Low Ocular Perfusion Pressure Values at Rest and during Resistance Exercise in Offspring of Glaucoma Patients

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Abstract

Purpose: To compare the ocular perfusion pressure (OPP) response during physical exercise in individuals with and without a family history (FH+, FH−) of glaucoma.

Methods: Thirty-four subjects, divided into FH+ and FH− groups, realized 3 min at rest, 3 min of isometric handgrip exercise at 30% of maximal voluntary contraction, followed by 3 min of recovery. Blood pressure (Dixtal® automatic device) and intraocular pressure (Goldmann applanation tonometer) were measured during rest, exercise, and recovery. The mean OPP (mOPP) was calculated.

Results: In the FH+ group (17 subjects), baseline mOPP values were significantly lower than in the FH− group (17 subjects) (right eye: $P < 0.001$, left eye: $P < 0.001$, respectively). During exercise, both the FH+ and FH− groups showed a similar increase in mOPP in both eyes (right eye: FH+: 38 ± 4 mmHg vs. 51 ± 7 mmHg, FH−: 48 ± 5 mmHg vs. 57 ± 9 mmHg, $P < 0.001$; left eye: FH+: 39 ± 3 mmHg vs. 51 ± 7 mmHg; FH−: 46 ± 5 mmHg vs. 58 ± 8 mmHg, $P < 0.001$, respectively). However, the FH+ group maintained significantly lower mOPP values compared to the FH− group in the right and left eyes (group effect: $P = 0.002$, $P = 0.002$, respectively). The percentage of increase in mOPP in the FH+ group was greater compared to the FH− group during exercise (right eye: 34.1% ± 15.9% vs. 22.1% ± 13.2%, respectively; $P = 0.025$; left eye: 33.2% ± 17.7% vs. 22.4% ± 13.7%, respectively, $P = 0.056$).

Conclusions: mOPP increased during physical exercise in both groups, but the FH+ group had lower absolute values. In addition, the FH+ group appears to demonstrate a higher percentage increase in mOPP compared to the FH− group.

Keywords: Exercise, Glaucoma, Heredity, Ocular physiological phenomena

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Introduction

The main risk factor for primary open-angle glaucoma (POAG) is increased intraocular pressure (IOP).[1] Age, race, atherosclerosis, corneal thickness, and positive family history (FH+) of POAG also contribute.[1] First-degree relatives have a 9-fold higher risk of developing POAG.[2,3] Epidemiological studies have correlated low mean ocular perfusion pressure (mOPP) values with the incidence of POAG.[4-9]

It is unknown how exercise affects OPP in individuals with FH+. Thus, we aimed to compare the mOPP at baseline and during physical exercise in individuals with FH+ and without a family history (FH-) of glaucoma.

Methods

As criteria for sample inclusion, volunteers should be between 18 and 55 years old. A total of 34 volunteers of both genders

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were included, divided into two groups: FH+ for POAG (17 subjects) and FH− for POAG (17 subjects). The groups were age-matched.

Exclusion criteria included the presence of cardiovascular and ocular diseases, prior ocular surgeries, the use of antihypertensive and antidiabetic medications, IOP ≥21 mmHg, and musculoskeletal abnormalities that would prevent the execution of the handgrip exercise.

The present study protocol was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee under approval number 3.177.330. All individuals included in the study participated voluntarily and signed the informed consent form.

The experimental protocol consisted of anamnesis, which included information on the volunteer's clinical data and the presence or absence of glaucoma in their parents, as well as anthropometry for measuring body weight and height. For this purpose, a *Filizola* scale with an accuracy of 0.1 kg and a stepped stadiometer with an accuracy of 0.5 cm attached to it were used, respectively. Body mass index (BMI) was calculated by dividing body weight by height squared (kg/m^2). All these variables were measured according to the criteria described by the American College of Sports Medicine.[10]

Systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were measured in the seated position using an automatic oscillometric method, with the DIXTAL 2023® automatic device (Biomédica Indústria e Comércio Ltda), with the cuff placed on the nondominant upper limb of the volunteer.

