

THE EFFECT OF RELIGIOUS FASTING ON WAVEFRONT ABERROMETER PARAMETERS

Oruç Tutmanın Wavefront Aberometre Değerlerine Etkisi

Soner GÜVEN¹

¹Kayseri City Hospital,
Department of Ophthalmology,
Kayseri,
Türkiye

ABSTRACT

Objective: Increased tear osmolarity and ocular surface inflammation during Ramadan fasting have been associated with alterations in anterior segment parameters. The primary aim of this study was to investigate the effect of religious fasting on refractive measures.

Material and Methods: Spherical equivalent, keratometry (K1, K2), and wavefront of all order aberrations and high order aberrations were scanned by iDesign Advanced WaveScan Studio (Abbott®, USA). Effective blur, high order percentages, polar Zernike coefficients at 6 mm and root mean square errors were also analysed. Thinnest pachymetry, corneal volume and anterior chamber volume were evaluated by Pentacam HR (Oculus®, Germany). The IOLMaster 500 (Zeiss®, Germany) was used to measure the axial length. Only the measurements of right eyes were used for statistical analysis. All measurements were performed at 4 pm one week prior to Ramadan (non-fasting period) and during last week of Ramadan (fasting period, 1 month later).

Results: Thirty-two eyes of 32 healthy volunteers (21 male and 11 female) were analysed. The mean age was 35.44±7.5 (18-49) years. No significant differences were found between fasting and non-fasting periods both in iDesign aberrometer corneal topography and biometry devices ($p>0.05$).

Conclusion: The refractive measures seem not to be altered during religious fasting period. There is no need to postpone the preoperative refractive measures in refractive surgery candidates during religious fasting.

Keywords: Religion; Cornea; Fasting; Refractive Surgical Procedures

ÖZET

Amaç: Ramazan ayında oruç tutmaya bağlı gözyaşı ozmolaritesinde ve oküler yüzey iltihabında artış olması ön segment parametrelerinde değişikliklere neden olabilmektedir. Bu çalışmanın ana amacı oruç tutmanın refraktif ölçümlere etkisinin incelenmesidir.

Gereç ve Yöntemler: Sferik eşdeğer, keratometri değerleri (K1, K2), tüm sıralı aberasyonlar ve yüksek sıralı aberasyonlar iDesign Advanced WaveScan Studio (Abbott®, ABD) cihazı ile tarandı. Efektif bulanıklık, yüksek sıra yüzdeleri, 6mmlik alandaki polar Zernike katsayıları ve kare kök ortalama hataları analiz edildi. En ince kornea kalınlığı, kornea hacmi, ön kamara hacmi Pentacam HR (Oculus®, Almanya) ile değerlendirildi. Aksiyel uzunluk ise IOLMaster 500 (Zeiss®, Almanya) ile ölçüldü. İstatistik analiz için sadece sağ gözden alınan ölçümler kullanıldı. Tüm ölçümler saat 16:00'da ramazan ayından 1 hafta önce oruçsuz dönemde ve ramazan ayının son haftasında (1 ay sonra) oruçlu iken yapıldı.

Bulgular: Toplam 32 sağlıklı gönüllünün (21 erkek ve 11 kadın) 32 gözü incelendi. Ortalama yaş 35,44±7,5 (18-49) yıl idi. Ramazan öncesi ve ramazan ölçümleri arasında incelenen tüm ölçümlerde istatistiksel olarak anlamlı fark saptanmadı ($p>0,05$).

Sonuç: Oruçlu olunan dönemde refraktif ölçümler değişmiyor olarak gözükmektedir. Refraktif cerrahi adaylarında oruçlu oldukları dönemde cerrahi hazırlığının refraktif sonuçlar açısından ertelenmesine gerek yoktur.

