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Resisted exercises for modulation of intraocular pressure in patients with primary open-angle glaucoma: A randomized clinical trial

Resisted exercise on intraocular pressure in patients with glaucoma

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Abstract
Aim: Primary open-angle glaucoma (POAG) is the most common type of glaucoma. Daily administration of topical medications for lowering the intraocular pressure (IOP) in POAG patients has many limitations, such as poor patient compliance and ocular allergy from repeated drug administration. Therefore, this study was conducted to investigate the therapeutic efficacy of adding resisted exercises to routine medical treatment on patients with primary open-angle glaucoma in comparison to routine medical treatment only. Material and Method: Thirty patients with primary open-angle glaucoma, aged between 40 and 50 years old, were randomly assigned into two equal groups: the study group and the control group. Both groups received their routine medical care. The study group received also resisted exercises for the upper limb 3 times a week for four weeks. Intraocular pressure (IOP) was measured using Goldmann Applanation Tonometry before (pre) and after (post) 4 weeks of application of resisted exercises treatment. Results: After training, significant improvements of IOP (decrease) were obtained in both eyes of patients in the study group whereas nonsignificant decrease was obtained in the control group. In addition, This study revealed that the reduction in IOP of both eyes (RT and LT) of patients in the study group post-exercise was significant in comparison to that of the control group after one month of treatment (p=0.001 and 0,000 respectively). The percentages of reductions of IOP in both eyes (RT and LT) of the study group were 13.5% and16.45% respectively while in the control were 0.95% and 1.7% respectively. Discussion: Adding upper limb resisted exercises to the traditional medical treatment of primary open-angle glaucoma has a clinical important in the reduction of intraocular pressure in those patients so open-angle glaucomatous patients should be encouraged to practice resisted exercises.

Keywords
Intraocular Pressure; Open Angle Glaucoma; Resisted Exercise

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Introduction

Glaucoma is the leading cause of irreversible blindness worldwide and the second most common cause of blindness after cataracts. The worldwide prevalence of glaucoma is increasing. The number of people with glaucoma worldwide will increase to 111.8 million in 2040, disproportionally affecting people residing in Asia and Africa [1]. Glaucoma is defined as a disturbance of the structural or functional integrity of the optic nerve that can usually be arrested or diminished by an adequate lowering of Intra Ocular Pressure (IOP) [2].

Primary open-angle glaucoma (POAG) is a chronic optic neuropathy with characteristic changes in the optic disc and visual field. It is the most common type of glaucoma which progresses slowly, painless, affects both eyes and often asymmetrical. As the central vision is relatively unaffected until late in the disease, visual loss generally progresses without symptoms [3-5].

Furthermore, intraocular pressure appears to be the only risk factor that can be easily modified and objectively monitored by eye care professionals thereby minimizing conversion rates of ocular hypertension (OHT), raised intraocular pressure, to glaucoma and disease progression in established glaucoma [6,7].

Recent medications which reduce IOP in patients with POAG are effective in delaying or preventing the onset of POAG. However, these medications may cause ocular irritation and other side effects in addition to the socioeconomic impact among patients with glaucoma [8-11]. Several studies demonstrated the effect of different types of exercises, including aerobic and resisted exercise for short time on IOP in normal population and patients with POAG [12,13]. Most of the studies examined the immediate effect of short time exercises on IOP as Conte et al. [14] who confirmed the immediate hypotensive effect of submaximal strength test on intraocular pressure and the significant increases of pulsatile ocular blood flow. Moreover, a study by Esfahani et al. [15] concluded that the IOP temporarily reduced after exercise test in patients who were suspected to coronary artery disease, however, it returned to baseline value shortly after the test.

To the best of our knowledge, no study has been conducted to determine the effect of upper limb resisted exercises on IOP in patient with POAG similar with our study parameters as the effect of IOP reduction varied with exercise type and intensity, as well as the duration after exercise [16].Therefore, the objective of the current study was to evaluate the therapeutic efficacy of resisted exercises on intraocular pressure in primary open angle glaucomatous patients.

Material and Method

Trial design

This study is a parallel-group, active-control, randomized clinical trial, single-blind, pre-post-test. Patients were randomly assigned into two equal groups (a study group and a control group). The study group received a routine medical care (topical ocular hypotensives) in addition to resisted exercises for the upper limb 3 times a week for four weeks, whilst the control group received the routine medical care only. Evaluative procedures were conducted before and after the treatment period by an ophthalmologist who was blind to treatment allocation.

