Effect of Aerobic Exercise Training on Cardiovascular Responses in Type 1 Diabetic Autonomic Neuropathy

Mohamed Abdulsattar Mohammed Hemida[1]

[1] Cairo university - Egypt

Received: 6 December 2015 Accepted: 1 January 2016 Published: 15 January 2016

Abstract

Background: Diabetes Mellitus is a chronic, multifaceted disorder caused by reduction in insulin action and secretion or the both, it?s characterized by hyperglycemia and disruption of the metabolism of carbohydrates, fats and proteins, over time, it results in small and large vessels complications and neuropathies. This disease is ranked as the third cause of death and leading factor of blindness. One of the most overlooked of all serious complications of diabetes is cardiovascular autonomic neuropathy (CAN), which encompasses damage to the autonomic nerve fibers that innervate the heart and blood vessels, resulting in abnormalities in heart rate control and vascular dynamics The complications of diabetes mellitus are macro and micro vascular disorders, central, Peripheral and autonomic neuropathy. The autonomic neuropathy is the most common complication of the long standing diabetes Autonomic neuropathy is a well recognised complication of diabetes mellitus, and its incidence has been reported to be 20 - 40

Index terms— aerobic exercise, type 1 diabetes mellitus, cardiac autonomic neuropathy.

1 I. Introduction

iabetes Mellitus is a chronic, multifaceted disorder caused by reduction in insulin action and secretion or the both, it's characterized by hyperglycemia and disruption of the metabolism of carbohydrates, fats and proteins, over time, it results in small and large vessels complications and neuropathies. This disease is ranked as the third cause of death and leading factor of blindness (Boulton AJ et al 2010).

The complications of diabetes mellitus are macro and microvascular disorders, central, Peripheral and autonomic neuropathy. The autonomic neuropathy is the most common complication of the long standing diabetes, It's due to the accumulation of sorbitol in nerve cell that result in abnormal fluid and electrolyte shift, which causes nerve cell dysfunction,. Balanced cardiac ANS function is based on strong impaired cardiovascular ANS function has been associated with type 1 diabetes (T1D) (Stevens et al., 2008).

Data from the 2008 Egypt Demographic and Health Survey ??EDHS 2008) were used to show the Prevalence of diabetes for selected socio-demographic variables was calculated by gender. Prevalence of co morbid conditions, and risk factors for complications of diabetes, were estimated by gender. Health care utilization among diabetics was estimated. The crude prevalence rate of known diabetes in Egypt in 2008 was 4.07% (0.25). It increased with age, to reach 19.8% among females aged 50-59. Only 18% of males, and 7.8% of females, had a normal body mass index. 37.5% of male diabetics smoked. The prevalence of hypertension among diabetics was 75% for males, and 66.9% for females; of these, only 2% of males, and 14.3% of females, were controlled to $< 130/80$ mmHg. 13.3% of males had a history of myocardial infarction or stroke. 44.9% of males, and 80.4% of females, had no insurance coverage. More than half of diabetics visited a private physician at their last visit. 9.3% of males, and 3.8% of females, had been hospitalized in the past year. They concluded that Diabetes is highly prevalent among older persons in Egypt. Public health policy should educate the public on the risk factors for diabetes, and should implement guidelines for adequate control of this disease (Naglaa et al 2010).

Autonomic neuropathy is a well recognised complication of diabetes mellitus, and its incidence has been reported to be 20 -40%. Numerous non-invasive tests have been in use for the diagnosis of cardiac autonomic neuropathy (Ewing DJ et al 1985).

CAN, manifested as changes in HRV, may be detected within 1year of diagnosis in type 2 diabetes and within 2 years of diagnosis in type 1 diabetes (Drake-Holland AJ et al, 2006) Resting tachycardia. Resting heart rates of 100 bpm with occasional increments up to 130 bpm usually occur later in the course of the disease and reflect a relative increase in the sympathetic tone associated with vagal impairment (Young et al., 2009).

Diabetic autonomic neuropathy (DAN) is classified as subclinical or clinical depending upon the presence or absence of symptoms. A wide spectrum of symptoms affecting many different organ systems can occur, including the cardiovascular, gastrointestinal, genitourinary, pupillary, sudomotor, and neuroendocrine systems (Tesfaye S et al 2005).

One of the most overlooked of all serious complications of diabetes is cardiovascular autonomic neuropathy (CAN), which encompasses damage to the autonomic nerve fibers that innervate the heart and blood vessels, resulting in abnormalities in heart rate control and vascular dynamics (Schumer MP 1998).

Our data and those of others confirm that early in the progression of CAN complicating type 1 diabetes, there is a compensatory increase in the cardiac sympathetic tone in response to subclinical peripheral denervation, CAN may critically influence myocardial substrate utilization (Drake-Holland AJ et al, 2006) and contribute to mitochondrial uncoupling regional ventricular motion abnormalities, functional deficits, and cardio myopathy (Pop-Busui R, 2004) Aerobic exercise is a physical exercise that intends to improve the oxygen system Aerobic means "with oxygen", and refers to the use of oxygen in the body's metabolic or energy-generating process. Many types of exercise are aerobic, and by definition are performed at moderate levels of intensity for extended periods of time The two types of exercise differ by the duration and intensity of muscular contractions involved, as well as by how energy is generated within the muscle. Initially during aerobic exercise, glycogen is broken down to produce glucose, which then reacts with oxygen (Krebs cycle) to produce carbon dioxide and water and releasing energy. In the absence of these carbohydrates, fat metabolism is initiated instead (Colberg S et al., 2003).

2 II. Patients and Methods

This study was consists of fifty type 1 diabetes mellitus(IDDM)patients with autonomic neuropathy (36 males and 14 females) attended to the Outpatient Clinic in National Institute for Diabetes and Endocrine Glands. Their age ranged from 45 to 65 years with a mean value of (49 ± 7.2), height ranged from 162 to 181 cm with a mean value of (172 ± 9), and the body weight ranged from 67 to 91 Kg with a mean value of (170 ± 11). Their body mass indexes ranged from 19 to 31 Kg / m 2 with a mean value of (25 ± 3.3 Kg / m 2). The all patients under medical control by specialized physician. All patients were randomly divided into two equal groups.