Anahtar Kelimeler: Din; Kornea; Oruç; Refraktif Cerrahi İşlemler

Soner GÜVEN, Dr.
(0000-0002-4497-5235)

İletişim:

Dr. Soner GÜVEN
Mevlana mh. Tamer cd. 5/14 Talas,
Kayseri, TÜRKİYE

Geliş tarihi/Received: 10.06.2021

Kabul tarihi/Accepted: 31.03.2022

DOI: 10.16919/bozoktip.950347

Bozok Tıp Derg 2022;12(2): 38-44

Bozok Med J 2022;12(2): 38-44

INTRODUCTION

A refractive surgery candidate should undergo full ophthalmic evaluation (latent and manifest refraction, aberrations, thinnest corneal thickness (TCT), corneal volume (CV), anterior chamber volume (ACV), pupil size, intraocular pressure (IOP)) to achieve satisfactory results after surgery. Patient selection for refractive surgery is as important as performing the surgical procedure. Questioning the social habits (e.g., cigarette smoking), medical history (previous surgery or medications), expectations from the surgery and eating habits are beneficial tools in decision making to perform or deny the surgery.

It has been shown that intermittent fasting (time-restricted feeding) has beneficial effects of on human health (1, 2). Intermittent fasting diets gained popularity as a way of weight loss in recent years due to increasing overweight problem all over the world. Religious fasting in the Ramadan is a type of intermittent fasting which restricts food and fluid intake between sunset (suhour) and dawn (iftaar) in Muslim religion. According to Islamic lunar calendar, Ramadan is the ninth month, lasts for 29 or 30 days including a daytime fasting period of 12-18 hours depending on the season. Eating habits and sleep schedule change during Ramadan. Systemic alterations (weight loss or weight gain, circadian hormone variations (melatonin, cortisol and prolactin etc.), dehydration, enhanced neurotrophic factors, reduced mitochondrial oxidative stress and pro-inflammatory cytokines) could also reflect to many ophthalmic alterations (3-6).

Ramadan fasting has been associated with increased tear osmolarity, ocular surface inflammation, alterations in anterior segment parameters and IOP (7-9). Besides, no significant links were found between Ramadan fasting and contrast sensitivity, topographic measures and corneal biomechanics (7, 10, 11). However, refractive status of healthy subjects during Ramadan fasting has not been well-described before (12). No data is available how to act in a refractive surgery candidate who is on religious fasting period.

The primary aim of this study was to investigate the alterations of refractive measures in fasting period by wavefront analysis. The potential alterations in biometric measures, corneal topographic measures, IOP and basal tear secretion variations were also

aimed secondarily to conclude whether to perform or postpone the surgery in a refractive surgery candidate who is on his/her religious fasting period.

