Does Treadmill Exercise Affect Endothelial Functions In Type 2 Diabetic Patients?

Azza F. Ismail, Alsayed A.shanb*, Soheir A. Abu El Fadl**, Laila Rashed****

*Physical Therapy for Cardiopulmonary Disorders and Geriatrics Department, Faculty of Physical Therapy, Cairo University; ****** Internal Medicine Department, Faculty of Medicine, Cairo University; *** Biochemistry Department, Faculty of Medicine, Cairo University

ABSTRACT

***Purpose**: The aim of this study was to determine the effect of treadmill exercise training program on nitric oxide (one of endothelial function) in patients with type 2 diabetes mellitus. **Subjects and Methods**: Thirty type 2 non-smoker diabetic patients selected from the outpatient diabetes clinic of Kasr El Aini hospital. Another thirty age and sex matched non-diabetic healthy control subjects were included in this study. The patients were medically controlled. They were not participating in any form of physical activity and any dietary changes throughout the study. Nitric oxide was measured for the patients and the control subjects at the beginning and at the end of the study. The diabetic patients were divided into two equal groups: **Group-I**: Fifteen patients practiced moderate treadmill exercise for 40 minutes per session three times weekly for 8 weeks in addition to the oral hypoglycemic drugs. **Group-II:** Fifteen patients received only the oral hypoglycemic drugs. **Results**: There was significant reduction in nitric oxide level in diabetic patients (15.59$\pm$1.52) than control subjects (23.3$\pm$1.99) **(P = 0.000)**. The nitric oxide levels were negatively correlated to the blood glucose levels (fasting & PPBG) in diabetic patients (r= –0.57 & -0.49; P = 0.008 & 0.01 respectively). Nitric oxide significantly increased after treadmill exercise in group-I (22.08 $\pm$1.8), (**P = 0.000)** and its mean value approach that of the control **(P= 0.052)**. There was non- significant change in nitric oxide levels in group-II at the end of the study (15.35 $\pm$ 1.68) **(P = 0.797)**. **Conclusion**: Treadmill exercise training program with moderate intensity in addition to the oral hypoglycemic drugs increase production of nitric oxide (improves endothelial function) in type 2 diabetic patients so it was recommended to be applied for those patients.*

***Key words:** Diabetic patient type 2, endothelial function, nitric oxide, Treadmill exercise*

INTRODUCTION

Diabetes mellitus is a chronic metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes,

kidneys, nerves, heart and blood vessels[2]. Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the ß-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The vast majority of cases of diabetes fall into two types. Type-1 diabetes (5-10%), where the cause is an absolute deficiency of insulin secretion and Type-2 diabetes (90-95%), as the cause is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response[1]. The vascular endothelium plays a vital role in vascular homeostasis by synthesizing and releasing a number of active factors which are involved in the regulation of vascular tone, and thrombus formation[6,13,37]. The vascular endothelium plays an important role in maintenance of vasodilatation through the release of nitric oxide (NO)[12,41]. Nitric oxide relaxes the smooth muscle surrounding the vessels and inhibits the adhesion and aggregation of platelets[3]. It limits vascular recruitment of leukocytes by inhibiting the expression of pro-inflammatory cytokines and leukocyte adhesion molecules[13] Insulin has an important vascular action to stimulate production of (NO) from endothelium. This leads to capillary recruitment, vasodilatation, increased blood flow, and subsequent augmentation of glucose disposal in classical insulin target tissues (e.g. skeletal muscle)[32]. Type 2 diabetes mellitus is characterized by insulin resistance and, depressed NO functions[28].

Endothelial cell dysfunction represents a common pathophysiological pathway of diabetic complications. Gradual accumulation of advanced glycated end products (AGEs) and induction of plasminogen activator inhibitor-1 that result in the decreased expression of endothelial NO Synthase (NOS) and reduced generation of NO[40,24] .The importance of the NO pathway is demonstrated by the strong link between endothelial dysfunction and cardiovascular diseases as arterial hypertension, hypercholesterolemia, coronary heart disease and heart failure[23]. Nitric oxide synthesis may be stimulated by a variety of physiological agonists as shear stress and pharmacological agents. Regular exercises may represent a non-pharmacological therapeutic option to delay the decrease in endothelial function associated with aging, atherosclerosis or heart failure [26,31].

