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PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

OPEN ACCESS Pakistan Journal of Biological Sciences

ISSN 1028-8880
DOI: 10.3923/pjbs.2019.400.405

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Research Article
Isometric Versus Aerobic Training Effects on Vascular Adaptation in Patients with Type 2 Diabetes

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Abstract
Background and Objective: Diabetes is known to be associated with arterial remodeling and dysfunction which predispose to different microvascular complications. This study was aimed to find out the effect of isometric versus aerobic training on vascular adaptation in patients with type 2 diabetes. **Materials and Methods:** The study was carried out on 40 type 2 diabetic patients (20 men and 20 women). Patients were selected from the outpatient clinic of El-Agouza Police Authority Hospital. They were assigned into 2 matched and equal groups in number. Group A with mean age of 49.55 years, received unilateral isometric handgrip exercise 22 min per session, 3 sessions per week for 8 weeks and group B with mean age 50.15 years, received aerobic exercise in form of arm ergometry for 30 min, 3 sessions per week for 8 weeks. They were assessed by a Doppler ultrasound for brachial artery adaptation (the brachial artery diameter, blood velocity and shear rate) before and after 8 weeks of training. **Results:** Group A showed significant improvement in brachial artery adaptation as increased brachial artery diameter from 4.28±0.19 to 4.43±0.18, baseline vessel velocity from 7.09±0.41 to 8.62±0.46 and its shear rate from 66.24±4.19 to 77.65±5.27, while in group B who received the aerobic exercise the results showed a minimal change between pre training and post-training results 4.24±0.23 to 4.26±0.21 for brachial artery diameter, 7.26±0.54 to 7.46±0.67 for blood velocity and 67.8±3.16 to 68.81±4.29 for shear rate respectively. **Conclusion:** Isometric handgrip exercise improved brachial artery diameter, blood velocity and shear rate in patients with type 2 diabetes.

Key words: Vascular adaptation, Isometric exercise, aerobic exercise, brachial artery diameter, blood velocity, shear rate

Citation: Nesreen G. El-Nahas and Manar Mohamed Badawy, 2019. Isometric versus aerobic training effects on vascular adaptation in patients with type 2 diabetes. Pak. J. Biol. Sci., 22: 400-405.

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The global incidence and prevalence of diabetes mellitus has increased significantly with the heightened risk of adverse micro vascular and cardiovascular events, the medical management mandates risk factor modification[1].

Diabetes is not only a group of metabolic disorders that characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both but also, a cause of vascular disease affecting nearly all blood vessel types and sizes. It is associated with long-term damage, dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart and blood vessels[2].

The increased risk of cardiovascular disease (CVD) in diabetes includes premature atherosclerosis[3], together with Diabetes-related endothelial dysfunction which has been reported leading to morphologic and structural vascular changes[4].

Exercise had proven to affect the blood flow, luminal shear stress, arterial pressure and tangential wall stress. There are important clinical implications of the adaptation that occurs as a consequence of repeated hemodynamic stimulation associated with exercise training[5].

The beneficial effects of exercise on the vasculature may contribute to the cardiovascular disease risk reduction by improving the endothelial nitric oxide synthase (eNOS) expression and phosphorylation, enhanced acetylcholine-induced vasomotor function and a reduction in pro-oxidant enzymes[3], with also an impact on arterial diameter decreasing cardiovascular risk gained by both aerobic and isometric exercises[6].

Physical activity and diabetes correlated with each other as they play an important role in the prevention of the progression of peripheral neuropathy and its impact is primarily on the development of muscle strength and the ability to replace the function of nerve fibers damaged disabilities[7].

High-resolution duplex ultrasound was used to examine resting diameter, wall thickness, peak diameter and blood flow. The results of these data suggested that the localized effects of exercise were obvious in the remodeling of arterial wall size, thickness and function[8].

People with diabetes have physiologic exercise limitations including insulin resistance, decreased limb and skeletal muscle blood flow with decreased cardiorespiratory fitness. They also, have slower oxygen uptake kinetics indicating decreased ability to adapt to an acute change in the demand for oxygenation at the beginning of exercise[9].

Muscle capillary density, oxidative capacity, lipid metabolism and insulin signaling proteins had been increased by regular training. Both aerobic and resistive training promote adaptations in vascular functions associated with enhanced insulin action and considered as risk modulators of exercise-related cardiovascular events. Combining endurance exercise with resistance exercise may provide greater improvements in adults with diabetes[10].