The study group was twenty five (19 male and 6 female) IDDM patients with autonomic neuropathy, Who practiced aerobic exercise training with a moderate intensity from 60 to 75 % of their HR max for each patient three sessions /week for three months on an electronic treadmill for forty minutes to each session, and Control group include twenty five patients (17 male and 8 female) IDDM, all patients received their medical treatment.

Exclusion criteria: Patients with, Varicose veins, Severe ischemic heart diseases and Chest infection patients were excluded.

Before starting the study, a meeting was done for all patients to explain for all of them our study (patient information sheet PIS) and also to collect consent form of each patient and to record demographic data, fasting blood glucose, heart rate (HR) responses to valsalva maneuver, HR response to deep breathing ,HR response to change of position, systolic blood pressure (BP) response to valsalva maneuver, systolic BP response to sustained hand grip and systolic BP response to change of position. ECG machine and its accessories will be used to do stress test for each patient by attending physician and to monitor heart rate, rhythm, R-R interval and Q-T interval for each patient of both groups.

Each patient of study group was asked to perform aerobic exercise training on electronic treadmill with moderate intensity from 60 to 75 % of each individualized (HR max), three times per week for three months for forty minutes of each session, accordingly to self limiting intensity of each patient the program started with: Warming up phase; for 5 minutes on treadmill with low speed (0 watt) with horizontal line, then the speed of electronic treadmill increased to reach Active phase (Soligard et al., 2008). Stimulus phase; in which each patient of group A performed self limiting exercises on treadmill with individualized moderate intensity from 60 to 75 % of HR max . For 30 minutes (Laskowski., 2013) Cool Down phase; about 5 minutes on treadmill with low speed (Woods et al., 2007).

Data were analyzed with SPSS software version 23. The level of significance was set at P ? 0.05. Paired t-test was applied for each group to compare pre and post values within the same group. Unpaired t-test was applied to compare pre and post values between both groups of the study.

3 III. Results

Mean value of body mass index (BMI) had shown a significant improve by significantly decreased post exercise in study group (P value = 0.001) as compare to control group which increased significantly (P value = 0.047) (Table **??**). In study group The value of Q-T interval had shown significant improve after exercise (P value =

0.001) but in control group had shown significant increase in Q-T interval (P value = 0.001) (Table **??**). The reduction of Q-T interval was considered as improvement. In study group R-R interval had shown a significant improve post exercise (P value = 0.001) and no significant change in control group (Table **??**). The increment of R-R interval was considered as improvement. The mean value of fasting blood glucose was shown high significant (decrease) improve post exercise (P value = 0.000) and control group had shown significant increase (P value = 0.002) (Table **??**). The mean value of systolic blood pressure responses to (change position, sustained hand grip and valsalva Maneuver) respectively had shown significant improve after exercise (P value = 0.003) (P value = 0.000) and (P value = 0.008) respectively but in control group had shown significant increase in systolic blood pressure responses to change position, sustained hand grip (P value = 0.000) and (P value = 0.001) (Table **??**) and no significant changes in response to valsalva Maneuver) (P value = 0.098) (Table **??**).

4 IV. Discussion

In this study, The mean value of BMI was significantly decreased post exercise from (29.2400 ± 2.61852) to (27.76 ± 2.38537). The mean value of fasting blood glucose pre exercise was (137.48 ± 10.85557) and significantly reduced post exercise to (127.00 ± 5.01664). The mean value of systolic blood pressure before exercise (change position, sustained hand grip and valsalva Maneuver) were (139.36 ± 6.52482), (139.68 ± 6.10137) and (137.60± 6.45497) respectively which were significantly changed after exercise by decreasing to (change position, sustained hand grip and valsalva Maneuver) (134.80 ± 5.50757), (134.16 ± 5.91383) and (134.24± 5.84009) respectively. The mean values of the heart rate responses to (change position, Deep breathing and valsalva Maneuver) were (98.36 ± 7.65876), (92.68 ± 6.47251) and (80.12 ± 4.04475) respectively, That were significantly decreased post exercise to (93.96 ±5.78417), (88.56 ± 5.61308) and (76.32 ± 4.75850) respectively. The value of Q-T interval pre exercise was (448.88 ± 47.39666). and significantly reduced post exercise to (414.68 ± 45.37503) (Table **??**0). The reduction of Q-T interval was considered as improvement. R-R interval pre exercise was (487.60 ± 53.32448) and significantly increased post exercise to (599.12 ± 49.92438), The increment of R-R interval was considered as improvement.

Results of this study were supported by Neil J et al 2006, who studied the Differences among the effects of aerobic, resistance, and combined training on HbA 1c (A1C) were trivial for training lasting in diabetic patients. There were generally moderate benefits for other measures of glucose control. For other risk factors, although combined training was generally superior to aerobic and resistance training. but there were small additional benefits of exercise on glucose control with increased disease severity. They concluded that All forms of exercise training produce benefits in the main measure of glucose control: A1C. The effects are similar to those of dietary, drug, and insulin treatments. These results were supported by **??**homas H et Improvement of FBG can be explained by several mechanisms as exercise training improve impairment of the muscular glucose transport protein system and the decreased of enzymatic activity, which regulate storage and oxidation of glucose in the skeletal muscle (Ebeling et al;. Also exercise training increase the conversation of low oxidative type (II a) fibers that have a greater capillary density and high concentration of the muscle glucose transport system that make them exhibit a greater response to insulin action than type (II b) fibers (Ivy, 1997).

In this study The value of Q-T interval pre exercise was (448.88 ± 47.39666). and significantly reduced post exercise to (414.68 ± 45.37503).The reduction of Q-T interval was considered as improvement. R-R interval pre exercise was (487.60 ± 53.32448) and significantly increased post exercise to (599.12 ± 49.92438), The increment of R-R interval was considered as improvement. Mathur et al 2006 said that QTc prolongation in diabetic subjects stands favourably as an autonomic dysfunction parameter as compared to other autonomic neuropathy function test (ANF) tests. Further, QTc prolongation has linear positive correlation with the degree of CAN. It is inferred from the present observations that QTc prolongation in diabetics with an otherwise normal heart can be used as a diagnostic test for assessment of cardiac autonomic neuropathy and may even be considered as a cardiac autonomic function test with prognostic significance. These results were supported by Veglio et al;(2000) who assessed the relationship between QT interval prolongation and mortality in type 1 diabetic patients. Data on survival after 5 years were obtained from 316 of 379 patients (83.3%) who took part in a study on the prevalence of diabetic neuropathy and QT interval prolongation. They found that mortality at 5 years was 6.32%, patients who survived were significantly younger, had a shorter duration of diabetes, had lower systolic and diastolic blood pressure levels, and had a shorter QT interval corrected for the previous cardiac cycle length (QTc) than subjects who died. In univariate analysis, patients had a higher risk of dying if they had a prolonged QTc or if they were affected by autonomic neuropathy. QTc prolongation was the only variable that showed a significant mortality they concluded that the first cohortbased prospective study indicating that QTc prolongation is predictive of increased mortality in type 1 diabetic patients.