SUBJECTS & METHODS

I – Subjects: Thirty non-smoker type 2 diabetic patients (16 males and 14 females) and 30 age and sex matched non diabetic healthy control subjects (16 males and 14 females) participated in this study. Patients, age ranged from 40 to 55 years old with a disease duration of (4.12±1.64) years. They were selected from the outpatient diabetes clinic of Kasr El Aini hospital. The study has been conducted in the out-clinic of the Faculty of Physical Therapy, Cairo University. They were under medical control and supervision. Patients with any complications or received any medications that interfere with the

study were excluded. Each patient signed a written informed consent. The patients were assigned into two equal groups:

Group-I: Fifteen patients (8 males and 7 females) received the oral hypoglycemic drugs and participated in a supervised treadmill exercise program with moderate intensity (score 12-14 on Borg scale) of rate of perceived exertion (RPE) for 30 minutes, 3 times per week, for 8 weeks. RPE is generally believed to be a valid and reliable marker of physiological intensity during exercise and is recommended to monitor exercise intensity[7] .

Group-II: Fifteen diabetic patients (8 males and 7 females) received only the oral hypoglycemic drugs.

II – Equipment

A) Evaluation equipment

- Disposable plastic syringes were used to draw venous blood samples. Polypropylene tubes with EDTA were used to keep blood samples.
- Centrifuge was used to separate serum from plasma. Analyzing chemicals and commercial kits were used to measure nitric oxide.
- Spectrophotometer (Assay Design, Inc. Ann Arbor. MI No.48108 USA) was used for estimation of nitric oxide.
- Standard weight and height scale (floor type, Health Scale, made in China) was used to determine patient weight and height to calculate body mass index (BMI) for every patient.

B) Treatment equipment: Electronic treadmill (Enraf Nonius, made in Holland) was used for exercise training.

III– Procedures

A. Evaluation: A complete history and physical examination were taken for every patient. Each patient underwent the following measurements before and after the study.

I. Laboratory Investigations: Three milliliters of venous blood were drawn from the anti-cubital vein of each patient and control subject before and after the study to determine nitric oxide, fasting and post-prandial blood glucose levels.

II. Calculation of BMI: The weight and height were measured for each patient using weight and height scale, then the BMI (kg/ m^2) was calculated. Obese patients with BMI>30 kg/ m^2 were excluded.

B. Study Program

Group-I: Fifteen diabetic patients participated in a supervised treadmill exercise training program. They practiced exercise with moderate intensity (score 12-14 on Borg scale of RPE) for 30 minutes, three sessions per week, for 8 weeks in addition to the oral hypoglycemic drugs. The training program consisted of three phases which are:

1. Warm-up: Every patient started each session with a lowest speed on the treadmill for 5 minutes to enhance patient performance by facilitating the circulatory adjustment and minimizing the formation of lactic acid.

2. Stimulus: After warming-up the speed of the treadmill was increased to achieve the score 12-14 on Borg scale for 20 minutes per session for each patient. The treadmill inclination

was fixed at 0% grade during the program so the intensity of the exercise can be increased or decreased only by changing the speed of the treadmill.

3. Cool-down: The speed of the treadmill was reduced gradually for 5 minutes to prevent the pooling of the blood in the lower extremities and orthostatic hypotension.

Group-II: Fifteen diabetic patients received only the oral hypoglycemic agents.

Statistical Analysis: The collected data were statistically analyzed by using **Paired "t" test** to determine the significant difference within each group. **Independent "t" test** to compare the significant difference of group-I with group-II. **Correlation test** was done to detect the relation between nitric oxide level and the blood glucose level in diabetic patients. P<0.05 is considered significant

RESULTS

1- The characteristics of the subjects

This study was carried out on thirty type 2 diabetic patients and another thirty non-diabetic healthy control subjects. The disease duration of patients was (4.12±1.64) years. There were non-significant differences in regarding to age, sex and BMI. There was significant reduction in nitric oxide level in diabetics (15.59±1.52) than control subjects (23.3 ± 1.99) **(P = 0.000)** table (1).

