ORIGINAL ARTICLE

Intraocular Pressure: the Effect of Short-term Fasting and Its Association With Fluid and Fat Status

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ABSTRACT

Introduction: Short-term fasting may influence intraocular pressure (IOP) due to alteration of fluid (total body water; TBW, and water intake) and fat (total body fat; TBF). This study aimed: i) to compare IOP values within and between, fasting and non-fasting periods; and ii) to assess the association between IOP and, TBW and TBF. **Methods:** Thirty healthy participants aged 21.8±1.1 years were assessed on two different periods (fasting vs. non-fasting). During each period, the IOP, TBW and TBF values were assessed for four times (morning, afternoon, evening, late-evening). The IOP was measured using AccuPen® tonopen, while TBW and TBF were assessed by using a Tanita body composition analyser. **Results:** During fasting, the IOP value in the afternoon (14.53±2.33 mmHg) was significantly higher than in the evening (12.43±2.73 mmHg, p=0.009) and late-evening (12.60±2.44 mmHg, p=0.003). No significant difference in IOP was observed during non-fasting period. The mean of IOP in the evening was significantly lower during fasting compared to non-fasting (12.43±2.73 mmHg vs 13.75±2.53 mmHg, p=0.044). The IOP and TBW were negatively correlated (r=-0.268; p=0.011) during non-fasting and showed no association during fasting period. There was no significant correlation between IOP and TBF during both fasting and non-fasting periods. **Conclusion:** IOP reduction during short-term fasting, together with the no association with TBF and TBW suggested that IOP is an independent factor that reduces during fasting in healthy population.

Keywords: Intraocular pressure, Fasting, Total body water, Total body fat, Total fat intake

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INTRODUCTION

Glaucoma is regarded as the "silent thief" of sight as patients are usually asymptomatic for a long time (1). It is a chronic, non-curable eye disease, which is caused by optic nerve damage and visual field loss (2). The number of people with glaucoma worldwide is projected to increase from 76.0 million in 2020 to 111.8 million in 2040 (3). Elevation of IOP is a strong risk factor that contributes to the development and progression of glaucoma (4). In fact, it is the only modifiable risk factor through the use of medications or surgical interventions (5,6). In addition, IOP has also been demonstrated to significantly reduce with fasting (7).

Fasting is an action of refraining the intakes of food and beverages. In Islamic religious practice, fasting lasted from sunrise to sunset, and can either be performed as a compulsory one-month period during Ramadan (long-term fasting), or as non-compulsory days outside of Ramadan (short-term fasting) (7). The IOP during long-term fasting were reported to be lower as compared to during non-fasting period (8). Long-term fasting may cause IOP reduction due to the modification of eating patterns. Eating behavior during fasting period changes in terms of frequency, timing composition as well as calories and nutrients content of meals, as compared to non-fasting period (7). Habitually, during non-fasting period people commonly consume three main meals daily which include breakfast, lunch and dinner. However, the number of meals normally changes into two meals per day which include a large breaking-fast meal (dinner) and a light pre-dawn meal during fasting which may cause reduction in daily nutrient intakes thus influence IOP values (9).

Abstaining oneself from drinking water for 12-14 hours during daytime may result in reduction of total body water (TBW) and thus may lead to IOP variation (8). A healthy eye normally demonstrates a small IOP fluctuation of about 2 to 6 mmHg, in comparison to those of glaucomatous eye, about ≥10 mmHg (10). The IOP fluctuation may be affected by abrupt changes of

TBW in the body. This is due to the reduction of water intake during fasting which causes greater impact in glaucomatous eyes than healthy eyes (11). Other than that, in primary open angle glaucoma, high total body fat (TBF) and dietary fat intake may result in significant increase of IOP as compared to healthy eye (12). It was speculated to be due to excessive intraorbital fat volume in the lower eyelid that leads to increased episcleral venous pressure thus causing a marked increase of IOP (13,14).

