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EFFECTS OF EXERCISE AND METFORMIN ON LIPID PROFILE AND GYLCEMIC INDEX IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM)

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ABSTRACT

The present study describes effects of exercise in T2DM patients receiving Metformin and determination of consequential changes in lipoidal components in addition to glucose and glycated Hemoglobin (HbA1c) levels. Patients were categorized accordingly into two groups, T2DM patients with exercise and T2DM patients without exercise, both on metformin, with males = 25 and females = 10 in both groups. Consequential changes in blood's triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), including glucose and glycated Hemoglobin (HbA1c) levels were determined in both groups by prescribed methods. Anthropometric parameters were also assessed to compare and analyze T2DM patients doing regular exercise with those with no exercise-life-style. Data is reported as mean ± SD. TC (mg/dL), LDL-C (mg/dL), HDL-C (mg/dL), TG (mg/dL), BSF (mg/dl) and HbA1c (%), all exhibited strong significant ($P < 0.0001$) difference between T2DM patients doing exercise and taking metformin as compared to those T2DM+metformin patients, not in habit of performing any exercise. Results showed a more effective activity of metformin in T2DM patients who performed exercise regularly.

Key-words: Metformin, Type 2 Diabetes Mellitus (T2DM), glycemic control.

Abbreviations: T2DM = Type 2 Diabetes Mellitus, TG = triglyceride, LDL-C= low-density lipoprotein cholesterol, HDL-C= high density lipoprotein cholesterol, HbAlc = glycated Hemoglobin, CVS = cardiovascular diseases,

INTRODUCTION

Life style modification, routine exercise and diet control are some of the factors that help an individual with type 2 diabetes mellitus (T2DM). Moreover those T2DM patients who routinely exercise and receives glucose controlling medicine, metformin, showed a much better glucose control and betterment in blood pressure, resulting in a much better healthy normal life (Bosi *et al*., 2009; Kitao *et al*., 2017; Mariël *et al*., 2018). Metformin is routinely used a prime medicine for the treatment of T2DM. Moreover, it was also established that metformin usage also slow down transition of Pre-diabetics to T2DM (Cededdu *et al*., 2014; Knowler *et al*., 2002). American Diabetic association also endorses this established fact and recommends treatment with metformin in patients with Pre-diabetes condition (Nathan *et al*., 2009; Rhee *et al*., 2010). Pre-diabetic condition or full-blown T2DM also influence lipid and cholesterol metabolism, resulting in abnormal values of triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C) (Rosenblit, 2016; Wu and Parhofer, 2014). These metabolic abnormalities in lipid profile components are known risk factors for development of atherosclerosis or cardiac abnormalities (Bosi *et al*., 2009; Grundy *et al*., 2004; Rhee *et al*., 2010). Excess of food with slowed metabolism is also known to induce insulin resistance, leading to T2DM with dyslipidemia (Mariël *et al*., 2018).

Therefore, present study described effects of exercise in T2DM patients receiving Metformin (as compared to those T2DM patients with no exercise) and determination of consequential changes in triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), including glucose and glycated Hemoglobin (HbA1c) levels.

MATERIALS AND METHODS

Selection of study group and Research Design: It's an observational prospective study conducted at Departments of Biochemistry Laboratory services & Chemical Pathology, Liaquat National Hospital, Karachi and Department of Physical Education, Karachi, for the period from January 2018 to Dec 2018. Demographic data of all patients were collected and documented through review their cases, files, HIMS and LIS and categorized accordingly into two

groups, T2DM patients with exercise and T2DM patients without exercise (Table 1), with males = 25 in both groups and females = 10 in both groups. Inclusion criteria is dependent on history of diabetes > 5 years and age >30 yrs and <45 years. Patients with multiple surgeries, <30 yrs and >45 yrs, missing history of co-morbid and who do not exercise regularly were excluded. Data of a total of 60 T2DM patients from both groups were reviewed, were documented as per availability of all demographic data, T2DM information, follow medication of diet recommendation, exercise regularly (and those who doesn't) including availability of complete and relevant biochemical parameters.

Analytical determination: Objective of the present study is to assess effects of exercise in T2DM patients receiving Metformin and determination of consequential changes in triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), including glucose and glycated Hemoglobin (HbA1c) levels. Blood samples, in fasting state were collected and analyzed according to the methods described earlier (Alam *et al*., 2012; 2014). Normal ranges for biochemical parameters are; Glucose fasting < 100 mg/dl; Glycated hemoglobin (HbA1c) = < 6.0 %, in triglyceride (TG) = 70-150 mg/dl, low-density lipoprotein cholesterol (LDL-C) = < 130 mg/dl, high density lipoprotein cholesterol (HDL-C) = 35 mg/dl. Anthropometric parameters were also asses to compare and analyze T2DM patients doing regular exercise with those with no exercise-life-style. Data is reported as mean ± SD.

Statistical analysis: Biochemical parametric data were compared and analyzed by SPSS ver 20.0. Results were considered significant at $P < 0.05$.

