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Effect of Inspiratory Muscle Training on Blood Glucose Levels and Serum lipids in female patients with type 2 diabetes

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Abstract : Chronic hyperglycemia and hyperlipidemia can lead to serious long-term complications in type 2 diabetes. Physical exercise can effectively lower blood glucose levels and serum lipids. However, women with type 2 diabetes are more likely to have limited physical activity due to comorbidities, and/or reduced physical exercise opportunities due to personal, social, and cultural barriers. This would address the need for exploring alternative exercise forms. Thus, the purpose of this study is to investigate the effect of inspiratory muscle training (IMT), as a potential alternative, on blood glucose levels and serum lipids in female patients with type 2 diabetes. Twenty eight female patients with type 2 diabetes were included in this study. The patients gave their written consents and were equally assigned to either a study (n=14) or a control (n=14) group. Patients in both group received oral anti-diabetic pharmacological therapy. Only patients in the study group received inspiratory muscle training at 30% of maximal inspiratory pressure, once daily, five days/week, for 8 weeks. Fasting and 2-h post-prandial blood glucose, cholesterol, low density lipoproteins, triglycerides, and HOMA-IR were measured at baseline and after the intervention. Unpaired t-test was used to calculate differences between the two groups, and Paired t-test was used to calculate changes within each group. none of the measured variable has been significantly changed in either group, and nor were there any significant differences between the two groups. IMT with low inspiratory loading fails to demonstrate any significant improvements in blood glucose levels, serum lipids, and/or HOMA-IR in female patients with type 2 diabetes.
Key words : Type 2 diabetes, Inspiratory muscle training, Blood glucose, Serum lipids, HOMA-IR.

Introduction

Type 2 diabetes is a major health problem, and accounts for about 90% of all diabetes worldwide. The number of patients with type 2 diabetes is growing rapidly in every country, which is caused by rapid increases in obesity and physical inactivity [1]. There were over 7.8 million cases of diabetes in Egypt in 2015, and this number is expected to increase to 15.1 million by 2040. This ongoing growth in the prevalence of type 2 diabetes means that, an all-out effort is required to establish effective interventions for better management of type 2 diabetes[2].

Regular physical activity is a major key element in the management of type 2 diabetes, and helps to normalize blood glucose levels and serum lipids profile [3,4]. However, many patients with type 2 diabetes, particularly women, may have limited physical activity due to obesity, musculoskeletal problems or other comorbidities. Women are also more likely to have reduced exercise opportunities due to lack of time with daytime involvement in household chores and family matters, absence of appropriate exercise facilities, and overcrowded streets that interfere with outdoor activities [5,6]. Because of that, there has been growing interest, for researching alternative forms of exercise for type 2 diabetic patients, especially women, who might have difficulties in participation in traditional physical exercise programs.

Inspiratory muscle training (IMT) may represent an alternative option of exercise, as recently, it has been shown to acutely improve blood glucose levels in patients with type 2 diabetes, in a way similar to aerobic exercise session[7]. Nevertheless, the long-term efficacy of IMT on blood glucose levels in type 2 diabetic patients needs more research. In addition, though the effect of IMT on blood lipids has been previously studied in older adults with fasting hyperglycemia [8] and in elderly subjects with insulin resistance [9], further research is needed to investigate that effect in patients with type 2 diabetes.

Therefore, the purpose of this research is to investigate the long term effect of IMT on blood glucose levels and serum lipids in female patients with type 2 diabetes. The results of this study may aid efforts to design alternative choices of exercises for women with type 2 diabetes.

Methods

This study was approved by the Ethics Committee for Scientific Research at the Faculty of Physical Therapy, Cairo University (no.: P.T.REC/012/001486).