The short-term fasting effect on IOP, on the other hand, is still unclear. Therefore, this study was conducted to study the relationship of IOP, between and within, short term fasting and non-fasting periods, in healthy eyes. In addition, potential association between IOP and dietary intakes of fluid and fat, as well as TBW and TBF, was also investigated.

MATERIALS AND METHODS

Study population

This cross-sectional study was conducted on healthy Malay participants aged 20 to 25 years, and had less than ±2.00DS spherical equivalent of refractive error (RE). Individuals with any chronic systemic diseases such as diabetes mellitus, hypertension and cardiovascular disease, active ocular pathologies such as glaucoma, diabetic retinopathy and hypertensive retinopathy and previous refractive and ocular surgery were excluded.
The sample size for this study was calculated based on the difference in the mean value of the outcome variable between the study groups, aided by the standardized effect size table (15). Critical level, α, of 0.05 at 95% confidence interval and the power, β, of 0.20 were chosen to determine the sample size. Using data from Baser et al., (2015), the mean differences of IOP between fasting and non-fasting periods were ~1.61±0.95 and ~0.93±0.65, respectively. Using a two-tailed $\alpha = 0.05$ and $\beta = 0.20$, the minimal required sample size was 21. However, the sample size was increased to 30 participants to include 20% attrition rate.

This study was ethically approved by the International Islamic University Malaysia Research Ethics Committee (IREC; ID No: IIUM/ 310/ G/ 13/ 4/ 4-199). Written consent was obtained from all participants which followed the tenets of the Declaration of Helsinki.

Measurement of IOP

A tonopen (AccuPen® Handheld Tonometer, Accutome Inc, The Hague, Netherlands) was used to measure the IOP. Tonopen was chosen to be used in this study due to its portability. Prior to IOP measurement, one drop of proparacaine hydrochloride 0.5% (AlcaineTM, Alcon Inc, Fort Texas, USA) was instilled in one eye which was randomly chosen using random number generator in Microsoft® Office Excel 2013 (Microsoft Corporation, Santa Rosa, California). The sensor tip of the tonopen was tapped at 90 degree on the participant's eye while fixating a target at 40cm for accurate measurement. Three readings were produced by the instrument and average value was taken for analysis. In the second visit, the IOP value was measured on the same eye as in the first visit.

Measurement of Body Composition

Body composition analyzer (SC-331S, Tanita Corporation of America, Inc., Illinois, USA) was utilized to measure the TBF, TBW and body weight, based on bioelectrical impedance analysis technique. The TBF, TBW and body weight were measured three times (morning, late-evening and night) during each fasting and non-fasting periods. Personal information such as body type, sex, age, height and standard target body fat (20% for male and 30% for female) were entered into the equipment. The participants' height was measured using a stadiometer height-rod (Seca 213, Seca gmbh & co. kg, Hamburg, Germany). The body mass index (BMI) was calculated by dividing total body weight in kilogram with height in meter squared (kg/m2).

Study Protocol

The IOP values were measured for four times on each fasting and non-fasting periods: in the morning (between 7.00 am to 9.00 am), afternoon (between 12.00 pm to 1.00 pm), evening/before fast breaking (*iftar*) (between 6.00 pm to 7.00 pm), and night/after *iftar* (between 9.00 pm to 10.00 pm). Similarly, other measurements including TBF, TBW and dietary intakes of fat and fluid, were recorded during fasting and non-fasting periods. Blood glucose levels were measured using glucometer (Accu-Chek® Active, Accu-Chek, Mannheim, Germany) to affirm fasting.

Assessment of Dietary Intake

The dietary intakes of total fluid and total fat during fasting and non-fasting periods were also assessed for comparison purposes. By using 24-hour diet recall, study participants were asked to specify all the foods and drinks that they had eaten throughout the day in detail. This is based on the regular mealtimes (breakfast, morning tea, lunch, afternoon tea and dinner) during non-fasting period. During fasting period, the participants were asked to report the food and drinks taken at pre-dawn meal (*suhur*) and during *iftar*. Household utensils (cups, bowls, glasses, and spoons) were utilized to assist respondents in estimating the amounts of foods and drinks consumed. These data were analyzed using a computerized diet analysis software, Nutritionist ProTM (Axxya Systems, Washington, USA) to obtain intakes of total fluid (ml/day) and total fat (g/day).

