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Original Article

Evaluation of corneal biomechanical properties in mustard gas keratopathy

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Abstract

Background: Degenerative biomechanical factors and immunologic processes with effect on collagen and corneal reparative process are known as the main cause of ocular surface dysfunction in mustard gas keratopathy (MGK) and may cause changes in the corneal biomechanical values. Therefore, we evaluate corneal biomechanical properties of these patients.
Methods and materials: This case-control study includes 61 chemical warfare victims with MGK. After omission according to our exclusion criteria, 88 eyes of patients with MGK were enrolled as the case group and also a group of 88 normal eyes, which were matched regarding their age and sex in the control group, were enrolled. Measurements of corneal biomechanical properties which reported by ORA and Corvis ST (CST) devices were compared. The SPSS software version 23.0 was used in the statistical analysis. For comparisons between groups, if the data had a normal distribution, were analyzed by Student's *t*-test and ANOVA, and if the data didn't have a normal distribution, Mann–Whitney U test, and Kruskal-Wallis were used. Furthermore, to identify a relationship between two groups of data Spearman's rank Correlation test was used. P value < 0.05 were considered statistically significant.
Results: In the MGK group, A1 length (A1L), A1 velocity (A1V), A2 velocity (A2V), deformation amplitude (DA) and peak distance (PD) were higher than the control group ($P < 0.001$). However, the corneal hysteresis (CH) ($P = 0.003$), corneal resistant factor (CRF), non-corrected IOP (IOPnct), corrected IOP based on corneal thickness (IOPpachy), and central corneal thickness (CCT) were lower than the control group ($P < 0.001$). The visual acuity according to the LogMAR scale and severity of MGK was positively associated with IOPpachy and negatively associated with CH, CRF, CCT and highest concavity radius (Radius).
Conclusion: Measurement of corneal biomechanical properties may be, have a useful role in the classification, monitoring or diagnosis of MGK.

Keywords: Mustard gas keratopathy, Corneal biomechanical, ORA, Corvis ST

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Introduction

Mustard gas is a very toxic alkaline chemical that can cause acute and chronic damage to the eye.[1] Acute lesions include swelling and redness of the eyelid, photophobia, chemosis, subconjunctival hemorrhage, corneal abrasion and anterior uveitis. The severity of this manifestation depends on the amount of contact with the mustard gas. In most cases, after

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a few weeks, the lesions are healed, and the patient's vision returns to the previous state. However, in some patients, the disease progresses and leads to chronic keratitis, which is known as a mustard gas keratopathy (MGK), and signs include corneal sensory disturbances, corneal erosion, corneal neovascularization, visual disturbances, and even blindness. MGK can create from 0.5 to 40 years after exposure to mustard gas, and exact pathophysiology of this disease remains unknown.[2–5]

The keratopathy according to the intensity of involvement can be divided among three groups:

(A) Mild: changes in the conjunctival vessels include tortuosity, segmentation, and telangiectasia without adjacent corneal involvement.
(B) Moderate: conjunctivalization, limbal ischemia and peripheral vascular invasion with or without corneal opacity.
(C) Severe: ischemic conjunctiva, corneal neovascularization, thinning and melting of the cornea and secondary degenerative changes.[5]

Corneal involvement in MGK is clinically diagnosed and investigated by many researchers. Degenerative biomechanical factors and immunologic processes with effect on collagen and corneal reparative process are known as the leading cause of ocular surface dysfunction in MGK.[6,7]

Corneal tissue is a complex viscoelastic structure that should describe as a system. Corneal biomechanical properties can affect many of the ophthalmic measurements, and the ability to measure these characteristics can enhance our ability to detect ophthalmic disorders.[8] ORA was introduced by the applanation tonometry technology in late 2005 and was the first device to enable us to investigate corneal biomechanical changes in various disorders. The measured parameter by ORA has included: CH (Corneal Hysteresis), CRF (Corneal Resistance Factor), IOPcc (Corneal-compensated IOP) and IOPg (Goldmann-correlated IOP).