Table (1): The characteristics of the patients and control subjects

Variables	Control subjects	Diabetic patients	P- value
Age	48.17 ± 5.21	47.4±3.86	NS (P>0.05)
Sex M : F	16 : 14	16 : 14	NS(P>0.05)
BMI (kg/ m^2)	27.08 ± 1.77	28.14 ± 1.1	NS (P>0.05)
NO (µmol/L)	23.3 ±1.99	15.59 ± 1.52	0.0000* (HS)

*M: male, F: female, BMI: body mass index, NO: nitric oxide, NS: non significant, HS: highly significant**

Nitric oxide levels were negatively correlated to the blood glucose levels (fasting & PPBG) in diabetic patients (r = –0.57 & -0.49; P = 0.008 & 0.01 respectively). This means that the higher the blood glucose levels the lower the nitric oxide levels table 2.

Table (2) the correlation between NO and blood glucose levels in diabetic patients:

Parameters	NO (µmol/L)	
	r	P-value
FBG (mg/dl)	-0.57	0.008
PPBG (mg/dl)	-0.49	0.01

2- The comparison between both groups (I, II) at the beginning of the study:

The patients were divided into two equal groups **Group-I** and **Group-II.** Before the study there were non-significant differences between them in regarding to age, BMI, duration of the disease, fasting and post-prandial blood glucose and nitric oxide levels table 3, fig. (1).

Table (3): Comparison between group I and group II at the beginning of the study.

Variables	Group-I mean ±SD	Group-II mean ±SD	P- value
Age (Years)	47.4±3.86	47.87±4.24	**0.76 (NS)**
BMI(kg/ m^2)	28± 0.9	27.93±1.15	**0.46 (NS)**
Duration of disease (years)	4.29 ± 1.7	3.9 ± 1.59	**0.42 (NS)**
FBG (mg/dl)	163.93 ± 35.15	159.9 ± 41.09	**0.776 (NS)**
PPBG (mg/dl)	188.87 ± 40.82	183.2 ± 45.97	**0.724 (NS)**
NO (µmol/L)	15.67 ± 1.39	15.51 ± 1.68	**0.779 (NS)**

SD: Standard deviation, BMI: Body Mass Index, FBG: fasting blood glucose PPBG: post-prandial blood glucose, NO: nitric oxide, NS: non significant

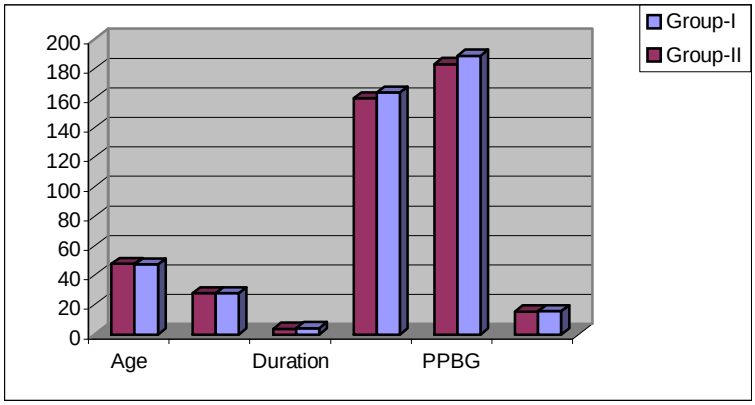

Figure1 comparison between group-I and group-II at the beginning of the study

3- The comparison between both groups (I, II) at the end of the study:

There were significant reductions in the fasting blood glucose levels (FBG) in group-I after exercise than group-II (P=0.049). There was a non significant reduction in the post-prandial blood glucose levels in group-I after exercise training than group-II (P= 0.089). There were highly significant increases in nitric oxide levels in group-I after exercise (P=0.000) table (4).

Table (4): comparison between group I and II at the end of the study.

Variables	Group-I mean ±SD	Group-II mean ±SD	P- value
FBG (mg/dl)	137.67 ± 26.38	160.87 ± 34.85	**0.049 (S)**
PPBG (mg/dl)	157.27 ± 24.38	176.47 ± 34.42	**0.089 (NS)**
NO (µmol/L)	22.08± 1.8	15.35±1.683	**0.000*(HS)**

FBG: fasting blood glucose, PPBG: post-prandial blood glucose, NO: nitric oxide
*.S: significant, NS: non significant, HS: highly significant**

The mean value of nitric oxide in group-I pre exercise training was (15.67 ± 1.39) µmol/L. It increased significantly after exercise training to (22.08 ± 1.80) µmol/L. P <0.05 table 5, while the mean value of nitric oxide in group-II was (15.51±1.68) µmol/L before the study and became (15.35±1.683) µmol/L at the end of the study without significant difference (P=0.779) table 5 figure. (2).- Group-I showed significant reductions in the fasting and post-prandial blood glucose levels after exercise P-value = (0.028 and 0.016) respectively. There were non-significant differences in group-II, before and after the study in regarding to fasting and post-prandial blood glucose levels (P= 0.95 & 0.65) respectively table 5.