Participants

Thirty patients, from both sexes, with primary open-angle glaucoma (60 eyes RT and LT) were recruited from the ophthalmology outpatient clinic. They were enrolled and assessed via preliminary ophthalmologic examination for their eligibility to participate in the study according to the following inclusion criteria: ages ranging from forty to fifty years old; (IOP) between 20-30 mmHg; normal open angle of anterior chamber; normal blood pressure and received at least 3 months of standard medical treatment. The exclusion criteria were closed angle of anterior chamber; diabetes; experiences of laser trabeculoplasty or ocular surgery and inflammation on the eye within the past year which may affect the results and any contraindications to resisted exercise. Random allocation was performed by a blinded and an independent researcher using sealed opaque envelopes for random allocation of the recruited patient into two groups of 15 patients each (the study group (Group A) or the control group (Group B)).

Ethical consideration

The aim and protocol of the study were fully explained for each patient and a signed informed consent was obtained from each patient before participation in the study. This study was approved by the Ethical Committee of the Faculty of Physical Therapy, Cairo University and it is in accordance with the Declaration of Helsinki.

Outcome measure

Measuring patients' intraocular pressure (IOP):

The ophthalmologist measured patients IOP using the Goldmann Applanation Tonometry before starting the exercise program and by the end of the program (48hours after the end of the program). Measurement of IOP by Goldmann Applanation Tonometry is considered to be the gold standard test and is the most widely accepted method. In comparison with other measurement techniques, the Goldmann device is thought to give more accurate results over a wider range of IOP values [17,18]. Patients were asked not to take their antiglaucoma drugs at the morning of (IOP) measurement and the procedures were explained clearly to each patient. The ophthalmologist recorded all measurements at the same time of the day between 12 pm and 2 pm to minimize the effects of diurnal variation.

Assessment procedure of the One-repetition maximum test (1-RM):

The one repetition maximum (1RM) test is considered as the gold standard for assessing muscle strength in non-laboratory situations. It is a baseline measurement to quantify the intensity of resisted exercise at the beginning of the training. The testing protocol has been previously described by Kraemer et al.[19]. One-repetition maximum (1-RM) of biceps brachii was determined using mechanical resistance, dumbbells. The highest load lifted (kg) in proper form was used as the 1-RM test score then used as a resistance for trained group (A).

Therapeutic intervention:

The study group (A) participated in a supervised individual resistive training program three times per week for 4 weeks.

This program was applied by an expert physical therapist with 15 years of experience. Each resisted training exercise session started with a general warm-up in the form of stretching for approximately 5–10 minutes, then the active phase of 20 minutes progressive resistance exercise. At the end of the session cool-down period was performed for 5 minutes in form of stretching. Dumbbells of different weights were used for training. Three sets of 8 repetitions, with a rest period of 2 minutes between sets, with intensity at 40% of 1- RM in the first week then increased gradually to 60% of 1- RM in the following three weeks. Patients were instructed to avoid holding their breath by counting to avoid Valsalva maneuver during exercise. Patients in the control group were instructed to avoid vigorous activities [20].

Statistical Analysis

Numerical data were explored for normality by checking the distribution of data, calculating the mean, median, and SD values, using the tests of normality (Kolmogorov-Smirnov and Shapiro-Wilk tests), drawing box plot, and histogram. Age, weight, height and IOP data showed parametric (normal) distribution. Data were expressed as the mean and SD. Paired t-test was used to compare results of the same group and unpaired t-test was used to compare the two groups. The alpha level of statistical significance was set at p< 0.01. Analysis for data was performed using IBM SPSS Statistics Version 20.

Results

Overall, 27 patients (14 in the control group, 13 in the study group) completed the duration of the study for 4 weeks, and we could not follow up 3 patients due to illnesses or withdrawal. Therefore, we used intention-to- treat in statistical analysis by the approach of imputing the mean of the missing subject's own group. The analysis of baseline values between the two groups, as shown in Table 1, revealed that there were no statistically significant differences (P>0.01) with respect to age (P=0.271), weight (P=0.668), height (P=0.766), sex (P=0.515), IOP for RT Eye (P=0.446), and IOP for LT Eye (P=0.239).

Regarding IOP, within-group comparison between the pretreatment and post-treatment values, results revealed that a significant improvement in the study group (A) both eyes (RT&LT) (P=0.000) and nonsignificant improvement in the control group (B) RT and LT eye (P=0.486 and 0.265, respectively) as shown in Table 2. Between-group comparison IOP (for RT and LT eyes) values before the treatment revealed a nonsignificant difference (P=0.446 and 0.239, respectively) as shown in Table1, whereas post-treatment comparison revealed a statistically significant difference in favor of the study group both eyes RT and LT (P=0.001 and 0.000, respectively) (Tables 2).

Discussion

This study extends the evidence from previously published studies on the effect of exercises on IOP. The aim of this study was to evaluate the therapeutic efficacy of resisted exercises on intraocular pressure (IOP) in primary open angle glaucomatous patients. This study demonstrated a significant improvement in the study group that received resisted exercises for 4 weeks with no significant changes in the control group, indicating an augmented effect of resisted exercises training as additional therapy to decrease intraocular pressure in patient with primary open-angle glaucoma.