As Oka et al, (1996) had attempted to clarify the relationship of Q-T interval to alpha and beta sympathetic, as well as, parasympathetic function tests including spectral analysis of R-R interval and systolic blood pressure. Q-T interval in 76 diabetic patients and 76 ages matched healthy control whose R-R interval was comparable. They also investigated the relationship of Q-T interval to various clinical features of diabetes mellitus and to autonomic function tests, Q-T interval in diabetic patients was significantly greater than in healthy control, but were prolonged in patients with long duration of disease as compared with short duration one. There were a significant correlation between Q-T interval and postural hypotension, also between Q-T interval and both high and low frequency component of spectral analysis of R-R interval, whereas, no relation was observed with spectral analysis and systolic blood pressure. An abnormal Q-T interval is an indicator of cardiac sympathetic and parasympathetic nervous dysfunction, but not vasomotor dysfunction.

On the other hand, Laptev DN et al 2012 Studid effect of graded physical exercise on glycemia level and interval QT duration in children and adolescents with type 1 diabetes mellitus. they found that there were two periods of significant and prolonged lowering of glycemia: in 120-420 min and 19-21 hours after exercise. Lowering of glycemia after physical exercise was associated with prolongation of QT interval. Also Zravenboer et al, (1993) investigated the corrected QT interval as a test for diagnosing autonomic dysfunction in 60 type I diabetic patients with proven peripheral neuropathy, Significant increase in QTc interval was observed after dynamic exercise, however, no change in QTc was observed following static exercise, and hence we conclude that static exercises may not be useful in assessing the cardiovascular status of an individual or in predicting cardiovascular events. they concluded that the corrected QT interval should not be used for the diagnosis of the severity of diabetic autonomic neuropathy. The result of study of Suarez GA et al 2005 came in contradict with our result, they studied the relationship between cardiac autonomic neuropathy (CAN) and major cardiovascular events in 2 prospective studies. Specifically, the relationship between baseline CAN and the subsequent incidence of a fatal or nonfatal cardiovascular event, defined as an myocardial infarction MI, heart failure, resuscitation from ventricular tachycardia or fibrillation, angina, or need for coronary revascularization, was examined. The relative risks associated with CAN in these studies were 2.2 and 3.4, respectively, with the latter result just achieving statistical significance ($P<0.05$). There seems to be an association between CAN and major cardiovascular events, but given the small number of events that occurred in each of these studies, The significance of CAN as an independent cause of sudden death has, however, been questioned recently. They suggested that although CAN could be a contributing factor, it was not a significant independent cause of sudden death. Heart failure is, however, common in individuals with diabetes; it is identified in these patients by the presence of neuropathy, even in those without evidence of coronary artery disease or LV dysfunction. Several long-term studies have demonstrated a consistent beneficial effect of regular exercise training on carbohydrate metabolism and insulin sensitivity, which can be maintained for at least 5 years. These studies used exercise regimens at an intensity of 50-80% Vo 2max three to four times a week for 30-60 min a session. Improvements in HbA 1c were generally 10-20% of baseline and were most marked in patients with mild type 2 diabetes and in those who are likely to be the most insulin resistant. It remains true, unfortunately, that most of these studies suffer from inadequate randomization and controls, and are confounded by associated lifestyle changes. Data on the effects of resistance exercise are not available for type 2 diabetes although early results in normal individuals and patients with type 1 disease suggest a beneficial effect. It now appears that long-term programs of regular exercise are indeed feasible for patients with impaired glucose tolerance or uncomplicated type 2 diabetes with acceptable adherence rates. Those studies with the best adherence have used an initial period of supervision, followed by relatively informal home exercise programs with regular, frequent follow-up assessments. A number of such programs have demonstrated sustained relative improvements in Vo 2max over many years with little in the way of significant complications.

Takebayashi K et al 2002 concluded that QTc intervals showed a significant positive correlation with systolic and diastolic blood pressure although it did not correlate with serum lipid concentrations. QTc also tended to be long in obese diabetic subjects (body mass index > 25 and QTc intervals might also be affected by other factors such as arteriosclerotic macroangiopathy and obesity, and not only autonomic nerve function. Therefore it might be considered as an overall index for complications, and not for pure autonomic impairment.

