EVALUATION OF OCULAR RESPONSE ANALYZER IN ASSESSMENT OF CORNEAL BIOMECHANICS AND OCULAR PRESSURE IN GLAUCOMA SUSPECT INDIVIDUALS

By

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ABSTRACT

Background: The cornea exhibits viscoelastic properties, which give it the quality of hysteresis. Corneal hysteresis (CH) is an important indicator of the biomechanical properties of the cornea.

Objective: To evaluate the effect of ocular response Analyzer in assessment of corneal biomechanics and intraocular pressure in glaucoma suspect individuals.

Individuals and Methods: We conducted our study on 60 eyes which was divided into 30 eyes of normal populations and 30 eyes of glaucoma suspect patients.

Results: Elevation of intraocular pressure (IOP) led to decrease in corneal biomechanics as corneal hysteresis (CH) and corneal resistance factor (CRF).

Conclusion: Increase of IOP led to decrease in corneal biomechanics as CH and CRF.

Keywords: Goldmann applanation tonometry, laser peripheral iridotomy, Corneal hysteresis

INTRODUCTION

Ophthalmologists have long recognized ocular hypertension (IOP>21 mm Hg) as a risk factor for glaucoma. Other factors include African Caribbean race, a family history of glaucoma, and advanced age. The Ocular Hypertension Treatment Study helped define baseline ocular factors that increase the risk of converting to glaucoma in eyes in which the pressure is elevated and the optic disc and visual field are normal. Those risk factors include a central corneal thickness

of >556 μm , a C/D >0.4, and a larger-than-average pattern standard deviation on an otherwise normal threshold visual field. Other ocular and systemic risk factors are diabetes, hypertension, high myopia, cardiovascular disease, and migraine/vasospasm, all of which the practitioner must take into account (*Suzuki et al., 2006*).

The diurnal variation for normal eyes is between 3 and 6 mmHg which is more in the morning. The variation may increase in glaucomatous eyes. During the

night, intraocular pressure may not decrease despite the slower production of aqueous humor. In the general population, IOP ranges between 10 and 21 mm Hg with a mean of about 15 or 16 mm Hg (plus or minus 3.5 mm Hg during a 24-hour cycle). In glaucoma patients, their 24-hour IOP profiles may be different from healthy individuals (*Liu and Weinreb, 2011*).

Glaucoma suspect is a diagnosis reserved for individuals who do not definitively have glaucoma at the present time but have characteristics suggesting that they are at high risk of developing the disease in the future based on a variety of factors.: ocular hypertension, optic nerve features suggestive of glaucoma, visual field abnormalities, and other characteristics placing them at greater risk than the average population (*Ahmad, 2018*).

Corneal Hysteresis is an assessment of the ability of the cornea to absorb and dissipate energy. Corneal hysteresis is independently predictive of visual field progression in glaucoma. It is used as a predictor of glaucoma risk and may help to assess the effect of corneal thickness on intraocular pressure. The clinical significance of CH in the diagnosis and efficacy of glaucoma will become more explicit. In the future, CH can also play an important role in the diagnosis and treatment of glaucoma (*Liang et al., 2018*).

In 2005 The Ocular Response Analyzer (ORA) was introduced as a tonometer that uniquely measures and then integrates corneal biomechanical data into its intraocular pressure (IOP) estimates in an

effort to improve accuracy of IOP assessment (*Medeiros et al., 2013*).

This work aimed to evaluate the effect of ocular response analyzer in measurement and assessment of corneal biomechanics, corneal hysteresis, corneal resistance factor and IOP in patients with glaucoma suspect and normal individuals.

PATIENTS AND METHODS

Sixty eyes of 60 subjects were enrolled. Subjects were selected from Ophthalmology outpatient clinic in Al-Azhar University Hospital and Kobri El Kobbah Military hospital in Cairo. The study was carried out from April to October 2019. According to the principle of the declaration of Helsinki, the study was explained to the subjects and was asked to sign written informed consents. The study was approved by the ethics board of Al-Azhar University. The study was prospective. Patients were divided into two equal groups: Group A: Normal individuals. Group B: Glaucoma suspects.

