Influence of Dynamic exercise on Ocular Perfusion Pressure in Patients with Type 2 Diabetes

Azza Fekry Ismail*, Nesreen Ghareeb Elnhas, Kadria Hosny Battecha*****
* Department of Physical Therapy for Cardiovascular/ Respiratory Disorder and Geriatrics, Faculty of Physical Therapy, Cairo University.
** Department of Cardiovascular /Respiratory Disorder and Geriatrics, Faculty of Physical Therapy, Cairo University.
*** Department of Basic Science, Faculty of Physical Therapy, Cairo University.

ABSTRACT

The aim of the study was to investigate the influence of treadmill exercise on ocular perfusion pressure in patients with type 2 diabetes. Twenty diabetic patients were enrolled in this study (10 women and 10 men) they were with age ranges between 40-55 years. They performed a supervised treadmill exercise program (3 sessions/week, 40 minutes/session for 3 months) where blood pressure, intraocular pressure and ocular perfusion pressure were measured before exercise, immediately after and 30 minutes after exercise. Patients underwent measurement procedures for weight, blood glucose level, blood pressure, intraocular pressure and ocular perfusion pressure at baseline, after 1 month, after 2 month and after 3 months. The results showed significant decline in blood glucose level, weight as well as intraocular pressure and ocular perfusion pressure after training period especially after 3 months. Conclusion; It was concluded that regular treadmill exercise was of great benefit to diabetic patients as it keeps ocular perfusion pressure within normal limits as to keep steady blood flow to retina as well as keeping blood glucose level within control.
Key Words: *Treadmill exercise, Diabetes, Intraocular pressure, ocular perfusion pressure.*

INTRODUCTION

Diabetes mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hypreglycemia. Several types of DM exist and are caused by complex interaction of genetics, environmental factors, and lifestyle choices. In the United States, DM is the leading cause of end stage renal disease, non-traumatic lower extremity amputations, and adult blindness. With an increasing world-wide, DM will likely contribute to be a leading cause of morbidity and mortality for the foreseeable future[22].

Nowadays treatment of Diabetes are directed to its complications because cardiovascular morbidity and mortality in patients with diabetes are caused by micro and macrovascular complications, with clinical manifestation beginning 15–20 years after the onset of diabetes[7].

Diabetic retinopathy is the damage to the blood vessels in the retina that may leak fluid or blood and grow scar tissue. This leakage affects the ability of the retina to detect and transmit images. In some people with diabetic retinopathy, blood vessels may swell and leak fluid. May lead to abnormal new blood vessels to grow on the surface of the retina[23].

Many studies had been reported abnormalities of structure, distensibility, myogenicity, and endothelium-dependent dilation in the medium seized arteries for diabetic patients and this impaired endothelial function has been implicated as an early sign of a proatherogenic vascular environment, and diabetics are certainly prone to this upstream in medium-sized arteries. A failure to autoregulate blood flow efficiently might lead to increased high blood pressure flow to target organs, effecting downstream damage, as observed in the kidney and eye, for example[25].

Vascular tone is decreased by hyperglycemia, resulting in increased blood pressure. Extracellular matrix accumulation also occurs, causing basement membrane thickening, which can lead to occlusion and ischemia. Compensatory growth of abnormal new blood vessels (i.e., neovascularization) that are fragile and prone to hemorrhage occurs in many cases as in DR. In the progression of diabetic retinopathy, Macular ischemia, macular edema, retinal and vitreous hemorrhage, and retinal detach-ment are the primary causes of blindness in patients with diabetic retinopathy[17].

Diabetic retinopathy burden in Egypt recorded the risk of blindness is about 25 times greater in diabetics than in non-diabetics. Diabetic retinopathy (D.R.) is the commonest cause of legal blindness in individuals between the ages of 20 and 65 years. The incidence of D.R. is related more to the duration of diabetes than to any other factor. 50% of diabetic patients of age less than 30 years will have D.R. after 10 years. Also; Glaucoma burden in Egypt: The data estimates burden of glaucoma in adults of age group 50+ to be 1.1% as a cause for low vision and 4.6 % as a cause for blindness from all causes of visual impairment[1].