Subjects

Twenty eight female patients with type 2 diabetes were included in this study. Diabetes Mellitus was diagnosed according to International Expert Committee, based on HbA_{1c} of ≥6.5% [10].The patients were recruited from Outpatient Diabetes Clinic of Omm El Misryeen Hospital in Giza, Egypt. The inclusion criteria were females with type 2diabetes, aged from 30-53 years old, patients undertaking oral hypoglycemic medications, and patients with stable clinical condition. The medical history of patients was obtained to identify any conditions that could exclude them. The exclusion criteria were male patients, smoker female patients, patients with pulmonary disease or exercise-induced asthma, patients under current insulin or corticosteroid treatment, patients who were pregnant, and/or patients who were practicing any form of physical exercise. The eligible patients gave their written consents and were equally assigned to either a study (n=14) or a control (n=14) group. Patients in both groups received oral anti-diabetic pharmacological therapy, and medications were similar between the two groups. Only patients in the study group received an 8-weeks inspiratory muscle training program. Three patients had dropped out from the study; one patient from the control group, and two patients from the study group.

Measurements

Anthropometric parameters

Body weight, and height were measured for all patients at baseline, and BMI was calculated as: (weight (in kg) / height in $(m)^2$) [11]

Maximum inspiratory pressure (MIP)

MIP values were measured at baseline; the patients were instructed to inhale with maximum effort against an occluded tube attached to an aneroid manometer gauge. During this measurement the nose was blocked and the lips were sealed tightly around the tube to prevent air leaks [12,13,14].

Biochemical blood analysis

After 6-8 hours of fasting, venous blood samples were withdrawn for detection of fasting blood glucose, and again after about 2 hours for detecting 2-HPP blood glucose. Blood glucose concentrations were measured with the glucose oxidase method [15]. Blood samples were collected on edita vacationer tube for measurement of A_{1c} at baseline. After at least 12 hour fasting, venous blood samples were withdrawn, serum was isolated for detection of blood lipids; cholesterol levels determination was done by using cholesterol oxidase of bacterial origin [16]. Serum triglyceride levels were determined according to the colorimetric method of **Fossati and Principe** [17]. Low density lipoprotein was calculated through this equation: (Total cholesterol – HDL – TG / 5) (18). Biotecnica Instrument diagnostic kits and biochemistry auto analyzer (BT-1500, Biotecnica Instrument, Italy) were used for analysis of HbA_{1c} and serum lipids. Fasting insulin was also measured using DRG-ELISA kit, by immunoassay device (Hitech, Expert plus, Austria). Homeostatic model assessment (HOMA-IR), as an index of insulin resistance was calculated according to this equation: (HOMA-IR= Fasting insulin (μ/ml) x fasting glucose (mg/dL) / 405) [19].

Interventions

Inspiratory muscle training program

Patients in the study group received supervised IMT once daily , 5 days per week, for 8 weeks. Threshold® Inspiratory Muscle Training device (Threshold IMT, Koninklijke Philips Electronics N.V., UK) was used. The inspiratory muscle training sessions were performed and supervised at the Outpatient Diabetes Clinic of Omm El Misryeen Hospital, in Giza. The inspiratory load was set at 30 % of baseline MIP. In the first two weeks; to familiarize patients with the training process; they were instructed to perform 5 sets of 20 breaths/set, with 2 minutes rest between sets. Then, for the next three weeks; the inspiratory muscles were overloaded by increasing the duration of the session to 15-20 min (5 sets× 30 breaths/set) in order to obtain a training response [20]. Afterwards, and till the end of the study; the exercise session duration was further increased to 25-30 min (8 sets × 30 breaths/set). During the training session, the patients were encouraged to adopt slow deep diaphragmatic pattern of breathing.

Unmeasured diabetic diet

Foods not to be eaten altogether, foods to be eaten in moderation only, and foods to be eaten as desired were prescribed to the patients in both groups [21].

