



Evaluation of the Effect of Fasting on Glaucoma Patients

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Abstract

Objectives: The aim of this research was to evaluate the effect of daytime Ramadan fasting and dehydration on intraocular pressure (IOP) and biometric parameters in primary open-angle glaucoma (POAG) patients.

Methods: This prospective study included 30 eyes of 30 POAG patients who were fasting during Ramadan (Group 1), 40 healthy participants who were fasting (Group 2), and 40 healthy individuals who were not fasting (Group 3). The eyes were evaluated twice a day at approximately 8 am and 4 pm during Ramadan and 1 month after Ramadan.

Results: IOP values at 4 pm were higher in Group 1 than Groups 2 and 3 in Ramadan ($p=0.029$ and 0.007 , respectively). The diurnal reduction in IOP was significantly smaller during fasting in the glaucoma patients compared with Groups 2 and 3 ($p=0.012$ and 0.007 , respectively). Comparisons of biometric parameters revealed less reduction in central corneal thickness (CCT) values from 8 am to 4 pm in glaucoma patients than in Groups 2 and 3 ($p<0.05$ for all comparisons) during Ramadan and after Ramadan.

Conclusion: POAG patients had a higher IOP at 4 pm during the fasting period than was seen following Ramadan. In addition, the diurnal reduction of IOP and CCT was smaller in patients with POAG compared with healthy subjects.

Keywords: Central corneal thickness, fasting, intraocular pressure, primary open-angle glaucoma

Introduction

Millions of Muslims all over the world fast as a religious practice during the month of Ramadan. Muslims do not eat, drink, or smoke from pre-dawn until sunset (1,2). Dehydration is one of the changes that can be seen in the body.

Among the effects of fasting are changes to the eyes and eye functions (3). It can influence ocular blood flow, intraocular pressure (IOP), and anterior and posterior segment parameters (4-8). Studies that have focused on the effects of fasting on IOP values have suggested that higher sympathetic nervous system activity as well as elevated levels of free fatty acids, cortisol, and norepinephrine may lead to an increased IOP during fasting (3,9-12). It has been also suggested that

excessive water intake at the pre-dawn meal before beginning the daily fast can be a factor that may increase morning IOP values (10). Other investigators have reported that dehydration and prostaglandin release during the fast may cause the IOP to decrease (4,5,7). The effects of fasting on the eyes, including IOP, visual acuity, refraction, anterior segment parameters, ocular blood flow, and tear secretion have been examined in healthy participants in numerous studies (3-7,10,13). However, a literature review revealed no studies that assessed the effect of fasting on glaucoma patients.

The objective of the present study was to investigate the effects of fasting on IOP in glaucoma patients at 8 am and 4 pm. Biometric parameters were also analyzed for a better understanding of the effects of fasting on glaucoma patients.

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Methods

The study was conducted prospectively with glaucoma patients and healthy volunteers who were fasting during Ramadan, as well as healthy volunteers who were not fasting during Ramadan, at the ophthalmology clinic of Medical Faculty Hospital between June 6 and July 4, 2016. In all, 30 eyes of 30 glaucoma patients (Group 1), 40 eyes of 40 healthy volunteers who were fasting (Group 2), and 40 eyes of 40 healthy volunteers who were not fasting (Group 3) were included in the study. Written, informed consent was provided by all of the participants. The Ethical Committee of the University approved the study, which was conducted in accordance with the Helsinki Declaration (Resolution no: 2016/58, date: 2016, June).

The patient group consisted of medically controlled glaucoma patients who had been diagnosed with primary open-angle glaucoma (POAG). POAG was defined by an open anterior chamber, >21 mm Hg IOP, glaucomatous optic disc changes, and retinal nerve fiber layer (RNFL) and/or visual field damage with no other underlying disease. The inclusion criteria were a best visual acuity of 20/20 or better, no acute or chronic eye disease (other than glaucoma in Group 1) or systemic disease, and no history of ocular surgery. Participants who had a spherical or cylindrical refraction error of $> \pm 3$ D, and an eye pathology (corneal disease, ocular surface disorders, etc.) preventing ocular examination were excluded. The participants were examined twice on the same day, once at 8 am and again at 4 pm during Ramadan, and the same measurements were taken 1 month later, after Ramadan.