The causes of diabetic retinopathy were discussed in many reviews, one of the most common causes is changes in blood-sugar levels in which high blood sugar can damage blood vessels in the retina, and when they are damaged, they can leak fluid or bleed. This causes the retina to swell and form deposits. This is an early form of diabetic retinopathy called nonproliferative or background retinopathy.In a later stage, called proliferative retinopathy, new blood vessels grow on the surface of the retina. These new blood vessels can lead to serious vision problems because they can break and bleed into the vitreous, the clear, jelly-like substance that fills the center of the eye. Proliferative retinopathy is a much more serious form of the disease and can lead to blindness[14].

According to, Jain et al., 2003[11]; Duration of disease and control of blood sugar are the most important variables in the development and progression of diabetic retinopathy. After 10 years, 70% of those with type 2 diabetes demonstrate some form of retinopathy, and nearly 10% show proliferative disease. Diet control, exercise, and proper glucose management with frequent daily glucose testing and the use of oral hypoglycemics or insulin, or both, are crucial in maintaining glycosylated hemoglobin levels lower than 7%.

Because the eye is a closed structure, if the drainage area for the aqueous humor called the drainage angle is blocked, the excess fluid cannot flow out of the eye. Fluid pressure within the eye increases, pushing against the optic nerve and causing damage and result in vision loss[6].

In many people, increased pressure inside the eye causes Glaucoma which is an eye disease in which the normal fluid pressure inside the eyes slowly rises, leading to vision loss or even blindness. Glaucoma is a dangerous eye condition because it frequently progresses without obvious symptoms. This is why it is frequently referred to as "the sneak thief of sight"[8].

Glaucoma is defined as a disturbance of the structural or functional integrity of the optic nerve that causes characteristic atrophic changes in the optic nerve, which may also lead to specific visual field defects over time. This disturbance usually can be arrested or diminished by adequate lowering of intraocular pressure (IOP)[3].

Both hyperpermeability and breakdown of the blood-retinal barrier are major early functional disorders observed in diabetic retina. Vascular endothelial growth factor (VEGF) is thought to play an essential role in intraocular neovascularization in the breakdown of the blood-retinal barrier[2].

Ocular perfusion pressure (defined as the arterial pressure in the ocular vessels minus the intraocular pressure [IOP], or often calculated as two thirds of the mean arterial pressure minus the IOP). Therefore, a decrease in mean arterial Pressure (MAP) or an increase in IOP can decrease ocular perfusion.

Choroidal blood flow (ChBF) depends, not only on ocular perfusion pressure (OPP), but also on absolute mean arterial pressure (MAP) and intraocular pressure (IOP). Studies confirm that the choroid shows some auto regulatory capacity during changes in OPP. In addition, the choroid regulates its blood flow better during exercise-induced changes in MAP than during an experimental increase in IOP[21].

According to Hilton, 2003[10], in normal healthy eye, ocular blood flow is auto regulated to remain constant when ocular perfusion is increased. Exercise cause increase in systolic blood pressure and a decrease in IOP. These two components are strongly influenced by the autonomic nervous system, and the result is an increase in ocular perfusion pressure. While a normal healthy eye can often cope with this stress of altered ocular perfusion pressure, a diseased eye, or an eye whose vasculature is compromised by a pre existing systemic state, may not.

Dynamic exercise
↓
•Increased metabolic activity in skeletal muscle proportional to exercise intensity
↓
•Fluid efflux from plasma to skeletal muscle interstitium
↓
•< Plasma colloid Osmotic pressure
↓
*Dehydration and reduction of vitreous volume?
*Decreased ciliary body filteration forces?
*Direct hypothalamic actions?
↓
< IOP

Several Studies confirm that regular exercise can enhance the release of nitric oxide (NO) that leads to a functional consequence of the good nourishment of the delicate and sensitive tissues to blood deprivation such as EYE and normalize intraocular pressure that will save it from occular complications as diabetic retinopathy (DR) which is the major cause of blindness in adults aged 25-74 years[24].