Inclusion criteria:

Age ranged from 30-70 years old of both genders and normal individuals as regard eye.

Exclusion criteria:

No previous ocular surgery, not known to be glaucoma, and corneal degenerative disease as keratoconus. Methods: Subjects were evaluated by history, examination and investigation.

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (SPSS) version 20. Qualitative data were presented as number

and percentages, while quantitative data were presented as mean, standard deviations and ranges.

The comparison between two independent groups with quantitative data and parametric distribution was done by using **Independent t-test and qualitative data by Chi-square test.**

Pearson correlation coefficients were used to assess the relation between two studied parameters in the same group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant when: $P > 0.05$.

RESULTS

There was no statistically significant difference between the study groups as regard age and sex. (**Table 1**)

Table (1): Demographic results of the study groups in %.

		parameters		Total no. = 60
Sex		Female		29 (48.3%)
		Male		31 (51.7%)
Age		Mean $\pm$ SD		45.57 $\pm$ 7.67
		Range		32 – 62
CD ratio		Mean $\pm$ SD		0.75 $\pm$ 0.07
		Range		0.7 – 0.9
		Control group	Patients group	P-value
		No. = 30	No. = 30	
Sex	Female	16 (53.3%)	13 (43.3%)	0.438
	Male	14 (46.7%)	17 (56.7%)	
Age	Mean $\pm$ SD	43.83 $\pm$ 7.23	47.30 $\pm$ 7.83	0.080
	Range	32 – 60	36 – 62	

*: Chi-square test; •: Independent t-test

This table shows no statistically significant difference between the study groups as regard to age (p-value = 0.080).

There was a statistically significant difference between the study groups as regard visual acuity. (**Table 2**)

Table (2): Comparison between IOPcc and IOPg in control group and patient group

Groups		Control group	Patients group	P-value
Parameters		No. = 30	No. = 30	
Baseline				
IOPcc	Mean $\pm$ SD	16.76 $\pm$ 2.65	22.85 $\pm$ 3.67	0.001
	Range	10.4 – 20.3	16.4 – 32.1	
IOPg	Mean $\pm$ SD	15.47 $\pm$ 2.44	20.67 $\pm$ 3.42	0.001
	Range	10.2 – 19.3	16.1 – 30.2	
Follow up				
IOPcc	Mean $\pm$ SD	16.62 $\pm$ 2.33	22.62 $\pm$ 3.49	0.001
	Range	12.1 – 20.1	16.1 – 30.1	
IOPg	Mean $\pm$ SD	15.27 $\pm$ 2.45	20.62 $\pm$ 3.40	0.001
	Range	10.2 – 19.1	16 – 30.1	
% of change				
IOPcc	Mean $\pm$ SD	0.05 $\pm$ 12.14	-0.91 $\pm$ 1.35	0.010
	Range	-17.20 – 61.54	-6.23 – 1.05	
IOPg	Mean $\pm$ SD	-1.33 $\pm$ 1.20	-0.25 $\pm$ 0.58	0.001
	Range	-5.43 – 0.00	-1.47 – 0.98	

•: Independent t-test

≠: Mann-Whitney test

There was significant different between the study group as regard IOPcc and IOPg, % of change in IOPcc and % of change in IOPg. (Table 1)

Table (3): Comparison between CH and CRF in control and patient groups

Groups		Control group	Patients group	P-value
Parameters		No. = 30	No. = 30	
Baseline				
CH	Mean $\pm$ SD	9.47 $\pm$ 0.88	7.63 $\pm$ 1.34	0.001
	Range	7.9 – 11.3	5.3 – 10	
CRF	Mean $\pm$ SD	9.34 $\pm$ 0.87	8.17 $\pm$ 1.71	0.002
	Range	7.5 – 11.1	5.6 – 11.2	
Follow up				
CH	Mean $\pm$ SD	9.41 $\pm$ 0.86	7.56 $\pm$ 1.35	0.001
	Range	7.9 – 11.2	5.2 – 10	
CRF	Mean $\pm$ SD	9.31 $\pm$ 0.89	8.12 $\pm$ 1.70	0.001
	Range	7.4 – 11.1	5.6 – 11.1	
% of change				
CH	Mean $\pm$ SD	-0.48 $\pm$ 5.40	0.64 $\pm$ 18.51	0.473
	Range	-14.15 – 20.88	-48.00 – 50.00	
CRF	Mean $\pm$ SD	0.34 $\pm$ 11.26	-0.69 $\pm$ 0.94	0.803
	Range	-27.03 – 33.73	-3.13 – 0.91	