However, the parameters measured by the ORA device did not capture the amount of corneal deformation at the time of occurrence, as in recent years, the development of the Corvis ST, which carries the image of the cornea with Scheimpflug Technology, made significant progress in this regard.[9,10]

The measured parameter by Corvis ST has included: the length in millimeter, in two times at first and second applanation of the cornea (A1Length (A1L)/A2Length (A2L)), and the speed in square of meter per second in two times of corneal applanation (A1Velocity (A1V)/A2 Velocity (A2V)). In addition, the maximum distance, radius, and range of deformation in the highest corneal curvature (Peak Distance (PD), highest concavity radius (Radius) and Deformation Amplitude (DA)), central corneal thickness (CCT), non-corrected IOP (IOPnct) and corrected IOP based on corneal thickness (IOPpachy) are calculated.

Therefore, the hypothesis was that, the changes in ocular surface function in MGK might cause a change in the corneal biomechanical values. In this study, we evaluated corneal biomechanical properties in these patients and compared them to the normal people. Since few studies have been done in this field globally, the results from this study are expected to help identify corneal biomechanical changes in MGK.

Materials and methods

This case-control study includes 61 chemical warfare victims with MGK. All of them was male. We gave informed consent from all patients before using their data. Patients with a minimum one of the following criteria are excluded from the sample:

History of diabetes, blood pressure, chronic kidney disease, glaucoma, cornea and retina disorder, myopia < −5.00, hyperopia > +3.00, any strabismus disorder and ocular surgery, including corneal transplantation, cataract surgery and other recent (less than six months) ocular surgery.

After omission according to these exclusion criteria, 88 eyes from chemical warfare victims were remained, Which were enrolled as the MGK groups with average age 50.8 ± 4.1 years and also a group of 88 normal eyes, which were matched regarding their age and sex as a control group, were enrolled (average age 50.5 ± 4.6 years).

Best-corrected visual acuity (BCVA) values of the patients were obtained by Snellen's chart and for statistical analysis, converted into Logarithm of Minimum Angle of Resolution (LogMAR) scale. Complete ophthalmic examination including slit lamp examination, taking slit photo imaging, refraction and measurement of IOP with air-puff tonometer (air-puff IOP) was done for all patients. Also, according to this examination, severity of MGK was determined, and patients were divided into three groups (Mild, Moderate, Severe). Measurements of corneal biomechanical properties which reported by ORA (Reichert, Depew, NY, USA) device and, which reported by Corvis ST (Oculus, Wetzlar, Germany) device were compared.

The SPSS software version 23.0 was used for statistical analysis. For comparisons between groups, if the data had a normal distribution, were analyzed by Student's *t*-test and ANOVA, and if the data didn't have a normal distribution, Mann–Whitney U test and Kruskal-Wallis were used. Also to identify relationships between two groups of data Spearman's rank Correlation test was used. All data were displayed as mean ± SD and *P* value less than 0.05 were considered statistically significant.

Results

Demographic data of all participants is summarized in Table 1. The results of biomechanical data in the case and control groups are shown in Table 2.

In the MGK group, Spearman's rank correlation test was used to identify a relationship between the ORA and Corvis ST corneal biomechanical variables (Table 3). Furthermore, BCVA according to the LogMAR scale had a positive correlation with IOPpachy (Coefficient = 0.219, $P = 0.040$) and had a negative correlation with CH (Coefficient = −0.216, $P = 0.044$), CRF (Coefficient = −0.243, $P = 0.023$), CCT (Coefficient = −0.405, $P < 0.001$), and Radius (Coefficient = −0.290, $P = 0.006$).

88 eyes of the MGK group according to the severity of MGK were divided into three groups: 63 (71.6%) of the eyes

Table 1. Demographic data of all participants.

Group	MGK (N = 88 eyes)	Control (N = 88 eyes)	P value
Age	50.8 ± 4.1	50.5 ± 4.6	0.654

Table 2. Corneal biomechanical characteristics in all participants.