According to, Chous, 2005[5]; Hemodynamic Risk Factors for Sight-Threatening Retinopathy: Recent evidence demonstrates that hyperglycemia increases blood flow into the eye by impairing retinal vascular auto-regulation. High retinal blood flow damages vascular endothelium, increases capillary permeability and promotes capillary non-perfusion hallmarks of diabetic retinopathy. In type 1 patient especially; elevated retinal perfusion pressure (RPP > 50.1mm) strongly predicts development of sight-threatening retinopathy (STR) (four to six times relative risk). In type 2 patients, elevated mean arterial pressure (MAP > 97.1mm) is highly predictive of STR (four to six times relative risk).

As mentioned in many studies that in healthy subjects, choroidal blood flow is regulated when the mean ocular perfusion pressure increases, as it is contolled by the autonomic nervous system. Since capillary vascular beds are altered in diabetic patients, the regulation of choroidal blood flow could be affected by this pathology. So in DR patients, the absence of this control could be due to the failure of the autonomic nervous system. Thereby they must exercise to keep their IOP within normal limits with keeping in mind the other risk factors[18].

It was reported that exercise also induces blood flow changes in all organs in the body, including the eye and the brain that are auto regulated in order to maintain a constant blood supply in the face of metabolic stress or imbalance. Blood flow auto regulation refers to the ability of the vascular bed to maintain a relatively constant flow despite moderate alterations in the perfusion pressure, or in terms of eye, ocular perfusion pressure[10].

So many studies were based on glycemic control to decrease the occurrence of these complications, Findings showed that improving glycemic control prevents the onset or progression of diabetic microvascular complications, such as diabetic retinopathy, nephropathy and neuropathy[20].

Dynamic exercise changes Ocular perfusion pressure (OPP), and produces increased tissue blood flow in the retina in the immediate post exercise period, while blood flow increases more persistently in the choroid-retina. Difference in control of blood flow in these two regions may be related to stronger auto regulatory mechanism of blood flow in the retina. Nitric oxide may play a role in the regulation of blood flow[12].

According to, Kinshuck, 2007[12], Exercise lowers the eye pressure 1mmHg. A 1mmHg reduction in pressure will cause a 10% reduction in loss of visual field. Thus exercise would be expected to result in a 10% reduction in the progression of glaucoma.

SUBJECTS, MATERIALS AND METHODS

Twenty diabetic patients were enrolled in this study, (10 women and 10 men), they were chosen from Kasr El Eini internal medicine and Faculty of Physical therapy out clinic departments. All patients were with age ranges between 40-55 years.

Diabetic patients were diabetic for at least 4-6 years duration with a sedentary life style before enrollment and were non-smokers, they were diagnosed clinically by plasma glucose levels (fasting and post prandial), clinical presentation and patients were under medical control.

Exclusion criteria: Subjects with systemic hypertension (defined as systolic blood pressure > 145 mmHg, diastolic blood pressure > 90 mmHg. Patients with glaucoma.

The procedures of the study were conducted in the out-clinic of Faculty of Physical Therapy, Cairo University.

The following parameters were measured for assessment: Blood glucose level by blood sample, Blood pressure by using sphygnomanometer, Quetlet index by the aid of weight and height scale, Intraocular pressure measurement for both eyes using Schiotz tonometer Improved (SK Speidel & Keller (€ 0123), Ocular perfusion pressure were calculated by the equation:

Ocular perfusion pressure = (2/3 MAP)- IOP Where;
Mean arterial pressure (MAP) = (2/3 diastolic BP+ systolic BP) /3 (Hilton, 2003)[10].