MATERIAL AND METHOD

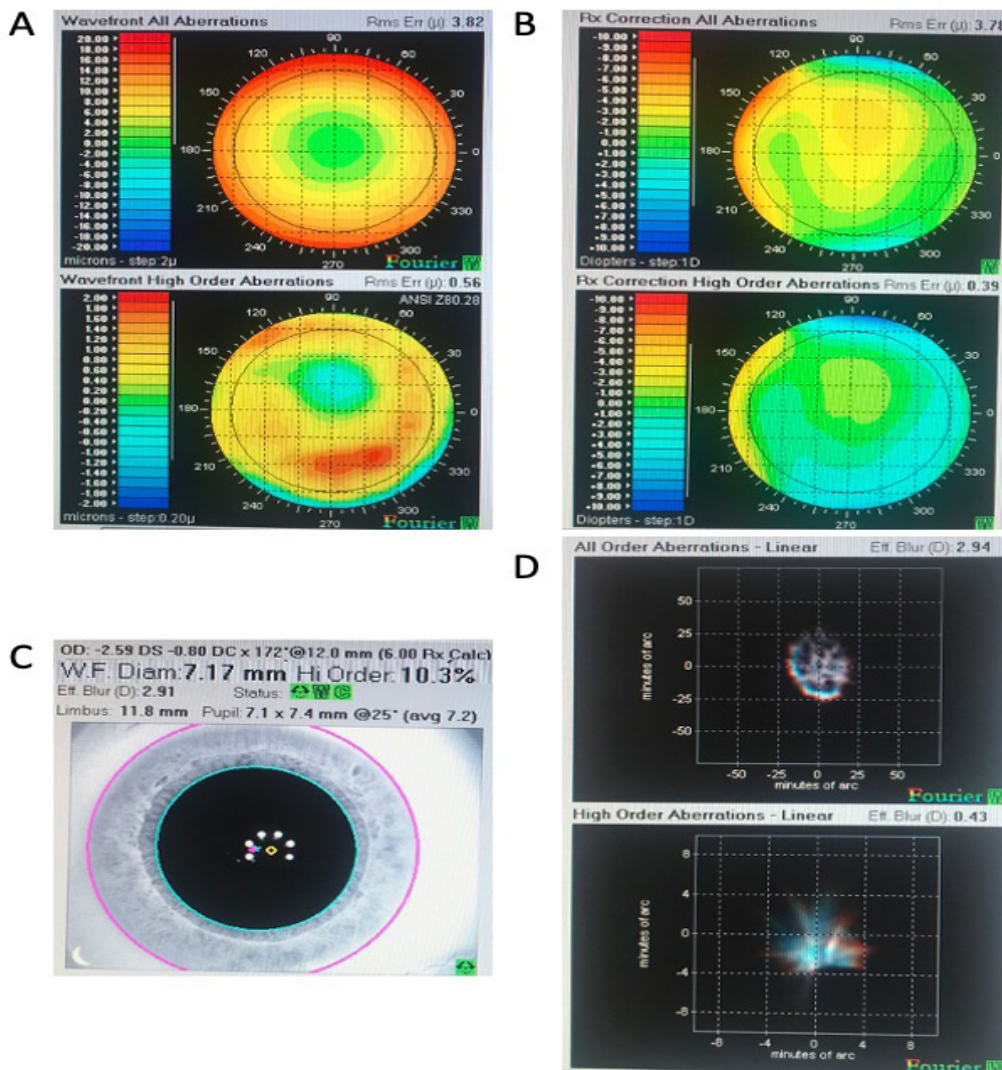
This current study was conducted according to Tenets of Helsinki following ethics committee approval (Erciyes University, Clinical Investigations Ethics Committee, 15.01.2020/2020-28) in Kayseri, Turkey in Ramadan 2020 (24 April-23 May). Verbal and informed consent forms were obtained from all participants. All volunteers were invited to undergo ophthalmic examinations in two points: one week before Ramadan (non-fasting period) and last week of Ramadan (fasting period). Healthy subjects aged >18 years who intended to fast during Ramadan at least 21 days with no history of any systemic and ophthalmic disorders were included. Subjects aged <18 years, any history of ophthalmic or systemic diseases, ophthalmic surgery, contact lens wear and any kind of medication use were excluded. Pregnant women and the women participants who were on their menstrual cycle periods were also excluded.

Spheric equivalent (SE) in both devices (Nidek®, ARK-700-A, Tokyo, Japan) and Wavefront iDesign Advanced WaveScan Studio (Abbott®, USA) were computed by adding half the minus cylinder to the sphere. This new iDesign aberrometer device captures images up to more than 1200 points with Hartmann-Schack principle to provide ocular aberrations. Topography, autorefractometry, pupillometry and keratometry measurements could also be provided by the same device in addition to ocular aberrations. iDesign has a spheric range from -16.00 to +12 dioptres (D), astigmatic range of 0 to 8.00 D and root-mean-square (RMS) range from 0 to 8 μ m high-order aberrations (HOA). The data acquisition is achieved by a Fourier algorithm. The data computed for a 6-mm diameter wavefront scan was used in the analysis. After the quality-check signals of the device turned green (all 3 of them), then the data were used for analysis. The high-order percentage (HOP) (%), HOA (in RMS, μ), all-order aberrations (AOA) (RMS, μ), point spread function (PSF) for HOAs' and AOAs' effective blur (D), HOA and AOAs for Rx correction (RMS, μ), total RMS error (μ) and polar Zernike coefficients (μ) (defocus,

astigmatism, coma, trefoil, spheric aberration, second order astigmatism and tetrafoil) were recorded (Figure 1). Flat (K1) and steep (K2) keratometry values computed in iDesign were also analysed. TCT (μm), CV (mm^3), ACV (mm^3) and iridocorneal angle (ICA, degree) measures were obtained by Pentacam HR (Oculus, Germany). Axial length (AL) was computed by