	MGK group	Control group	P-value
IOPg	14.32 ± 3.56	14.47 ± 3.51	0.540
IOPcc	17.25 ± 3.86	16.26 ± 2.51	0.117
CH	8.25 ± 2.29	9.18 ± 2.51	0.003
CRF	8.23 ± 2.25	9.32 ± 2.51	<0.001
IOPnct	15.39 ± 2.65	16.96 ± 3.51	<0.001
IOPpachy	18.03 ± 3.35	19.70 ± 0.51	<0.001
CCT	483.25 ± 74.77	534.97 ± 2.51	<0.001
A1L	2.14 ± 0.38	1.79 ± 1.51	<0.001
A1V	0.13 ± 0.02	0.12 ± 1.51	0.004
A2L	1.04 ± 0.36	1.16 ± 0.51	0.069
A2V	-0.43 ± 0.05	-0.94 ± 4.51	<0.001
DA	1.14 ± 0.90	1.03 ± 1.51	<0.001
PD	5.02 ± 0.25	4.87 ± 0.51	0.001
Radius	7.60 ± 0.89	7.70 ± 6.51	0.263

were in the Mild group, 12 (13.6%) eyes in the Moderate group and 13 (14.8%) of the eyes were in the Severe group.

To compare the corneal biomechanical data in these three groups, we used ANOVA test and Kruskal-Wallis test (Table 4). Among these three groups, the result showed a statistically significant difference between IOPg, CH, CRF, CCT, IOPpachy, A1L, and HCR. The rest data in the groups were not statistically significant. Also, between these three groups, BCVA had statistically significant difference ($P < 0.001$).

Discussion

Mustard gas has a destructive effect on the cornea, and the changes in ocular surface function in MGK maybe cause a change in the corneal biomechanical values. Therefore, this study was done to evaluate corneal biomechanical properties in the patients with MGK and compared them to the normal people. It should be noted that a similar study has not been performed about corneal biomechanical properties in these patients.

However, confocal microscopy studies on patients with MGK have been shown; decrease in corneal thickness, a significant loss of keratocytes, increase in corneal midstromal nerve thickness, small stromal spots, amyloid degeneration and lipid keratopathy.[11] In the pathology of MGK, chronic inflammation, increased activity of the matrix metalloproteinase (MMP), and limbal cell injury has been reported.[12] This finding was similar to the ocular alkali burn injury, which was reported by many studies[13] but, no study about corneal biomechanical properties in the ocular alkali burn, has been performed. Thus, the results of this study are expected to

Table 3. Correlation between ORA data and Corvis ST in MGK group.

	IOPg		IOPcc		CH		CRF	
	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value	Coefficient	P-value
IOPnct	0.730**	<0.001	0.453**	<0.001	0.257*	0.016	0.531**	<0.001
IOPpachy	0.370**	<0.001	0.428**	<0.001	−0.241*	0.024	−0.063	0.560
CCT	0.299**	0.005	−0.027	0.800	0.536**	<0.001	0.602**	<0.001
A1L	0.340**	0.001	0.286**	0.007	−0.075	0.488	0.084	0.437
A1V	−0.537**	<0.001	−0.495**	<0.001	0.109	0.311	−0.147	0.172
A2L	0.425**	<0.001	0.316**	0.003	0.142	0.187	0.302**	0.004
A2V	0.310**	0.003	0.236*	0.027	0.105	0.332	0.220*	0.040
DA	−0.554**	<0.001	−0.542**	<0.001	0.104	0.336	−0.157	0.143
PD	−0.466**	<0.001	−0.471**	<0.001	0.092	0.395	−0.140	0.193
Radius	0.453**	<0.001	0.257*	0.016	0.270*	0.011	0.437**	<0.001

* Correlation is significant at the 0.05 level.
** Correlation is significant at the 0.01 level.

Table 4. Comparison of BCVA and corneal biomechanical properties between three groups of MGK.