These parameters were operated to all patients at the beginning of the study, after 4 weeks (12 sessions), 8 weeks (24 sessions) and at the end of the training program that lasted for 12 weeks (36 sessions).

Training program

The patients were trained in the form of controlled walking exercise on the treadmill (Enraf Nonius, EN-TRED). At each training session, walking speed will be slowly increased on an individual basis until the heart rate 140 beats/minute (using pulsometer) that was proved to induce ocular perfusion changes[15]. Each exercise session lasted for 40 minutes; 10 minutes warming up and then the speed were increased as prescribed previously. The actual training period was about 20 minutes that was followed by 10 minutes for cooling down. The exercise will be stopped when any symptom limiting exercise appears as chest pain, leg pain, fatigue, dyspnea, disturbance in breathing or heart rates.

In each session the blood glucose level was checked before the exercise as a safety precaution for the patient. The blood pressure as well as the IOP was measured before the exercise, immediately after exercise, and 30 minutes after the end of exercise. After 4 weeks (12 sessions), 8 weeks (24 sessions) and at the end of the training program that lasted for 12 weeks (36 sessions).

Statistical analysis

Descriptive analysis using measures of central tendency in the form of arithmetic mean and measures of dispersion in the form of standard deviation (SD) for the age, weight, height, BMI and other variables among the intervention group. Paired student "t" test was used to compare between means for paired series at the baseline and after the end of the training program (3 months) for weight, BMI and blood glucose level within each group. The statistical analysis of the variables went on the view of NON-PARAMETRIC TESTS for multiple related samples were used, as it is the useful alternatives to a repeated measures analysis of variance. {They are especially appropriate for small samples and can be used with nominal or ordinal test variables}. (Tests for several related samples) as Friedman test. This test was used to analyze intraocular pressure (IOP) and the ocular perfusion pressure (OPP) for both eyes referenced by different exercise intervals (pre, Immediately after, and after 30 minutes) throughout the course of the study at one spot to mark which of the exercise intervals was significant. Then by the use of Wilcoxon signed-rank test analysis took place to study the difference between different times of exercise intervals to mark the significance.

RESULTS

Table (1): Demographic data for the intervention group.

	Intervention Group Mean ± SD
Number/Sex	20 Diabetic patients 10 women and 10 men
Age (yrs)	45.7 ± 6.63
Weight (Kg)	79.5 ± 10.6
Height (cm.)	161.95 ± 5.7
BMI (Kg/m²)	30.3 ± 3.8

Table (2): Plasma glucose level throughout the course of the study.

		Training period		
Plasma glucose level mg /dl	At baseline Mean ± SD	1-month Mean ± SD	2-month Mean ± SD	3-month Mean ± SD
Intervention Group	192 ± 16	140 ± 15	125 ± 16*	113 ± 10*

