Effect of Gestational Diabetes Mellitus on Corneal Biomechanical Characteristics

Gestasyonel Diabetes Mellitus'un Kornea Biyomekanik Özellikleri Üzerine Etkisi

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Abstract

Objective: This study aimed to investigate whether gestational diabetes mellitus (GDM) affects the corneal biomechanical parameters.

Material-Method: Thirty-eight pregnant women, newly diagnosed with GDM and, age- and gestational age-matched 34 healthy pregnant females were enrolled in the study. Individuals having any ocular or systemic disorders (such as glaucoma, thyroid disorders, rosacea, connective tissue diseases, etc.) and history of ocular surgery or trauma, contact lens or those using any topical medication were excluded from the study. The right eye of the participants was examined. The corneal parameters including corneal hysteresis (CH), corneal resistance factor (CRF), Goldmann-correlated intraocular pressure (IOPg), and the corneal compensated IOP (IOPcc), obtained by The Ocular Response Analyzer (ORA) device were compared statistically.

Results: The mean and gestational age of the participants was 30.71±5.09 years, 25.95±1.56 weeks and 29.97±4.10 years, 25.76±1.30 weeks in pregnant females with GDM and healthy pregnant females, respectively. No significant differences in age (p=0.502) or gestational age (p=0.594) were noted. The values of CH, CRF, IOPg, and IOPcc were determined to be higher in pregnant females with GDM as compared to that in healthy pregnant females. However, there was no statistically significant difference in any other parameter (p=0.183, p=0.303, p=0.732 and p=0.330, respectively).

Conclusions: Hyperglycemia in diabetic patients causes pathological changes in the cornea, along with all the other layers of the eye. Short-term hyperglycemia does not affect the corneal biomechanical parameters.

Keywords: Cornea, Corneal Biomechanics, Gestational Diabetes Mellitus, Hyperglycemia, Ocular Response Analyzer.

Özet

Amaç: Bu çalışmada gestasyonel diyabetes mellitus'un (GDM) korneal biyomekanik parametreler üzerindeki etkisini araştırmak amaçlanmıştır.

Materyal-Metot: Çalışmaya GDM tanısı alan 38 hasta ile yaş ve gebelik haftaları uyumlu 34 sağlıklı gebe kadın katıldı. Herhangi bir oküler veya sistemik bozukluğu (glokom, tiroid bozuklukları, rosacea, bağ dokusu hastalıkları, vb.) ve oküler cerrahi veya travma öyküsü, kontakt lens veya herhangi bir topikal ilaç kullanan kişiler çalışma dışı bırakıldı. Katılımcıların sağ gözü incelendi. Oküler response analiz (ORA) cihazı ile elde edilen kornea histerezisi (CH), kornea direnç faktörü (CRF), Goldmann-korelasyonlu göz içi basıncı (IOPg) ve korneal kompanse edilmiş IOP (IOPcc) içeren kornea parametreleri istatistiksel olarak karşılaştırıldı.

Bulgular: Katılımcıların ortalama yaş ve gebelik haftası GDM'li ve sağlıklı hamile kadınlarda sırasıyla 30,71±5,09 yıl, 25,95±1,56 hafta ve 29,97±4,10 yıl, 25,76±1,30 hafta idi. Yaş (p=0,502) veya gebelik haftası (p=0,594) arasında anlamlı fark bulunmadı. CH, CRF, IOPg ve IOPcc değerleri, GDM'li hamile kadınlarda, sağlıklı hamile kadınlardakine kıyasla daha yüksek bulunmuştur. Ancak parametrelerde istatistiksel olarak anlamlı bir fark yoktu (sırasıyla, p=0,183, p=0,303, p=0,732 ve p=0,330).

Sonuç: Diyabetik hastalarda hiperglisemi, gözün diğer tüm katmanlarıyla birlikte korneada patolojik değişikliklere neden olur. Ancak kısa süreli hiperglisemi korneal biyomekanik parametreleri etkilemez.

Anahtar kelimeler: Kornea, Korneal Biyomekanik, Gestasyonel Diyabet, Hiperglisemi, Oküler Cevap Analizörü.

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Introduction

Hyperglycemia in diabetic patients causes pathological changes in the cornea, along with all the other layers of the eye (1–3). Increased oxidative stress and glycolysis products as a result of hyperglycemia produce a number of biomechanical changes in both the retina and the cornea (4–7). Dysfunction of corneal endothelial cells observed in diabetic patients may be another pathogenic factor for the same (7).