Statistical Analyses

Statistical procedures were performed using the Statistical Package for the Social Sciences (SPSS) for Windows Version 12.0 (IBM Corporation, New York, USA). All data were presented as mean ± standard deviation.

Normality of data was tested using the Shapiro-Wilk test. The significance level was set at p-value less than 0.05. The comparison of IOP values at different time points between fasting and non-fasting periods were conducted by using paired sample t-test. The IOP values at different time points within each fasting or non-fasting periods were compared using repeated measures (RM) ANOVA. Correlations between IOP and TBF and TBW were assessed by using Pearson correlation. Comparison of the total fluid and total fat intakes between periods were conducted using paired sample t-test.

RESULTS

A total of 30 Malay participants (15 of which were males) aged 21.8 ± 1.1 years with mean refractive error of -0.66 ± 0.78 DS were enrolled in this study. The mean BMI value was 22.3 ± 3.8 kg/m2. The mean fasting blood glucose level of the participants during fasting (4.1 ± 0.3 mmol/l) was significantly lower (p<0.001) compared to during non-fasting (4.9 ± 0.8 mmol/l). Lower blood glucose during fasting showed that all the participants performed fasting.

Comparison of IOP between fasting and non-fasting periods

The IOP during fasting period were significantly different (RM ANOVA p<0.001; Table I). The Bonferroni post-hoc test (Fig. 1) indicated that the IOP value in the afternoon was significantly higher by 2.10 mmHg (p=0.009) and 1.93 mmHg (p=0.003) than the IOP values before *iftar* and after *iftar* respectively. On the other hand, the IOP does not significantly change throughout different time point of measurements during the non-fasting period (Table I).

Comparing IOP between fasting and non-fasting periods, it was found that the IOP was significantly lower during fasting (12.43±2.73 mmHg) compared to during non-fasting period (13.75±2.53 mmHg; p=0.044) only in the evening, as shown in Table II. The IOP showed no differences at other time points between fasting and non-fasting periods.

Association between IOP and fat & fluid status

No significant linear correlation was found between the mean IOP and TBF values during both periods. However, there was a trend for a weak positive relationship between IOP and TBF values during fasting (r=0.204, p=0.054). There was no significant association between IOP and TBW during fasting period. However, there was a significant inverse relationship (r=-0.268; p=0.011) during non-fasting period (Fig. 2). Table III presented the correlation between IOP and TBF during fasting and non-fasting periods.

Table I: Comparison of IOP at different time intervals during fasting and non-fasting periods (n=30)

Periods	IOP (mmHg) Morning Mean ± SD	IOP (mmHg) Afternoon Mean ± SD	IOP (mmHg) Before *iftar* / evening Mean ± SD	IOP (mmHg) After *iftar* / late-evening Mean ± SD	p-value (RM ANOVA)
Fasting	13.62 ± 2.25	14.53 ± 2.33	12.43 ± 2.73	12.60 ± 2.44	<0.001
Non-fasting	13.97 ± 2.59	14.10 ± 3.01	13.75 ± 2.53	12.90 ± 2.95	0.101

IOP, intraocular pressure; mmHg, millimeter mercury; *iftar*, fasting break; RM, repeated measure; SD, standard deviation
Morning, 7.00 to 9.00 am
Afternoon, 12.00 to 1.00 pm
Before *iftar* / evening, 6.00 to 7.00 pm
After *iftar* / late-evening, 9.00 to 10.00 pm

