A moderate-intensity exercise program with a weekly duration not adherent to international guidelines improves blood glucose in women with type 2 diabetes

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Summary

Introduction: Current international guidelines recommend a range of 150–300 min per week of moderate physical activity/exercise in adults with type 2 diabetes. However, type 2 diabetic patients, particularly obese women, may fail to adhere to these guidelines because of reduced functional capacity or lack of time due to household responsibilities. Therefore, this study aimed to investigate the effect of low-volume, moderate-intensity aerobic exercise of < 150 min/week on average blood glucose in type 2 diabetic women.

Material and methods: Twenty-two obese women with type 2 diabetes were assigned to an exercise group (n_1 = 10, age = 41 ±2.92 years, body mass index (BMI) = 35.22 ±2.59 kg/m^2) and a control group (n_2 = 12, age = 44 ±6.87 years, BMI = 36.75 ±5.69 kg/m^2). Patients in both groups received oral antidiabetic medications, and only patients in the exercise group received supervised moderate-intensity treadmill walking at 65–75% of peak heart rate (HR_{peak}) for 30 minutes/session, 3 days/week, and 8 weeks. A 5–10-min warm-up and a 3–5-min cool-down period of low-intensity walking were combined with the 30-min work phase of the exercise session. A symptom-limited maximal exercise test was performed to determine the HR_{peak}. Average blood glucose was estimated from glycosylated haemoglobin.

Results: There were statistically significant reductions in estimated average blood glucose levels in the exercise group compared to the baseline ($p < 0.001$) and to the controls ($p = 0.040$).

Conclusions: Combined with oral antidiabetic therapy, an 8-week moderate-intensity walking exercise program, with weekly duration lower than that recommended by the international guidelines, could induce significant reductions in blood glucose levels in middle-aged obese women with type 2 diabetes and seems to be a better choice than no exercise at all.

Key words: low-volume, moderate-intensity, aerobic exercises, average glucose, obese women, type 2 diabetes.

Introduction

Diabetes mellitus (DM) is a global health problem, with 537 million cases of DM were estimated worldwide in 2021 [1]. Type 2 DM is the most common type of DM and accounts for 90% of all cases of DM around the world [1]. This prevalence of DM is going to increase over the next years, with the greatest growth being in lower-income countries [1]. In Egypt, the 10th highest age-adjusted diabetes prevalence worldwide was reported [2]. Women with type 2 diabetes have 25–50% increased risk of cardiovascular diseases (CVD) than diabetic men because women have a lower physical activity level and develop diabetes at a higher body mass index (BMI) than their male counterparts with diabetes, which means that women are subjected to excess body fatness and co-existing cardiovascular risks for a longer duration than men before developing type 2 diabetes [3].

Hyperglycaemia is a major risk factor for CVD and all-cause mortality in patients with type 2 diabetes. Treatment interventions that reduce hyperglycaemia to near-normal levels could prevent cardiovascular events and mortality of type 2 diabetic patients [4]. Exercise therapy is an effective intervention for normalizing blood glucose levels and reducing the risk of cardiovascular disease in patients with type 2 diabetes [5]. Current guidelines for the management of type 2 diabetes consider physical exercise training to be an essential component of the management plan, and recommend a minimum of 150 minutes up to 300 min of moderate-intensity activity per week [6]. However, many patients with type 2 diabetes, particularly obese women,

may be unable to meet the recommended exercise volume because of reduced cardiopulmonary fitness [3], or because of time constraints owing to household activities or family commitments. Therefore, the purpose of this study was to investigate the effect of low-volume, moderate-intensity aerobic exercise training, defined as moderate-intensity exercise of < 150 minutes/week, on estimated average glucose in obese type 2 diabetic women. The results of this study may aid health professionals interested in exercise therapy of type 2 diabetes.

Material and methods

Ethical considerations

This study was conducted according to the Helsinki Declaration and approved by the Ethics Committee of Scientific Research of the Faculty of Physical Therapy at Cairo University (Approval No.: P.T.REC/012/004119). Patients gave their written consent prior to participation in this research.

Subjects

Twenty-two women with type 2 diabetes were recruited for this study. Patients were assigned to either an exercise group (n_1 = 10) or a non-exercising control group (n_2 = 12). For patient selection, a thorough medical history was taken, and patients were selected according to certain criteria. Inclusion criteria were type 2 diabetic women diagnosed by glycosylated haemoglobin (HbA_{1c}) > 6.5%, age 30–50 years, obese patients with BMI > 30 kg/m^2, and patients under oral hypoglycaemic agents. Exclusion criteria were male patients, pregnancy, patients with regular exercise habits, and/or patients with cardiopulmonary, neurological, or musculoskeletal limitations to exercise training. Patients in both groups received oral antidiabetic medications and maintained their usual lifestyle throughout the study. No dietary intervention was included in this study.

