ASSESSING THE INFLUENCE OF AEROBIC EXERCISE ON THE OCULAR PERFUSION PRESSURE AND INTRAOCULAR PRESSURE IN SUBJECTS HAVING PRIMARY OPEN ANGLE GLAUCOMA: A CLINICAL STUDY

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Abstract

Background: Glaucoma is the irreversible and most common cause of the blindness globally. POAG (primary open angle glaucoma) is the most common subtype of glaucoma constituting to majority of glaucoma cases. The literature data is scarce on assessing effect of aerobic exercise in POAG subjects.

Aim: The present study was aimed to assess the influence of short and long-term aerobic exercises on the ocular perfusion pressure and intraocular pressure in subjects having primary open angle glaucoma.

Methods: The present study assessed 62 subjects having primary open angle glaucoma and using prostaglandin analog. 62 subjects were randomly divided into 2 groups of control and exercise. For short-term effects, all subjects did cycle exercise at moderate and high intensity of 20% and 60% Wmax for 10 and 5 minutes respectively. For long-term effects, control group comprised of subjects doing irregular exercise and exercise group subjects did jogging for 30 minutes at 6:00-10:00 am for 3 months and minimum 20 days a month with intensity reflected by target heart rate.

Results: Following short-term aerobic exercise, a significant increase in ocular perfusion pressure and a significant decrease in intraocular pressure was seen. Reduced intraocular pressure was related to gender, intensity of exercise, and baseline intraocular pressure. After long-term exercise of 3 months, alterations in intraocular pressure in exercise group showed a reduction.

Conclusion: The present study concludes that a significant increase of ocular perfusion pressure and decrease of intraocular pressure depicts that aerobic exercise is advantageous for subjects having primary open-angle glaucoma and adequate aerobic exercises are appropriate in managing glaucoma subjects.

Keywords: Aerobic exercise, ocular perfusion, intra-ocular pressure, primary open angle glaucoma

Introduction

Presently, glaucoma is the irreversible and most common cause of the blindness. PAOG/primary open angle glaucoma is the most prevalent subtype of glaucoma accounting for nearly 75% of all the cases of glaucoma. Primary open angle glaucoma is a chronic, irreversible, potentially blinding, and progressive eye disease that leads to the loss of retinal nerve fiber layer and optic nerve rim with associated defects in the VF (visual field). The appearance of angle in PAOG is normal.[1] The major risk factors for PAOG being old age and level of IOP (intraocular pressure). It has been estimated that by 2040, nearly 79.76 cases of adults of age 40-80 years will have PAOG. Glaucoma progression is been linked to level of IOP making it prominent risk factor. With every 1mm Hg decrease of IOP, glaucomatous progression reduces by 10% as suggested by results of EMGT (Early Manifest Glaucoma Trial).[2]

The treatment of PAOG mainly focus on decreasing the intraocular pressure. The present management strategies for all PAOG includes medicine, laser surgery, and incisional surgery. However, surgical management have clinical side effects and high cost, monotherapy might not be able to achieve the desired reduction in the intraocular pressure. In some subjects, monotherapy can have only partial efficacy. Other treatment and adjuvant therapy with various different mechanism can be fused to make combination therapy. Reduction in intraocular pressure with exercise as an adjuvant to other therapies is prevalent in glaucoma subjects owing to convenience and low cost and is easy for the self-management of the subjects.[3]

Janiszewska-Zygier in 1963 was first to establish the role of dynamic exercises in reducing the intraocular pressure. He reported a significant decrease in IOP following dynamic exercise.[4] Cycling, jogging, and walking are joint aerobic exercises that leads to slight and significant reduction in the intraocular pressure with the increase in the heart rate with 15 to 20 minutes of endurance. Previous literature data showed that following exercise, in ordinary subjects, a 1 to 8mm decrease in the intraocular pressure is seen.[5]

A significant decrease in intraocular pressure has been extensively assessed in the previous literature data. However, increase or decrease in the ocular perfusion pressure is still a controversial topic in the literature. The ocular blood flow highly correlates to the level of intraocular pressure comprise of the choroidal and retinal circulation. The ocular perfusion pressure is the net pressure gradient that represents the eye blood flow, and is referred to relation between intraocular pressure and systemic blood pressure. Ocular perfusion pressure is calculated as $2/3^{rd}$ of MAP (mean arterial pressure)-IOP where mean arterial pressure is 1/3 (systemic blood pressure-diastolic blood pressure) +diastolic blood pressure.[6] Both isometric and dynamic exercises can increase the ocular perfusion pressure suggesting its beneficial effect on glaucoma subjects as subjects having low ocular perfusion pressure have high chances of developing glaucoma.