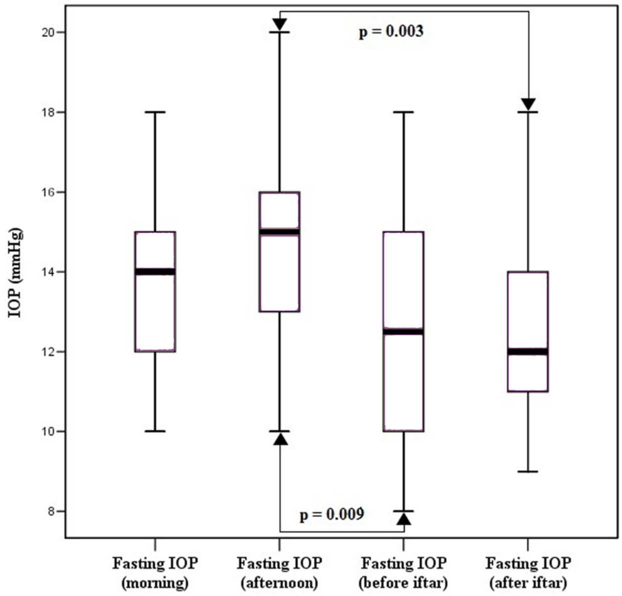

Figure 1: Boxplot of IOP at different time points during fasting period

Table II: Comparison of IOP at different time points during fasting and non-fasting periods (n=30)

Sessions	Fasting IOP (mmHg) Mean ± SD	Non-fasting IOP (mmHg) Mean ± SD	p-value (paired sample t-test)
Morning	13.62 ± 2.25	13.97 ± 2.59	0.525
Afternoon	14.53 ± 2.33	14.10 ± 3.01	0.509
Before *iftar* / evening	12.43 ± 2.73	13.75 ± 2.53	**0.044**
After *iftar* / late-evening	12.60 ± 2.44	12.90 ± 2.95	0.601

IOP, intraocular pressure; mmHg, millimeter mercury; *iftar*, fasting break; SD, standard deviation
Morning, 7.00 to 9.00 am
Afternoon, 12.00 to 1.00 pm
Before *iftar* / evening, 6.00 to 7.00 pm
After *iftar* / late-evening, 9.00 to 10.00 pm

The fluid and total fats intakes were compared between fasting and non-fasting periods (Table IV). It was demonstrated that fluid intake was significantly lower during fasting compared to during non-fasting period (789 ± 75 ml/day vs 1238 ± 627 ml/day; p<0.001). Similarly, total fats consumed during fasting (43.8 ± 29.4 g/day) was also significantly lower during fasting than during non-fasting period (65.2 ± 40.2 g/day; p=0.011).

DISCUSSION

This study was conducted to compare the IOP between fasting and non-fasting periods at four selected time points; morning, afternoon, evening/before *iftar* and late-

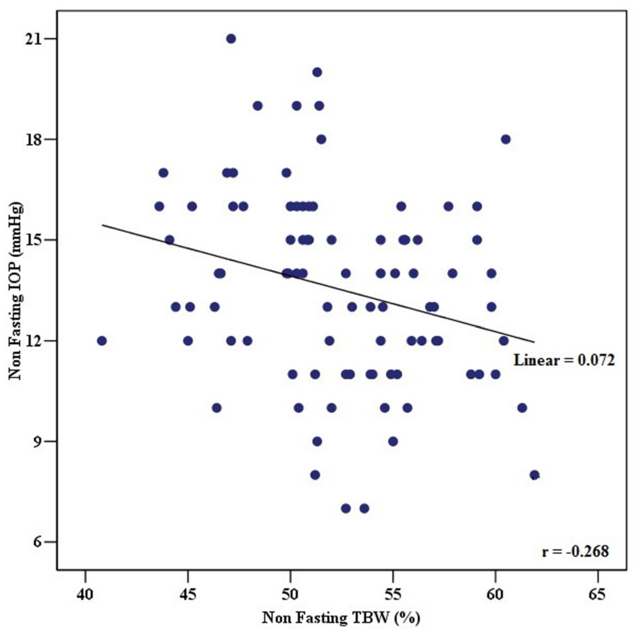

Figure 2: Inverse relationship between IOP and TBW values during non-fasting

Table III Correlation analysis between IOP and TBF values during fasting and non-fasting periods (n=30)