First, all of the participants underwent a complete ophthalmologic examination, including assessment of best corrected visual acuity, biomicroscopy, and a fundus examination. A history of prior treatment was documented. Central corneal thickness (CCT), anterior chamber depth without CCT (ACD), and axial length (AL) measurements using a low-coherence optical biometry device (LCOB) (LS-900 biometer; Haag-Streit AG, Köniz, Switzerland), and RNFL thickness measurements were performed using spectral-domain optic coherence tomography (SD-OCT) (Spectralis; Heidelberg Engineering Inc., Heidelberg, Germany). Global RNFL values were obtained from an average of 6 sectors without changing the default RNFL measurement mode parameters using a 3.6-mm, fixed-diameter circle screen. IOP measurements were performed in a seated position using a Goldmann applanation tonometer.

The data obtained were statistically analyzed with IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). The data obtained in the morning and afternoon measurements during Ramadan and a month after Ramadan and the associated diurnal variations were com-

pared. A paired samples t-test was performed for within group comparisons. One-way analysis of variance followed by the Tukey honest significant difference test was used for post-hoc comparisons between groups.

Results

Thirty eyes (14 right eyes and 16 left eyes) of 30 POAG patients (Group 1), 40 right eyes of 40 healthy volunteers who were fasting (Group 2), and 40 right eyes of 40 healthy volunteers who were not fasting (Group 3) were included in the present study. Of the total of 110 participants, 52 were male (47%) and 58 were female (53%), with an average age of 60.9 ± 6.8 years (range: 49-77 years). The mean age and gender of groups did not differ significantly ($p=0.180$ and 0.322 , respectively). The IOP, AL, CCT, ACD, and RNFL values of the fasting groups are presented in Table 1; the same values of the groups recorded after Ramadan can be seen in Table 2. The mean cup/disc ratio was 0.53 ± 0.16 (range: 0.3-0.9) in the glaucoma patients. The topical medications used by the patients were a prostaglandin analog (2 eyes), timolol+dorzolamide/brinzolamide (10 eyes), prostaglandin analog+timolol+dorzolamide/brinzolamide (4 eyes), and prostaglandin analog+timolol+dorzolamide/brinzolamide+brimonidine tartrate (4 eyes).

Post-hoc tests of variance analysis indicated that the IOP value obtained at 4 pm was higher in the POAG patients than in Group 2 and 3 during Ramadan ($p=0.029$ and 0.007 , respectively). Comparison of diurnal IOP variation revealed that there was less of a reduction in IOP from 8 am to 4 pm in the POAG patients compared with that of Groups 2 and 3 during Ramadan ($p=0.012$ and 0.007 , respectively) (Table 3). However, a significant difference was not seen in measurements after Ramadan ($p=0.646$ and 0.898 , respectively). When the biometric parameters were compared, only the CCT values were significantly different. The CCT was thinner in Group 1 at 8 am compared with that of Groups 2 and 3 ($p<0.05$ for all comparisons); however, the difference was not significant at 4 pm ($p>0.3$ for all comparisons) either during or after Ramadan. In addition, there was less reduction in CCT values from 8 am to 4 pm in the POAG patients than in Groups 2 and 3 ($p<0.05$ for all comparisons) during and after Ramadan (Table 3).

Within Group 1, the IOP value measured at 4 pm was higher during Ramadan ($p=0.022$) and the diurnal change in IOP was lower, though the difference was not statistically significant ($p=0.707$). The CCT measurements of Group 1 were slightly lower during Ramadan, while they increased after Ramadan, but the difference was not statistically significant ($p=0.480$). In Group 2, the CCT values during the fasting period were greater at 8 am and 4 pm compared with the values after Ramadan ($p=0.026$ and 0.016 , respectively).

Table 1. Refractive, IOP, and biometric values of the groups during Ramadan

Parameters	Time	Group 1 (n=30) (Mean±SD)	Group 2 (n=40) (Mean±SD)	Group 3 (n=40) (Mean±SD)	p*
SPEQ (D)	8:00am	+0.15±1.04	-0.11±0.77	-0.21±1.10	0.312
	4:00pm	+0.03±0.90	-0.11±0.83	-0.19±0.93	0.589
IOP (mm Hg)	8:00am	16.77±3.51	15.79±3.06	15.22±2.57	0.250
	4:00pm	16.61±4.06	13.94±2.34	14.05±2.70	0.005
AL (mm)	8:00am	23.41±0.77	23.47±0.90	23.43±0.80	0.557
	4:00pm	23.42±0.86	23.45±0.83	23.44±0.84	0.509
CCT (µm)	8:00 am	531.44±20.77	545.28±30.02	547.72±28.32	0.024
	4:00 pm	530.00±25.99	540.65±31.77	543.20±30.16	0.428
ACD (mm)	8:00 am	2.67±0.40	2.75±0.44	2.69±0.29	0.256
	4:00pm	2.70±0.42	2.78±0.50	2.70±0.39	0.343
RNFL (µm)	8:00am	82.25±13.94	100.65±11.16	101.50±10.04	<0.001
	4:00pm	85.47±11.47	100.70±11.05	101.80±9.80	<0.001