Table 5: The mean values of group I and II pre and post the exercise

Variables	Group-I (pre-ex)	Group-I (post ex)	Group-II (pre)	Group-II (post)
	mean ±SD	**mean ±SD**	**mean ±SD**	**mean ±SD**
FBG (mg/dl)	163.93 ± 35.15	137.67 ± 26.38	159.9 ± 41.09	160.87 ± 34.85
P- value	**0.028 (S)**		**0.95 (NS)**	
PPBG (mg/dl)	188.87 ± 40.82	157.27 ± 24.38	183.2 ± 45.97	176.47 ± 34.42
P- value	**0.016(S)**		**0.65 (NS)**	
NO (µmol/L)	15.67 ± 1.39	22.08± 1.8	15.51 ± 1.68	15.35±1.683
P- value	**0.00(HS)***		**0.79 (NS)**	

*.S: significant, NS: non significant, HS: highly significant**

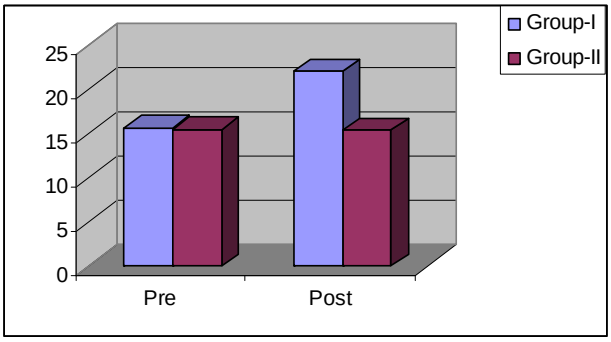

Fig (2): The mean values of nitric oxide of group-I and II pre and post study

4- The Comparison of NO levels among three groups at the end of the study

The mean value of nitric oxide of group-I increased after exercise and approached to the level of NO of control subjects without significant difference **(P=0.052),** while this didn't occur in group -II at the end of the study P=0.00 table (6).

Table 6: the Comparison of NO levels among group I, II and control subjects at the end of the study

Variables	Group-I (post -ex) mean ±SD	Control subjects mean ±SD	Group-II (post-study Mean ±SD
NO (µmol/L)	22.08± 1.8	23.3 ±1.99	15.35±1.683
P- value (group I vs. control)	**0.052 (NS)**		
P -value (group II vs. control)		**0.000 (S)**	

NS: non significant, .S: significant

DISCUSSION

Abnormal vascular endothelial function and atherosclerosis are prominent features of diabetes mellitus[36]. The patho-physiology of vascular disease in diabetes involves abnormalities in vascular endothelium, vascular smooth muscle cells, and platelet function. The metabolic abnormalities that characterize diabetes are hyperglycemia, increased free fatty acids, and insulin resistance. Each one provokes molecular mechanisms that contribute to vascular dysfunction and decreased nitric oxide (NO) bioavailability[33] **.**

In the current study, it was found that nitric oxide levels were significantly lower in diabetic patients than non-diabetic subjects **(P=0.00)**. These were supported with previous data indicating that vessels of diabetic patients show marked abnormalities in endothelial function characterized by reduced NO bioactivity[19,5]**.** Evidence from experimental studies suggests that increased superoxide production accounts for a significant proportion of the NO deficit in diabetic vessels. In addition to NO scavenging, superoxide may alter the activity and regulation of endothelial NO synthase activity in endothelial cells[35,42]**.** Insulin stimulates NO production from endothelial cells by increasing the activity of Nitric Oxide Synthase (NOS) [30]**.** Type 2 diabetes mellitus is characterized by insulin resistance and depressed endothelial function[28]**.**

From this study nitric oxide levels were negatively correlated with the blood glucose levels, so more hyperglycemia was associated with lower nitric oxide levels and more endothelial dysfunction. Several hypotheses explained the adverse effects of hyperglycemia on the vasculature. High concentrations of glucose have been shown to be associated with endothelial dysfunction. Mechanisms underlying this endothelial dysfunction could include a decreased activity and/or expression of NOS III or an increased

degradation of NO secondary to an enhanced superoxide production[9,22]. Formation of AGEs results in decreased expression of endothelial NO Synthase (NOS) and reduced generation of NO[40].