Period	r	p-value (Pearson)
Fasting	0.204	0.054
Non-Fasting	0.117	0.273

Table IV Comparison of dietary intakes (fluid and fat) between fasting and non-fasting periods (n=30)

Dietary Intakes	Fasting (Mean ± SD)	Non-fasting (Mean ± SD)	p (Paired sample t-test)
Total fluid intake (g/day)	789 ± 75	1238 ± 627	<0.001
Total fat intake (g/day)	43.8 ± 29.4	65.2 ± 40.2	0.011

SD, standard deviation

evening/after *iftar*. Mean IOP value in the evening was found to be significantly lower during fasting compare to during non-fasting period. This study findings in agreement with the previous study which reported there was significant reduction of IOP during fasting compared to non-fasting (17).

A study comparing IOP values during the fasting month of Muslims, Ramadan, to non-fasting periods outside of Ramadan reported that IOP values at all four different times (9.00am, 12.00pm, 3.00pm and 6.00pm) during fasting were significantly lower than the values of the paired times during non-fasting period (8). In this current study, there is no significance difference in IOP values during fasting and non-fasting, except in evening/before *iftar*. The slight difference in the result of this study may be due to the different type of fasting. Long-term fasting (as performed by the participants of Dadeya et al. study (8)) was believed to have induced more dehydration compared to short-term fasting, as performed in the current study. The changes of eating pattern in the long term fasting may have led to overall reduction in fluid and other nutrients intake which may render IOP reduction in a whole day relative to period of non-fasting (17). Another possible explanation, the IOP values in Dadeya et al. were compared between values at the end of the month of long term fasting, to values 45 days after the long term fasting (8). This is in contrast with the current study where IOP values were compared between values during a short term fasting to a random non-fasting day. Nevertheless, another study comparing IOP during a long-term fasting and non-fasting demonstrated significant reduction in IOP during fasting at the time point measured towards the end of the day (evening) (17). The findings yielded similar results with the current study. This may be due to the fact that both studies were conducted in a same climate (hot and humid). A study stated fasting during hot and humid climate induced more dehydration due to increment of some renal function markers and serum electrolytes (18). In the current study, significant reduction of IOP values between fasting and non-fasting may be influenced by changes in dietary intake. It was recorded that total fluid intake showed significant reduction during short-term fasting as compared to non-fasting. Fluid intake during fasting was found to be significantly lower at 789 ± 75 ml/day than during non-fasting period at 1,238 ± 627 ml/day ($p<0.001$). Loss of water during fasting stimulates excessive secretion of antidiuretic hormone (ADH), which simultaneously causes an increase in plasma osmolality (19). This results in ocular dehydration as water is prone to be absorbed from aqueous humor into plasma and this eventually reduces IOP. Other than that, a study suggested that reduction of IOP because of dehydration is due to depletion of aqueous humor secretion by non-pigmented ciliary epithelium (20). Using a color-Doppler ultrasound, the authors found that dehydration caused the ocular blood flow in the ophthalmic artery, central retinal artery and temporal short ciliary artery, to be decreased. This indirectly lead to a reduction in IOP (20). In the current study, a reduction in IOP value was seen predominantly at the end of the 14 hours of fasting. Our finding is similar to another study's which had also found a significant reduction in IOP after 14 hours of fasting due to dehydration (21). The fasting duration which affected IOP values in other studies however, was more varied. A case-control study on healthy adults demonstrated that IOP was significantly decreased after only ten hours of dehydration (22). On the other hand, another study found that IOP value was significantly reduced after 18 hours of dehydration (23). More research is needed to determine the duration of fasting and its effect on IOP values.