*One-way analysis of variance;ACD:Anterior chamber depth;AL:Axial length; CCT: Central corneal thickness; IOP: Intraocular pressure; RNFL: Retinal nerve fiber layer; SPEQ: Spherical equivalent.

Table 2. Refractive, IOP, and biometric values of the groups after Ramadan

Parameters	Hours	Group 1 (n=30) (Mean±SD)	Group 2 (n=40) (Mean±SD)	Group 3 (4=20) (Mean±SD)	p*
SPEQ (D)	8:00am	+0.18±1.06	-0.10±0.93	-0.18±0.99	0.414
	4:00pm	-0.04±0.96	-0.09±0.83	-0.14±1.05	0.603
IOP (mm Hg)	8:00am	15.91±3.28	15.28±3.27	15.49±2.67	0.821
	4:00pm	15.79±2.93	14.20±2.51	14.50±2.62	0.219
AL (mm)	8:00am	23.40±0.81	23.48±0.83	23.46±0.80	0.401
	4:00pm	23.41±0.89	23.46±0.88	23.46±0.85	0.389
CCT (µm)	8:00am	528.44±22.51	543.33±29.23	547.61±25.46	0.017
	4:00pm	530.19±26.26	539.50±31.84	543.75±29.87	0.461
ACD (mm)	8:00am	2.69±0.41	2.73±0.39	2.66±0.20	0.335
	4:00pm	2.73±0.58	2.70±0.38	2.68±0.33	0.407
RNFL (µm)	8:00am	83.35±11.82	100.60±10.70	101.30±10.10	<0.001
	4:00pm	84.13±12.37	100.50±10.64	101.00±9.89	<0.001

*One-way analysis of variance;ACD:Anterior chamber depth;AL:Axial length; CCT: Central corneal thickness; IOP: Intraocular pressure; RNFL: Retinal nerve fiber layer; SPEQ: Spherical equivalent.

There was no significant difference in any comparison of the non-fasting participants (Group 3), as expected.

Discussion

To the best of our knowledge, the present analysis of the changes in IOP in fasting glaucoma patients is the first in the literature. The IOP value of the healthy subjects was not significantly affected during the fasting period. However,

glaucoma patients who were fasting had higher IOP values at 4 pm compared with the values recorded after Ramadan. Moreover, the diurnal decline in IOP during fasting was smaller in POAG patients compared with that of the healthy fasting and non-fasting subjects.

Many studies have been performed to examine the effects of fasting on IOP values in different settings and with various hypotheses (1,3-5,10,12,14). One study indicated

Table 3. The mean diurnal change in IOP and biometric values

Parameters	Period	Group 1 (n=30) (Mean±SD)	Group 2 (n=40) (Mean±SD)	Group 3 (n=40) (Mean±SD)	p*
dc IOP (mm Hg)	Fasting	-0.97±2.86	1.33±1.82	1.47±2.39	0.004
	Control	0.11±2.09	0.81±2.33	0.46±2.70	0.670
dc AL (mm)	Fasting	-0.01±0.02	-0.01±0.01	-0.02±0.01	0.776
	Control	-0.03±0.05	0.01±0.02	-0.01±0.03	0.221
dc CCT (µm)	Fasting	0.21±3.75	2.95±4.45	3.16±4.63	0.021
	Control	-1.93±3.73	3.44±5.37	2.94±3.06	0.002
dc ACD (mm)	Fasting	-0.02±0.02	-0.01±0.04	-0.01±0.03	0.800
	Control	-0.02±0.03	-0.01±0.03	-0.01±0.04	0.687

*One-way analysis of variance; ACD: Anterior chamber depth; AL: Axial length; CCT: Central corneal thickness; dc: Diurnal change (8:00 am value subtracted from 4:00 pm value); IOP: Intraocular pressure.

that the morning IOP values during fasting were significantly higher than non-fasting morning IOP values. In another study, significantly a lower IOP value was recorded in the afternoon during fasting. The expected diurnal decline in IOP value was reported to be greater during Ramadan (4,11). The findings of Kerimoğlu et al. (10) were consistent with other published studies in the literature, which reported higher morning IOP values and lower afternoon IOP values than ordinarily seen during fasting. They also reported that healthy non-fasting subjects had a higher IOP value in the afternoon. According to I hypothesis, a high IOP value in the morning during a fasting period may create conditions similar to those of a water loading test. Significant fluid consumption at a pre-dawn meal approximately 4 hours before the measurements may explain higher IOP values (10,11,15).