Both eyes had their IOP measured using the Goldmann applanation tonometer performed by the ophthalmologist. For this purpose, anesthetic eye drops containing 4 mg/mL of oxybuprocaine hydrochloride and dye eye drops containing 1% sodium fluorescein were used. Subsequently, the mOPP was calculated as follows: ⅔MAP – IOP.[11]

The physical exercise protocol consisted of three stages: 3 min of rest, 3 min of isometric exercise at 30% of maximum voluntary contraction (MVC), and 3 min of recovery. For the exercise stage, a Jamar® Hand Dynamometer (Jamar Hand Dynamometer – Hydraulic - 200 lb Capacity/Fabrication) was used. Initially, the maximum isometric handgrip strength was calculated by taking the arithmetic mean of three MVC attempts on the dominant limb. At the end of the 3rd min of each stage, SBP, DBP, MAP, heart rate (HR), and IOP of both eyes were measured, and subsequently, the mOPP of both eyes was calculated.

After the protocol, the volunteers were instructed to rate their level of physical exertion during the handgrip maneuver using the Borg Scale for ratings of perceived exertion.[12]

The statistical analysis of the data was performed using SPSS® (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Data were presented as mean ± standard deviation and absolute values. The assumption of sphericity was assessed using Mauchly's test, and when violated, Greenhouse–Geisser correction was applied. A comparison between groups regarding demographic and baseline characteristics as well as the percentage change of mOPP during exercise was conducted using the independent samples *t*-tests, after testing for equality of variances (Levene's test). Cohen's D was used for effect size, considering reference values (small: 0.2–0.5/medium: 0.5–0.8/large: Above 0.8). To investigate potential differences in BP, HR, IOP, and mOPP during the entire experimental protocol, a two-way repeated measures analysis of variance was used, followed by the Bonferroni *post hoc* tests. The Fisher exact test or Chi-square test, when appropriate, was used to compare categorical variables. A significance level of $P \leq 0.05$ was adopted.

Results

The demographic, baseline hemodynamic, and ocular pressure characteristics of both the FH+ group (17 subjects) and the FH− group (17 subjects) are shown in Table 1. Age, height, body weight, HR, and BMI were similar between the FH+ and FH− groups. However, the baseline variables SBP, DBP, MAP, and mOPP in the right eye and mOPP in the left eye were significantly lower in the FH+ group when compared to the FH− group. There was no significant difference in IOP (right and left eye) between the groups.

During exercise, SBP, DBP, MAP, and HR variables increased similarly between the groups. SBP, DBP, and MAP return to baseline values during the recovery period. However, the FH+ group consistently exhibited significantly lower SBP, DBP, and MAP values throughout the entire experimental protocol (group effect: $P = 0.015$; $P = 0.001$; $P = 0.002$, respectively) [Figure 1a-c]. HR increased during exercise and decreased after the recovery period to values below baseline for both groups remaining similar between the groups [Figure 1d].

There was no increase in IOP in the right eye during exercise in both groups (time effect: $P = 0.109$). On the other hand, the IOP of the left eye increased significantly and similarly in both the FH+ and FH− groups (14 ± 3 mmHg vs. 15 ± 3 mmHg; 14± 2 mmHg vs. 15 ± 2 mmHg, time effect: $P = 0.022$, group effect = 0.967; interaction effect = 0.772, respectively). However, during the recovery period, the IOP of both eyes, in both the FH+ and FH− groups, significantly decreased compared to baseline (right eye: FH+:14 ± 4 mmHg vs. 13 ± 3 mmHg, FH−: 14 ± 2 mmHg vs. 13 ± 2 mmHg, time effect: $P = 0.028$; left eye: FH+: 14 ± 3 mmHg vs. 13 ± 3 mmHg; FH−: 14 ± 2 mmHg vs. 13 ± 2 mmHg, time effect: $P = 0.017$, respectively [Figure 2]).

During the physiological handgrip maneuver, both the FH+ and FH− groups showed a similar increase in mOPP in both eyes (right eye: FH+: 38 ± 4 mmHg vs. 51 ± 7 mmHg, FH−: 48 ± 5 mmHg vs. 57 ± 9 mmHg, $P = 0.000$; left eye: FH+: 39 ± 3 mmHg vs. 51 ± 7 mmHg; FH−: 46 ± 5 mmHg vs. 58 ± 8 mmHg, $P = 0.000$, respectively). However, throughout

Table 1: Baseline demographic, hemodynamic, and ocular pressure characteristics of the with and without a family history groups