•: Independent t-test

There was a significant difference between the study groups as regard CH and CRP, and non significant difference between the study groups as regard % of change in CH and CRP. (Table 4)

Table (4): Comparison between VArt and VAlt in control and patient groups

Groups		Control group	Patients group	P-value
Parameters		No. = 30	No. = 30	
Baseline				
VA rt	Mean $\pm$ SD	0.72 $\pm$ 0.11	0.63 $\pm$ 0.10	0.002
	Range	0.5 – 0.9	0.4 – 0.8	
VA lt	Mean $\pm$ SD	0.72 $\pm$ 0.11	0.59 $\pm$ 0.11	0.001
	Range	0.5 – 0.9	0.4 – 0.8	
Follow up				
VA rt	Mean $\pm$ SD	0.72 $\pm$ 0.11	0.63 $\pm$ 0.10	0.001
	Range	0.5 – 0.9	0.4 – 0.8	
VA lt	Mean $\pm$ SD	0.72 $\pm$ 0.11	0.58 $\pm$ 0.11	0.000
	Range	0.5 – 0.9	0.4 – 0.8	
% of change				
VA rt	Mean $\pm$ SD	0.00 $\pm$ 0.00	0.06 $\pm$ 3.59	1.000
	Range	0.00 – 0.00	-12.50 – 14.29	
VA lt	Mean $\pm$ SD	0.00 $\pm$ 0.00	-1.90 $\pm$ 8.16	0.154
	Range	0.00 – 0.00	-42.86 – 0.00	

•: Independent t-test

There was a non significant difference between the study groups as regard visual acuity and significant difference between baseline IOPg and their follow up, baseline IOPcc, CH, CRF, VA and their follow up. (Table 5).

Table (5): Comparison between baseline parameters as IOPcc, IOPg, CH, CRF, VA rt and VA lt and their follow up values in control group

Control Groups Parameters		Control group		P-value
		Baseline	Follow up	
IOPcc	Mean $\pm$ SD	16.76 $\pm$ 2.65	16.62 $\pm$ 2.33	0.595
	Range	10.4 – 20.3	12.1 – 20.1	
IOPg	Mean $\pm$ SD	15.47 $\pm$ 2.44	15.27 $\pm$ 2.45	0.000
	Range	10.2 – 19.3	10.2 – 19.1	
CH	Mean $\pm$ SD	9.47 $\pm$ 0.88	9.41 $\pm$ 0.86	0.544
	Range	7.9 – 11.3	7.9 – 11.2	
CRF	Mean $\pm$ SD	9.34 $\pm$ 0.87	9.31 $\pm$ 0.89	0.904
	Range	7.5 – 11.1	7.4 – 11.1	
VA rt	Mean $\pm$ SD	0.72 $\pm$ 0.11	0.72 $\pm$ 0.11	–
	Range	0.5 – 0.9	0.5 – 0.9	
VA lt	Mean $\pm$ SD	0.72 $\pm$ 0.11	0.72 $\pm$ 0.11	–
	Range	0.5 – 0.9	0.5 – 0.9	
IOPcc	Mean $\pm$ SD	22.85 $\pm$ 3.67	22.62 $\pm$ 3.49	0.003
	Range	16.4 – 32.1	16.1 – 30.1	
IOPg	Mean $\pm$ SD	20.67 $\pm$ 3.42	20.62 $\pm$ 3.40	0.018
	Range	16.1 – 30.2	16 – 30.1	
CH	Mean $\pm$ SD	7.63 $\pm$ 1.34	7.56 $\pm$ 1.35	0.778
	Range	5.3 – 10	5.2 – 10	
CRF	Mean $\pm$ SD	8.17 $\pm$ 1.71	8.12 $\pm$ 1.70	0.001
	Range	5.6 – 11.2	5.6 – 11.1	
VA rt	Mean $\pm$ SD	0.63 $\pm$ 0.10	0.63 $\pm$ 0.10	0.423
	Range	0.4 – 0.8	0.4 – 0.8	
VA lt	Mean $\pm$ SD	0.59 $\pm$ 0.11	0.58 $\pm$ 0.11	0.211
	Range	0.4 – 0.8	0.4 – 0.8	