The literature reports many studies, most of which employed the Ocular Response Analyzer (ORA, Reichert Technologies, Depew, NY) and proved the fact that diabetes mellitus (DM) affects the corneal biomechanical characteristics (8–15). The ORA measures two metrics of corneal biomechanics in vivo: (i) corneal hysteresis (CH), which reflects the viscous dampening properties of the cornea, and (ii) corneal resistance factor (CRF) which is mostly associated with corneal stiffness (16, 17). The ORA also acts as a non-contact tonometry device which serves to yield the Goldmann-correlated intraocular pressure (IOPg) and the corneal compensated IOP (IOPcc).

With the increasing prevalence of obesity in recent years, gestational diabetes has been affecting 5% of pregnant women. (18). The duration of hyperglycemia in GDM patients is much shorter as compared to that in other diabetic patients. In this study, we investigated the effects of short-term hyperglycemia on the cornea in gestational pregnancy. To date, there is no study on the biomechanical properties of corneas in gestational diabetes.

Material and Methods

This study is an observational, cross-sectional study. The power analysis was performed by GPower 3.1.9.2 (Universitaet Kiel, Germany). In the analysis, preprandial blood glucose, HbA1C, and IOPcc pilot study measurements were recruited. The sample size for each group was determined as 34 cases according to 5% type-I error, 0.57 effect size (determined by real values) and 90% power for ANOVA.Thirty-eight pregnant females with newly diagnosed GDM and 34 age- and gestational age-matched healthy pregnant women were enrolled in the study. The diagnostic criteria given by the American Diabetes Association, performed by employing 75 g oral glucose tolerance test, was used for the diagnosis of GDM (19). Written informed consents were obtained from the participants prior to the study, which was conducted in accordance with the Helsinki Declaration and approved by the local ethics committee.

Pregnant women with normal ocular and systemic findings, with or without GDM were included in the study. Individuals having any ocular or systemic disorders (such as glaucoma, thyroid disorders, rosacea, connective tissue diseases, etc.) and history of ocular surgery or trauma, contact lens or those using any topical medication were excluded from the study. Before the measurements, all participants underwent a detailed ophthalmic examination by a single ophthalmologist (UA), to rule out the possibility of any ocular pathology. The right eye of the participants was examined. In order to eliminate the effects of diurnal variations of corneal biomechanics and IOP, all measurements were performed between 12:30 and 13:30 h.

The ORA device and its operating principles were presented for the first time in 2005 in detail by Luce (16). The ORA device helps perform a dynamic bi-directional applanation of the cornea during the measurement. A fast air-flow with increasing density forces the cornea to move inwards until it reaches a concave state. This is followed by a decrease in the density of the air-flow. The cornea then returns to its natural form depending on the internal flexibility it bears. The device calculates the CH and CRF from the differences in the acting pressures, by an infrared beam and an optical sensor (16).

The 4 parameters that were statistically compared between the healthy pregnant females and the pregnant women with GDM included CH, CRF, IOPg, and IOPcc.

Statistical Analysis

Mean±Standard deviation (SD) values were used to describe the quantitative variables, while nominal data were presented by frequency and percentages. Normality assumption was checked by Shapiro Wilk's test. Since data did not conform to the normal distribution, nonparametric statistical tests were used throughout the study. Mann-Whitney U test was used to compare the two groups in terms of quantitative variables. For all analyses, the IBM-SPSS version 20.0 was used and the statistical significance was set at $p<0.05$. The power analysis was performed by GPower 3.1.9.2 (Universitaet Kiel, Germany). In the analysis, blood glucose, HbA1C, and IOPcc pilot study measurements were recruited. The sample size for each group was determined as 34 cases according to 5% type-I error, 0.57 effect size (determined by real values) and 90% power for ANOVA.

Results

Demographic features and blood glucose levels of all study participants are summarized in Table 1. The mean age and gestational age of the participants were 30.71±5.09 year, 25.95±1.56 weeks and 29.97±4.10 years, 25.76±1.30 weeks, respectively, in pregnant females with GDM and healthy pregnant women, in the same order. There were no significant differences in age ($p=0.502$) and gestational age ($p=0.594$). Yet, the mean fasting blood glucose and HbA1c levels were significantly higher in pregnant females with GDM ($p<0.001$, for both).

Table 1. The demographic features and the laboratory results regarding blood glucose among of the healthy pregnant and pregnant with GDM participants

	The Mean±SD		p-value
	Pregnant with GDM (n=38)	Healthy pregnant (n=34)	
Age (year)	30.71±5.09	29.97±4.10	0.502
Gestational age (week)	25.95±1.56	25.76±1.30	0.594
FBG (mg/mL)	104.79±6.80	73.79±5.21	<0.001
HbA1c (%)	5.53±0.51	4.97±0.27	<0.001

GDM: Gestational diabetes mellitus, FBG: Fasting blood glucose.