	FH+ (17)	FH- (17)	*P*	Cohen's D
Men/women	3/14	6/11	-	-
Age (years)	32±10	29±7	0.327	0.35
Height (m)	1.67±0	1.65±0	0.606	0.02
Weight (Kg)	71±11	66±14	0.253	0.40
BMI (Kg/m²)	25±4	24±3	0.215	0.28
SBP (mmHg)	111±11	124±9	0.001	-1.29
DBP (mmHg)	64±6	74±7	0.000	-1.53
MAP (mmHg)	79±6	91±7	0.000	-1.84
HR (bpm)	79±2	75±7	0.473	0.78
IOP_R (mmHg)	14±3	14±3	0.487	0.00
IOP_L (mmHg)	14±3	14±2	0.817	0.00
mOPP_R (mmHg)	38±4	46±5	0.000	-1.77
mOPP_L (mmHg)	39±3	46±5	0.000	-1.70

FH+: With a family history, FH-: Without a family history, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, HR: Heart rate, IOP_R: Intraocular pressure-right eye, IOP_L: Intraocular pressure-left eye; mOPP_R: Mean ocular perfusion pressure-right eye, mOPP_L: Mean ocular perfusion pressure-left eye. The test used to obtain the *P* values was the unpaired *t*-tests ($P \leq 0.05$)

the entire experimental protocol, the FH+ group maintained significantly lower mOPP values compared to the FH− group in both the right and left eyes (group effect: $P = 0.002$, $P = 0.002$, respectively). During the recovery period, mOPP returned to baseline values in both the right and left eyes (right eye: FH+: 41 ± 6 mmHg vs. 38 ± 4 mmHg, FH−: 45 ± 5 mmHg vs. 48 ± 5 mmHg, $P = 1.000$; left eye: FH+: 41 ± 5 mmHg vs. 39 ± 3 mmHg; FH−: 45 ± 5 mmHg vs. 46 ± 5 mmHg, $P = 1.000$, respectively [Figure 3]).

Furthermore, the percentage of increase in mOPP in the FH+ group was greater compared to the FH− group during physical exercise (right eye: 34.1% ± 15.9% vs. 22.1% ± 13.2%, respectively; $P = 0.025$; left eye: 33.2% ± 17.7% vs. 22.4% ± 13.7%, respectively, $P = 0.056$).

Discussion

The main finding of this study was that healthy individuals with a positive FH of glaucoma exhibited a preserved response of increased mOPP during resistance exercise. However, the absolute mOPP values were significantly lower compared to the FH− group throughout the entire experimental protocol.

Several epidemiological studies have investigated the relationship between OPP and glaucoma, and they have observed that reduced OPP is a risk factor for the prevalence, incidence, and progression of the condition.[4-9,13-15]

The Barbados Eye Study[7] was a longitudinal study that assessed the incidence of glaucoma after 9 years of follow-up. The study indicated that participants with mOPP lower than 40 mmHg had a 2.6 times higher risk of developing glaucoma.[7] In the present study, the FH+ group exhibited mOPP values, in both eyes, below 40 mmHg, which increases the risk of glaucoma development for these individuals.

In addition, during physical exercise, there was a significant increase in mOPP in both groups, in line with data from various studies[16-26] that demonstrate that resistance exercise increases mOPP. Consequently, the FH+ group, during exercise, reached absolute mOPP values above those cited as a risk for glaucoma,[7] although after recovery, the values of the variables in both groups returned to baseline values.

Another relevant finding of the present study was that the FH+ group exhibited a higher percentage of increase compared to the FH− group, particularly in the right eye. An important fact is that Movaffaghy *et al*. conducted a study on healthy individuals to investigate the effect of increasing OPP on ocular blood flow through squatting exercise. The authors observed that blood flow in the optic nerve head remained unchanged until mOPP increased by approximately 34% in relation to baseline.[27] In the present study, the FH+ group demonstrated a 34% increase in the right eye and 33% in the left eye, aligning with the threshold identified by Movaffaghy *et al*. for the consistent maintenance of blood flow.

Autoregulation, defined as the vascular bed's ability to adjust its vascular resistance to changes in OPP, is crucial for maintaining relatively constant blood flow, thereby stabilizing tissue perfusion and capillary hydrostatic pressure during normal variations in BP. In a nonautoregulated vascular bed, any alteration in OPP directly affects perfusion.[24]

Although our study utilized handgrip exercise, which requires less muscle recruitment compared to squats, we observed a greater variation in the percentage of increase in the FH+ group. This suggests that there could be more significant fluctuations in blood flow within the FH+ group during routine physical activities, potentially posing risks for a population with impaired autoregulation.