In this study The mean value of systolic blood pressure before exercise (change position, sustained hand grip and valsalva Maneuver) were (139.36 ± 6.52482), (139.68 ± 6.10137) and (137.60 ± 6.45497) respectively which were significantly improved after exercise by decreasing to (change position, sustained hand grip and valsalva Maneuver) (134.80 ± 5.50757), (134. 16 training is an effective method to lower blood pressure and improve other cardiovascular risk factors. Our result were supported by Jamie F. Burr 2012 who concluded that Aerobic exercise has significant and particular benefits for people with type 1 diabetes. It increases sensitivity to insulin, lowers blood pressure, improves cholesterol levels, and decreases body fat. patients with type 1 diabetes who are physically more active have a lower overall risk of cardiovascular events than their sedentary counterparts. Also Gail and Francis, (1984) concluded that physical exercise training altered the cardiovascular responses to exercise training as decreased heart rate and pressure load on myocardium. Also Gert-van-Dijket al (1994) confirmed that aerobic exercise training is currently promoted as life style modification that lowers the resting BP especially in persons with elevated BP, it was supported with that the dynamic exercise training reduces resting SBP and DBP by approximately 3%and 4 % respectively. On the other hand Campainge and Lampman, (1994) found that patients with type 2DM displayed a greater SBP in response to exercise training. Also Donckier et al; found that in cardiac autonomic neuropathy there was increasing of SBP in response to exercise training. found that patients with cardiac autonomic neuropathy have severely exaggerated increase in SBP and DBP. Also Bottini et al; found that in diabetic autonomic neuropathic patients, SBP was significantly increased in response to exercise training. Pamella Karoline et al concluded that a single session of aerobic exercise resulted in 24 h BP reductions in individuals with T2D, also **??**015 Radice et al; found that in diabetic autonomic neuropathic patients in response to exercise training there was no significant difference in blood pressure either at rest or at peak of exercise training between diabetic patients with autonomic neuropathy and diabetic patients without autonomic neuropathy and during exercise training diabetic patients showed lower values of SBP and DBP. Agreed with these results, Thomas H et al 2009 who said that both aerobic and resistance training have important roles in DM. Recent work comparing the individual and combined effects of aerobic and/or resistance training revealed that both forms of exercise were equally beneficial for glycemic control, although aerobic training had a greater effect on body composition (except with regard to increasing muscle cross-sectional area). Caution should be used when interpreting these results given double the volume of exercise performed in the combined training. It is recommended that patients with Type 2 Diabetes Mellitus (T2DM) perform both aerobic and resistance training. They concluded that Exercise training in patients with T2DM is feasible, well tolerated, and beneficial to improve cardiovascular risk. It is recommended that patients with T2DM accumulate a minimum of 150 minutes per week of at least moderateintensity and/or 90 minutes per week of at least vigorous-intensity cardiorespiratory exercise.

The mean values of the heart rate responses to (change position, Deep breathing and valsalva Maneuver) were (98.36 ± 7.65876), (92.68 ± 6.47251) and (80.12 ± 4.04475) respectively, That were significantly decreased post exercise to (93.96 ± 5.78417), (88. 56 Sheri Colberg 2013 said that if cardiac autonomic neuropathy (CAN) is present, the heart rate response is abnormal at rest, when standing, and when during strain related to holding the breath (Valsalva maneuver). Blood pressure responses can be abnormal when changing positions or performing isometric exercise. Moreover, the potential for exercise-related dehydration is a concern, as is impaired thermoregulation during activities in environmental extremes, and extra fluids may need to be consumed to protect against both dehydration and hyperthermia. Care must be taken with all components of the exercise prescription. In addition to developing a safe exercise prescription and considering exercise precautions for those with autonomic neuropathy, attention must be given to factors that will assist patients in maintaining a regular physical activity program. Marrero and Size more have developed the Ease of Access Index and Ease of Performance Index to help patients determine how realistic their activity selections are **??**Marrero DGet al 1996).

Aaron I. Vinik et al 2003 concluded that, knowledge of early autonomic dysfunction can encourage patient and physician to improve metabolic control and to use therapies such as ACE inhibitors and ?-blockers, proven to be effective for patients with CAN.

The insulin sensitivity, lipid profile, blood pressure, coagulation properties, body composition, and psychological well be improved in diabetic patients by aerobic exercixses (Mayer et al; 1998).

Scognamiglio et al; (1995) they investigated role of myocardial contractility recruitment in determining an abnormal left ventricular response to isometric and isotonic exercise in 14 diabetic patients with autonomic neuropathy (A.N), they studied left ventricular and myocardial functions at rest and during exercise by twodimensional echocardiography, they excluded ischeamic heart diseases by the absence of left ventricular wall motion abnormalities induced by exercises and by coronary angiography, they found that there was an abnormal response of left ventricular ejection fraction to isometric and dynamic exercise in these patients.

Bottini et al; (1995) investigated cardiovascular and plasma catecholamine response during incremental exercise and recovery in diabetic patients with and without autonomic neuropathy, all the patients underwent a submaximal or symptom limited incremental exercise test using a cycle ergometer, air flow and respiratory gases fractions were sampled at the level of the mouth allowing a breath-by-breath analysis of oxygen consumption (VO 2max), the heart rate and systolic blood pressure were recorded and venous samples were obtained from the patients at rest and during each minutes of exercise and recovery to measure to measure epinephrine and nor-epinephrine plasma level, the heamodynamic parameters and plasma catecholamine were completed at rest and at 25, 50, 75 and 100 % of the peak of (VO 2max) , they found that during exercise heart rate, systolic blood pressure, nor-epinephrine, and epinephrine increase was different among diabetic groups being significantly blunted in diabetic patients with autonomic neuropathy. (Lampman, 1991) said that Physical activity has the potential to yield several health benefits for people with diabetes. These benefits can include improvements in glucose control

5 V. Conclusion

The result of this study support the importance of using exercise training program as general and especially walking training for IDDM with autonomic neuropathy.

The aerobic exercise training has a positive effect on blood glucose level, heart rate, blood pressure, R-R interval and Q-T interval in IDDM patients with autonomic neuropathy. So the exercise training generally should be recommended as a protective factor against the major risk factors. [1]

Figure 1: F

(

Variables	Study group			Control group			P value for both groups after program
	Pre program	Post program	P Value	Pre program	Post program	P Value	
	Mean ±SD	Mean ±SD		Mean ±SD	Mean ±SD		
BMI	29.2 ± 2.6	27.7 ± 2.3	0.001 S	28.8±1.7	29.2±1.8	0.047	0.018 S
Q T interval	448.8 ± 47.3	414.6 ± 45.3	0.001 S	426.2±34.8	450.4±39.3	0.001	0.023 S
R R interval	487.6 ± 53.3	599.1 ± 49.9	0.001 S	613.6±71.1	574.0±84.4	0.14	0.207
Fasting Blood Glucose	137.4 ± 10.8	137.4 ± 5.0	0.000 S	129.0±6.9	135.6±8.8	0.002	0.001 S

SD=Standard Deviation, Significant level: P?0.05 S.

Figure 2: Table (1

(

in study group the mean values of the heart rate responses to (change position, Deep breathing and valsalva Maneuver) had shown significant improve post exercise (P value = 0.000), (P value = 0.000) and (P value = 0.001) respectively and in control group had shown significant increase in heart rate responses t change position (P value = 0.009), Deep breathing value = 0.026), and no significant changes in heart responses to valsalva Maneuver (P value = 0.098) (Table 3).