Isometric hand grip exercise is beneficial and came with associated improvement for brachial artery adaptation in patients with diabetes type 2. As evidenced by the significant increase in brachial artery diameter, blood flow velocity and shear rate. Vascular adaptation in a diabetic has a significant role to prevent or delay the vascular complications of diabetes related to atherosclerosis and peripheral neuropathy so this study was examined the effect of isometric versus aerobic training on vascular adaptation in patients with type 2 diabetes.

MATERIALS AND METHODS

Participants: Forty patients of both sexes (20 men and 20 women) with type 2 Diabetes for at least 10 years were selected from the outpatient clinic for internal medicine, El-Agouza police authority hospital. They were assigned into 2 matched and equal groups in number, with mean age of 49.55 years for group A and 50.15 years for group B. The purpose and nature of this study were explained to all participants who signed a consent form before participation in the study with assuring confidentiality.

Inclusion criteria: patients diagnosed with type 2 diabetes with FBG level (129-134 mg dL^{-1}) for duration of 10-15 years. Body mass index (BMI) was ranging between 31.53-36.39 kg m^{-2}. Medical treatments were optimized prior to participation in the study for all participants. The exclusion criteria were autonomic neuropathy, cardiovascular instability, smoking, nephropathy and diabetic retinopathy, patients on medication affecting peripheral blood flow.

Protocol: Patients were evaluated before and after 8 weeks of training for blood glucose level using fasting postprandial glucose testing maneuvers, BMI by calculation of weight and height of each patient and brachial artery diameter, blood flow and shear rate through Doppler ultrasound imaging using a Toshiba Power-vision 6000 with a multi-frequency linear array transducer (7-11 MHz) as: Images were measured approximately 3-5 cm. proximal to antecubital fossa where the patient is in supine position with extended arm. All blood velocity measurements were collected at a pulse wave frequency of 4.0 MHZ, a velocity range gate of 500 cm sec^{-1} . Blood velocity in brachial artery was assessed from a 10-s pulse wave Doppler signal obtained from the entire brachial artery. Its diameter was measured from leading edge to leading edge. Shear rate was calculated using formula:

$$\text{Shear rate} = 4\ Vm/D$$

where, Vm is mean blood velocity (cm sec^{-1}) and D is mean arterial diameter (cm) {B-mode ultrasound}.

Patients were assigned into two equal groups in number and gender distribution as:

- **Group A:** Patients were positioned in sitting position with forearm supported by a table throughout the training session holding hand grip dynamometer (HG). Being instructed to breathe normally and to avoid performance of a Valsalva maneuver, they completed four sets of 2 min isometric HG contractions (The contraction and relaxation time was set at 2 sec each) using a programmed HG dynamometer 3 times per week for 8 weeks. Isometric contractions were performed at 30% maximal voluntary contraction and each contraction was separated by a 2 min rest interval. All isometric HG training sessions took place under the direct supervision of an exercise trainer 3 times per week for 8 weeks[11]
- **Group B:** Training sessions were conducted 3 times per week. The aerobic training session was 30 min in duration and consisted of a 5-7 min warm-up in form of arm cycling with slow rate represented as 30-40% of the maximum heart rate (MHR) detected by strapless heart rate monitor, 20 min of aerobic training, at 65% of (MHR) and 5-7 min of cooling down as done in warming up, 3 times per week for 8 weeks[12]

Statistical analysis: The statistical analysis was done by SPSS program with representing data as mean and standard deviation with expressing standard error values, using paired t-test to analyze the difference within each group pre and post treatment and unpaired t-test to analyze the difference between both groups, also at level of significance ($p<0.05$). Also, the statistical analysis showed the percentage of improvement in all measured parameters in the study.

I-Demographic data:

- **For Group A:** Twenty patients (10 men and 10 women) were included in this group A with the mean values of their ages, weight, height, body mass index (BMI) and fasting blood glucose (FBG) levels were 49.55±1.73, 92.05±3.72, 165.25±5.17, 33.76±2.01 and 132.75±1.68, respectively as shown in Table 1
- **For Group B:** Twenty patients (10 men and 10 women) were included in this group B with the mean values of their ages, weight, height, body mass index (BMI) and fasting blood glucose (FBG) levels were 50.15±1.46, 91.85±2.83, 164.45±4.67, 33.99±1.35 and 131.8±1.47, respectively as shown in Table 1

II-Studied parameter analysis: The results showed that there is no significant difference between group A and group B at the beginning of the study in the Doppler measurements of the brachial artery diameter, velocity and shear rate. After 8 weeks of isometric training of group A the results for vessel diameter showed significant improvement determined by mean value at baseline diameter from 4.28±0.19 to be 4.43±0.18 at post training period and for baseline vessel velocity from 7.09±0.41 that increased to be 8.62±0.46 and its shear rate from 66.24±4.19 that significantly increased to be 77.65±5.27, while in group B who received the aerobic exercise the results showed a minimal change between pre training and post-training results 4.24±0.23-4.26±0.21 for brachial artery diameter, 7.26±0.54-7.46±0.67 for blood velocity and 67.8±3.16-68.81±4.29 for shear rate, respectively, as shown in Fig. 1-3.