	Mild (1)	Moderate (2)	Severe (3)	P-value (1 vs 2 vs 3)	P-value (1 vs 2)	P-value (1 vs 3)	P-value P-value (2 vs 3)
BCVA (LogMAR)	0.186 ± 0.162	0.358 ± 0.320	0.415 ± 0.089	<0.001	0.128	<0.001	0.176
IOPg	14.88 ± 3.34	12.37 ± 3.47	13.39 ± 4.12	0.048	0.025	0.165	0.467
IOPcc	16.89 ± 3.84	17.28 ± 2.89	18.97 ± 4.53	0.210	–	–	–
CH	9.04 ± 2.00	6.71 ± 1.24	5.83 ± 1.99	<0.001	<0.001	<0.001	0.251
CRF	9.07 ± 1.83	6.32 ± 1.69	5.88 ± 1.90	<0.001	<0.001	<0.001	0.548
IOPnct	15.68 ± 2.64	14.67 ± 2.92	14.61 ± 2.38	0.128	–	–	–
IOPpachy	17.14 ± 2.52	17.84 ± 3.02	22.49 ± 3.77	<0.001	1.000	<0.001	0.018
CCT	513.40 ± 38.79	470.42 ± 33.48	349.00 ± 85.28	<0.001	0.005	<0.001	<0.001
A1L	2.13 ± 0.36	1.89 ± 0.23	0.44 ± 2.38	0.011	0.148	0.163	0.008
A1V	0.14 ± 0.02	0.13 ± 0.03	0.12 ± 0.02	0.190	–	–	–
A2L	1.03 ± 0.35	1.06 ± 0.42	1.03 ± 0.35	0.868	–	–	–
A2V	-0.42 ± 0.05	-0.46 ± 0.05	-0.44 ± 0.04	0.127	–	–	–
DA	2.13 ± 0.36	2.13 ± 0.36	2.13 ± 0.36	0.765	–	–	–
PD	2.13 ± 0.36	2.13 ± 0.36	2.13 ± 0.36	0.094	–	–	–
Radius	7.83 ± 0.77	7.31 ± 0.89	6.74 ± 0.92	<0.001	0.065	0.001	0.900
Air-puff IOP	11.80 ± 2.55	10.04 ± 2.23	9.32 ± 2.01	0.001	0.081	0.003	1.000

help us to identify corneal biomechanical changes in MGK and maybe other alkali agents.

So far, according to many studies in normal people, some ORA and Corvis ST variables like CH, A1V, A1L, A2V, and DA had a relationship with age, and some of them like PD had a relationship with sex.[14–16] Therefore, we compare our results with a control group which was matched regarding their age and sex to the MGK group.

In our study, the levels of A1L, A1V, A2V, DA and PD in the MGK group were higher than the control group, and the levels of CH, CRF, IOPnct, IOPpachy, and CCT were lower than the control group. Furthermore, in the MGK group, IOPg had a positive relationship with IOPnct, IOPpachy, CCT, A1L, A2L, A2V, and Radius and had a negative relationship with A1V, DA, and PD. IOPcc also had a positive correlation with IOPnct, IOPpachy, A1L, A2L, A2V, and Radius, and had a negative correlation with A1V, DA and PD. CH had a positive relationship with IOPnct, CCT, and Radius and had a negative relationship with IOPpachy. CRF had a positive correlation with IOPnct, CCT, A2L, A2V, and Radius. In the control group, there was no correlation between the data of the ORA and the Corvis ST.

In a similar study in patients with glaucoma, data from the ORA device and the Corvis ST device were correlated, but the strength of this relationship was moderate and weak,[17,18] but there is no further study comparing the data of these two devices in patients with MGK. Our study showed that there are a lot of relations between the data of the ORA device, such as IOPg and IOPcc, with the Corvis ST data in the MGK group, which is mostly strong to the moderate relationship. However, this relation was less in data such as CH and CRF.

Additionally, in the studies, CCT is positively related to A1L, A2L, A2V, DA, and Radius.[16] In our study, CCT had a positive relationship with IOPg, CH, CRF, IOPnct, A2L, and Radius and had a negative relation with IOPpachy.

In our study, there was a statistically significant difference between BCVA, IOPg, CH, CRF, CCT, IOPpachy, A1L, Radius and air-puff IOP level in three groups of patients based on the severity of MGK (Mild, Moderate, Severe). As the visual acuity according to the LogMAR scale and severity of MGK was increased, the level of the IOPpachy was increased and level of the CH, CRF, CCT and Radius was decreased.

One of the limitations of this study is the low number of patients with moderate to severe MGK severities that have not undergone corneal transplantation surgery. Patient's IOP was also not measured by the Goldman Tonometer, which, if done, could make the comparison between IOP measured by the two devices more valuable.

It is suggested that similar studies should be carried out with larger sample size to find out the clinical application of corneal biomechanical data in the diagnosis or treatment of MGK. We hope that our study could be the basis for further studies in this field.

Conclusion

Measurement of corneal biomechanical properties may have a useful role in the classification, monitoring or diagnosis of MGK.

Conflict of interest

The authors have no conflict of interest to declare.

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