SD: Standard deviation * Significant

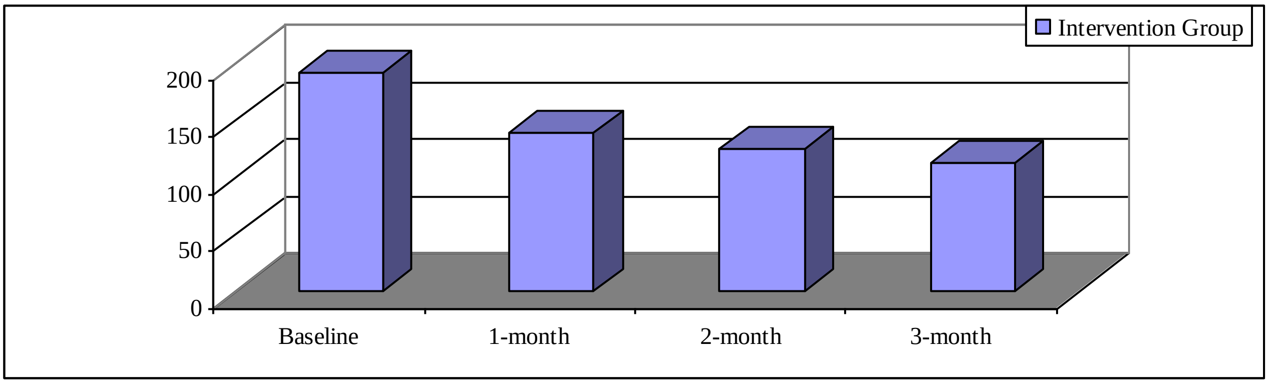

Fig. (1): Plasma glucose level for both groups throughout the course of the study.

Table (3): Ocular perfusion pressure of the right and left eyes for the intervention group throughout the course of the study.

	Pre-exercise Mean ± SD		Imm. After Mean ± SD		After 30 min. Mean ± SD	
	Rt. eye	Lt. eye	Rt. eye	Lt. eye	Rt. eye	Lt. eye
At Baseline	21.8 ± 4.7	21.7 ± 5	24.5 ± 3.8	24.4 ± 3.8	22.4 ± 5	22.5 ± 5
After 1-month	21.7 ± 4.6	21.8 ± 5.9	24.1 ± 4.6	24.5 ± 4.7	22.1 ± 5.6	22.1±6.3
After 2-month	22 ± 4.3	22.3 ± 5.3	24.3 ±3.9	25 ± 4.5	23.7 ± 5.5	23.9±5.5
After 3-month	22.7 ± 3.7	23 ± 4.1	28.4 ± 3.7	28.3 ± 3.6	23.8 ± 4.2	23.8±4.1

Imm.: immediately min.: minutes SD: Standard deviation

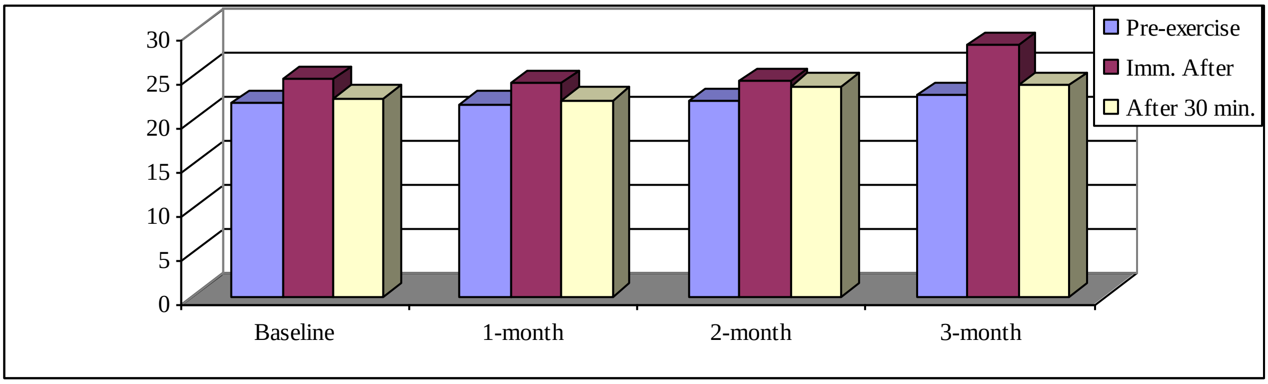

Fig. (2): Ocular perfusion pressure measuring of the right eye of the intervention group throughout the study.