Year 2016 Volum XVI Issue Version I D D I D) F (

Variables	Study group			Control group			P value for both groups after progra
	Pre program	Post program	P Value	Pre program	Post program	P Value	
	Mean ±SD	Mean ±SD		Mean ±SD	Mean ±SD		
systolic B P response to change position	139.3 ± 6.5	134.8 ± 5.5	0.003 S	137.7± 7.6	143.7± 6.4	0.000 S	0.000 S
systolic B P response to sustained Hand Grip	139.6 ± 6.1	134.1 ± 5.9	0.000 S	138.4± 6.8	142.9± 7.1	0.001 S	0.000 S
systolic BP response to valsalva maneunver	137.6 ± 6.4	134.2 ± 5.8	0.008 S	134.4± 8.5	136.7± 5.6	0.098	0.135

SD=Standard Deviation, Significant level: P?0.05 S.

Figure 3: Table (2

(

Variables	Study group			Control group			P valu
	Pre program	Post program	P Value	Pre program	Post program	P Value	for b group after progr
	Mean ±SD	Mean ±SD		Mean ±SD	Mean ±SD		
Heart Rate response to change position	98.3±7.6	93.9±5.7	0.000 S	98.3± 6.7	101.6 ± 2.7	0.009 S	0.001 S
Heart Rate response to Deep Breathing	92.6±6.4	88.5±5.6	0.000 S	84.2 ± 6.7	86.7 ± 6.1	0.026 S	0.005 S
Heart Rate response to valsalva maneunver	80.1±4.0	76.3±4.7	0.001 S	87.8 ± 1.6	86.8± 4.7	0.098	0.001 S
SD=Standard Deviation, Significant level: P?0.05 S							

Figure 4: Table (3

Also result of Anna Chudyk et al 2011 supporeted our result who said that 645 articles retrieved, 34 met our

inclusion criteria; most investigated aerobic exercise alone, and 10 reported combined exercise training.

Aerobic alone or combined with resistance training (RT) significantly improved HbA 1c ?0.6 and ?0.67%, respectively (95% CI ?0.98 to ?0.27 and ?0.93 to ?0.40, respectively), systolic blood pressure (SBP) ?6.08 and ?3.59 mmHg, respectively (95% CI ?10.79 to ?1.36 and ?6.93 to ?0.24, respectively), and triglycerides ?0.3 mmol/L (95% CI ?0.48 to ?0.11 and ?0.57 to ?0.02, respectively). Waist circumference was significantly improved ?3.1 cm (95% CI ?10.3 to ?1.2) with combined aerobic and resistance exercise. they concluded that Aerobic exercise improves glycemic control, SBP, triglycerides, and waist circumference in diabetic patients. Hordern M D et al 2009 proved that resisted exercise training for 6 weeks significantly increased rate of glucose disposal and insulin sensitivity in sedentary NIDDM patients, they concluded that discrepancy of blood
?12 weeks,

Figure 5:

Year 2016
Volume XVI Issue 1 Version I
D D D D) F
(

Figure 6:

exercised on bicycle, there was an increase in HR and can be used as a preventive measure in patients who

SBP, they concluded that increasing in resting work are at risk of developing cardiovascular diseases due to

product and decrease cardiac output in response to obesity.

exercise training program in diabetic patients due to

decrease parasympathetic activity, While Bottini et al;

(1995) found that diabetic autonomic neuropathy in

response to exercise training program there was a

significant increase in HR. Also Irace et al; (1991) found

a significant increase in HR in response to exercise

training program and higher in diabetic autonomic

Volume XVI Issue 1 Version I Year 2016 (D D D D) F

± 5.61308) and (76.32 ± 4.75850) respectively This improvement of hemodynamic responses come in agreement of Alsayd et al, (1999) he found decreasing in resting HR after moderate aerobic exercise training on treadmill for 6 weeks in NIDDM patients. Also Kahn et al; (1986) found that during exercise training program of diabetic cardiac autonomic neuropathy patients there were lower resting HR, although cardiac autonomic neuropathy have higher resting HR. Wiese et al; (1990) studied heart rate variability (HRV) in diabetic patients with and without autonomic neuropathy in response to orthostatic load and found significant lower in HRV in diabetic patients with autonomic neuropathy. Also Clarie and David (1981) found that strengthening exercise training program for 6 months significantly decreased HR. Gail and Francis, (1984) reported that exercise training program was associated with cardiovascular impairment. This was supported with reducing the HR after the exercise training program. On the other hand, Oka et al; (1995) found that in diabetic with mild autonomic neuropathy the R-R of low frequency component wasn't different from those of healthy of different intensities of aerobic exercise on 24-hour blood pressure (BP) responses in individuals with type 2 diabetes mellitus (T2D) and prehypertension. [Subjects and Methods] Ten individuals with T2D and prehypertension (55.8 ± 7.7 years old; blood glucose 133.0 ± 36.7 mg?dL ?1 and awake BP 130.6 ± 1.6/ 80.5 ± 1.8 mmHg) completed three randomly assigned experiments: non-exercise control (CON) and exercise at moderate (MOD) and maximal (MAX) intensities. Heart rate (HR), BP, blood lactate concentrations ([Lac]), oxygen uptake (VO 2), and rate of perceived exertion (RPE) were measured at rest, during the experimental sessions, and during the 60 min recovery period. After this period, blood pressure was monitored for 24 h. thier results indicate that [Lac] (MAX: 6.7±2.0 vs. MOD: 3.8±1.2 mM), RPE (MAX: 19±1.3 vs. MOD: 11±2.3) and VO 2 peak (MAX: 20.2±4.1 vs. MOD: 14.0±3.0 mL?kg ?1 ?min ?1) were highest following the MAX session. Compared with control group, only MAX single session of aerobic exercise resulted in 24 h BP reductions in individuals with T2D, especially while sleeping, and this reduction seems to be dependent on the intensity of the exercise performed. Sarika Chaudhary et al 2010 evaluated the effects of aerobic and strength training on cardiac variables such as blood pressure, heart rate (HR), and metabolic parameters like cholesterol, high density lipoprotein (HDL), triglycerides and anthropometric parameters of obese women. Their findings of the study indicate statistically significant differences in recovery heart rate [Pre-exercise: 97.40± 5.378 (mean±standard deviation (SD)), post-exercise: 90.70±4.599, t=8.066, P<0.001] and in post-diastolic blood pressure [Pre-exercise: 85±3.265, post-exercise: 86.20±2.820, P<0.001] in aerobic training and in systolic blood pressure [Pre-and post-exercise] in both training groups (P<0.001). Significant differences were observed in very low-density lipoprotein [pre-exercise: 28.10±1.415, post-exercise: 26.86±0.760, t=5.378] and HDL [pre-exercise: 45.40±3.533, post-exercise: hypotension. Pamella Karoline et al 2015 studed the effects neuropathy than in diabetic without autonomic neuropathy.