Another possible factor which leads to decrement in

IOP is dietary fat intake. In the current study, the result of fat intake showed significant reduction during fasting (43.8 ± 29.4 g/day) compared to non-fasting (65.2 ± 40.2 g/day; p=0.001) as demonstrated in Table III. It was recorded in the current study that dietary fat intake showed significant reduction during short-term fasting as compared to non-fasting period. A study investigated the association between dietary fat intake and primary open angle glaucoma (POAG) revealed that a decrease in fat intake would reduce the IOP and thus lowering the risk of POAG (12). Low fat intake during fasting caused reduction of ocular hypotensive agent, prostaglandin to be secreted which consequently resulted in the reduction of IOP (24). Nevertheless, more investigation needs to be conducted to further understand the association between IOP and dietary intakes.

Conversely, there have been previous studies which reported no significant differences of IOP between fasting and non-fasting measured in the evening (20,25,26). These studies concluded that this might be due to none occurrence of significant body weight loss thus minimizing dehydration. The other reason for the disparity of their findings with the current study's may be due to the fact that their studies were conducted during winter season (26). This current study was conducted in a tropical location where dehydration may play a factor in IOP values. In addition, different distribution of age group enrolled between previous studies and the current study may also give influence to the parameters (20).
In addition, current study showed the highest IOP during fasting and non-fasting were recorded in the afternoon. This may be related to prolonged binocular convergence and accommodation usage during office hours which influences the IOP value in the afternoon (14). It was found that increment in accommodation creates a deformation of the globe hence narrowing the anterior chamber and thickening of crystalline lens (27). Accommodation elicitation results in transient elongation of axial length which is stimulated by scleral tension changes (28,29). These factors give rise to the IOP elevation (27).

In the current study, no significant correlation was recorded between IOP and TBF during fasting and non-fasting periods. Based on the literature search, association between IOP and TBF is scarcely available. However, IOP and TBF relationship was indirectly assessed in the earlier studies among normal weight and obese individuals (classified based on BMI status) and demonstrated variable results (14,30–32). A study reported that increased BMI was associated with increment of obesity parameters which included waist circumference, TBF mass, as well as, total and regional body fat percentage that lead to mark increment of IOP (30). However, no correlation was found between IOP and TBF values of underweight and normal BMI participants which represent similar findings to the current study (14,32). In contrast, BMI and TBF were found to be positively correlated with IOP in which higher BMI and TBF leads to higher IOP (30,31). The plausible hypotheses on this relationship were increment of episcleral venous pressure as well as blood viscosity, which may cause reduction of aqueous outflow facility, leading to an increase in IOP (14).

In terms of TBW, a previous work reported no significant association between TBW and IOP (33). This is similar to the finding of the current study during fasting period where no significant relationship between IOP and TBW was found. On the other hand, the current study found a significant inversed relationship between IOP and TBW during non-fasting, which indicated that a reduction of TBW causes increased IOP. This finding could be influenced by caffeine intake. It was recorded that 57% of the participants in this study drank caffeinated beverages with their meals during non-fasting period. Previous study has shown that each 180 mg of caffeine in 200ml of beverage may increase 1 to 4 mmHg of IOP in healthy individuals. This finding could be influenced by hydration status (34). Fluid intake is expectedly higher during non-fasting hence better hydration status compared to fasting period. A study have shown that water-loading (rehydration) process significantly increased IOP value in healthy eyes due to elevation of episcleral venous pressure (35).

The current study investigated the effect of short-term fasting and its association with fat and fluid status. Existing research so far has only looked at the influence of long-term fasting period such a in the month of Ramadan, on IOP, and relationship with weight and waist circumference. This study, however, was conducted on young and healthy individuals, and thus may not be generalizable to other populations. A similar study conducted on elderly or those with ocular hypertensive and glaucoma may yield different outcomes. In terms of dietary intake, the current study takes consideration of the total fat and fluid intakes from data of a whole day, instead of by meal times. Due to limitation, the relationship between IOP to both fat and fluid intakes, are not available by specific time points or according to meal times. A detailed analysis by time point may be beneficial for future studies.

CONCLUSION

Short-term fasting caused significant reduction in IOP only in evening, and not associated with TBF and TBW. The probability of dietary intake of fluid and fat influencing the significantly lower IOP values during short-term fasting compared to non-fasting period is promising and warrants thorough investigation.

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