IOL Master 500 (Carl Zeiss Meditec AG, Jena, Germany). All participants underwent for full ophthalmic examination including slit lamp and funduscopy prior to ophthalmic examinations. All ophthalmic measures were performed by the same investigator (S.G.) at least three times both in non-fasting and fasting periods at 4 pm. Only the averages of the measurements of right

Figure 1. Example to explain data collection of a participant on iDesign WaveScan Studio



- A:** Wavefront error map for high-order aberrations (HOA) and all-order aberrations (AOA) in root-mean-squares (RMS) (μ) using Fourier reconstruction.
- B:** Wavefront error map for Rx correction for HOA and AOA in RMS (μ) using Fourier reconstruction.
- C:** Eye image and refraction error power in dioptres (D), wavefront reconstruction based on Zernike polynomials for AOA RMS (μ), HOA percentage (%), AOA effective blur (D), and quality check signal lights.
- D:** Point spread function for AOAs and HOAs effective blur (D).

eyes were used in statistical analysis. Due to Islamic belief issues no participants allowed to any eye drop instillations including cyclopentolate and fluoresceine. Thus, IOPs were assessed by non-contact pneumotometry (Topcon, CT-80, Japan) and only manifest refraction was analysed. Schirmer I test (without anaesthesia) was performed to measure tear secretion.

Statistical Analysis

Statistical Package for Social Sciences software version 23 for Mac (IBM Corp. Released 2015. IBM SPSS Statistics for Macintosh, Version 23.0. Armonk, NY: IBM Corp.) licensed for Erciyes University was used for analysis. The percentage (%) and number (n) were used for frequency values. The mean ± standard deviation (SD) and upper/lower limits of 95% confidence interval of the differences were used to present descriptive statistics. The normality of the variables was explored by both Shapiro-Wilk test and Q-Q plots and histograms. In continuous variables Paired samples t or Wilcoxon signed rank tests were used according to the distribution of the variable. A p value less than 0.05 was considered statistically significant. All p values were 2-sided.

RESULTS

Of 45 volunteers who intended to participate in this study, 8 participants did not undergo the Ramadan

examinations, ophthalmic measurements failed to pass quality check in 4 participants and 1 subject was diagnosed with keratoconus in initial tests. Thus, 13 of 45 subjects were excluded from the study. In total, 32 eyes (right) of 32 healthy subjects (21 male, 11 female) were included in statistical analysis.

The mean age was 35.44±7.5 (19-49) years. No significant differences were found in any analysed parameters between fasting and non-fasting measures except for SE computed in Nidek autorefractometer (Table 1). SE values computed in autorefractometer in fasting period were significantly higher than the non-fasting values (p=0.016). Wavefront measures between fasting and non-fasting periods are shown in Table 2 and Table 3.

DISCUSSION

The results of this study revealed that religious fasting has not a significant effect on refractive measures of healthy subjects to postpone the surgery preparations of refractive surgery candidates. Moreover, this study showed no significant alterations in refractive surgery parameters used in decision making process such as corneal topography (TC), IOP, AL, tear secretion values. The current literature has mostly focused on ocular surface, IOP, and corneal topography/ biomechanical alterations in religious fasting studies (7, 9, 11). There have been few published studies reporting the effect

Table 1. Comparison of ocular biometry, corneal topography and ocular surface characteristics of participants between fasting and prefasting periods (n:32).

	Fasting Mean±SD	Prefasting Mean±SD	Paired Differences			95% CI of the Difference		p [†]
			Mean	SD	St. Err Mean	Lower	Upper	
TCT, µm	523.28±40.69	521.53±42.25	1.75	5.78	1.02	-0.33	3.83	0.097
CV, mm ³	58.91±4.05	58.39±13.11	0.52	12.59	2.23	-4.02	5.06	0.817
ACV, mm ³	173.69±32.44	170.53±32.31	3.16	9.80	1.73	-0.38	6.69	0.078
ICA, degree	34.67±4.23	34.45±5.92	0.22	6.07	1.07	-1.97	2.40	0.842
SE*, diopter	-0.16±1.07	-0.40±1.01	0.24	0.52	0.09	0.05	0.42	0.016
IOP, mm hg	13.97±3.30	14.03±3.56	-0.06	2.33	0.41	-0.90	0.78	0.88 [†]
Schirmer	16.63±11.13	15.38±13.25	1.25	12.97	2.29	-3.42	5.92	0.589 [†]
AL, mm	23.44±0.75	23.45±0.74	-0.01	0.03	0.00	-0.01	0.00	0.313