[Bottini et al.] , P Bottini , C Tantucci , L Scionti , M L Dottrorini , E Puxeddue , G Reboldi , G B Bolli , G Casucci , F Santeusanio , C A Sorbin .

[Suarez et al.] , G A Suarez , V M Clark , J E Norell , T E Kottke , M J Callahan , P C O'brien , P A Low , P J Dyck . (Sudden cardiac death in diabetes mellitus: risk factors in the)

[Vinik et al. ()] , Aaron I Vinik , M D Roy Freeman , Tomris Erbas . *Diabetic Autonomic Neuropathy Seminars in Neurology Semin Neurol* 2003. (4) p. 23.

[Laskowski (2013)] , E R Laskowski . *Mayo Clinic* July 9. 2013. (expert opinion)

[Klem et al. ()] 'A descriptive study of individuals successful at long-term maintenance for substantial weight loss'. M L Klem , R R Wing , M T Mcguire , H M Seagle , J O Hill . *Am -J -Clin -Nutr* 1997. 66 p. .

[Radice et al. (1996)] 'Abnormal responses to exercises in middle aged NIDDM patients with and without autonomic neuropathy'. M Radice , A Rocca , E Bedon , N Musacchio , A Morabito , G Segalinin . *Diabet-Med* Mar. 1996. 13 (3) p. .

[Ebeling et al. ()] 'Athletes with NIDDM exhibit imparted metabolic control and increased lipid utilization with no increase in insulin sensitivity'. P Ebeling , J A Tumoinen , R Bourey . *Diabetes* 1995. 44 p. .

[Ewing et al. ()] 'Autonomic neuropathy, QT interval lengthening, and unexpected deaths in male diabetic patients'. D J Ewing , O Boland , J M Neilson , C G Cho , Clarke , BF . *Diabetologia* 1991. 34 p. .

[Koullam et al. (2009)] 'BROWN Effect of High Intensity Interval Training on Heart Rate Variability in Individuals with Type 2'. Koullam , Marcos A Parpa , Michaelides , Barry S . *Diabetes Journal of Exercise Physiologyonline* August 2009. 12 (4) . (JEPonline))

[Young et al. ()] 'Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial'. L H Young , F J Wackers , A E Iskandrian , S D Wittlin , N Filipchuk , R E Ratner , S E Inzucchi , Investigators . *AMA* 2009. 301 p. .

[Irace et al. (1991)] 'cardiovascular adaptation during cycloergometer exercise test in IDDM with or without autonomic cardiopathy'. L Irace , D Iarussi , S Langella , L Santangelo , V Coppola , A Iacono . *Cardiologia* Aug. 1991. 36 (8) p. .

[Schumer et al. ()] 'Cardiovascular autonomic neuropathy testing in patients with diabetes'. M P Schumer , S A Joyner , M A Pfeifer . *Diabet Spectr* 1998. 11 p. .

[Cardiovascular responses in diabetes: influence of autonomic neuropathy of different severity Diabetologia (1995)] 'Cardiovascular responses in diabetes: influence of autonomic neuropathy of different severity'. *Diabetologia* Feb. 1995. 38 (2) p. .

[Gail ()] 'Changes in rate pressure product with physical training of individuals with coronary artery disease'. A Gail , Francis , N . *Physical Therapy* 1984. 64 (9) p. .

[Charlotte Bjork Ingul Aerobic interval training reduces blood pressure and improves myocardial function in hypertensive patients 'Charlotte Bjork Ingul Aerobic interval training reduces blood pressure and improves myocardial function in hypertensive patients'. *European Journal of Preventive Cardiology* April 2012. 19 (2) p. .

[Drake-Holland et al. ()] 'Chronic catecholamine depletion switches myocardium from carbohydrate to lipid utilisation'. A J Drake-Holland , V Van D , T Roemen , J W Hynd , M Mansaray , Z M Wright , M I Noble . *CardiovascDrugs Ther* 2006. 15 p. .

[Soligard ()] 'Comprehensive warm-up programme to prevent injuries in young female footballers: Cluster randomized controlled trial'. T Soligard . *BMJ* 2008. 337 p. 2469.

[Kahn et al. ()] 'Decreased exercise heart rate and blood pressure response in diabetic subjects with cardiac autonomic neuropathy'. J K Kahn , B Zola , J Juni , A Vinik . *Diabetes Care* 1986. 9 p. .

[Landry and Allen ()] 'Diabetes mellitus and exercise'. G L Landry , D B Allen . *Clin. Sports Med* 1992. 11 (2) p. .

[Davidson ()] *Diabetes Mellitus. 4 th ed.W.B saunder company*, M B Davidson . 1981. p. .

[Vinik et al. ()] 'Diabetic autonomic neuropathy'. A I Vinik , R E Maser , B D Mitchell , R Freeman . *Diabetes Care* 2003. 26 p. .

[Alsayed ()] *Effect of exercise on macro and micro circulating blood flow in diabetic patients. Doctoral thesis, Faculty of physical therapy, Cairo university*, A Alsayed . 1999. p. .

[Didangelos et al. ()] 'Effect of quin april or losartan alone and in combination on left ventricular systolic and diastolic functions in asymptomatic patients with diabetic autonomic neuropathy'. T P Didangelos , G A Arsos , D T Karamitsos , V G Athyros , S D Georga , ND . *J Diabetes Complications* 2006. 20 p. .

[Gert-Van-Dijk et al. (1994)] 'Effect of supine blood pressure on interpretation of standing up test in 500 diabetic patients'. J Gert-Van-Dijk , - A M Tjon-A-Tsien , - B A Kamzoul , - C G Kramer , H H Lemkes . *J-Auton-Nerv-syst* Apr. 1994. 47 (1-2) p. .