The current results could be attributed to the effect of exercise on intraocular pressure and pulsatile ocular blood flow [12]. Intense exercise causes tissues to resort to anaerobic respiration, the end products of which are energy in the form of adenosine triphosphate and lactic acid due to the hydrogenation of pyruvic acid. As lactic acid enters the general circulation blood lactate levels rise, which causes an increase in blood osmolarity. The increased lactate levels cause an outflux of water from the eye which is responsible for fall in IOP with exercise [21]. In addition to the release of large quantities of epinephrine and norepinephrine from adrenal medulla, in response to resisted exercise, stimulating the synthesis of cyclic adenosine monophosphate (cAMP) which regulate the activity of the protein kinases, it has been shown that activation of (cAMP) decreases IOP by decreasing in aqueous humor production [22-26]. Another possible mechanism, hormonal regulation by an increased release of adrenaline has been suggested [27]. The exact mechanism of IOP decrease by adrenaline has not been fully explained yet, but it is likely that adrenaline increases trabecular outflow facility and reduces aqueous humor formation [28].

The findings of this study are supported by the results of previous studies. A study by Natsis et al. [29] demonstrated a sta-

Table 1. Demographic values and IOP measurements at baseline (Pre) in the two study groups.

Characteristics	Study Group A (n=15)	Control Group B (n=15)	p-value
Age (yrs.)	46.93±3.173	48.20±2.678	0.271
Weight (Kg)	79.40±3.942	78.60±5.448	0.668
Height (cm)	167.93±3.712	168.33±3.177	0.766
IOP for RT Eye(mmHg)	20.27±3.615	21.07±1.335	0.446
IOP for LT Eye(mmHg)	21.87±2.475	20.93±1.486	0.239
Sex (male/female)	(9/4)	(8/6)	0.515

Values of age, weight, height, and IOP are expressed as mean ± SD; sex distribution is expressed as frequency. SD: standard deviation, P: probability, IOP: intraocular pressure.

Table 2. Statistical analysis of intraocular pressure within each group and post-treatment comparison between groups.

	Study group (n=13)				Group B control (n=14)				Between- group p-value
	pre	post	mean % of reduction in IOP	p-value	pre	post	mean % of reduction in IOP	p-value	
IOP OF RT.EYE (mmHg)	20.27±3.62	17.53±3.31	13.5%	0.000*	21.07±1.34	20.87±1.06	0.95%	0.486	0.001*
IOP OF LT.EYE (mmHg)	21.87±2.48	16.60±2.38	16.45%	0.000*	20.93±1.49	20.27±1.71	1.7%	0.265	0.000*

Values are expressed as mean ± SD; IOP, intraocular pressure; RT, right; LT, left; % percentage; Between-group P-value, post-treatment comparison between groups; P-value, before versus after treatment within each group; *Significant tistically significant decrease in IOP in patients with glaucoma during jogging and they concluded that there was no ocular restriction for glaucoma patients in performing physical activity; although they did not use the same type of exercise intensity or duration of our study. Furthermore, Recep et al. [30] concluded that exercises reduce the intraocular pressure both in athletes as well as individuals leading sedentary lives.

Chromiak et al. [20] confirmed in his study the hypotensive effect of dynamic resisted exercise on IOP in physically active people and they showed that the upper-body resistance training had a more lasting effect on IOP lowering compared with lower-body training. Although these results supported our selection of upper limb resisted exercise as a therapeutic intervention for POAG patients, it was conducted only on healthy individuals.

Price et al. [12] examined the effect of exercise on intraocular pressure and pulsatile ocular blood flow in young normal population and they found a significant decrease in IOP with strenuous exercise then it recovered gradually toward baseline over a period of 30 min and they also concluded that pulsatile ocular blood flow increased significantly immediately after exercise then returned to baseline levels between 5 and 10 min after stopping exercise although the type of exercise used was aerobic in the form of a 4-min period of bicycle ergometry.

Vieira et al. [31] studied intraocular pressure (IOP) variations in healthy volunteers after a session of weight lifting with 85% top load for 8 repetitions and they found a small, but significant intraocular pressure (IOP) decrease. Qureshi et al. [27] found that hard-working is associated with physical fitness and physical fitness is associated with reduced resting intraocular pressure (IOP) and they conclude that the intensity of exercise seems responsible for the magnitude of the initial IOP decrease after short-term exercise [13].

This study has some limitations such as small sample size and short duration of the training period. The long-term effects after stopping resisted training were not measured; therefore, further research, with larger sample size, about the long-term effect of resisted training on patients with glaucoma and comparison between males and females results may also be required.

Conclusion

In summary, the information presented in this study contributes to the growing evidence that encourages adding upper limb resisted exercise as additional therapy for decreasing intraocular pressure in patients with primary open-angle glaucoma.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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