Statistical analysis

At first to determine whether the data set is normally distributed or not, the normal probability plot was used and interpreted, as described by McPherson[22].Unpaired t-test was used to calculate difference between the two groups at baseline and after the end of the study. Paired t-test was used to calculate changes within each group. All values were expressed as means and standard deviations. The values of $P< 0.05$ were considered as statistically significant. All statistical calculations were done using GraphPad software and Microsoft Excel 2010.

Results

Baseline physical and clinical characteristics of patients are shown in Table.1. Of the variables presented, no significant differences were observed between the two groups at the baseline. After the intervention; none of the measured variable has been significantly changed in either group, and nor were there any significant differences between the two groups, as shown in Table 2.

Table.1 Baseline anthropometric and clinical characteristics of patients

Variables	Control group n=14	Study group n=14	P Value
Age (yrs)	44.28±6.87	42.21±5.91	0.400
Height (Cm)	155.28±6.74	156.35±6.20	0.665
Body weight (Kg)	88.57±14.32	84.50±13.03	0.438
BMI (Kg/m^2)	36.75±5.69	34.55±4.60	0.272
Duration of DM (yrs)	2.87±3.36	3.99±3.07	0.386
HbA$_{1c}$(%)	6.75±1.21	6.65±1.16	0.829
FBG (mg/dL)	145.28±46.67	134.92±37.30	0.522
2HPP (mg/dL)	217.38±102.81	201.07±59.24	0.624
Cholesterol (mg/dL)	200.5±41.23	211.42±30.34	0.432
LDL (mg/dL)	130.28±33.86	139.78±20.55	0.377
TG (mg/dL)	159.00±65.91	146.50±66.56	0.621
HOMA-IR	7.71±3.70	6.16±5.38	0.383

Data are expressed as means± SD. P< 0.05 is statistically significant
BMI, Body mass index; DM, Diabetes mellitus; HbA1c, glycosylated haemoglobin; FBG, Fasting blood glucose; 2HPP, 2-hours post prandial; LDL, Low density lipoprotein; TG, Triglycerides; HOMA-IR, Homeostatic model assessment as an index of insulin resistance

Table 2. Comparison of biochemical characteristics of patients within each group & between the two groups after intervention

Variable	Control group n=13			Study group n=12			Control vs. Study After intervention
	Pre	Post	P Value	Pre	Post	P Value	P Value
FBG (mg/dL)	143.85±48.26	133.23±65.72	0.621	134.08±39.83	126.83±51.16	0.628	0.789
2HPP (mg/dL)	220.42±106.7	211.92± 90.16	0.775	198.92±64.07	187.33± 72.19	0.526	0.461
Cholesterol (mg/dL)	203.08±41.73	206.15±52.02	0.740	205.83±26.95	208.92±40.48	0.738	0.883
LDL (mg/dL)	132.92±33.71	132.54±41.96	0.955	137.33±19.21	137.50±37.20	0.984	0.758
TG (mg/dL)	159.46±68.58	153.31±83.79	0.766	128.75±53.19	123.58±57.98	0.613	0.317
HOMA-IR	7.89±3.79	5.84±2.69	0.18	6.62±5.65	6.42±4.59	0.925	0.70

Data are expressed as means± SD. P< 0.05 is statistically significant.
Fasting blood glucose; 2HPP, 2-hours post prandial; LDL, Low density lipoprotein; TG, Triglycerides; HOMA-IR, Homeostatic model assessment as an index of insulin resistance

Discussion

This study fails to report any significant changes in blood glucose levels, HOMA-IR, or serum lipids, after 8 weeks of IMT performed at low inspiratory resistance, in female patients with type 2 diabetes. Future efforts to implement effective protocols for inspiratory muscle training in type 2 diabetics; will need to take those findings into considerations, to produce clinically important improvements in blood glucose levels and serum lipids.