Nitric oxide is an important hemodynamic and metabolic regulator during the performance of physical activity. There are adaptations in this system in response to exercise training to increase the functional capacity and the cardio-protective effects. Exercise has a particular efficacy in restoring dysfunction of the vascular endothelial NO system [38]. These results proved that treadmill exercise program with moderate intensity for 30 minutes, three days per week, for 8 weeks significantly increased the concentration of nitric oxide from (15.67 ± 1.39) to (22.08 ± 1.80).

Many studies demonstrated positive effect for exercise on endothelial functions in patients and healthy subjects. But there is little information about the effects of aerobic exercise training on NO in adults with type 2 diabetes[43]. In recent study the investigators found that a two times/week for 6-months of progressive aerobic-training is associated with improvement of endothelial function in overweight, non-smoking, old type 2 diabetic individuals [43].

Results of current study came in agreement with previous studies [25, 16]. The exercise training by ergometer on healthy young subjects at 70% of VO2max for 1 hour, 3-4 days/week for 8 weeks significantly increased plasma concentration of NO[25]. In addition twelve weeks of moderate-intensity ergometer exercise significantly augmented acetyl-choline-induced vasodilatation through increased production of nitric oxide in the forearm blood flow in healthy subjects[16,2]. Exercise training increases NO production, enhances antioxidant enzyme levels, and ameliorates endothelial dysfunction in hypertensive patients[39]. The forearm blood flow increased significantly by physical exercise for 12 weeks for 30 minutes of brisk walking; 5 to 7 times per week in patients with mild essential hypertension. This finding suggests that long-term physical exercise improves endothelium-dependent vaso-relaxation through the release of nitric oxide in normal as well as hypertensive subjects[21]. In addition supine ergometer exercise stimulates the release of NO in patients with effort angina.[34] Also twelve weeks of endurance exercise training in patients with coronary artery disease led to an improvement in endothelial function as measured by brachial artery flow-mediated dilation (7.9% at baseline vs. 11.1% at 12 weeks).[10]

Cycling exercise at 50% of maximal oxygen consumption for 30 min/day, 5 days/ week for two consecutive menstrual cycles increases endogenous NO release in patients with peripheral vascular disease [4] Also endurance-training with sub-maximal exercise test for 30 minutes at 60% of their individual maximal work capacity increased the formation of nitric oxide this may contribute to vasodilatation during physical exercise [15]. Basal production of NO increases in hyper-cholesterolemic patients in response to 4 weeks of cycling moderate

intensity whereas brisk walking improves the forearm blood flow in response to acetylcholine in hypertensive subjects by increasing vascular shear stress [31].

Recently acute exercise induced a significant increase in nitrite/nitrate plasma levels in both sedentary and active subjects and it seems that either acute exercise even for a short time training period can induce an increase in circulating NO[11]. There are some molecular mechanisms underlying the enhanced endothelial function in response to exercise. They may be due to a direct effect of exercise on the vasculature by generating a recurrent intermittent increase in shear stress, a well known physiological stimulus to NO bioactivity, increased expression of endothelial NOS and enhanced antioxidant enzyme levels [12,17,26,39].