Table 1: Demographic data of patients included in the study

	Group A		Group B		Comparison		
Items	Mean±SD	SE	Mean±SD	SE	t-value	p-value	S
Age (years)	49.55±1.73	0.38	50.15±1.46	0.32	1.185	0.240	NS
Weight (kg)	92.05±3.72	0.83	91.85±2.83	0.63	0.191	0.840	NS
Height (cm)	165.25±5.17	1.15	164.45±4.67	1.04	0.513	0.611	NS
BMI (kg m^{-2})	33.76±2.01	0.44	33.99±1.35	0.30	0.420	0.670	NS
FBG level (mg dL^{-1})	132.75±1.68	0.37	131.80±1.47	0.33	1.900	0.950	NS

SD: Standard deviation, SE: Standard error, P: Probability, S: Significant, NS: Non significant, kg: Kilogram, cm: Centimeter, kg m^{-2}: Kilogram per meter square, BMI: Body mass index, FBG: Fasting blood glucose, mg dL^{-1}: Milligram per deciliter

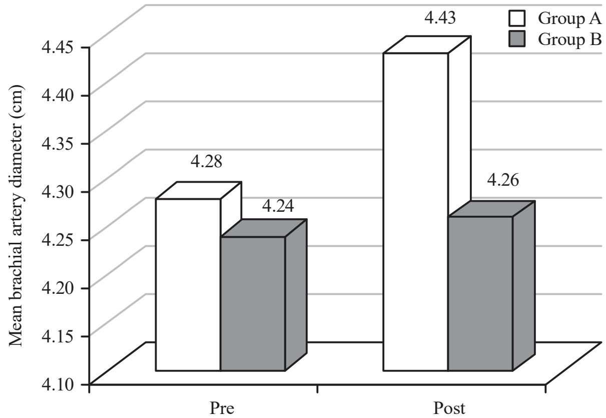

Fig. 1: Mean brachial artery diameter pre and post training between groups

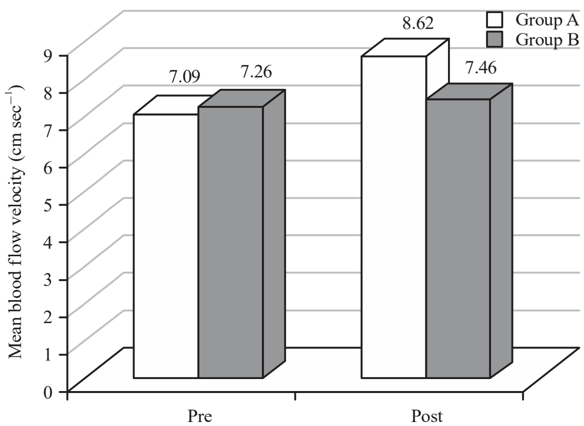

Fig. 2: Mean brachial artery blood velocity pre and post training between groups

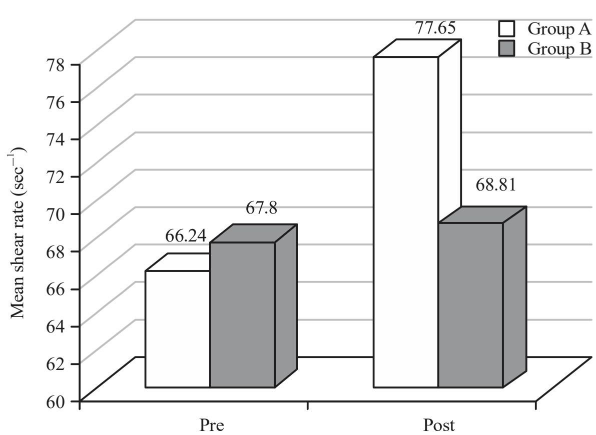

Fig. 3: Mean brachial artery shear rate pre and post training between groups

DISCUSSION

Diabetes exerts a pro-atherogenic action by disturbing endothelial homeostasis where the endothelium-dependent vasodilation (NOs) which is a marker of atherosclerosis is impaired in diabetes[13]. This study was aimed to assess the effect of isometric vs. aerobic training on vascular adaptation in patients with type 2 diabetes, where the endothelial dysfunction manifested in diabetes disorder is considered a precursor of atherosclerosis and CVD and evidence directed to that exercise training results in increased shear stress on vascular endothelium and increased NO production[14].