The present study assessed if subjects with primary open angle glaucoma showed an increase in ocular perfusion pressure or decrease in intraocular pressure after 3 months of aerobic exercise that can help guiding the clinical management of subjects having primary open angle glaucoma.

MATERIALS AND METHODS

The present prospective clinical study was aimed to assess the influence of short and long-term aerobic exercises on the ocular perfusion pressure and intraocular pressure in subjects having primary open angle glaucoma. The study was done at Department of Ophthalmology, SMBT Institute of Medical Science and Research Center, Dhamangaon-Ghoti, Nashik, Maharashtra. The study was done at Department of Ophthalmology of the Institute. A written and verbal informed consent was taken from all the subjects before study participation.

The study included subjects from both the genders and in the age range of 20-70 years with primary open angle glaucoma. The inclusion criteria for the study were subjects with an open-normal appearing anterior chamber angle, characteristic glaucomatous visual field defect (glaucoma hemifield test results outside normal limits and the presence of at least three contiguous test points within the same hemifield on the pattern deviation plot at $P < 1\%$, with at least one at $P < 0.5\%$, excluding points on the edge of the field or those directly above and below the blind spot),[7,8] localized defects of the neuro-retinal rim or retinal nerve fiber layer with no other anomalies that could lead to these defects, asymmetry between eyes ≥0.2, or cup-to-disc ratio > 0.6 depicting glaucomatous optic neuropathy, subjects using prostaglandin analog locally, good compliance, morning jog habits, and subjects willing to participate. Exclusion criteria for the study were subjects with previous intra-ocular surgery, one-eyed subjects, primary angle-closure glaucoma subjects, and subjects with secondary glaucoma including trauma, uveitis, pigment dispersion, and pseudo-exfoliation. The study also excluded subjects on systemic medications, any systemic disease not allowing mild to moderate physical activity, osteoarthritis, and coronary heart disease subjects.

After inclusion criteria, 62 subjects were eligible to participate in the study and were randomly divided into two groups namely control and exercise groups. The final sample size comprised of 124 eyes. Before inclusion in the study, all subjects were subjected to clinical assessment for maximum exercise power at baseline with the cycle ergometer. This was done to evaluate the exercise capacity of all the subjects. This assessed the short-term and long-term aerobic exercise.

Concerning short-term exercise, the change in ocular perfusion pressure and IOP was assessed in two groups after short-term exercise at different levels. Also, correlation between exercise intensity and variation in intraocular pressure was assessed. The IOP was assessed in sitting position with tonometry attached with slit lamp. At both stages, IOP was assessed by a single technician expert in his work. Each measurement was taken for three times.

Short-term exercise measurement was done using a cycle ergometer as a tool. After the cycling of subjects as fast as possible for 30 seconds, the reading of the cycle ergometer was taken as maximum watt (%Wmax) that assessed the exercise difficulty level. To evaluate the effect of aerobic exercise on blood circulation, diastolic blood pressure, systolic blood pressure, and ocular perfusion pressure was assessed.

For the clinical assessment and prior to all experiments, the subjects were asked to cycle for 30 seconds as fast as possible to attain individual maximum exercise power known as Wmax. 62 study subjects were included in the study. One subject did not turn for follow-up and was excluded making a sample size of 61 subjects where 31 subjects were allotted to control group and 30 subjects were allotted to exercise group.

The effect of short-term exercise on intraocular pressure was assessed in two stages after 10 minutes of cycling at 20% Wmax and after 2 minutes to assess IOP and after 5 minutes of exercise at 60% Wmax where IOP was again assessed. The IOP was assessed before the initiation of exercise, stage 1, and after stage 2.

In long-term aerobic exercise stage, the jogging was done daily by the subjects from the exercise group during 6:00 to 10:00 am daily. The intensity was assessed with sports watch to attain and maintain the targeted heart rate assessed as 220-age of the subjects * (0.5-0.7) for 30 minutes and performed jogging for minimum 20 times a month. The intervention was continued for 3 months. The subjects doing irregular exercise comprised the control group. 24-hour intraocular pressure was assessed at initiation and end of the long-term exercise.