Physical exercise plays an important role in the regulation of ocular BP. [28] As it is already known, acute resistance exercise can increase BP through sympathetic stimulation.[28] However, this increase in BP is directly related to the exercise intensity, the number of sets, the load mobilized, and the muscle groups involved.[29] Typically, during strength exercise, both SBP and DBP tend to rise, resulting in a significant increase in MAP, even if only for a short period.[30] Similarly, mOPP also increases during physical exercise.[16-26]

It can be inferred that low mOPP values presented by individuals with a FH of glaucoma put this population at a higher risk of developing glaucoma when compared to those without an FH.

Given the potential influence of genetic factors on glaucoma, it is important to note that the sample being discussed has a high level of admixture, likely referring to a mix of different

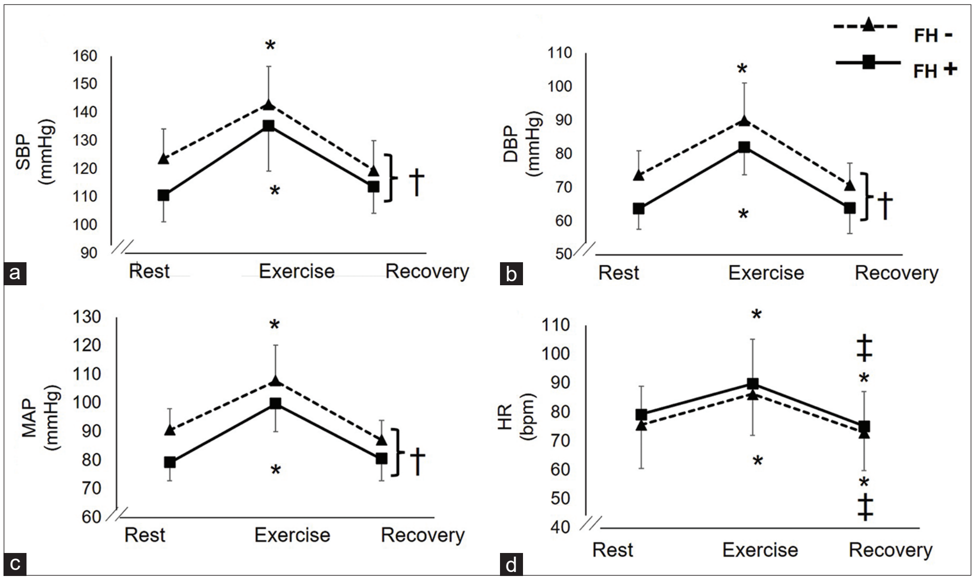

Figure 1: Response of (a) systolic blood pressure, (b) diastolic blood pressure, (c) mean arterial pressure, and (d) heart rate at rest, during handgrip exercise, and in postexercise recovery. **P* < 0.05 versus baseline, †*P* < 0.05 versus group, ‡*P* < 0.05 versus exercise. MAP: Mean arterial pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FH: Family history

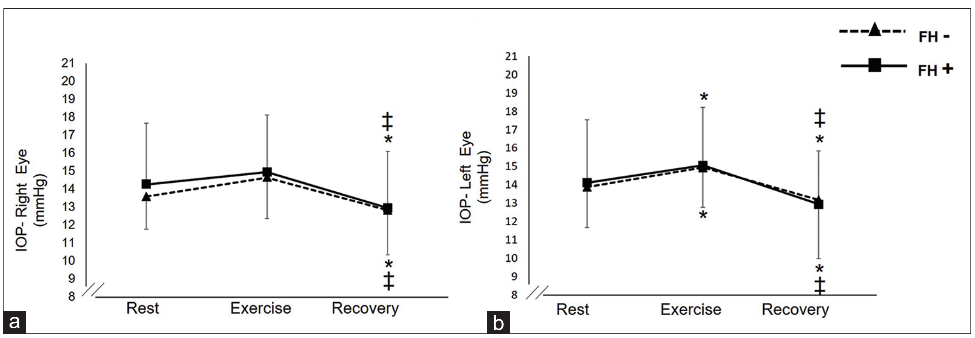

Figure 2: Response of intraocular pressure at rest, during handgrip exercise, and in postexercise recovery in the (a) right and (b) left eyes. **P* < 0.05 versus baseline, †*P* < 0.05 versus group, ‡*P* < 0.05 versus exercise. IOP: Intraocular pressure, FH: Family history

genetic backgrounds or ancestries. There is a known higher risk of POAG among individuals of African descent.[1] Siesky *et al*., examining ocular blood flow disparities between individuals of African and European descent with open-angle glaucoma, found notably lower blood flow in individuals of African descent compared to their European counterparts. These findings imply that the role of ocular blood flow in the progression of the disease may differ between these ethnic groups.[31] Consequently, it is essential to refrain from generalizing our findings to all populations.

