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Evaluation of the Diurnal Intraocular Pressure Fluctuations and Blood Pressure under Dehydration due to Fasting

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ABSTRACT

Introduction: This study aimed to investigate the diurnal intraocular pressure fluctuations under dehydration conditions and the relationship between the intraocular pressure fluctuations and blood pressure.

Methods: The intraocular pressures (IOP), body weights, as well as systolic and diastolic blood pressures (SBP, DBP) of 36 fasting healthy volunteers were recorded at 8:00 a.m. and 5:00 p.m. in the Ramadan of 2014 and two weeks after it. The data were analyzed using paired Student's t-test and Pearson correlation analysis.

Results: As the results demonstrated, the mean diurnal IOP differences of IOP, SBP, DBP, and weight were 2.67±1.33 mmHg, 9.44±8.02 mmHg, 3.33±5.94 mmHg, and 0.90±0.46 kg during the fasting period, respectively. In addition, the mean diurnal IOP differences of IOP, SBP, DBP, and weight were -0.33±1.4 mmHg (P=0.001), 0.55±7.25mmHg (P=0.003), -3.33±5.94 mmHg (P=0.001), and 0.12±0.45 kg (P=0.001) during the control period, respectively. There was a moderate correlation between the diurnal IOP and SBP differences (r=0.517, P=0.028).

Conclusion: Based on the findings of the current study, the total fluid volume might have a more dominant effect on IOP peaks than the sympathetic system activity. Furthermore, the SBP was found to correlate with the IOP.

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Introduction

The intraocular pressure (IOP) follows a diurnal rhythm. Typically, the morning IOP values are slightly higher than the evening measurements (1, 2). The IOP is the only risk factor of glaucoma, one of the most major causes of legal blindness, which can be controlled and managed. High fluctuations of IOP are assumed as a risk factor for the progression of glaucoma (3). However, the diurnal fluctuations vary between ethnic groups, systemic blood pressure, and various conditions (4-6). It has been demonstrated that the diurnal fluctuations have seasonal variations in rabbits (7).

The IOP reflects a balance between inflow and outflow of aqueous humour. The suprachiasmatic nucleus, which controls the activities of sympathetic and parasympathetic innervations as well as the pterygopalatine and superior cervical ganglia, has significant impacts on the rhythmic regulation of the IOP (8, 9).

A main step in the medical treatment of glaucoma is reducing inflow, and thereby IOP. The IOP is an important risk factor for the progression of glaucoma. According to the literature, the primary open-angle and closed-angle glaucoma are associated with the increased sympathetic nervous system activity and decreased parasympathetic system activity, respectively (10, 11).

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Water loading is one of the factors, which increases IOP and alters other ocular parameters in the eye (12, 13). Water drinking significantly and rapidly raises sympathetic activity. Indeed, it elevates the plasma norepinephrine level as much as such classic sympathetic stimuli as caffeine and nicotine (14). After drinking water or any hypotonic fluid, water is absorbed into the blood and body tissues, including the eye. This is associated with a consequent increase of episcleral venous pressure and IOP (15-17).

Fasting results in various physiological alterations in the human body, which could be summarized as reduction of insulin secretion, elevation of glucagon, and activation of the sympathetic system, which leads to the increase of secretion of fatty acids as well as serum cortisol and norepinephrine levels. Increased blood levels of these hormones may result in the augmentation of renal hyperperfusion and systemic blood pressure (18-20).

Since water loading increases IOP, a decrease in IOP can be expected during water loss. However, the mechanisms of these processes have remained unclear. With this background in mind, we aimed to investigate the factors that influence the diurnal IOP measurements under dehydration conditions due to fasting. In our previous study, we concluded that the total fluid volume has an important effect on the IOP fluctuations (21). The present study aimed to investigate the relationship between the blood pressure and intraocular pressure fluctuations.

Material and methods

For the purpose of data collection, 36 eyes of 36 healthy voluntary participants were included in the study. The measurements were taken on a random day in the second decade of the 2014 Ramadan (July 2014-August 2014) at 8.30 a.m. and 5.00 p.m. as well as two weeks after this month. After obtaining the participants' informed consent, they underwent complete ophthalmologic and refractive examinations with IOP measurements.

Subsequently, the weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) of the participants were measured. The exclusion criteria were as follows: 1) diabetes, 2) hypertension, 3) any metabolic disease, 4) any ocular disease such as cataract, glaucoma, undergoing intraocular surgery or congenital disorder, 5) refractive errors > ±1.00 diopter, 6) age of < 20 and > 45 years, and 7) smoking.

In 2014, the fasting month occurred between July and August in the summer. That year, the fasting act lasted for approximately 17 h under a mean temperature of 33^0C in the shadow. In Islamic fasting, people wake up before dawn and prepare themselves for the fasting day ahead. They eat a full meal and especially drink large amount of water before dawn to endure the long fasting period on a summer day.