Measurements

Anthropometric measurements

Body weight, height, and waist circumference were measured at baseline. The body mass index (BMI) was calculated as BMI = body weight (kg)/height in metres squared.

Estimated average glucose

The glycosylated haemoglobin was measured for all patients, and the average blood glucose was estimated at baseline and after 8 weeks according to this equation: estimated average glucose [eAG] in (mg/dl) = 28.7 × HbA_{1c} – 46.7 [7].

Incremental exercise test

Prior to exercise intervention, the eligibility for exercise testing/training was checked and a symptom-limited maximal treadmill exercise test was performed according to the modified Bruce protocol [8, 9]. Compared with the original Bruce protocol that has 5 stages and begins with a speed of 1.7 miles/hour at an inclination of 10% (stage 1), the modified protocol has 7 stages and starts at a zero inclination with a speed of 1.7 miles/hour (stage 0) and then increases to a 5% inclination at the same speed (stage 0.5) [9]. Patients underwent the test safely and stopped because of maximal exertion. The peak heart rate (HR_{peak}) was recorded immediately after the end of the test using a fingertip pulse oximetry. The baseline HR_{peak} was needed for the calculation of the target heart rate (THR).

Interventions

Exercise training intervention

The exercise training was prescribed to the patients in the intervention group using the "FITT" principle of exercise prescription laid down by the American College of Sports Medicine [10], as follows:

- frequency – patients exercised for 3 days/week on alternate days;
- intensity – the intensity of the working phase of exercise was set at a THR of 65–75% of HR_{peak}, determined from the incremental exercise test. The THR was monitored during exercise sessions by a fingertip pulse oximetry. The speed of the treadmill was adjusted to make the patients achieve their THR. A low intensity walking at a THR of < 60% HR_{peak} was set for the warm-up and cool-down phases of exercise;
- time (duration) – the time of session was ≤ 45 minutes (5–10 minutes warm-up, 30 min working phase, and 3–5 min cool-down). The moderate-intensity exercise volume = frequency of sessions × actual duration of moderate-intensity exercising = 3 days/week × 30 minutes = 90 minutes/week, which is < 150 minutes per week. The total duration of exercise program was 8 weeks;
- type/mode – continuous treadmill walking exercise.

Antidiabetic drug therapy

Patients in both groups were on oral hypoglycemic medication throughout the entire period of the study.

Statistical analysis

Unpaired t-test was used to analyse the data between the 2 groups at baseline. A paired *t*-test was used to analyse the changes in eAG means within each group after the intervention. A one-way ANCOVA test was used to assess the difference in the postintervention

eAG means between the 2 groups after adjusting for the baseline differences in eAG means between the 2 groups [11, 12]. Descriptive statistics were used to present the data as means ± standard devision. *P*-values < 0.05 were considered statistically significant. GraphPad prism software was used for statistical analysis.

Results

The baseline age and anthropometric characteristics of the patients in the 2 groups are shown in Table 1. As shown in Table 1, there was no statistically significant difference in the anthropometric characteristics between the 2 groups. As shown in Table 2, there was a statistically significant reduction in average blood glucose compared to the baseline values in the exercise group only (paired t test, $p < 0.001$) (Fig. 1, Tab. 2). There was also a statistically significant difference in the eAG means between the 2 groups after the intervention in favour of the exercise group (ANCOVA test, $p = 0.040$) (Fig. 1, Tab. 2).

Discussion

The main findings of this study are as follows:

- low-volume, moderate-intensity exercise (i.e. < 150 minutes/week) combined with oral hypoglycemic therapy induced a highly statistically significant reduction in estimated average blood glucose (eAG) compared to the baseline value ($p < 0.001$);
- the statistically significant improvement in eAG reported in the exercise group was clinically meaningful; the eAG reduced significantly from 187.3 ±18.29 to 147.7 ±10.50 mg/dl, which corresponds to a 1.4% reduction in HbA_{1c}. For each 1% reduction in HbA_{1c} there is an 18% reduction in cardiovascular risk [13] and a 37% decrease in micro-vascular complications [14] in patients with type 2 diabetes;
- compared to the non-exercising control group, the low-volume, moderate-intensity aerobic exercise in addition to oral hypoglycemic medication induced significantly greater improvement in eAG in type 2 diabetic women.

