [11]. Due to it’s shape, the human cornea has variable thickness, being thicker in the periphery and thinner centrally. It’s refractive power is about 40 D [11].

Cornea can be defined as a sum of properties such as: optical, geometrical (topography, curvature and thickness) and biomechanical (corneal hysteresis and corneal resistance factor) [12, 13]. Like many biological materials cornea is viscoelastic, which means that it has both viscous and elastic properties [10]. These types of materials are characterized by hysteresis.

Starting from geometrical properties and their influence on the IOP measurements, authors have investigated corneal reaction and found that corneal response is very important in a glaucoma suspect or a diagnosed glaucomatous patient. It shows us that cornea can adjust in front of IOP variations and protect the eye against raised IOP. As a result, today we know that a thick cornea tends to overestimate IOP measurement, so it has a protective role, while a thin cornea tends to underestimate IOP measurements and it represents a risk factor [14–16]. Nowadays, there are devices capable of measuring not just corneal geometrical, but also its biomechanical properties.

3. CORNEAL BIOMECHANICAL PROPERTIES MEASUREMENT

One of these devices is ocular response analyzer (ORA; Reichert Ophthalmic Instruments, Buffalo, NY)[17]. ORA was initially designed to be a noncontact tonometer. It uses an air pulse to indent the cornea centrally, generating an applanation pressure (P1). The air pulse is than stopped and the cornea regains its initial state, so this is recorded as the second applanation pressure (P2). The machine uses an electro optic infrared system that records corneal changes taking place within 3 mm of the central cornea and the two applanation pressure points (15), (16). After data acquisition, an algorithm is applied and the device reveals four parameters regarding intraocular pressure and corneal biomechanics: IOPg (IOP equivalent to Goldmann measured IOP), IOPcc (corneal compensated IOP), CH (corneal hysteresis) and CRF (corneal resistance factor) [14, 16].

Corneal hysteresis displays cornea’s capacity to deform when an external pressure is applied at its surface and then to come back to its original form when the external force is stopped, but the cornea does not regain its exact initial shape, absorbing some energy [7]. This makes the second applanation pressure measurement to be lower than the first one. The difference between the initial and the final pressure is recorded as corneal hysteresis (P1–P2) [7, 14, 16, 17]. CH shows corneal ability to absorb energy and reveals its response to IOP variations revealing that a cornea with a high CH can absorb more energy and protect the eye against raised IOP effects [14–16].

Corneal resistance factor is an indicator of the entire corneal resistance and is closely related to CCT. CRF is dependent on the CH and it is calculated using the formula P1–(kP2), where k is a constant derived from an empirical

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analysis of P1, P2 and CCT [7, 16, 17]. IOPg represents an IOP measurement equivalent to Goldmann measured IOP and is calculated by the formula (P1+P2)/2. IOPcc is adjusted by corneal biomechanical properties and represents corneal compensated IOP [17].

4. PURPOSE

The purpose of this study was to investigate if CH is an independent risk factor for glaucoma and to see whether this parameter changes in primary open angle glaucoma (POAG), ocular hypertension (OH) or normal eyes even if we group the eyes by the IOP and examine them accordingly.

5. MATERIAL AND METHODS

This was a retrospective study that included 214 observed eyes from 115 patients. These observed eyes were divided into 3 groups: first group included 79 POAG eyes, the second group included 68 OH eyes and the last group included 67 normal eyes (NE).

5.1. INCLUSION CRITERIA

Inclusion criteria for the first group consisted of diagnosed POAG patients with glaucomatous optic neuropathy, open angle on gonioscopy, RNFL and visual field defects, disregarding the IOP value. The second group includes OH patients with open angle on gonioscopy, without glaucomatous optic neuropathy, RNFL and visual field defects and with IOP higher than 21 mmHg measured at two different consults/checkups. The last group includes normal patients without glaucomatous optic neuropathy, RNFL and visual field defects and with normal IOP.

5.2. EXCLUSION CRITERIA

Exclusion criteria consisted of any kind of corneal pathology (history of refractive surgery, pellucid marginal degeneration, keratoconus, keratoglobus, corneal dystrophies or degenerations), closed angle on gonioscopy, optic nerve changes other than glaucomatous and neurological pathology that could influence the RNFL thickness or visual field.