[Karoline De Morais et al. (2015)] 'Effects of aerobic exercise intensity on 24-h ambulatory blood pressure in individuals with type 2 diabetes and prehypertension'. Pamella Karoline De Morais , Marcelo Magalhães Sales , Jeeser Alves De Almeida , Daisy Motta-Santos , Caio Victor De , Herbert Gustavo Sousa , Simõe . *J Phys Ther Sci* Jan. 2015. 27 (1) p. .

[Snowling and Hopkins ()] *Effects of Different Modes of Exercise Training on Glucose Control and Risk Factors for Complications in Type 2 Diabetic Patients A meta-analysis*, Neil J Snowling , Will G Hopkins . 2006. American diabetes association.

[Lampman and Schteingart ()] 'Effects of exercise training on glucose control, lipid metabolism, and insulin sensitivity in hypertriglyceridemia and non-insulin dependent diabetes mellitus'. R M Lampman , D E Schteingart . *Med Sci Sports Exercise* 1991. 23 p. .

[Howorka et al. (1997)] 'Effects of phsical training on heart rate variability in diabetic patients with varios degree of autonomic neuropathy'. K Howorka , J Pumprla , P Haber , J Koller , J Mondrzyk , A Schambmann . *Cardiovasc-Res* Apr. 1997. 34 (1) p. .

[Stevens et al. ()] 'EURODIAB Prospective Complications Study Group. Relationship between risk factors and mortality in type 1 diabetic patients in Europe: the EURODIAB Prospective Complications Study (PCS)'. L K Stevens , M Porta , J H Fuller . *Diabetes Care* 2008. 31 p. .

[Schneider and Ruderman ()] 'Exercise and NIDDM'. S H Schneider , N B Ruderman . *Diabetes Care* 1990. 13 (7) p. .

[Colberg et al. (2010)] *Exercise and Type 2 Diabetes The American College of Sports Medicine and the American Diabetes Association: joint position statement Diabetes Care*, Sheri R Colberg , Ronald J Sigal , Judith G Regensteiner , Bryan J Blissmer , Richard R Rubin , Lisa Chasan-Taber . 2010 Dec. 33 p. .

[Albright et al. (2010)] *Exercise and Type 2 Diabetes The American College of Sports Medicine and the American Diabetes Association: joint position statement Diabetes Care*, Ann L Albright , R D Phd , Barry Braun . Dec. 2010. 33 p. .

[Wing et al. ()] 'Exercise in a behavioral weight control program for obese patients with Type 2 (non-insulindependent) diabetes'. R R Wing , L H Epstein , M Paternostro-Bayles . *Diabetologia* 1988. 31 (12) p. .

[Russell and White ()] *Exercise in Diabetes Management The Phyisi-Sport-Med*, D Russell , M D White , Carl , S . 1999. p. 27.

[Campaigne and Lampman ()] *Exercise in the clinical management of diabetes*, B N Campaigne , R M Lampman . 1994. p. . (st ed. Human Kinetics)

[Thomas et al. (2009)] *Exercise Training for Type 2 Diabetes Mellitus: Impact on Cardiovascular Risk: A Scientific Statement From the American Heart Association Circulation*, H Thomas , Matthew D Marwick , Todd Hordern , Miller , A Deborah . June 30. 2009. 119 p. .

[Beernbaum et al. (1989)] 'Exercise training in diabetic with retinopathy and blindness'. M Beernbaum , S G Albert , J D Cohen . *Arch-phys-Med-Rehabil* Aug. 1989. 70 (8) p. .

[Donckier et al. (1989)] *Exercises and posture related changes of arterial natriuretic factor and cardiac function of diabetes. Diabetic Care*, J E Donckier , B M De-Coster , M Buysschear , D P Pieters , F M Cauwe , A Robert , C M Brichabnt , J M Ketelslegers . Jul-Aug. 1989. 12 p. .

[Hansen Tomas Stolen1Arnt Erik Tjonna1Inger Lise Aamot2Inga Schjerve Ekeberg1Gjertrud Aunet Tyldum1Ulrik Wisloff1] *Hansen Tomas Stolen1Arnt Erik Tjonna1Inger Lise Aamot2Inga Schjerve Ekeberg1Gjertrud Aunet Tyldum1Ulrik Wisloff1*,

[Weise et al. ()] *Heart Rate Variability in Diabetic Patients during Orthostatic Load*, F Weise , W Gerhing , U Runge , L Klin . 1990. 4 p. .

[Hilsted et al. ()] 'Impaired cardiovascular responses to graded exercise in diabetic autonomic neuropathy'. J Hilsted , H Galbo , N J Christensen . *Diabetes* 1979. 28 p. .

[Rogers et al. ()] 'Improvement in glucose tolerance after one week of exercise in patients with mild NIDDM'. M A Rogers , C Yamamoto , D S King . *Diabetes Care* 1988. 11 (8) p. .

[Vinik and Neuropathy (ed.) ()] *In The Health Professional's Guide to Diabetes and Exercise*, A I Vinik , Neuropathy . Alexandria, Va. (ed.) 1995. American Diabetes Association. p. .

[Mayer-Davis et al. ()] 'Intensity and amount of physical activity in relation to insulin sensitivity'. E J Mayer-Davis , R Agostino , A J Karta , S M Haffner , M J Rewers , M Saad , R N Bergman . *JAMA* 1998. 279 p. .

[Takebayashi et al. ()] 'Inukai Clinical usefulness of corrected QT intervals in diabetic autonomic neuropathy in patients with type 2 diabetes Diabetes &'. K Takebayashi , Y R Aso , Y Sugita , T Takemura . *Metabolism* 2002. 28 (2) p. .

[Zravenboer et al. ()] 'Is the corrected Q-T interval a reliable indicator of the severity of diabetic autonomic neuropathy'. B Zravenboer , P H Hendriksen , L P Oey , W H Gispen , A C Huffelen , D W Erkelens . *Diabetes Care* 1993. 16 p. .

[Laptev et al. ()] 'Korneeva IT Effect of short term graded physical exercise on the level of glycemia in children and adolescents with type 1 diabetes mellitus: data of long term ECG monitoring and registration of motor activity'. D N Laptev , M N Kruzhkova , G V Riabykina , S D Poliakov . *Kardiologiia* 2012. 52 (6) p. .