Contrary to our results, two studies have reported significant improvement in blood glucose levels as a result of IMT in patients with fasting hyperglycemia [8], and in patients with insulin resistance [9]. The intensity of inspiratory load and the duration of inspiratory exercises may explain these discrepancies; the first study had incorporated higher inspiratory loading (i.e. 40% of the maximal inspiratory pressure), and exercise sessions of 30 minutes from the early beginning of the study, 7days/week, and for 8 weeks .The second one had also recruited the IMT for 30 minutes per session throughout the entire period of the study, 7 days/week, and for 12 weeks. Both the intensity and total exercise training time were higher than in the present study.Thus, the absence of significant improvement in blood glucose levels (FBG and 2-HPP) after the intervention, could be due to the low intensity of inspiratory loading (i.e. 30 % MIP) used in this study. In addition, it appears that exercise session duration was not long enough at the initial weeks of the study, to affect blood glucose levels. Besides, the total cumulative time of all exercise sessions, also might have been not sufficient for any significant changes to occur in any of the measured variables. This explanation could be supported by what was reported by The American College of Sports Medicine and the American Diabetes Association, both of which stated that the reductions in blood glucose levels are related with exercise intensity and duration [3]. So, this is likely the case here; if a higher inspiratory load was recruited, together with exercise sessions of a longer duration, and for a longer period of time, this could have led to different outcomes in blood glucose levels.In addition, lack of significant changes in blood glucose levels in the study group, could also be attributed to lack of significant improvement in insulin resistance (HOMA-IR). Other possible explanation for the absent significant improvement in blood glucose in the study group; could be that, there were daily hassles and family stress experienced and reported by some patients in this group. This could have led to elevated plasma glucose levels most of the time. The mechanism is through the direct physiological effects of stress on counter-regulatory hormones, which in turn increase blood glucose [23]. We do believe that, this association between daily hassles and elevated blood glucose levels, might have underestimated any possible influence of inspiratory muscle exercises on blood glucose.

Another finding in the present study is that, low intensity IMT was also not effective in inducing any significant changes in blood lipids, in women with type 2 diabetes. This finding was in accordance with two previous studies, which have also shown that IMT had no significant effects on blood lipids [8,9]. This could be also because the IMT in the present study was performed at a lower intensity (i.e.30% of MIP). It has been confirmed that, the intensity of exercise seems to be an important modulator of lipid profile, and there is an intensity threshold for exercising to elicit changes in plasma lipid profile (24,25).Accordingly, lack of significant improvement in cholesterol, LDL, or triglycerides could be attributed to the low intensity of inspiratory loading used in this study, which was not sufficient to elicit the appropriate stimulus for reducing blood lipids. Perhaps, if IMT of a higher intensity was implemented in this study, this could have elicited an adequate stimulus for inducing positive changes in blood lipids. In addition, the patients were instructed to maintain unmeasured diabetic diet, and were not on a calorie restricted diet. Larson- Mayer et al, [26] shown that, when caloric restriction was added to physical activity, there were significant improvements in cholesterol and LDL-C. Also, Church et al.,[27] reported that 4 months of exercise without caloric restriction had no effect on blood lipids compared to the control. Thus, if calorie restriction was added to IMT in the present study, a combined effect could have been more beneficial in reducing blood lipids.The present study also showed that, HOMA-IR was not changed significantly, as a result of 8 weeks of low intensity inspiratory training, which is inconsistent with what was reported by Silva et al, [9]. This could be, as we discussed earlier, due to the methodological difference between our study and theirs.

Conclusion

Our data suggest that, exercising inspiratory muscles for 8 weeks, once daily, 5 days/week, with low inspiratory loading (i.e. 30% MIP), has failed to induce any significant improvements either in blood glucose levels, HOMA-IR, and/ or serum lipids. Efforts to design alternative forms of exercises for type 2 diabetic patients; particularly women with limited physical activity or reduced exercise opportunities, will need to consider these observations. Low intensity IMT has proved to be an inappropriate alternative to physical exercise training, when the target is to lower blood glucose levels, enhance insulin sensitivity and/or improve blood lipids.

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