Acetylcholine may represent another mechanism mediating NO-dependant dilation during physical activity. The neuromuscular junction of motor nerves that synthesize, store and release Ach may represent a physiological source of acetylcholine during exercise that stimulates endothelial release of NO, triggering vaso-relaxation and increased blood flow[14]. It was found that short-term exercise- increased endothelial NO synthesis in skeletal muscle arterioles and increased the vasodilator responses to acetylcholine and L-arginine [15,26]. It was found that two bouts of lower limb exercise separated by a 30-min recovery increased systemic production of NO during exercise even in resting vessel beds which was not directly involved in the exercise stimulus[18]

On the other hand, results of this study contradicted with some previous studies [29,27]. Some investigators reported that 8 weeks of supervised circuit training with moderate intensity in 19 healthy men did not significantly affect endothelium-dependent function[29]. This may be due to the impairment of NO-related endothelial function in diabetic patients. The individuals with impaired endothelial function appear to be more sensitive to exercise training than healthy individuals[20,27]. In this study, there was significant reduction of blood glucose levels (both FBG & PPBG) after exercise in spite of unchanging the medical treatment. This improvement of hyperglycemia may be a possible contributor to the improved endothelial dysfunction and NO production in the exercised group[8].

Conclusion: Treadmill exercise with moderate intensity increases production of nitric oxide (improves endothelial function) in type 2 diabetic patients so it was recommended to be applied for those patients in addition to the medical treatment to protect them against cardiovascular complications.

REFERENCES

1. **American Diabetes Association (2006)**: Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 29:S43-S48.
2. **American Heart Association (2003):** Effect of different intensities of exercise on endothelium-dependent

vasodilatation in humans. Diabetes Care 30: 49-54.

3. **Andrew J. (2006):** Biological chemistry of nitric oxide as it pertains to the extra pulmonary effects of inhaled nitric oxide. The American Thoracic Society, 3:150-152.
4. **Arosio E**.; **Cuzzolin L**.; **and De Marchi S.; (1999):** Increased endogenous nitric oxide production induced by physical exercise in peripheral arterial occlusive disease patients. Life Sci., 65(26):2815-2822.
5. **Bitar MS**, **Wahid S**, **and Mustafa S, (2005)**. Nitric oxide dynamics and endothelial dysfunction in type II model of genetic diabete Eur J Pharmacol.1; 511(1):53-64s.
6. **Bonora E. and Muggeo M. (2001):** Postprandial blood glucose as a risk factor for cardiovascular disease in type two diabetes. Diabetologia, 44: 2107-2114.
7. **Borg G. (1998):** Borg's rating of perceived exertion and pain scales. Champaign, IL: Human Kinetics, pp.49.
8. **Boulé NG, Haddad E, and Kenny GP, (2001)**: Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA 286:1218–1227
9. **Cosentino F, Hishikawa K, and Katusic ZS, (1997)**. High glucose increases nitric oxide synthase expression and superoxide anion generation in human aortic endothelial cells. Circulation; 96: 25–28
10. **Edwards DG**, **Schofield RS**, **and Lennon SL**, **(2004):** Effect of exercise training on endothelial function in men with coronary artery disease. Am J Cardiol. 1;93(5):617-620
11. **Franco L.; Doria D. and Mattiucci F. (2001):** Effect of acute exercise on plasma nitric oxide level in humans. Medical principles and practice, 10(2):106-109.
12. **Fuchsjäger-Mayrl G.; Pleiner J.; and Günther F.; (2002):** Exercise training improves vascular endothelial function in patients with type 1 diabetes. Diabetes Care; 25:1795-1801**.**
13. **Ganz P and Joseph A (2003):** testing endothelial vasomotor function: nitric oxide; a multipotent molecule. Circulation, 108: 2049-2055.
14. **Gielen S and Hambrecht R (2001):** Effect of exercise training vascular function and myocardial perfusion. Cardiol CLIn; 19: 357 – 368
15. **Gordon P.; Visich P.; Ehrman J. and Keteyian S. (2004):** Clinical exercise physiology," Diabetes" Chap. 8,2**nd** ed. University of California, San Francisco, P. 129-151.
16. **Goto C.; Higashi Y.; and Kimura M.; (2003):** Effect of different intensities of exercise on endothelium-dependent vasodilatations in humans: Role of endothelium-dependent nitric oxide and oxidative stress. **Circulation,** 108:530-543.
17. **Green D.; Cheetham C.; and Mavaddat L.; (2002):** Effect of lower limb exercise on forearm

vascular function: contribution of nitric oxide. Am J Physiol. Heart Circ. Physiol**.,** 283(3): H899-H907**.**