All subjects were kept under observation and were instructed to not do any physical activity on waking up and were asked to be in supine position 15 minutes prior to commencing the test. All measurements of IOP were taken at 6:00 am, 8:00 am, 10:00 am, 2:00 pm, 6:00 pm, 10:00 pm, and 2:00 am to minimize diurnal variation effects and were IOP assessment under rest for 24 hours. Before every measurement, one drop comprising of combined 0.25% fluorescein sodium and 0.4% benoxinate hydrochloride was dropped in eye. Every IOP assessment was done twice, and if difference of >2mm was seen in two readings, a third reading was taken and mean of two high values was taken.

The data gathered were age, gender, heart rate, exercise watt, diastolic blood pressure, systolic blood pressure, treatment, IOP, and adverse outcomes. IOP and ocular perfusion pressure was assessed along with success of short-term and long-term exercise where short-term success was reaching the 20% Wmax and 60% Wmax. For long-term study, success was reaching and maintaining target heart rate for 30 minutes.

The data gathered were analyzed statistically using SPSS software version 25.0 (IBM Corp., Armonk, NY, USA) with t-test and Mann-Whitney U test. Intragroup and intergroup comparison was done using t-test. The significance level was kept at $p<0.05$.

RESULTS

The present prospective clinical study was aimed to assess the influence of short and long-term aerobic exercises on the ocular perfusion pressure and intraocular pressure in subjects having primary open angle glaucoma. On initial screening, the study had 32 males and 30 female subjects. The study subjects were in the age range of 20-70 years and the mean age of 49.2±1.3 years. These subjects were randomly allocated to regular aerobic exercise or optional exercise group. The target heart rate was assessed by the expert examiner unaware of the study protocol and groups. In short-term analysis, 32 subjects each were allocated to control group and exercise group and in long-term analysis25 subjects each were divided to study and control group. Concerning the family history of glaucoma and gender of the study subjects, no statistical difference was seen in two groups with $p=0.34$ and 0.07 respectively. All the study subjects were Indians.

The baseline demographic and treatment characteristics of the study subjects are listed in Table 1. It was seen that the mean age, heart rate, intraocular pressure, diastolic blood pressure and systolic blood pressure had non-significant difference in exercise and control group and were comparable with $p=0.35$, 0.08, 0.97, 0.12, and 0.15 respectively. Wmax in control and exercise group was 204.7±7.36 and 219.8±8.63 respectively which was statistically comparable with p=0.15. Also, ocular perfusion pressure was 43.06±1.23 and 45.8±0.95 respectively for control and exercise group with p=0.13 as shown in Table 1.

For the ocular perfusion pressure and intraocular pressure following aerobic exercise for short-term at various intensities, it was seen that a baseline ocular perfusion pressure was 44.38±8.24 mmHg which increased to 46.76±7.47 at 20% Wmax for 10 minutes and to 49.69±5.56 at 60% Wmax for 5 minutes. The difference was statistically significant with p=0.00. Concerning intraocular pressure, it was 19.02±4.79 at baseline and decreased significantly to 16.42±4.68 at 20% Wmax (10 minutes) and further to 13.05±4.26 at 60% Wmax (5 mins) with p=0.00 as depicted in Table 2.

On assessing the average intraocular pressure and 24 hours variations in the intraocular pressure before and after 3 months of the study, in control group, a reduction was seen in IOP from baseline to 3 months during 24-hour assessment at all the times. However, the reduction was statistically non-significant with p=0.54. In exercise group, a positive effect was seen in decreasing the intraocular pressure at all the time intervals during 24 hours assessment. The decrease was statistically significant with p=0.002. For the change of intraocular pressure in the control and exercise group, a decrease in intraocular pressure was seen at all the time during 24 hours assessment with a statistically significant difference in variation of intraocular pressure of the control group with p=0.001 (Table 3).

The success rate of short-term aerobic exercise at intensity of 20% Wmax and 60% Wmax was 100%. In attaining the heart rate, long-term aerobic exercise showed success in 82% and 81% subjects respectively from exercise and control group respectively with p=0.83. However, no difference was seen in baseline heart rate and Wmaxin the non-responders and responders of two groups with p=0.24 and 0.35 for heart rate in control and exercise group respectively and 0.53 and 0.63 for Wmax in control and exercise groups respectively.