The corneal biomechanical characteristics obtained with the ORA device are summarized in Table 2. The values of CH, CRF, IOPg, and IOPcc were determined to be higher in pregnant women with GDM as compared to that in the healthy pregnant females. However, there was no statistically significant difference in any other parameter studied (p=0.183, p=0.303, p=0.732 and p=0.330, respectively).

Table 2. The biomechanical characteristics of the cornea obtained with the Ocular Response Analyzer device

Measurements (mmHg)	The Mean±SD		p-value
	Pregnant with GDM (n=38)	Healthy pregnant (n=34)	
Corneal hysteresis	10.57±1.12	10.18±1.30	0.183
Corneal resistance factor	10.41±1.53	10.08±1.44	0.303
IOPg	14.61±3.28	14.86±3.05	0.732
IOPcc	15.08±3.44	14.32±3.07	0.330

GDM: Gestational diabetes mellitus, IOPcc: Corneal compensated intraocular pressure, IOPg: Goldmann-correlated intraocular pressure.

Discussion

This study shows that short-term hyperglycemia does not affect corneal biomechanical characteristics. However, Bao et al. (20) measured the corneal stiffness (tangent modulus) in healthy and diabetes-induced rabbits by injecting alloxan monohydrate intravenously for six weeks. They found that the mean corneal stiffness values were significantly higher in diabetic rabbits at four different stress levels. Furthermore, tangent modulus at the stress of 2.0 kPa was significantly correlated to the blood glucose and AGEs levels of diabetes-induced rabbits (20).

Although the literature reports several studies evaluating the effect of chronic DM on corneal biomechanical features, no study investigating corneal biomechanical alterations in pregnant females with GDM has been reported. The literature also presents conflicting reports regarding the effects of DM. Ramm et al. (8) and Goldich et al. (15) found that while CH and CRF values increased significantly in diabetic patients, IOPcc and IOPg did not differ significantly. Perez-Rico et al. (9) found that while CH was significantly lower, IOPcc and IOPg were significantly higher, and CRF was similar in uncontrolled DM patients. On the other hand, controlled DM patients showed parameters that were statistically similar to those of the healthy subjects. Sahin et al. (14), in their study, found the same outcomes as that of Perez-Rico et al. regardless of the fact that blood sugar was controlled in diabetic patients. On the contrary, Scheler et al. (10) and Kotecha et al. (11) reported that both CH and CRF values were significantly higher in poorly-controlled diabetics as compared to that in the healthy participants and well-controlled diabetics. Hence, they determined that the corneal biomechanical features changed depending on the glucose level. In contrast to these authors, Bekmez and Kocaturk (12) suggested that both IOPg and IOPcc measurements were significantly higher while CH and CRF values were non-significantly lower in patients with DM as compared to that in healthy subjects. Although there were no statistically significant differences in CH and CRF values, Bekmez and Kocaturk interpreted that the rise in IOP measurements, associated with lower CH and CRF values, appeared interesting. Yazgan et al. (13) found that all parameters (CH, CRF, IOPg, and IOPcc) were significantly higher in diabetic patients as compared to that in the healthy subjects; they also observed that IOP elevations were positively related to HbA1c levels.

Though all these studies employed the same device, the different measurements could be a result of differences in the duration and regulation of diabetes and the participants' age. The mean ages of the diabetic patients were reported to be 55.39±11.64 years, 67.6±10.3 years, 63.3±9.0 years by Sahin et al., Ramm et al., and Bekmez and Kocaturk, respectively.

The present study also has some limitations. One such limitation is that the participant number was relatively limited since the patient group included only GDM patients. Another limitation was that the corneal biomechanical characteristics could also be affected by the pregnancy of the participants. Tabibian et al. (21) reported that the hormonal changes affected the corneal biomechanics and topography during pregnancy. Unlike them, Santiagu et al. (22), Naderan et al. (23) and Sen et al. (24) determined that the differences between topographic and biomechanical corneal parameters before pregnancy, during pregnancy and during postpartum were not found to be statistically or clinically significant.

Conclusion

In conclusion, the present study reports that corneal biomechanical parameters appear to be unaffected by short-term hyperglycemia. This result may also be confirmed by performing similar studies on newly-diagnosed diabetic patients, with larger sample size.

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