There was a significant difference in IOPcc, IOPg and CRP in patient group between baseline and their follow up and non significant difference in CH, VA rt, VA lt in patient group between baseline and their follow up (p value > 0.05). (**Table 6**).

Table (6): Comparison between CD ratio and it relation to other parameters as IOPcc, CH, CRF, VA and age, their up, % of change

Parameters \ CD ratio	r	P-value
Age	-0.302	0.184
baseline		
IOPcc	-0.059	0.799
IOPg	0.133	0.565
CH	0.249	0.276
CRF	0.236	0.304
VA rt	0.084	0.717
VA lt	0.099	0.668
Follow up		
IOPcc	-0.062	0.788
IOPg	0.140	0.546
CH	0.169	0.463
CRF	0.292	0.199
VA rt	0.084	0.717
VA lt	0.027	0.907
% of change		
IOPcc	0.133	0.566
IOPg	0.149	0.519
CH	-0.096	0.678
CRF	0.355	0.115
VA lt	-0.209	0.362

Spearman correlation coefficient

DISCUSSION

The human cornea is a viscoelastic tissue that can be described by two principal properties: A static resistance component (characterized by the CRF), for which deformation is proportional to applied force, and a dynamic resistance component (characterized by CH), for which the relationship between deformation and applied force depends on time. Both CH and the CRF are measured using a dynamic bidirectional applanation process using the ORA (*Ambrósio et al., 2013*).

The value of CH reflects the ability of corneal tissue to absorb and release energy during bidirectional flattening. It is an

important biomechanical parameter of the cornea. The CH value of healthy adults is about 11 mmHg. The measurement of CH is reproducible and different. People have different CH values, which are determined by the shape of the individual's cornea. The study found that all types of glaucoma, including primary open angle glaucoma, angle-closure glaucoma, normal tension glaucoma, congenital glaucoma, binocular asymmetrical glaucoma, CH values are lower than normal people. Therefore, CH is a good indicator of glaucoma diagnosis and screening. Lower CH values are associated with thinner retinal nerve fiber layer (RNFL), larger linear cup/disk ratio (LCDR) and degree of optic disc defect. A

lower CH value can also result in a lower visual field index. CH and the basic intraocular pressure play a synergistic role in the progression of glaucoma. The study found that CH can change with changes in basic intraocular pressure, means CH increases when intraocular pressure decreases, while the CH decreases conversely when intraocular pressure increases.. CH has its limitations, such as corneal damage or corneal surgery, but in general, CH is a risk factor for glaucoma progression

Our groups were divided into two equal subgroups: Controlled group of normal individuals, and patients group of glaucoma suspect individuals.

Mean IOP was statistically significant in patients group when compared with control group.

Mean IOPg was statistically significant in patients group when compared with control group.

Mean CH was statistically significant in patients group when compared with control group.

Kamiya et al. (2012) it was statistically highly significant in patients group when compared with control group.

Hoban et al. (2017) it was statistically highly significant in patients group when compared with control group.

Meanwhile *Jin et al. (2016)* disagreed with our results as they noted that there was no statistically significant difference between the control and diseased groups regarding CH values.

Mean CH in control group was 9.41 ± 0.5 mmHg and mean CH in diseased group was 9.44 ± 0.62 mmHg.

Wei et al. (2014) it was statistically highly significant in patients group when compared with control group.

In our study the mean CRF in the control group was 9.34 ± 0.87 mmHg in comparison with the mean CH in diseased group which was 8.17 ± 1.71 mmHg.

It was statistically highly significant in patients group when compared with control group.

Zuo et al. (2019) it was statistically highly significant in patients group when compared with control group.