18. **Green D.; Maiorana A.; O'Driscoll G. and Roger T. (2004):** Effect of exercise training on endothelium-derived nitric oxide function in humans. J Physiol, 561(1):1-25.
19. **Guzik TJ**, **Mussa S**, **and Gastaldi D**, **(2002):** Mechanisms of increased vascular superoxide production in human diabetes mellitus: role of NAD (P)H oxidase and endothelial nitric oxide synthase. Circulation; 9;105(14):1656-1662
20. **Hambrecht R.; Wolf A.; and Geilen S.; (2000):** Effect of exercise on coronary endothelial function in patients with coronary artery disease. N Engl J Med., 342: 454–460.
21. **Higashi Y.; Sasaki S.; and Kurisu S. (1999):** Regular aerobic exercise augments endothelium-dependent vascular relaxation in normotensive as well as hypertensive subjects: role of endothelium-derived nitric oxide. Circulation, 100:1194–1202.
22. **Hink U, Li H, and Mollnau H, (2001);** Mechanisms Underlying Endothelial Dysfunction in Diabetes Mellitus. Circulation Research; 88: e14-e19.
23. **Kim JA**, **Montagnani M**, **Koh KK**, **and Quon MJ (2006)**. Reciprocal relationships between insulin resistance and endothelial dysfunction: molecular and pathophysiological mechanisms. Circulation. 18; 113(15):1888-1898.
24. **Lapolla A, Piarulli F, and Sartore G, (2007):** Advanced glycation end products and antioxidant status in type 2 diabetic patients with and without peripheral artery disease. Diabetes Care; 30(3):670-676.
25. **Maeda S.; Miyauchi T.; and Kakiyama T.; (2001):** Effects of exercise training of 8 weeks and detraining on plasma levels of endothelium-derived factors, endothelin-1 and nitric oxide, in healthy young humans. Life Sciences, 69: 1005-1016.
26. **Maeda S.; Tanabe T.; and Otsuki T.; (2004):** Moderate regular exercise increases basal production of nitric oxide in elderly women. Hypertens Res., 27(12):947-953.
27. **Maiorana A., O'Driscoll G., and Dembo L. (2000):** Effect of aerobic and resistance exercise training on vascular function in heart failure. Am J Physiol., 279: H1999–H2005.
28. **Maiorana A., O'Driscoll G., and Cheetham C.; (2001) a:** Effect of combined aerobic and resistance exercise training on vascular function in type 2 diabetes. J Am Coll Cardiol., 38:860-866.
29. **Maiorana A., O'Driscoll G., and Dembo L.; (2001) b:** Exercise training, vascular function, and functional capacity in middle-aged subjects. Med Sci Sports Exerc, 33(12):2022-2028.
30. **Montagnani M.; Golovchenko I.; and Kim I, (2002):** Inhibition of phosphatidylinositol 3-kinase

enhances mitogenic actions of insulin in endothelial cells. J Biol Chem., 277: 1794–1799.

31. **Moyna N. and Thompson P. (2004):** The effect of physical activity on endothelial function in man. Acta Physiol Scand., 180:113–123.
32. **Muniyappa R**, **Montagnani M**, **Koh KK**, and **Quon MJ (2007)**. Cardiovascular Actions of Insulin. Endocr Rev. 24; [Epub ahead of print]
33. **Nesto R. and Rutter M. (2002):** Impact of the atherosclerotic process in patients with diabetes. Acta Diabetol, 2:S22-S28.
34. **Node K.; Kitakaze M.; and Sato H; (1998):** Increased release of nitric oxide in ischemic hearts after exercise in patients with effort angina**.** J Am Coll Cardiol., 32(1):63-68.
35. **Peterson TE, Poppa V, and Ueba H, (1999).** Opposing effects of reactive oxygen species and cholesterol on endothelial nitric oxide synthase and endothelial cell caveolae. Circ Res.; 85: 29–37
36. **Pieper GM (1998).** Review of alterations in endothelial nitric oxide production in diabetes: protective role of arginine on endothelial dysfunction. Hypertension; 31: 1047–1060
37. **Ramesh K. and Ashok SH. (2003):** Endothelial dysfunction: many ways to correct-trends that promise. Indian Journal of Pharmacology; 35: 73-82.
38. **Richard B and Vahid-David S (2003):** Exercise and diabetes mellitus: Optimizing performance in patients who have type 1 diabetes. The physician and sports medicine, 31: 177-182
39. **Roberts C.; Vaziri N. and Barnard R. (2002):** Effect of Diet and Exercise Intervention on Blood Pressure, Insulin, Oxidative Stress, and Nitric Oxide Availability. Circulation, 106:2530-2539**.**
40. **Sampathkumar R**, **Balasubramanyam M**, **and Rema M**, **(2005):** A novel advanced glycation index and its association with diabetes and microangiopathy. Metabolism; 54(8):1002-1007.
41. **Vita J. and Keaney J. (2002):** Endothelial function: a barometer for cardiovascular risk (editorial). Circulation, 106:640–642.
42. **Wolin MS (2000).** Interactions of oxidants with vascular signaling systems. Arterioscler Thromb Vasc Biol.; 20: 1430–1442.
43. **Zoppini G**, **Targher G**, **and Zamboni C, (2006).** Effects of moderate-intensity exercise training on plasma biomarkers of inflammation and endothelial dysfunction in older patients with type 2 diabetes**.** Nutr Metab Cardiovasc Dis.; 16(8):543-549.