Dadeya et al. (5) measured IOP at 4 time points during the day in healthy subjects who were fasting and compared the data to the equivalent measured after Ramadan. The results showed a significant reduction in IOP values at each time point during the fasting period. Oltulu et al. (7) also observed reduced IOP values while fasting. The IOP-lowering effect of fasting was thought to be due to dehydration and elevated secretion of prostaglandin analogs during fasting (4,5,7). There are also studies that have demonstrated no significant changes in IOP values during Ramadan compared with controls (3,6,12,14).

There might be some additional reasons for glaucoma patients to have elevated IOP values at 4 pm. First of all, the changes in daily routine that occur during Ramadan may have affected the time of eye drop application. Higher IOP values may be a result of a decline in the activity of the drug by 4 pm, when the effect of fasting becomes apparent. Secondly, habit modifications during Ramadan have been

shown to affect the sleep cycle and circadian rhythms in several studies (16-19). Bogdan et al. (16) observed that during Ramadan the serum cortisol level increased in the afternoon; the ordinary morning rise was delayed. In a review article, Roky et al. (17) concluded that major chronobiological change patterns are flattened during Ramadan, which causes a shift in some circadian rhythms. Therefore, any changes of aqueous production associated with altered circadian rhythms or any alteration in the routine of medicine application that might affect aqueous production might be reasons for elevated IOP values at 4 pm in glaucoma patients.

The present study, to the best of our knowledge, is the first to examine the anterior segment parameters during fasting with an LCOB device. The AL and ACD values of the controls and fasting subjects were not significantly different; however, the CCT values were significantly different. Studies investigating the CCT values of patients with glaucoma have indicated that there were similar fluctuations to those observed in a healthy population and did not impact IOP measurements (20,21). In the present study, unlike the healthy population, the POAG patients had an increased CCT thickness at 4 pm following Ramadan. This difference may have been due to greater use of drops (antiglaucomatous, artificial tears, etc.) in POAG patients following Ramadan. Potential changes to the application schedule of eye drops during the fasting period may have prevented the diurnal increase of CCT in POAG patients. It has been suggested that the major chronobiological changes during Ramadan are a general flattening as well as a shift in the circadian rhythm (17).

Limitations of the study include the smaller size of the glaucoma patient group due to eligibility requirements, not performing patient evaluations more frequently throughout a

24-hour time period, and the lack of follow-up on drug compliance with the glaucoma patients. In addition, the POAG patients were not a homogeneous group in terms of use of the same medications or glaucoma grade. Nonetheless, the comparison of 3 experimental groups at the same time and under the same conditions can be considered a strength that will contribute to additional evaluation of the impact of fasting and dehydration.

Conclusion

In conclusion, many hypotheses have been proposed regarding increased IOP values during Ramadan, including increased sympathetic activity during fasting, altered cortisol rhythm, and increased fluid intake at the pre-dawn meal. It has also been suggested that increased dehydration and prostaglandin release may play a role in IOP values during Ramadan (3-5,9-11,16). Inconsistencies in published studies of the impact of fasting on IOP values may also be a result of the different response of each individual to fasting, including the effect of dehydration, altered hormonal rhythms, and changes in lifestyle, such as eating habits and sleep cycle. Variance in drug compliance in glaucoma patients also makes it more difficult to precisely determine the impact of fasting. The results of the present study demonstrated a mild increase in IOP values at 4 pm in the POAG patient group. The importance of regular eye drop application during Ramadan should be explained to glaucoma patients. Additional studies with larger and homogeneous groups with controlled drug application and more frequent daily evaluation are required to further understand the effects of fasting on glaucoma patients.

Disclosures

Ethics Committee Approval: Ethical Committee of Medical Faculty of Abant Izzet Baysal University, Resolution no: 2016/58, date: 2016, June.

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Authorship Contributions: Involved in design and conduct of the study (EU, FU, UD); preparation and review of the study (EU, FU, UD, SC); data collection (EU); and statistical analysis (EU, FU).

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