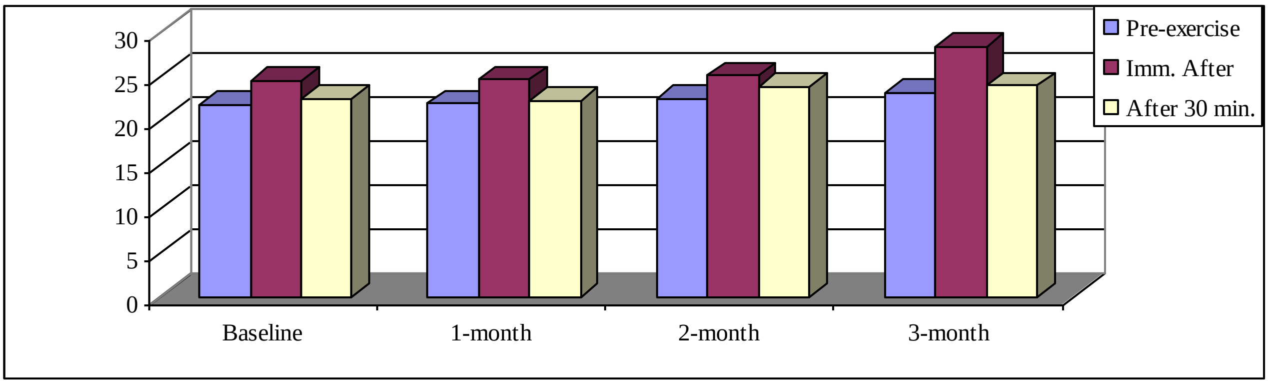

Fig. (3): Ocular perfusion pressure measuring of the left eye of the diabetic group throughout the study.

Table (4): Analytical analysis for ocular perfusion pressure of the right and left eye for the intervention group throughout the course of the study by the use of Friedman test.

		Mean Rank		t-value (Chi-square)		P-value	
		Rt. eye	Lt. Eye	Rt. eye	Lt. Eye	Rt. eye	Lt. Eye
At baseline	Pre-exercise	1.45*	1.55*	18.1	15.1	0.000*	0.001*
	Imm. After	2.75	2.70				
	After30min.	1.80	1.75				
1-month	Pre-exercise	1.90	1.95	6.7	7.3	0.035	0.026
	Imm. After	2.45	2.45				
	After30min.	1.65*	1.60*				
2-month	Pre-exercise	1.50*	1.50*	12.4	13.291	0.002*	0.001*
	Imm. After	2.60	2.63				
	After30min.	1.90	1.88				
3-month	Pre-exercise	1.45*	1.50*	26.30	26	0.000*	0.000*
	Imm. After	2.92	2.92				
	After30min.	1.69	1.53*				

Imm.: immediately * Significant min.: minutes SD: Standard deviation
Rt. : right Lt.: left

According to these data, the results manifest the variation in the mean ranks at the 2nd as well as 3rd month during the period after 30 minutes of exercise in which the data showed the best results.

DISCUSSION

Much of the burden of diabetes is due to the development of vascular complications, including cardiovascular diseases, retinopathy and nephropathy. Improvements in patient management to promote tight control of glycaemia have helped to reduce the prevalence of microvascular complications, but cardiovascular diseases continue to be the leading cause of death in patients with type 2 diabetes[4].

Mahmoud et al., 2006[16] showed that in a study on 15 diabetic patients were enrolled in treadmill exercise and No was investigated in those patients where the results supported that exercise has a positive effect on increasing the level of nitric oxide and hence decrease the incidence of vascular complications of diabetic patients.

Results from a study done by Singleton et al., 2003[27], indicate an association of systemic blood pressure with IOP in patients with autonomic dysfunction. There was a decline of IOP, MAP, and mean ocular perfusion pressures (MOPP) below normal values with a positional change from supine to standing in patients with peripheral or central autonomic dysfunction. These results suggested that the autonomic system has a significant role in stabilizing IOP and may act indirectly through blood pressure maintenance.

In the present study, the results showed that exercise training improved the level of blood glucose in diabetic patients which in turn had the effect on blood pressure and IOP as well as ocular perfusion pressure, these results came in consistent with the findings of Fuchsjäger-Mayrl et al., 2002[7] where the study demonstrated that endothelial function of conduit and resistance vessels can be improved by regular aerobic training in patients with diabetes.