Our results are supported by a recent meta-analysis by Pan *et al*. [15] which has shown that supervised aerobic exercises significantly reduced HbA_{1c} and fasting blood glucose compared to no exercise. Our results are also consistent with a very recent study, which has shown that moderate aerobic exercises are capable of inducing significant improvements in blood glucose levels in type 2 diabetes [16]. In addition, a single session of moderate-intensity exercises was enough to produce a significant reduction in blood glucose in patients with type 2 diabetes, particularly in patients with excess body fatness and worse glycaemic control [17]. Furthermore, a cross-sectional study by Park *et al*. [18] showed that the moderate aerobic exercise can reduce the risk of poor glycaemic control by 0.317 times [18].

Physical exercise training stimulates muscle blood glucose uptake through insulin-dependent and insulin-independent pathways [19]. The cellular mechanisms

Table 1. Baseline anthropometric and clinical characteristics

Parameters	Exercise group ($n_1 = 10$)	Control group ($n_2 = 12$)	*p*
Age [years]	41 ±2.92	44 ±6.87	0.2140
Body weight [kg]	87.58 ±6.16	88.57 ±14.32	0.8413
Height [cm]	157.7 ±2.05	155.28 ±6.74	0.2886
Body mass index [kg/m^2]	35.22 ±2.59	36.75 ±5.69	0.4427
Average blood glucose [mg/dl]	187.30 ±18.29	146.67 ±37.86	0.006**

*Data are presented as means ±SD. ** significant p < 0.05 from the unpaired-t test.*

Table 2. Results of estimated average glucose in the 2 groups before and after the intervention

Outcome measure		Exercise group ($n_1 = 10$)	Control group ($n_2 = 12$)	Exercise vs. Control *p*
Estimated average glucose [mg/dl]	Pre	187.3 ±18.29	146.7 ±37.86	0.006**
	Post	147.7 ±10.50	165.8 ±38.80	0.040‡
	p	< 0 .001*	0.1430	
	Absolute mean change [mg/dl]	–39.6	19.16	
	Relative mean change (%)	↓21.14	↑13.06	

*Data are presented as means ±SD and as absolute and percent mean changes. * significant p < 0.05 from the paired-t test. ** significant p-value < 0.05 based on the unpaired t-test.‡ significant p-value based on the ANCOVA test.*

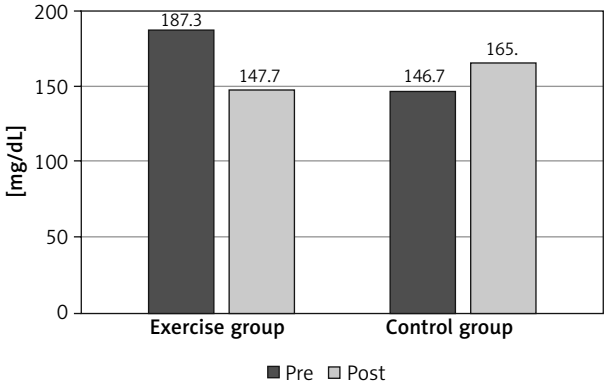

Fig. 1. Mean values of estimated average glucose before and after the intervention

responsible for exercise-induced glucose uptake could be as follows:

- exercise-induced improvement in insulin sensitivity. Moderate-intensity exercise has been found to improve insulin sensitivity within skeletal muscles [20];
- exercise-induced enhancement in mitochondrial function. Patients with type 2 diabetes have been shown to have damaged or dysfunctional mitochondria, which has been associated with insulin resistance [21]. Exercise training restores mitochondrial dysfunction found in type 2 diabetes partly due to increased mitochondrial content, which has been linked with enhanced insulin sensitivity and insulin-mediated glucose disposal [22];
- exercise-induced increased availability, translocation, and expression of glucose transporter 4 (GLUT4). Aerobic exercise training has been reported to increase GLUT4 protein levels within the muscles [23]. Physical exercise is a potent stimulus to increase GLUT4 translocation and expression within skeletal muscles, contributing to improved insulin action and enhanced glucose disposal [24];
- exercise-induced activation of 5' adenosine monophosphate-activated protein kinase (AMPK). Muscle contractions increase AMPK activity – this enzyme plays a major role in stimulating blood glucose uptake by the working muscles [23, 25];
- nitric oxide-mediated blood glucose uptake. Moderate-intensity exercise increases the bioavailability of nitric oxide [26], which plays an important role in the regulation of glucose uptake by muscles during exercise in patients with type 2 diabetes [24, 27]. Nitric oxide stimulates blood glucose uptake by skeletal muscles through modulation of blood flow (i.e. glucose delivery) or by regulation of intramuscular signalling involved in translocation of GLUT4 [28];
- calcium (Ca^{2+}) ion-induced glucose uptake. It has been reported that Ca^{2+} ions released during muscle contraction indirectly mediate glucose uptake through the increased energy expenditure needed for the action of Ca^{2+} pumps in the sarcoplasmic reticulum [23]. However, Jensen *et al*. [25] have suggested that sarcoplasmic reticulum Ca^{2+} plays no role in muscle contraction-stimulated glucose uptake;
- exercise-induced increased muscle temperature could play a role in glucose uptake regulation. There is evidence suggesting that the increased muscle temperature can directly stimulate glucose uptake by the muscle, partly, through the activation of AMPK [29];
- actin cytoskeleton reorganization within the muscles during physical exercise. The actin cytoskeleton is a composition of actin filaments with their accessory and regulatory proteins. The contraction/relaxation of muscle fibres during exercise leads to reorganization of the actin cytoskeleton, which modulates insulin signalling for GLUT-4 translocation, resulting in enhancement of glucose uptake by the muscles [19];
- a potential role of exercise-induced hypoxia in the regulation of blood glucose uptake. Heinonen *et al*. [30] have shown that moderate hypoxia during exercise increased glucose uptake by the muscles; however, this effect is yet to be confirmed;
- exercise-induced adenosine triphosphate turnover and mechanical stress feedback signalling has also been found to stimulate skeletal muscle glucose uptake [25].

Interestingly, the remarkable reductions in average blood glucose seen in the exercise group, compared to the baseline and the control group, occurred without dietary co-intervention. This finding is consistent with the American Diabetes Association position statement, which has reported that supervised aerobic exercise training can reduce blood glucose levels in type 2 diabetic patients regardless of any dietary co-intervention [31]. Limitations of this study include the relatively small number of participants. Also, a few variables were measured; however, the exercise training protocol was designed based on an accurate and individualized determination of targeted exercise intensity using a symptom-limited maximal exercise test to record patients' actual peak heart rate.

Conclusions

Complementary to oral antidiabetics, low-volume, moderate-intensity exercise, performed for less than 150 minutes/week, could be successful in inducing statistically and clinically significant reductions in average blood glucose in women with type 2 diabetes. This improvement can be attributed to exercise-mediated muscle glucose uptake through several cellular mechanisms recruiting insulin-dependent and insulin non-dependent pathways. This finding could be of great clinical relevance for obese patients with type 2 diabetes, particularly women unable to adhere to an exercise volume of ≥ 150 min/week as recommended by the cur-

rent international guidelines, because of low functional capacity or lack of time to exercise. Future research work with a large sample size and both genders may be needed to confirm our findings.

The authors declare no conflict of interest.