Table 1: Baseline and treatment parameters in the study subjects

Parameter	Control group (Mean ± S.D)	Exercise group (Mean ± S.D)	p-value
Age	47.46±1.8	49.81±1.7	0.35
Heart rate	76.17±1.46	73.86±1.26	0.08
IOP	19.3±0.46	18.96±0.36	0.97
Diastolic BP	77.39±1.27	80.37±1.28	0.12
Systolic BP	125.09±2.01	129.06±1.87	0.15
Wmax	204.7±7.36	219.8±8.63	0.15
Ocular perfusion pressure	43.06±1.23	45.8±0.95	0.13

Table 2: IOP and OPP after 5 mins of exercise at 20% Wmax and 10 minutes of exercise at 60% Wmax in study subjects

Intensity of exercise	Ocular perfusion pressure (Mean ± S.D)	p-value	Intraocular pressure (Mean ± S.D)	p-value
Baseline	44.38±8.24	**0.00**	19.02±4.79	**0.00**
20% Wmax (10 mins)	46.76±7.47		16.42±4.68	
60% Wmax (5 mins)	49.69±5.56		13.05±4.26	

Table 3: Changes in IOP/IOP of 24-hour levels at prior to study and 3 months after the study

Parameters	6:00 am	8:00 am	10:00 am	14:00 pm	18:00 pm	22:00 pm	2:00 am	p-value
Control Group								
Baseline IOP	21.05	19.23	19.63	18.07	18.18	17.89	21.18	0.54
IOP after 3 months	20.57	19.66	19.48	18.56	17.53	17.75	20.75	
Exercise group								
Baseline IOP	18.23	18.43	17.97	17.24	18.07	18.33	19.34	**0.002**
IOP after 3 months	19.63	18.63	19.26	18.14	18.77	18.66	20.16	
Variation in IOP								
Control group	-0.46	0.49	-0.17	0.55	-0.67	-0.16	-0.45	**0.001**
Exercise group	1.42	0.22	-0.17	0.55	-0.67	-0.16	-0.45	

DISCUSSION

On initial screening, the study had 32 males and 30 female subjects. The study subjects were in the age range of 20-70 years and the mean age of 49.2±1.3 years. These subjects were randomly allocated to regular aerobic exercise or optional exercise group. The target heart rate was assessed by the expert examiner unaware of the study protocol and groups. In short-term analysis, 32 subjects each were allocated to control group and exercise group and in long-term analysis25 subjects each were divided to study and control group. Concerning the family history of glaucoma and gender of the study subjects, no statistical difference was seen in two groups with p=0.34 and 0.07 respectively. All the study subjects were Indians. These data were similar to the studies of Caprioli J et al[9] in 2008 and Zhang N et al[10] in 2021 where authors assessed glaucoma subjects with comparable demographics and age range.

It was seen that concerning the baseline demographic and treatment characteristics of the study subjects, the mean age, heart rate, intraocular pressure, diastolic blood pressure and systolic blood pressure had non-significant difference in exercise and control group and were comparable with p=0.35, 0.08, 0.97, 0.12, and 0.15 respectively. Wmax in control and exercise group was 204.7±7.36 and 219.8±8.63 respectively which was statistically comparable with p=0.15. Also, ocular perfusion pressure was 43.06±1.23 and 45.8±0.95 respectively for control and exercise group with p=0.13. These data were comparable to Leske MC et al[11] in 2003 and Lichetr PR et al[12] in 2001 where the treatment characteristics of the glaucoma subjects coincided with the present study.

Concerning the ocular perfusion pressure and intraocular pressure following aerobic exercise for short-term at various intensities, it was seen that a baseline ocular perfusion pressure was 44.38±8.24 mmHg which increased to 46.76±7.47 at 20% Wmax for 10 minutes and to 49.69±5.56 at 60% Wmax for 5 minutes. The difference was statistically significant with p=0.00. Concerning intraocular pressure, it was 19.02±4.79 at baseline and decreased significantly to 16.42±4.68 at 20% Wmax (10 minutes) and further to 13.05±4.26 at 60% Wmax (5 mins) with p=0.00. These results were consistent with the findings of Lawson EC et al[13] in 2014 and Wylegala A et al[14] in 2016 where results similar to the present study were reported by the authors concerning intraocular pressure and ocular perfusion pressure following aerobic exercise.

The study results showed that the average intraocular pressure and 24 hours variations in the intraocular pressure before and after 3 months of the study, in control group, a reduction was seen in IOP from baseline to 3 months during 24-hour assessment at all the times. However, the reduction was statistically non-significant with p=0.54. In exercise group, a positive effect was seen in decreasing the intraocular pressure at all the time intervals during 24 hours assessment. The decrease was statistically significant with p=0.002. For the change of intraocular pressure in the control and exercise group, a decrease in intraocular pressure was seen at all the time during 24 hours assessment with a statistically significant difference in variation of intraocular pressure of the control group with p=0.001. These findings were in agreement with the results of Conte M et al[15] in 2014 and Najmanova E et al[16] in 2016 where similar variations in intraocular pressure were seen after jogging and exercise as seen in the results of the present study.