Elmazara et al. (2017) agreed with our results as they mentioned in their results that the mean CRF value of the control group (group A) was 7.1731 ± 0.97952 mmHg in comparison with 8.6902 ± 1.25195 mmHg in diseased group (group B).

Elmazara et al. (2017) it was statistically highly significant in patients group when compared with control group.

Meanwhile *Katz et al. (2018)* disagreed with our results as they noted that there was no statistically significant difference between the control and diseased groups regarding CRF values.

Mean CRF in control group was 8.81 ± 0.45 mmHg and mean CRF in diseased group was 9.11 ± 0.52 mmHg.

Wei et al. (2014) it was statistically highly significant in patients group when compared with control group.

Abitbol et al. (2010) it was statistically highly significant in patients group when compared with control group.

In our study the mean VA in the control group was 0.72 ± 0.11 in

comparison with the mean VA in diseased group which was 0.63 ± 0.10 .

It was statistically highly significant in patients group when compared with control group.

Zuo et al. (2019) it was statistically highly significant in patients group when compared with control group.

Allam and Khalil (2015) it was statistically highly significant in patients group when compared with control group.

Wei et al. (2014) it was statistically highly significant in patients group when compared with control group.

CONCLUSION

Our study reported that elevation of IOP leads to decrease in corneal biomechanics as CH and CRF. Also there is significant difference in IOP, CH, CRF, VA, FUNDUS (CD ratio) between glaucoma suspects versus normal individuals. Where IOP increase but CH, CRF decrease in glaucoma suspect individuals, CD ratio more than 0.5 in glaucoma suspect, optic disc may show a notch.

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تقييم استخدام جهاز محلل استجابة العين في دراسة الخواص الحيوية الميكانيكية للقرنية وضغط العين في الاشخاص المشتبه اصابته بمرض الجلوكوما

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خلفية البحث: للقرنية خواص المرونة واللزوجة، والتي تمنحها خاصية التباطؤ. التباطؤ القرني هو مؤثر مهم على الخواص الميكانيكية الحيوية للقرنية.

الهدف من البحث: تقييم تأثير محلل استجابة العين في قياس وتقييم الميكانيكا الحيوية القرنية المشتبه اصابته (التباطؤ عامل مقاومة القرنية). وضغط العين في مرضى الجلوكوما والأفراد العاديين.

الأشخاص وطرق البحث: أجرينا دراستنا على ٦٠ عيناً تم تقسيمها إلى ٣٠ عيناً من الأشخاص الطبيعيين، و ٣٠ عيناً من المرضى المشتبه باصابته بالجلوكوما.

نتائج البحث: ذكرت دراستنا أن ارتفاع ضغط العين يؤدي إلى انخفاض في الميكانيكا الحيوية القرنية كعامل التباطؤ القرنية وعامل مقاومة القرنية. الزرق هو السبب الرئيسي لفقدان البصر لا رجعة فيه. قدر تحليل تلوي حديث حدوث زيادة كبيرة في حدوث الجلوكوما على مدى العقود الثلاثة المقبلة في جميع أنحاء العالم - من ٠,٩ ٪ تأثر في عام ٢٠١٣ ، وارتفع إلى ١,١ ٪ في عام ٢٠٢٠ ، و ١,٦ ٪ في عام ٢٠٤٠.

الاستنتاج: ذكرت دراستنا أن ارتفاع ضغط العين يؤدي إلى انخفاض في الميكانيكا الحيوية القرنية مثل القرنية التخلفية و عامل مقاومة القرنية. أيضا هناك فرق كبير في ارتفاع ضغط العين، القرنية التخلفية، عامل مقاومة القرنية، حدة الأبصار، قاع العين (نسبة سي د) بين الجلوكوما المشتبه فيها وبين الأفراد الطبيعيين. عند زيادة ارتفاع ضغط العين لكن القرنية التخلفية ، انخفاض عامل مقاومة القرنية في الأشخاص المشتبه في كونهم زرق، نسبة سي د أكثر من ٠,٥ في الجلوكوما المشتبه بها ، قد يظهر القرص البصري درجة.