[Lehmann and Vokae ()] 'Loss of abdominal fat and improvement of the cardiovascular risk profile by regular moderate exercise training in patients with NIDDM'. R Lehmann , A Vokae , Agosti , K . *Diabetolgia* 1995. 38 p. .

[Lehmann and Vokae ()] 'Loss of abdominal fat and improvement of the cardiovascular risk profile by regular moderate exercise training in patients with NIDDM'. R Lehmann , A Vokae , Agosti , K . *Diabetolgia* 1995. 38 p. .

[Hordern et al. ()] 'Marwick Effects of exercise intervention on myocardial function in type 2 diabetes'. M D Hordern , J S Coombes , L M Cooney , L Jeffriess , J B Prins , T . *Heart* 2009. 95 p. .

[Chudyk and Petrella (2011)] *MD, Effects of Exercise on\Cardiovascular Risk Factors in Type 2 Diabetes: A meta-analysis Diabetes Care*, Anna Chudyk , Msc , Robert J Petrella . May 1. 2011. 34 p. .

[Marrero and Sizemore ()] *Motivating patients with diabetes to exercise*, D Marrero , J M Sizemore . 1996. American Diabetes Association. p. .

[Scognamiglo et al. (1995)] 'Myocardial dysfunction and an abnormal left ventricular exercise response in autonomic diabetic patients'. R Scognamiglo , G Fasoli , M Ferri , S Nistri . *Clin-Cardiol* May. 1995. 18 (5) p. .

[Burr ()] *Physical activity in type 1 diabetes mellitus Assessing risks for physical activity clearance and prescription Can Fam Physician*, Jamie F Burr . 2012. 58 p. .

[Boulton and Vinik ()] 'Position statement: Diabetes mellitus and exercise'. A J Boulton , A I Vinik . S 40-44. *Diabetes Care* 2010. American Diabetes Association. 21 (1) . (Suppl)

[Oka et al. ()] 'Prolongation of Q-T interval and Autonomic Nervous Dysfunction in Diabetic Patients'. H Oka , S Mohio , K Sato , K Katayama . *Diabetes-Res-Clin-Pract* 1996. 31 (1-3) p. .

[Panoulas et al. (2014)] 'Prolonged QTc interval predicts all-cause mortality in patients with rheumatoid arthritis: an association driven by high inflammatory burden'. V F Panoulas , T E Toms , K M Douglas . *Rheumatology* January 2014. 53 (1) p. .

[Veglio et al. ()] 'QT interval prolongation and mortality in type 1 diabetic patients. a 5-year cohort prospective study. Neuropathy Study Group of the Italian Society of the Study of Diabetes'. M Veglio , R Sivieri , A Chinaglia , L Cavallo-Perin , P . *Diabetes Care* 2000. 23 p. .

[Kahn et al. ()] 'QT interval prolongation and sudden cardiac death in diabetic autonomic neuropathy'. J K Kahn , J C Sisson , A I Vinik . *J-Clin-Endocrinol -Metab* 1987. 64 p. .

[Mathur and Gupta ()] 'QTc Prolongation in Diabetes Mellitus an Indicator of Cardiac Autonomic Neuropathy'. C P Mathur , Deepak Gupta . *JIACM* 2006. 7 (2) p. .

[Rochester Diabetic Neuropathy Study J Neurol Neurosurg Psychiatry ()] 'Rochester Diabetic Neuropathy Study'. *J Neurol Neurosurg Psychiatry* 2005. 76 p. .

[Ivy ()] 'Role of exercise training in the prevention and treatment of insulin resistance and NIDDM'. J L Ivy . *Sports Med* 1997. 24 (5) p. .

[Oka et al. (1995)] *Spectral analysis of R-R interval and systolic blood pressure in diabetic autonomic neuropathy. J-Auton-nervo-sys*, H Oka , S Mohio , K Sato , K Katayama , T Nohara , T Hasunuma , K Houi , Y Isogai . Apr. 1995. 8 p. .

[Standards of medical care in diabetes-2006 Diabetes Care ()] 'Standards of medical care in diabetes-2006'. *Diabetes Care* 2006. American Diabetes Association. 9 (1) p. .

[Suarez et al. ()] 'Sudden cardiac death in diabetes mellitus: risk factors in the Rochester Diabetic Neuropathy Study'. G A Suarez , V M Clark , J E Norell , T E Kottke , M J Callahan , P C O'brien , P A Low , P J Dyck . *J Neurol Neurosurg Psychiatry* 2005. 76 p. .

[Pop-Busui et al. ()] 'Sympathetic dysfunction in type 1 diabetes: association with impaired myocardial blood flow reserve and diastolic dysfunction'. R Pop-Busui , I Kirkwood , H Schmid , V Marinescu , J Schroeder , D Larkin , E Yamada , D M Raffel , M J Stevens . *J Am Coll Cardiol* 2004. 44 p. .

[Chaudhary et al. (2010)] 'The Effects of Aerobic Versus Resistance Training on Cardiovascular Fitness in Obese Sedentary Females Asian'. Sarika Chaudhary , Jaspal Singh Manpreet Kaur Kang , Sandhu . *J Sports Med* 2010 Dec. 1 (4) p. .

[Arafa and Amin ()] 'The epidemiology of diabetes mellitus in Egypt: Results of a national survey'. Naglaa Arafa , Ghada Amin . *Egyptian Journal of Community Medicine* 2010. 28 (3) .

[Ewing et al. ()] 'The value of cardiovascular autonomic function tests'. D J Ewing , C N Martyn , R J Young , B F Clark . *Diabetes Care* 1985. 8 p. 5.

[Colberg et al. ()] 'Use of heart rate reserve and rating of perceived exertion to prescribe exercise intensity in diabetic autonomic neuropathy'. S Colberg , D Swain , A Vinik . *Diabetes Care* 2003. 26 p. .

[Tesfaye et al. ()] 'Vascular risk factors and diabetic neuropathy'. S Tesfaye , N Chaturvedi , S E Eaton . *N Engl J Med* 2005. 352 p. 341.

[Woods ()] 'Warm-up and stretching in the prevention of muscular injury'. K Woods . *Sports Medicine* 2007. 37 p. 1089.