CI; confidence interval, SD; standard deviation, St. Err; standard error, TCT; thinnest corneal thickness, CV; corneal volume, ICA; iridocorneal angle, SE; spheric equivalent, IOP; intraocular pressure, AL; axial length †Paired samples t test *Nidek autorefractometry †Wilcoxon signed rank test

Table 2. Comparison of refractive measures of participants between fasting and prefasting periods in iDesign Aberrometer (n:32).

	Fasting Mean±SD	Prefasting Mean±SD	Paired Differences			95% CI of the Difference		p [‡]
			Mean	SD	St. Err Mean	Lower	Upper	
SE, D	-0.67±1.08	-0.75±0.90	0.08	0.41	0.07	-0.07	0.23	0.27
HOP, %	32.72±21.97	32.56±19.84	0.17	15.11	2.67	-5.28	5.61	0.95
Eff. Blur, D	1.18±0.77	1.13±0.64	0.05	0.40	0.07	-0.10	0.19	0.52
K1, D	43.05±1.50	43.15±1.66	-0.10	0.94	0.17	-0.44	0.24	0.55
K2, D	43.95±1.61	44.02±1.76	-0.07	0.94	0.17	-0.41	0.27	0.67
AOA, Rms (μ)	1.43±0.88	1.60±1.75	-0.17	1.48	0.26	-0.70	0.37	0.53
HOA, Rms (μ)	0.41±0.20	0.49±0.47	-0.08	0.47	0.08	-0.25	0.09	0.36 [‡]
Rx correction, AOA, Rms (μ)	1.38±0.90	1.25±0.84	0.13	0.44	0.08	-0.03	0.29	0.10
Rx correction, HOA, Rms (μ)	0.31±0.16	0.40±0.47	-0.09	0.47	0.08	-0.26	0.08	0.28 [‡]
PSF, AOA, Rms (μ)	1.24±0.76	1.13±0.62	0.11	0.44	0.08	-0.04	0.27	0.15
PSF, HOA, Rms (μ)	0.39±0.28	0.47±0.43	-0.08	0.37	0.07	-0.21	0.05	0.23 [‡]
Total RMS error, μ	1.38±0.90	1.25±0.90	0.13	0.45	0.08	-0.03	0.30	0.10

CI; confidence interval, SD; standard deviation, St. Err.; standard error, SE; spheric equivalent, D; diopter, HOP; high order percentage, Eff. Blur; effective blurring, K1; flat keratometry, K2; steep keratometry, AOA; all order aberrations, Rms; root-mean-square, HOA; high order aberrations, PSF; point spread function, ‡ Paired samples t test †Wilcoxon signed rank test

Table 3. Comparison of polar Zernike coefficients of participants between fasting and prefasting periods (n:32).

Rms (μ)	Fasting Mean±SD	Prefasting Mean±SD	Paired Differences			95% CI of the Difference		p [‡]
			Mean	SD	St. Err Mean	Lower	Upper	
Defocus	0.85±1.18	0.89±1.07	-0.04	0.42	0.07	-0.19	0.11	0.60
Astigmat	0.50±0.51	0.48±0.52	0.02	0.11	0.02	-0.02	0.06	0.25 [‡]
Coma	0.16±0.09	0.16±0.08	0.00	0.05	0.01	-0.02	0.01	0.64
Trefoil	0.17±0.08	0.17±0.14	0.00	0.06	0.01	-0.02	0.02	0.98 [‡]
Spheric aberration	0.05±0.15	0.05±0.14	0.00	0.05	0.01	-0.02	0.02	0.91
Astigmatism 2 nd order	0.06±0.05	0.06±0.06	0.00	0.03	0.01	-0.01	0.02	0.45 [‡]
Tetrafoil	0.06±0.03	0.07±0.03	-0.01	0.05	0.01	-0.02	0.01	0.36 [‡]

ACI; confidence interval, Rms; root-mean-square, SD; standard deviation, St. Err.; standard error, ‡ Paired samples t test †Wilcoxon signed rank test

of religious fasting on refractive changes (7, 12-14). Significantly increased SE values were computed with Nidek autorefractometer in fasting period in the current study. In contrast, no significant changes were reported in respect of SE measures between fasting and non-fasting periods in different autorefractometers (Topcon) in previous studies (12-14). The SE difference observed in autorefractometer was not evident in iDesign device indicating inter-device differences could

have led this result.