The handgrip exercise performed by the volunteers is related to functionality since manual grip is part of daily life and is essential for maintaining daily activities. The intensity of the exercise performed by the study population can be considered "moderately strong" for the FH− group (4) and "strong" for the FH+ group (5) according to the Borg Scale for Ratings of Perceived Exertion.[12]

Our study presented some limitations. Regarding the volunteers, the age range was broad (18–55 years old), but the mean age of both the FH+ and FH− groups was similar, reflecting young adults (FH+: 32 ± 10 vs. FH−: 29 ± 7 years; *P* = 0.327). The results may not be representative of older age groups or other demographic characteristics. Generalizing the findings to a broader population may require caution. The number of participants in the study may be limited; however, the mOPP response during exercise exhibited significant statistical power for group comparison (HF+ vs. HF−) with values of 0.895 for the right eye and 0.917 for the left eye. Furthermore, we achieved a statistical power of 1.000 when comparing rest and exercise.

As an exclusion criterion, we excluded individuals with no history of cardiovascular and ocular diseases because both conditions could impact IOP and OPP values. Our aim was to evaluate healthy individuals unaffected by systemic and ocular diseases. Our sample does not fully represent the diversity of individuals with an FH of glaucoma. This could limit the external validity of the findings.

Our study calculated mOPP using a single measurement during each stage of the exercise protocol. Continuous monitoring of

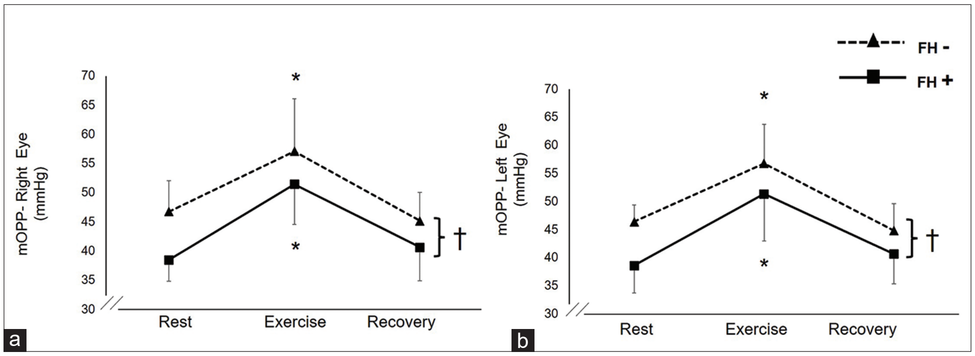

Figure 3: Response of mean ocular perfusion pressure at rest, during handgrip exercise, and in postexercise recovery in the (a) right and (b) left eyes. *$P < 0.05$ versus baseline; †$P < 0.05$ versus group; ‡$P < 0.05$ versus exercise. mOPP: Mean ocular perfusion pressure, FH: Family history

mOPP could provide a more comprehensive understanding of its dynamic changes during exercise. Furthermore, the subjective nature of self-reported physical exertion using the Borg Scale introduces an element of subjectivity. However, the protocol used was 30% of the MVC in both groups. Even so, objective measures of exercise intensity could contribute to understanding the results. The study primarily focuses on acute responses to resistance exercise. A longer-term follow-up could provide insights into the chronic effects of exercise on mOPP and the potential impact on the development or progression of glaucoma.

In our study, we did not evaluate peak oxygen consumption. However, in the anamnesis, we observed that 11 volunteers in the HF+ group and 6 volunteers in the HF− group reported practicing physical activity, with no difference in the proportion distribution between groups (Chi-square, $P = 0.17$). Only two volunteers in the HF− group were using medication for anxiety. Six women in the HF+ group and four women in the HF− group were using oral contraceptives with no difference in the proportion distribution between groups (Fisher's exact test, $P = 1.00$).

Thus, we conclude that mOPP increased acutely during physical exercise in both groups, but the FH+ group exhibited lower absolute values throughout the entire experimental protocol. In addition, the FH+ group appears to demonstrate a higher percentage increase in mOPP compared to the FH− group. However, more controlled and randomized clinical trials are needed to observe the acute and chronic effects of resistance exercise on mOPP, as well as clinical pharmacological and nonpharmacological strategies for increasing mOPP in individuals with a positive FH of POAG.

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Conflicts of interest

There are no conflicts of interest.

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