5.3. OPHTHALMOLOGIC EXAMINATION

All patients were submitted to a complete examination that included best corrected visual acuity, visual field examination (Humphrey Field Analyzer II, Carl Zeiss Meditec Inc, Dublin, California strategy 24), Goldmann IOP measurement and corneal biomechanical properties measurement using ORA (Reichert Ophthalmic Instruments, Inc. (Depew, NY), gonioscopy, pachymetry (Alcon® OcuScan® RxP Ophthalmic Ultrasound System), fundus examination and RNFL thickness measurements (Optical Coherence Tomography 3D OCT-2000 Series).

6. RESULTS

We started by investigating the IOP and the relationship between ORA measured and Goldmann measured IOP. First we determined means for IOPcc, IOPg and Goldmann measured IOP in all three groups. Goldmann IOP (measured by both aplanotometer and ORA) and IOP cc were higher in POAG and OH groups than in NE group, so we can confirm once again that high IOP represents a risk factor for glaucoma (Table 1). In addition, for the POAG and OH groups IOPcc was higher than IOPg and Goldmann IOP showing that Goldmann IOP tends to underestimate IOP. Table 1 also shows that ORA’s IOPg is comparable to Goldmann measured IOP.

More than that, we performed a linear regression test in order to demonstrate the correlation between IOPg, IOPcc and Goldmann measured IOP. The correlations were statistically significant, positive and strong in all three groups (Table 2). These findings prove once again that ORA parameters are reliable and useful in our patient’s management. Being a non contact device it can also be useful in cases where we can not use the aplanotonometer (corneal erosion, herpetic keratitis, etc).

Then, we investigated corneal biomechanical properties and, as well as other studies have shown, our study revealed lower values for CH in POAG group than in OH group and in OH lower than in NE. Also, CRF values were lower in POAG group than in OH group and NE group (Table 3).

We know that a low CH is usually associated to a high IOP, especially in an OH patient or POAG suspect [8, 9, 18]. In order to establish if the value of CH in glaucomatous patients is influenced or not by the IOP value or how much does the IOP counts, we tried to analyze corneal hysteresis value at the same value of the IOP in the three groups. First, we eliminated values that did not have data in all three groups. The statistical analysis showed that all data were statistically significant and revealed that means of CH were higher in normal individuals than in OH group and POAG and that means of CH in OH group was higher than in POAG group.

So, even if the CH value lowers in patients with raised IOP, regardless of the group in which it takes part, we saw that at the same value of the IOP, CH is lower in glaucomatous patients than in the other two groups and furthermore, that in the OH group CH is lower than in normal individuals. This shows that regardless of the IOP, CH lowers in POAG patients or suspects and that this is related to the biomechanical changes of the cornea that occur in glaucomatous patients and not just to the IOP. Linear regression reveals the relationship between CH and IOP in the three groups (Fig. 1).

7. DISCUSSIONS

CH may represent, along with IOP and CCT an useful parameter in the investigation of POAG suspects or patients. When dealing with such a patient we need to explore every option and to take into consideration all factors in order to be able to confirm an early diagnosis.

The practical value of finding lower values of CH in POAG group than in OH group and in OH lower than in NE was presented in Pillunat’s study which concluded that glaucomatous patients with a low CH need to be monitored more often [16]. This findings could make CH a parameter to be taken into account in front of an OH patient or POAG suspect.

Furthermore, knowing that CH is lower in POAG and OH patients regardless of the IOP, shows us that we can use CH as an independent parameter in glaucoma management, along with IOP and CCT and not just in addition to it. A glaucoma suspect or an OH patient that has a low CH has a higher risk than a patient with a high CH because its corneal biomechanical properties are modified.
Also, knowing that studies showed a connection between CH and visual field index (VFI) and mean deviation (MD), we can now say that a glaucoma patient with a low CH has a greater risk of progression than a patient with a high CH, and it needs to be monitored closely and treated more aggressively [18].

### CONCLUSIONS

Taking into account that ORA measurements are relatively inexpensive and easy to take, that ORA’s IOP is comparable to Goldmann measured IOP and that it provides us parameters that investigate corneal biomechanical properties, we could use it's program in order to investigate OH patients and POAG suspects.

This study confirmed once again that high IOP represents a risk factor for glaucoma. Also, considering that IOPcc was higher than IOPg and Goldmann IOP in POAG and OH groups we demonstrated that in these patients Goldmann IOP tends to underestimate IOP. Our study revealed that the value of CH in a glaucomatous patient is lower regardless of the IOP, so it represents an independent parameter that could help us reevaluate our patients rate of progression, using now two parameters instead of one, but it is not recommended to base out therapeutically decision on a normal or low value of the CH.

Further studies are needed to confirm these data and to make CH an independent risk factor for glaucoma.

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**Fig. 1 – Linear regression CH–IOP.**

### REFERENCES


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