هل تؤثر التمرينات بجهاز المشي الكهربائي على وظائف بطانة الأوعية الدموية في مرضى النوع الثاني من البوال السكري؟

يعتبر مرض البوال السكري من أهم أمراض العصر المزمنة و التي لها كثير من المضاعفات على مختلف أعضاء الجسم و خاصة.بطانة الأوعية الدموية التى لها كثير من الوظائف و منها إنتاج أكسيد النيتريك الذي يحمي الشرايين و القلب من تصلب الشرايين و جلطات القلب

اجرى هذا البحث لمعرفة تأثير التمرينات بجهاز المشي الكهربائي على وظائف بطانة الأوعية الدموية في مرضى النوع الثاني من البوال السكري عن طريق معرفة تأثيرها على مستوى أكسيد النيتريك في الدم

أجريت هذه الدراسة على ٣٠ مريضا من مرضى البوال السكري (النوع الثاني) و ٣٠ شخصا صحيحا للمقارنة تم قياس مستوى أكسيد النيتريك في الدم لجميع المرضى في المجموعتين واشخاص المجموعة الضابطة قبل وبعد نهاية الدراسةة. ثم تم تقسيم المرضى إلى مجموعتين متماثلتين:

مجموعة (١): وتشمل ١٥ مريضا مارسوا التمرينات بجهاز المشي الكهربائي لمدة ٨ أسابيع متتالية، و شملت ٢٤ جلسة بمعدل ثلاث جلسات أسبوعيا مدة كل منها ٣٠ دقيقة، يتم أداء فترة إحماء لمدة ٥ دقائق عبارة عن تمرينات منخفضة الشدة يتبعها أداء التمرينات ذات الشدة المتوسطة باستخدام جهاز المشي الكهربائي لمدة ٢٠ دقيقة ثم تنتهي الجلسة بخمس دقائق أخرى من التمرينات منخفضة الشدة للتهدئة هذا بالإضافة إلى العلاج الدوائي.

مجموعة (٢): و تشمل ١٥ مريضا تم علاجهم بالعلاج الدوائي فقط.

أظهرت النتائج وجود نقص ذو دلالة إحصائية في مستوى أكسيد النيتريك في مرضى البوال السكري (النوع الثاني) عنه في الأصحاء . وجود زيادة ذات دلالة إحصائية في مستوى أكسيد النيتريك في مرضى المجموعة (١) بعد ممارسة التمرينات بجهاز المشي الكهربائي مما يدل على تحسن وظائف بطانة الأوعية الدموية فيهم. مع عدم وجود فروق ذات دلالة

إحصائية في مرضى المجموعة (٢) التي لم تمارس التمرينات وتم علاجهم بالعلاج الدوائي فقط

خلاصة البحث: ان مرض البوال السكري (النوع الثاني) يؤثر سلبا على وظائف بطانة الأوعية الدموية ،تحسن وظائف بطانة الأوعية الدموية في مرضى البوال السكري (النوع الثاني) بعد ممارسة التمرينات بجهاز المشي الكهربائي لذا يوصى باستخدام التمرينات بجهاز المشي الكهربائي في علاج مرضى البوال السكري (النوع الثاني) بالإضافة إلى العلاج الدوائي لمنع حدوث مضاعفات على القلب والأوعية الدموية.