In a study analysing the effect of fasting on tear osmolarity, the authors also reported that no significant differences were found in respect of Zernike polynomials between fasting and non-fasting periods (7). Although the authors reported comparable results with this current study, no information was mentioned about the refractive status of subjects or AOA/HOA values. Moreover, the device used for Zernike polynomials

was OPD Scan II which has a different working principle from iDesign aberrometer (7). In this study, mean differences between fasting and non-fasting periods in respect of defocus and astigmatism were found to be -0.04μ and 0.02μ , respectively. Both differences in these parameters were not only statistically insignificant but also were far lesser than lower limits of noticeable blur (0.18 ± 0.08) for defocus and astigmatism which was described elsewhere (15).

It has been previously reported that tear osmolarity increases and tear secretion decreases during fasting periods indicating a shift from normal to dry eyes (7). This dehydration trend observed in ocular surface could cause refractive irregularities in aberrometer measurements (16). A decrease trend in AOA and HOA (both for Rx correction and PSF) whereas an increase trend in total RMS error and AOA (both for Rx correction and PSF) were observed in fasting period in the current study; however, the differences were not statistically significant. Similarly, even though it was not statistically significant; Koktekir et al also reported a slight increase in ocular aberrations in their cohort during fasting period (7). Unlike to aforementioned study, tear osmolarity values were not quantified in this current report (7). TCT, ICA, ACV, CV values on corneal topography did not significantly change between fasting and prefasting periods in the current study. Parallel to this, Kerimoglu et al found no significant effects of fasting on corneal and anterior segment parameters with Pentacam (17). Similarly, Baser et al found no significant differences in respect of corneal thickness measurements between fasting and non-fasting periods in their cohort (13). However, some authors reported that a slight rise trend occurs in ACV during fasting (9, 12, 13). Further studies are needed to conclude. Besides, keratometry values (K1, K2) on iDesign aberrometer did not significantly differ in fasting periods in this study which was parallel to previous similar reports (7, 12).

Nowroozzadeh and Baser et al reported that AL significantly decreased in fasting period which was different from the current study (12, 13). In contrast to this report, Nowroozzadeh et al included an older cohort (mean age was 65 years) (12). Furthermore, ultrasonic biometry was used for AL measurements in both studies instead of IOLMaster which could have caused the different results from this study (12, 13).

IOP alterations during fasting period have been investigated by many researchers (7, 9, 11, 13, 17, 18). Although being the most common parameter explored in fasting studies, IOP alteration reports are controversial. A decrease trend in IOP during fasting has been reported (7, 9, 13, 17). However, Kayikcioglu and Uysal et al found no significant alterations in respect of IOP during fasting (11, 18). Consistent with the latter reports, no significant alterations were observed in IOP values during fasting in the current study. According to Islamic belief that eye drops would disrupt fasting, IOP measurements were performed by pneumotometry device instead of applanation tonometry in the study. The insignificant results in IOP values in this study could be attributed to measurement method used.

This study has some limitations. One center without control group design limits the study. Morning measurements were lacking to rule out diurnal variations. Fasting period lasted 18 hours in May where this study was conducted but measurements of the subjects were done at 14th hour of the fasting time. Furthermore, weight loss and tear osmolarity values of subjects were not considered to estimate the level of dehydration quantitatively. The study group comprised healthy younger subjects without any ocular diseases, thus the results can only be commented for this group. Fasting may cause different alterations on eye in older ages or in subjects with a specific type of ocular disorder. Additionally, the participants of the study had relatively low refractive errors. The measures of subjects with greater amounts of refractive errors may show different results. However, to the best knowledge no study has evaluated the refractive alterations during fasting period via wavefront aberrometer before.