It was also seen that the success rate of short-term aerobic exercise at intensity of 20% Wmax and 60% Wmax was 100%. In attaining the heart rate, long-term aerobic exercise showed success in 82% and 81% subjects respectively from exercise and control group respectively with p=0.83. However, no difference was seen in baseline heart rate and Wmaxin the non-responders and responders of two groups with p=0.24 and 0.35 for heart rate in control and exercise group respectively and 0.53 and 0.63 for Wmax in control and exercise groups respectively. These results were in line with the Karabatakis VE et al[17] in 2004 and Heijl A et al[18] in 2002 where success rates reported by authors for the aerobic exercise in glaucoma subjects was comparable to the results of the present study.

CONCLUSION

Considering its limitations, the present study concludes that a significant increase of ocular perfusion pressure and decrease of intraocular pressure depicts that aerobic exercise is advantageous for subjects having primary open-angle glaucoma and adequate aerobic exercises are appropriate in managing glaucoma subjects. However, further prospective studies are needed to validate the results.

REFERENCES

1. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040:A systematic review and meta-analysis. *Ophthalmology.* 2014;121:2081–90.
2. European Glaucoma Society. Terminology and Guidelines for Glaucoma. *Br J Ophthalmol.* (5th Edition) 2021;105:1–169.
3. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol.* 2006;90:262–7.
4. Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, Keltner JL, Miller JP, et al. The ocular hyper–tension treatment study:A randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol.* 2002;120:701–13.
5. Bengtsson B, Leske MC, Hyman L, Heijl A Early Manifest Glaucoma Trial Group. Fluctuation of intraocular pressure and glaucoma progression in the early manifest glaucoma trial. *Ophthalmology.* 2007;114:205–9.

6. Riva CE, Grunwald JE, Sinclair SH, Petrig BL. Blood velocity and volumetric flow rate in human retinal vessels. *Invest Ophthalmol Vis Sci.* 1985;26:1124–32.

7. Swanson MW. The 97.5th and 99.5th percentile of vertical cup disc ratio in the United States. *Optom Vis Sci.* 2011;88:86–92.

8. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. *Br J Ophthalmol.* 2002;86:238–42.

9. Caprioli J, Coleman AL. Intraocular pressure fluctuation:A risk factor for visual field progression at low intraocular pressures in the advanced glaucoma intervention study. *Ophthalmology.* 2008;115:1123–9.

10. Zhang N, Wang J, Li Y, Jiang B. Prevalence of primary open-angle glaucoma in the last 20 years:A meta-analysis and systematic review. *Sci Rep.* 2021;11:13762.

11. Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff E, et al. Factors for glaucoma progression and the effect of treatment:The early manifest glaucoma trial. *Arch Ophthalmol.* 2003;121:48–56.

12. Lichter PR, Musch DC, Gillespie BW, Guire KE, Janz NK, Wren PA, et al. Interim clinical outcomes in the collaborative initial glaucoma treatment study:Comparing initial treatment randomized to medications or surgery. *Ophthalmology.* 2001;108:1943–53.

13. Lawson EC, Han MK, Sellers JT, Chrenek MA, Hanif A, Gogniat MA, et al. Aerobic exercise protects retinal function and structure from light-induced retinal degeneration. *J Neurosci.* 2014;34:2406–12.

14. Wylegala A. The effects of physical exercises on ocular physiology:A review. *J Glaucoma.* 2016;25:e843–9.

15. Conte M, Baldin AD, Russo MR, Storti LR, Caldara AA, Cozza HF, et al. Effects of high-intensity interval vs. continuous moderate exercise on intraocular pressure. *Int J Sports Med.* 2014;35:874–8.

16. Najmanova E, Pluhacek F, Botek M. Intraocular pressure response to moderate exercise during 30-min recovery. *Optom Vis Sci.* 2016;93:281–5.

17. Karabatakis VE, Natsis KI, Chatzibalis TE, Lake SL, Bisbas IT, Kallinderis KA, et al. Correlating intraocular pressure, blood pressure, and heart rate changes after jogging. *Eur J Ophthalmol.* 2004;14:117–22.

18. Heijl A, Leske MC, Bengtsson B, Hyman L, Hussein M. Reduction of intraocular pressure and glaucoma progression:Results from the early manifest glaucoma trial. *Arch Ophthalmol.* 2002;120:1268–79.