The IOPs were measured with a Goldmann applanation tonometer (GAT), which is considered the most accurate clinical method for measuring the IOP. This method indirectly measures the IOP by gauging how much force it takes to flatten the cornea over a fixed surface area. The systemic blood pressure was measured using a manual sphyngomanometer. The cuff was placed midway between the shoulder and elbow with a gap of 2-3 cm above the elbow. The brachial pulse was palpated with the first two fingers, and the cuff was placed so that the arrow of the arterial indicator was directly over the brachial artery. The cuff was located at the same height as the heart.

The chest piece of the stethoscope was placed firmly and directly over the brachial artery underneath the cuff. The cuff was inflated until no pulse was heard. The air valve was turned counter-clockwise to release the air at a rate of 2-3 mmHg per second. The systolic and diastolic pressures were noted on the gauge reading with the first and the last audible pulses, respectively. To determine the fluid loss during the fasting and control periods, the body weight was measured using an analogue platform scale.

This prospective study, which was approved by the Ethical Committee of Sifa University, adhered to the tenets of the Declaration of Helsinki.

Statistical Analysis

The data were checked for normality of distribution using graphical analytical techniques (e.g., histograms and probability plots) and analytical methods (e.g., Kolmogorov-Smirnov and Shapiro-Wilk tests). The descriptive analysis of the normally distributed data (i.e., SBP, DBP, IOP, and weight measurements [WM]) was presented as mean and standard deviation. Paired Student's t-test was used to compare the morning and evening measurements of the SBP, DBP, WM, and IOP during the control and fasting periods. Additionally, the relationship between the variables was investigated using Pearson product-moment correlation. The data were analyzed through SPSS version 15.0 (SPSS Science, Chicago, IL, USA).

Results

According to the results of the study, the mean age of the participants was 31.1±5.7 years (age range: 21-43 years). Furthermore, 25 of the subjects (69.44%) were male and 11 (30.55%) were female. The differences between the morning and evening measurements of the fasting and control periods are illustrated in Table 1.

Table 2 displays the IOP, SBP, DBP, and weight of the patients during the fasting and control periods.

According to the results of the study, the mean diurnal IOP differences (IOP in the morning and evening) were 2.67±1.33 mmHg and -0.33±1.4 mmHg during the fasting and control periods, respectively (P=0.001). In addition, the mean SBP differences (SBP in the morning and evening) were 9.44±8.02 mmHg and 0.55±7.25 mmHg during the two periods, respectively (P=0.003). The mean diurnal DBP differences (DBP in the morning and evening) were 3.33±5.94 mmHg and -3.33±5.94 mmHg during the fasting and non- fasting periods, respectively (P=0.001). Furthermore, the mean diurnal weight differences (weight in the morning and evening) were 0.90±0.46 kg and -0.12±0.45 kg during these two periods (P=0.001).

As the results demonstrated, there was a moderate correlation between the diurnal IOP and SBP differences (r=0.517, P=0.028). However, no significant correlation was observed between the diurnal IOP and DBP differences (r= -0.361, P=0.141). Likewise, there was no correlation between the differences of the diurnal IOP and weight (r=0.095, P=0.707).

Discussion

The findings of the present study contributed to the hypothesis that the total fluid volume has a significant impact on IOP fluctuations. In the current study, there was a significant difference in the IOP and diurnal weight measurements of the participants between the fasting and control periods. In the non-fasting control period, we observed even a slight increase of the body weight in the evening measurements.

Although there was no correlation between the body weight and IOP differences, the observed difference in the body weight can be partly due to the total fluid loss of the body during the fasting period, because the differences of the weight loss were significant during the fasting period. However, the

Table 1. The differences between the morning and evening measurements of the fasting and control periods

	Fasting period Morning/Evening	P-value	Control period Morning/Evening	P-value
IOP	17.00±2.19/14.33±2.47	0.001*	16.5±2.01/16.88±1.87	0.357
SBP	111.4±8.5/107.2±7.5	0.115	118.3±7.8/117.7±8.1	0.288
DBP	69.4±9.9/66.1±9.2	0.256	73.9±7.8/77.2±5.7	0.012*
BW	74.7±7.4/73.8±7.2	0.02*	75.1±7.1/75.2±7.2	0.556

IOP: Intraocular pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

*Statistically significant

Table 2. Mean IOP, blood pressure, and weight measurements between the fasting and control periods

	Fasting period	Control period	P-value
Mean IOP in the morning (mmHg)	17.00±2.19	16.5±2.01	0.163
Mean IOP in the evening (mmHg)	14.33±2.47	16.88±1.87	0.001*
Mean SBP in the morning (mmHg)	111.4±8.5	118.3±7.8	0.110
Mean SBP in the evening (mmHg)	107.2±7.5	117.7±8.1	0.001*
Mean DBP in the morning (mmHg)	69.4±9.9	73.9±7.8	0.072
Mean DBP in the evening (mmHg)	66.1±9.2	77.2±5.7	0.001*
Mean weight in the morning (kg)	74.7±7.4	75.1±7.1	0.279
Mean weight in the evening (kg)	73.8±7.2	75.2±7.2	0.002*

IOP: Intraocular pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

*Statistically significant

question regarding whether the IOP regulation reacts faster to fluid loss at a critical level remains unanswered.