CONCLUSION

The results of this report highlighted that no significant aberrometer changes occur during fasting period to postpone the surgery preparation of refractive surgery candidates. Further studies on subjects with moderate to high refractive errors are needed to confirm the results of this study.

ACKNOWLEDGMENTS

The authors declare that there is not any funding financial support for the study

REFERENCES

1. Horne BD, Muhlestein JB, Anderson JL. Health effects of intermittent fasting: hormesis or harm? A systematic review. *Am J Clin Nutr.* 2015;102:464-70.
2. Jane L, Atkinson G, Jaime V, Hamilton S, Waller G, Harrison S. Intermittent fasting interventions for the treatment of overweight and obesity in adults aged 18 years and over: a systematic review protocol. *JBI Database System Rev Implement Rep.* 2015;13:60-8.
3. Jahrami HA, Alsibai J, Clark CC, Mo'ez Al-Islam EF. A systematic review, meta-analysis, and meta-regression of the impact of diurnal intermittent fasting during Ramadan on body weight in healthy subjects aged 16 years and above. *Eur J Nutr.* 2020;59:1-26.
4. Roky R, Chapotot F, Hakkou F, Bencheikroun MT, Buguet A. Sleep during Ramadan intermittent fasting. *J Sleep Res.* 2001;10:319-27.
5. Kul S, Savaş E, Öztürk ZA, Karadağ G. Does Ramadan fasting alter body weight and blood lipids and fasting blood glucose in a healthy population? A meta-analysis. *J Relig Health.* 2014;53:929-42.
6. Michalsen A, Li C. Fasting therapy for treating and preventing disease-current state of evidence. *Forsch Komplementmed.* 2013;20:444-53.
7. Koktekir BE, Bozkurt B, Gonul S, Gedik S, Okudan S. Effect of religious fasting on tear osmolarity and ocular surface. *Eye Contact Lens.* 2014;40:239-42.
8. Armstrong BK, Coc IR, Agarwal P, Smith S, Navon S. Association of Ramadan daytime fasting with ocular surface inflammation and dry eye. *Int Ophthalmol.* 2019;39:2857-63.
9. Beyoğlu A, Karakucuk Y, Çömez A. Evaluation of the effect of fasting on intraocular pressure, anterior segment parameters and density of crystalline lens and cornea. *Int Ophthalmol.* 2020;40:2987-94.
10. Gok ZE, Gunduz A, Cankaya C. Effect of Fasting on Contrast Sensitivity in Healthy Males. *J Ophthalmic Vis Res.* 2019;14:315-20.
11. Uysal BS, Duru N, Ozen U, Yorgun MA, Akcay E, Caglayan M et al. Impact of dehydration and fasting on intraocular pressure and corneal biomechanics measured by the ocular response analyzer. *Int Ophthalmol.* 2018;38:451-7.
12. Nowroozzadeh MH, Mirhosseini A, Meshkibaf MH, Roshannejad J. Effect of Ramadan fasting in tropical summer months on ocular refractive and biometric characteristics. *Clin Exp Optom.* 2012;95:173-6.
13. Baser G, Cengiz H, Uyar M, Seker Un E. Diurnal alterations of refraction, anterior segment biometrics, and intraocular pressure in long-time dehydration due to religious fasting. *Semin Ophthalmol.* 2016;31:499-4.
14. Assadi M, Akrami A, Beikzadeh F, Seyedabadi M, Nabipour I, Larijani B et al. Impact of Ramadan fasting on intraocular pressure, visual acuity and refractive errors. *Singapore Med J.* 2011;52:263-6.
15. Atchison DA, Guo H, Charman WN, Fisher S. Blur limits for defocus, astigmatism and trefoil. *Vision Res.* 2009;49:2393-03.
16. Montés-Micó R. Role of the tear film in the optical quality of the human eye. *J Cataract Refract Surg.* 2007;33:1631-5.
17. Kerimoglu H, Ozturk B, Gunduz K, Bozkurt B, Kamis U, Okka M. Effect of altered eating habits and periods during Ramadan fasting on intraocular pressure, tear secretion, corneal and anterior chamber parameters. *Eye.* 2010;24:97-100.
18. Kayikcioglu O, Güler C. Religious fasting and intraocular pressure. *J Glaucoma.* 2000;9:413-4.