References

1. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation 2021. http://www.diabetesatlas.org.
2. Sayed Ahmed HA, Fouad AM, Elotla SF, et al. Prevalence and associated factors of diabetes distress, depression and anxiety among primary care patients with type 2 diabetes during the COVID-19 pandemic in Egypt: a cross-sectional study. Front Psychiatry 2022; 13: 937973.
3. Huebschmann AG, Huxley RR, Kohrt WM, Zeitler P, Regensteiner JG, Reusch JEB. Sex differences in the burden of type 2 diabetes and cardiovascular risk across the life course. Diabetologia 2019; 62: 1761-1772.
4. Pistrosch F, Natali A, Hanefeld M. Is hyperglycemia a cardiovascular risk factor? Diabetes Care 2011; 34: S128-S131.
5. Yang D, Yang Y, Li Y, Han R. Physical exercise as therapy for type 2 diabetes mellitus: from mechanism to orientation. Ann Nutr Metab 2019; 74: 313-321.
6. Kanaley JA, Colberg SR, Corcoran MH, et al. Exercise/physical activity in individuals with type 2 diabetes: a consensus statement from the american college of sports medicine. Med Sci Sports Exerc 2022; 54: 353-368.
7. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ. A1c-derived average glucose study group. Translating the A1C assay into estimated average glucose values. Diabetes Care 2008; 31: 1473-1478.
8. Bruce RA. Exercise testing of patients with coronary heart disease: principles and normal standards for evaluation. Ann Clin Res 1971; 3: 323-332.
9. Noonan V, Dean E. Submaximal exercise testing: clinical application and interpretation 2. Phys Ther 2000; 80: 782-807.
10. American College of Sports Medicine. ACSM's Guidelines for Exercise Testing and Prescription. 10th ed. Lippincott Williams & Wilkins, Philadelphia: PA 2016.
11. Vickers AJ, Altman DG. Statistics notes: analysing controlled trials with baseline and follow up measurements. BMJ 2001; 323: 1123-1124.
12. Twisk J, Bosman L, Hoekstra T, Rijnhart J,Welten M, Heymans, M. Different ways to estimate treatment effects in randomised controlled trials. Contemp Clin Trials Commun 2018; 10: 80-85.
13. Selvin E, Marinopoulos S, Berkenblit G, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med 2004; 141: 421-431.
14. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000; 321: 405-412.
15. Pan B, Ge L, Xun YQ, et al. Exercise training modalities in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. Int J Behav Nutr Phys Act 2018; 15: 72.
16. Shang-Lin C, McLean HM, Yi-Jen H, Wen-Chii T, Meei-Shyuan L, Chia-Huei L. Effects of a 12-week moderate-intensity exercise training on blood glucose response in patients with type 2 diabetes. Medicine 2019; 98: e16860.
17. Oguri M, Adachi H, Ohno T, Oshima S, Kurabayashi M. Effect of a single bout of moderate exercise on glucose uptake in type 2 diabetes mellitus. J Cardiol 2009; 53: 8-14.
18. Park JH, Lee YE. Effects of exercise on glycemic control in type 2 diabetes mellitus in Koreans: the fifth Korea National Health and Nutrition Examination Survey (KNHANES V). J Phys Ther Sci 2015; 27: 3559-3564.
19. Pereira RM, de Moura LP, Muñoz VR, et al. Molecular mechanisms of glucose uptake in skeletal muscle at rest and in response to exercise. Motriz Rio Claro 2017; 23: e101609.
20. Shambrook P, Kingsley M, Taylor N, Gordon B. Accumulated or continuous exercise for glycaemic regulation and control: a systematic review with meta-analysis. BMJ Open Sport Exerc 2018; 17: 1-12.
21. Patti ME, Butte AJ, Crunkhorn S, et al. Coordinated reduction of genes of oxidative metabolism in humans with insulin resistance and diabetes: potential role of PGC1 and NRF1. Proc Natl Acad Sci USA 2003; 100: 8466-8471.
22. Meex RC, Schrauwen-Hinderling VB, Moonen-Kornips E, et al. Restoration of muscle mitochondrial function and metabolic flexibility in type 2 diabetes by exercise training is paralleled by increased myocellular fat storage and improved insulin sensitivity. Diabetes 2010; 59: 572-579.
23. Stanford KI, Goodyear LJ. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ 2014; 38: 308-314.
24. Richter EA, Hargreaves M. Exercise, GLUT4, and skeletal muscle glucose uptake. Physiol Rev 2013; 93: 993-1017
25. Jensen TE, Sylow L, Rose AJ, et al. Contraction-stimulated glucose transport in muscle is controlled by AMPK and mechanical stress but not sarcoplasmatic reticulum Ca^{2+} release. Mol Metab 2014; 3: 742-753.
26. Goto C, Nishioka K, Umemura T, et al. Acute moderate-intensity exercise induces vasodilation through an increase in nitric oxide bioavailiability in humans. Am J Hypertens 2007; 20: 825-830.
27. Kingwell BA, Formosa M, Muhlmann M, Bradley SJ, McConell GK. Nitric oxide synthase inhibition reduces glucose uptake during exercise in individuals with type 2 diabetes more than in control subjects. Diabetes 2002; 51: 2572-2580.
28. Hong YH, Betik AC, McConell GK. Role of nitric oxide in skeletal muscle glucose uptake during exercise. Exp Physiol 2014; 99: 1569-1573.
29. Koshinaka K, Kawamoto E, Abe N, Toshinai K, Nakazato M, Kawanaka K. Elevation of muscle temperature stimulates muscle glucose uptake in vivo and in vitro. J Physiol Sci 2013; 63: 409-418.
30. Heinonen I, Kemppainen J, Kaskinoro K, et al. Effects of adenosine, exercise, and moderate acute hypoxia on energy substrate utilization of human skeletal muscle. Am J Physiol Regul Integr Comp Physiol 2012; 302: R385-R390.
31. Colberg SR, Sigal RJ, Yardley JE, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. Diabetes Care 2016; 39: 2065-2079.