RESULTS

No significant difference in Height (cm) 159.63 ± 10.20, and 161.71 ± 8.40 was noted in both groups; however weight (kg) 71.80 ± 18.65 and 59.34 ± 19.55 ($P < 0.001$) and BMI (kg/m2) 28.63 ± 4.10 and 23.80 ± 5.45 ($P< 0.01$) showed significant difference. Similarly TC (mg/dL), LDL-C (mg/dL), HDL-C (mg/dL), TG (mg/dL), BSF (mg/dl) and HbA1c (%), all exhibited strong significant ($P < 0.0001$) difference between T2DM patients doing exercise and taking metformin as compared to those T2DM+metformin patients not in habit of any exercise. For example TC (mg/dL) was 187.29 ± 30.35 in T2DM (without exercise patients) whereas 145.03 ± 16.20 T2DM (habitually doing exercise), LDL-C (mg/dL) from 100.11 ± 31.50 down to 85.91 ± 25.45 and TG (mg/dL) from 183.90 ± 25.50 down to 155.40 ± 18.65, respectively in T2DM without exercise and with exercise. Data suggested very strong physiological, pharmacological and metabolic influence of exercise on the effectiveness of metformin in patients with T2DM.

Table 1. Anthropometric and Blood chemistry Characteristics of T2DM Diabetic Individuals on Metformin with and without exercise.

Anthropometric values	Without Exercise	With exercise	T value	P < 0.05
Age (years)	44.54 ± 15.90	45.42 ± 19.10	- 4.759	NS
Gender, men/women	25/10	25/10	--	--
Height (cm)	159.63 ± 10.20	161.71 ± 8.40	-6.427	NS
Weight (kg)	71.80 ± 18.65	59.34 ± 19.55	42.243	< 0.001
BMI (kg/m2)	28.63 ± 4.10	23.80 ± 5.45	15.349	< 0.01
Blood Chemistry values				
TC (mg/dL)	187.29 ± 30.35	145.03 ± 16.20	67.958	< 0.001
LDL-C (mg/dL)	100.11 ± 31.50	85.91 ± 25.45	26.712	< 0.001
HDL-C (mg/dL)	36.58 ± 7.35	54.83 ± 10.40	-39.122	< 0.001
TG (mg/dL)	183.90 ± 25.50	155.40 ± 18.65	63.738	< 0.001
BSF (mg/dl)	99.63 ± 10.25	85.29 ±8.10	28.597	< 0.001
HbA1c (%)	7.49 ± 2.30	6.09 ± 1.80	34.991	< 0.001

DISCUSSION

T2DM patients adhering to healthy lifestyle, such as regular exercise, healthy food, proper sleep shows improved physiology and metabolic activities as healthy life style facilitate their body in induction of better efficacy of diabetic medications such as metformin (Bosi *et al*., 2019; Cededdu *et al*., 2014; Kitao *et al*., 2017; Knowler *et al*., 2002; Stee *et al*., 2018). This is in contrast to what a T2DM patient exhibits that are non-compliant, don't exercise and don't adhere to prescribed food regiments. Data from our study exhibited a more effective activity of metformin in T2DM patients who performed exercise regularly, which is confirmed by a comparatively lowered level of TG, LDL, CHOL, Blood glucose and HbA1c as compared with T2DM who do not exercise. A previous study clearly indicated that physical exercise alone or in combination with metformin induced a much better efficacy of the drug than treatment alone or exercise alone (Cededdu *et al*., 2014). Additionally, it was observed that exercise enhances the pharmacological effects of metformin and cardio-pulmonary performance of the individual by negating side-effects of metformin (Cededdu *et al*., 2014).

It is a known and well established fact that T2DM induce lipid abnormalities resulting in higher risk for developing cardiovascular diseases (CVD) (Rosenblit, 2016). In an interesting turn, CVD itself indicated as a factor that can increase the duration or early onset of T2DM (Rosenblit, 2016; Wannamethee *et al*., 2011). Furthermore, T2DM patients not only experience dyslipidemia, and if not controlled through medication and exercise, also are at risk for several risk factors such as hypertension, obesity and insulin resistance (Brunzell *et al*., 2008). Our study indicated that T2DM patients on metformin and does regular exercise showed much lower concentration of lipoidal components than those who don't exercise thus exposing themselves to probable risk factors for developing CVDs. It was reported previously that lack of exercise and sedentary life style in patients with T2DM increase the risk for CVDs, for which physician assistants are getting trained to counsel such patients (Dugan, 2016). A study reported earlier showed appreciable decrease in HbA1c in patients who regularly performed 100 to 150 minutes exercise (Dugan, 2016).

The effects of timing of exercise in T2DM patients with dyslipimedia is also an area of much interest (Horton *et al*, 2006; Huang *et al*., 2018; Weston *et al*., 2014). It was documented after a thorough study that post-exercise glycemic control and ultimately dyslipidemia can be modified in favor of the patients if metformin therapy is well-planned in combination with exercise (Huang *et al*., 2018). High Intensity Interval Training (HIIT) was recommended as a time-efficient exercise modality to enhance cardiovascular fitness, reduce cardiometabolic risk factors in T2DM patients with cardio-metabolic such as CVD and T2DM (Horton *et al*., 2006; Weston *et al*., 2014).

CONCLUSION

The present study described effectiveness of exercise in T2DM patients with dyslipidemia, who are on glycemic controlling medicine metformin. Our results showed a more effective activity of metformin in T2DM patients who performed exercise regularly, which is confirmed by a comparatively lowered level of TG, LDL, CHOL, Blood glucose and HbA1c as compared with T2DM patients who do not exercise.

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