In the present study, the impact of 3 months treadmill exercise is the most important variable that plays an important role in adjusting blood glucose level as well as intraocular pressure. That was in consistent with the results of a study by Silver and coworkers, 1991 that reported an increase in blood flow of the opthalamic artery, which is accompanied by a decrease in IOP following acute exercise.

In contrast, a separate study by Nemesure et al., 2002[19] which used color Doppler ultrasound imaging to measure blood flow velocities of the ophthalmic artery and central retinal artery in healthy volunteers before and after exercise, showed decreased blood flow in the ophthalmic artery, while blood flow in the central retinal artery remained stable. The authors concluded that efficient autoregulatory mechanisms existed for retinal blood flow, which was kept constant during the altered cardiac state, but not for the ophthalmic artery.

Dynamic exercise, such as biking, In spite of the rapid increase in PPm during biking, Choroidal blood flow (ChBF) remains very close (increase of about 6 %) to its value at rest (time 0 s). This study strongly supports the presence of an active regulatory mechanism for blood flow in the human choroid. Furthermore the study concluded that the increase in vascular resistance during biking is at the level of the choriocapillaris but the nature of the mechanism underlying this regulation remains to be elucidated.

Hilton, 2003[10], the reason why exercise results in reduced IOP in both the short and the long term are yet to be fully elucidated; however, it seems possible that the properties of IOP reduction during isometric exercise differ to that of isotonic (dynamic) exercise. She found that reduction in IOP with the latter (isotonic) exercise group showing largest reduction when it is compared to isometric. The authors proposed that the greater number of fibrils were recruited during the isotonic exercise due to a contraction of the muscle in the whole joint movement, which may have had a more profound effect on the rest of the body including the eyes.

In support with Kozobolis et al., 2008[13] who studied the effects of maximum dynamic physical exercise on ophthalmic artery (OA) blood flow and ocular perfusion pressure (OPP) on thirty male subjects and concluded that maximal physical exercise increases OPP and blood flow at the OA implying that auto-regulative mechanisms are active in both retinal and choroidal.

It was concluded that regular treadmill exercise had the effect of lowering intraocular pressure as well as ocular perfusion pressure which emphasis in good ocular nutrition especially in diabetic patients. So we can control diabetes and its complications to minimize its hazards and cost effectiveness of treating diabetic complications that increases the economic burden of diabetic management.

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الملخص العربي

تأثيرالتمرينات الديناميكية على الضغط المغذى للعين لدى مرضى البوال السكرى (النوع الثانى)

هدف الرسالة هو معرفة تأثير تمرينات جهازسير المشى المتحرك على الضغط المغذى للعين لدى مرضى البوال السكرى (النوع الثانى) . أجرى البحث على عشرين مريض بالبوال السكرى (النوع الثانى) وتتراوح أعمارهم ما بين 40-55 سنة. أجريت الدراسة لمدة ثلاثة أشهر حيث قام المرضى باجراء تمارين المشى على جهاز السير الكهربائى لثلاثة ايام فى الاسبوع مع قياس نسبة السكر فى الدم ، ضغط الدم والضغط الداخلى للعين والضغط المغذى للعين قبل بدء المشى وبعده مباشرة وبعد 30 دقيقة من الانتهاء من جلسة العلاج والتى استمرت لمدة 40 دقيقة . وقد أظهرت النتائج وجود فروق ذات دلالة احصائية تشير الى تحسن ملحوظ فى انخفاض مستوى السكر فى الدم مع انخفاض الضغط الداخلى للعين والضغط المغذى للعين بين مرضى البوال السكرى الذين قاموا بأداء التمرينات بجهازسير المشى المتحرك مما يؤدى الى الحفاظ على صحة العين من عواقب مرض البوال السكرى. لذلك يوصى بالمواظبة على اداء تمارين المشى لدى مرضى البوال السكرى .

الكلمات الدالة : جهازسير المشى المتحرك ، الضغط الداخلى للعين ، مرضى البوال السكرى (النوع الثانى) .