Similar results were achieved by Kerimoglu, Dadeya, and Hassan et al.; nevertheless, in a study conducted by Kayikcioglu et al., no alterations in diurnal body weight and IOP values were reported. This discrepancy might be due to the difference in the study period (22-24). Kayikcioglu et al. carried out a study in 2000, in which the fasting month hit the winter months in Turkey. In that time, the fasting period was short and the climate was cold. Consequently, the body weight loss reported in the mentioned study was less than that in other studies (25).

We found a moderate correlation between the SBP and IOP differences in the fasting period. During the fasting period, as expected, the sympathetic system activity increased in the evening, which was due to dehydration; nevertheless, the SBP values were lower than the morning measurements. This might be due to the water loss after an averagely-17-hour fasting period. The elevation of IOP after water drinking might be partially due to the thickening of the choroid, which results in a pressure gradient transmitted to the intraocular compartments and the outflow of humour aqueous from the anterior chamber to the drainage system (26).

Therefore, it could be expected that dehydration has an opposite effect. Another important factor might be the presence of innervation of the choroid by vasoconstrictor sympathetic and vasodilator parasympathetic nerves. This has been previously indicated by Steinle et al. in rat models, which demonstrated that the sympathetic denervation for six weeks led to significant increases in choroidal thickness and sympathetic nerves. Furthermore, they concluded that sympathetic nerves are involved in maintaining normal choroidal vascular architecture through actions mediated primarily by β-adrenoceptors (27).

As an important observation of our study, the expected increments of sympathetic system activity and blood pressure did not lead to the elevation of IOP. The increase of blood pressure can be ascribed to the fact that the dehydration was not at a critical level to keep the blood pressure in a normal status. Another reason for this increase can be the activation of sympathetic system, which kept the blood pressure in a tolerable status. On the contrary, in a study conducted by Klein et al., a higher BP was found to correlate with a higher IOP. They related this feature to the higher choroidal perfusion pressure that prevails in hypertension.

Furthermore, they stated that such IOP elevations were associated with the subsequent development of glaucoma (28). The higher blood pressure observed in this study indicates that the sympathetic system activity has an observable effect on IOP, at least in dehydration conditions. However, the blood pressure was low in the evening measurements, which can be ascribed to two possibilities: the sympathetic system activity was limited or the sympathetic system was activated and kept the blood pressure as stable as possible; however, this did not increase the resistance in the episcleral blood vessels.

Given the significantly lower values of the IOP measurements in the evening hours, it can be concluded that the total fluid volume of the human body has a more dominant effect on IOP peaks. There is a possibility that the choroid regulates the ocular perfusion pressure, which is sensitive to volume changes. Sympathetic innervation plays an important role in choroidal blood flow regulation.

Recent studies revealed that the choroid, mainly controlled by the sympathetic nervous system and metabolic factors, can be autoregulated in response to an increase or decrease in ocular perfusion pressure (29, 30). However, in which part of this system the choroid is involved is still an unresolved question.

There are some strengths and weaknesses in the present study. The first and the most important limitation was the impossibility of standardizing the amount of dehydration. Considering this, the findings of the present study can only give us an idea regarding how the autonomic nerve system might be involved in the regulation of IOP. Furthermore, the use of diurnal choroidal thickness measurements could provide us with additional information about the impact of the choroid on IOP peaks under dehydration conditions.

Additionally, it is stated that the dehydration also alters mean arterial blood pressure, stroke volume, and cardiac output as well as increases the plasma norepinephrine levels (12). Nevertheless, examining such parameters in the participants, which requires blood and ultrasonographic tests, is troublesome regarding the hard fasting conditions. Therefore, it is recommended to conduct a prospective study investigating these parameters to obtain more precise information about the autonomic nerve system and IOP relation.

On the other hand, to the extent of the researchers' knowledge, this study has been performed in the hardest fasting condition. In July 2015, the mean temperature in the Aegean region of Turkey was between 33^{0}C and 38^{0}C and an average fasting period lasted between 17-18 h. It is difficult to find these fasting conditions, because the fasting periods are changing every year due to the shorter period of the Islamic calendar (lunar calendar), compared to the solar calender. Consequently, this study provided valuable information about the IOP and body fluid volume homeostasis.

Conclusion

Based on the findings of the current study, the total fluid volume might have a more dominant effect on IOP peaks than the sympathetic system activity. As demonstrated in the study, the SBP correlated with diurnal IOP. Since the regulation of the IOP is a complex system, further studies and attention should be directed toward exploring the mechanism of the IOP peaks.

Conflicts of interest

The researchers of the present study certify that they have no affiliations with or involvement in any organization or entity with any financial interest (e.g., honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultations, stock ownership, or other equity interest, as well as expert testimony or patent-licensing arrangements) or non-financial interest (e.g., personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this study.

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