After 8 weeks of training for 40 diabetic patients, the results of this study had shown significant improvement within group A (isometric trained group) and these findings were consistent with those of Thijssen *et al*.[15], who found that Localized handgrip training induced a significant change in brachial artery flow mediated dilatation FMD = 3.6%. The diameter response significantly increased. While they found that there were no changes found across the localized handgrip training in the eliciting shear stress stimulus.

The findings of this study were agreed with Billinger *et al*.[16], who found that a 4 week SLE training program increased muscular activity in the hemiparetic limb and improved the femoral artery blood flow, diameter and peak velocity. Moreover, the results are also coincided with Spence *et al*.[11], Whaley *et al*.[12], Goldfine *et al*.[13], Lee *et al*.[14], Thijssen *et al*.[15], Billinger *et al*.[16] and Baross *et al*.[17], who found that resistance training increased brachial artery resting diameter and peak FMD diameter. Also, a study done on the vascular adaptation of femoral artery on the same variables of vessel diameter, blood velocity declared its response to the isometric training for lower limbs by significant improvement results that reflected the clue of that exercise had mechanical effects that provoked the endothelial cells that lined the intra-arterial walls to modify its arterial tone.

In accordance to these results related to isometric training effects on vascular adaptation, the results of Thijssen *et al*.[18], McKillop *et al*.[19], Horiuchi and Okita[20] had shown that, at the end of resistive exercise shear stress was stimulated and followed by greater vasodilatation and/or enhanced blood flow. Many researchers studied the impact difference between isometric versus aerobic training on vascular adaptation in healthy and in diabetic or even patients at risk to CVD diseases to denote which one had the desirable effect that was in line with a study done by Augustine *et al*.[21], who reported that resisted exercise prevents increased arterial stiffness that was ensured with the results of current study in Group A. Despite of the results of this study concerning to the significant effect of isometric exercise on vascular function, the results achieved by Gibbs *et al.*[22] showed that there was average percent change in brachial artery diameter by 5.56% with regular isometric exercise.

These findings were also in consistent to results achieved by Das *et al.*[23], who stated that protection of endothelium is not dependent on the mode of exercise training based on their study (aerobic vs. resistance vs. cross-training) on 45 participants engaged in 4 different exercise groups with a control one indicated that different modes of exercise performed metabolic changes with decrements in vascular function attenuated by exercise. The results related to group B were consistent with Thijssen *et al.*[18] results, who studied the changes of blood flow during cycling and walking (aerobic exercise) and the results showed only a minimal increase during cycling exercise that was induced by initial decrease in shear rate.

Regarding to the comparison between the two modes of exercise used in this study and their effect on vascular adaptation the results came conceptual to Green *et al.*[24], who reported that during handgrip, mean forearm blood flow increased with workload whereas forearm blood flow decreased at lower cycle workloads. The debate between the impact of significant or non significant effects of aerobic exercise on the endothelial functions of brachial artery was in continuous clinical trials as one performed by Gaenzer *et al.*[25] who found that in response to exercise (cycle ergometer), a clear rise of blood flow in the brachial artery and the changes in brachial artery diameter were not significant in smokers.

The consequences of another study performed by Mikus *et al.*[26] and Özcan *et al.*[27] were completely different after aerobic exercise program there was a dramatically improved femoral artery blood flow in individuals with type 2 diabetes as they stated. That was added to the results found that the brachial artery diameter and the brachial artery mean velocity following the aerobic exercise increased significantly. On the contrary, the results reported by Petrofsky *et al.*[28], who found that forearm blood flow was significantly lower at rest, during exercise and post aerobic exercise in subjects with diabetes compared to control subjects.

All the previous studies demonstrated the importance of both modes of exercises that induced changes in vascular adaptation that might mitigate the vascular effects and prevent complications to patients at risk and play a complementary role to each other depending on patients ability, lifestyle and health status either to use isometric or aerobic maneuvers.

CONCLUSION

It was concluded that isometric handgrip exercise was beneficial and came with associated improvements for brachial artery adaptation in patients with type 2 diabetes. As evidenced by the significance increase in brachial artery diameter, blood flow velocity and shear rate.

SIGNIFICANCE STATEMENT

This study was designed to determine the different effects of isometric and aerobic exercises on the vascular adaptation in diabetic patients as an attempt to prevent or delay the vascular complications of diabetes related to atherosclerosis and peripheral neuropathy which started accidentally and appeared suddenly to diabetic patients who have to deal with for lifetime.

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