

Moderate-intensity continuous training: is it as good as high-intensity interval training for glycemic control in type 2 diabetes?

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In Egypt, type 2 diabetes is higher in females than in males. Moderate-intensity continuous training (MICT) has been the most widely used exercise form in type 2 diabetes. This study aims to compare the classical MICT to the newly popular high intensity interval training (HIIT) with regard to changes in glycosylated hemoglobin (HbA_{1c}) and estimated average glucose (eAG) in female type 2 diabetics. Twenty-six female patients with type 2 diabetes were assigned into three groups: a control group (n=9), a MICT group (n=9), and a HIIT group (n=8). Patients in both groups exercised on treadmill three days/ week for 8 weeks. Patients in MICT exercised continuously for about 40 min at 65%–75% of peak heart rate (HR_{peak}). Patients in HIIT exercised for 4 × 4 min at 85%–90% of HR_{peak} with 3-min recovery in between at 65%–75% of HR_{peak}. Results showed that HbA_{1c} was reduced significantly from 8.2% (7.45%–

8.65%) to 6.9% (6.6%–7.15%) in MICT and from 8.23% (7.94%–8.85%) to 6.25% (6.1%–6.89%) in HIIT after interventions. Likewise, eAG was significantly reduced from 188.64 mg/dL (167.11–201.55 mg/dL) to 151.33 mg/dL (142.72–158.50 mg/dL) in MICT and from 189.64 mg/dL (181.18–207.29 mg/dL) to 136.69 mg/dL (128.37–151.04 mg/dL) in HIIT. No significant difference was found between HIIT and MICT in the measured variables. It is concluded that the less physically demanding MICT is as good as HIIT for normalizing hyperglycemia in type 2 diabetic females. Therefore, recent interests surrounding HIIT should not overemphasize it compared to the traditional MICT for improving glycemic outcomes.

Keywords: Moderate intensity, High intensity interval, Exercise, Glycemic control, Type 2 diabetes

INTRODUCTION

Type 2 diabetes is a major public health problem not only worldwide but in Egypt as well. According to The International Diabetes Federation Middle East and North Africa Region, there were more than 8 million cases of diabetes in Egypt in 2017 (International Diabetes Federation, 2017). The highest growth of type 2 diabetes in Middle East and North Africa has been found to be for women (Kautzky-Willer et al., 2016; Tobias, 2011). Accordingly, unless effective measures are taken to control this increasingly growing disease, the number of patients, particularly women suffering from the disease and/or its complications is going to increase. There is a huge body of literature that emphasizes

the essential and the central role of exercise in the management of type 2 diabetes. Recently, American Diabetes Association position statement included for the first time high intensity interval training (HIIT) as an alternative type of training that has been demonstrated to induce enhancement in insulin sensitivity and glycemic control in type 2 diabetic patients (Colberg et al., 2016). Nevertheless, for patients' safety, HIIT requires pre-training medical clearance by a health care provider and exercise stress testing may be ordered. In addition, HIIT is a physically demanding workout which can be difficult for sedentary type 2 diabetics, particularly female patients with reduced muscle mass. Moreover, many patients may be unable to keep up with the pace of the HIIT because of its complexity (Colberg et al., 2016; Colberg, 2017). All

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of previously mentioned drawbacks of HIIT represent important barriers to exercise, and do really make of HIIT a hard exercise training form to stick to. Contrary to HIIT, moderate intensity continuous training (MICT) simply does not need pre-exercise medical clearance and is a less physically demanding exercise form than HIIT (Colberg et al., 2016). This simplicity of MICT makes it more suitable for almost all patients with type 2 diabetes especially female patients.

Two recent meta-analysis studies (De Nardi et al., 2018; Jellyman et al., 2015), have investigated the benefits of HIIT versus MICT in patients with type 2 diabetes. Compared to HIIT, it was reported that MICT showed no significant difference with regard to glycosylated haemoglobin (HbA_{1c}) changes and fasting blood glucose (Hollekim-Strand et al., 2014; Karstoft et al., 2013; Mailard et al., 2016; Mitranun et al., 2014; Terada et al., 2013). On the other hand, one meta-analysis study by Liubaoerjijin et al. (2016) has shown that HIIT induced greater improvement in HbA_{1c} in type 2 diabetes. In addition, an earlier study by Tjønnhaug et al. (2008) had reported that HIIT induced significant reduction in fasting blood glucose compared to MICT group in patients with metabolic syndrome. However, a more recent study by Robinson et al. (2015) has conversely shown that MICT showed greater reductions in fasting glucose in prediabetics which was not the case after HIIT. Based on that inconsistency across the results, subsequent trials and further supporting research are needed in this field in an attempt to resolve the controversy about the best type of aerobic exercises which delivers the greatest glycemic benefits. Therefore, the aim of the present study is to compare the traditional MICT with HIIT in female patients with type 2 diabetes with regard to exercise-induced changes in average blood glucose and HbA_{1c}.

MATERIALS AND METHODS

Ethical consideration

The Ethics Committee of Human Scientific Research of the Faculty of Physical Therapy, at Cairo University, approved the study protocol (No.012/001623). After being informed about study procedures, consents were taken from all patients before beginning of the study.

Subjects

At the beginning, thirty female patients with type 2 diabetes were assigned to the present study, and were divided into three groups: a control group (n = 10), a MICT group (n = 10), and a

HIIT group (n = 10). Patients were recruited from Outpatient Diabetes Clinic at Omm El-Misryeen Hospital. Inclusion criteria included: type 2 diabetes, female patients, overweight and obese patients (body mass index [BMI] > 25 kg/m²), patients' ages between 30–50 years, patients undertaking oral hypoglycemic medications with HbA_{1c} either controlled or not. Patients were excluded if they were smokers, pregnant, under current insulin or corticosteroid therapy, and/or participating in any other exercise programs. Patients were also excluded if they had an evidence of cardiopulmonary disease, coronary artery disease, peripheral arterial disease, and orthopaedic or neurological limitations to exercise. Four patients had dropped out from the study as follows: one patient in the control group dropped out due to unknown reason and could not be contacted after 8 weeks; another patient in MICT group dropped out due to sickness after 2 weeks from the beginning; and two other patients in HIIT group dropped out, one due to difficulty of exercise after two sessions and the other one due to work commitments after 4 weeks from the start. The statistical analysis has been done only for patients who completed the study. The control group (n = 9) had mean values of age and BMI of 46 ± 3.9 years and 35.19 ± 3.58 kg/m² respectively. The MICT group (n = 9) had mean values of age and BMI of 40.8 ± 3 years and 35.22 ± 2.58 kg/m² respectively. The HIIT group (n = 8) had mean values of age and BMI of 42 ± 6.8 years and 33.08 ± 4.95 kg/m² respectively. Patients in all groups were instructed to regularly take their diabetic medications and were also allowed to keep up their usual daily physical activities throughout the entire period of the study. In addition, a healthy-eating diet for diabetics was explained to the patients.

Measurements

Demographic and anthropometric data

Age, body weight, and height were obtained from patients at baseline. BMI was calculated according to the following equation: BMI = weight (kg)/height (m²) (World Health Organization, 2000).

Lab analysis of HbA_{1c}

Venous blood samples were taken from patients and HbA_{1c} was measured before and after the study. Biotechnica Instrument diagnostic kits and biochemistry auto analyzer (BT-1500, Biotechnica Instrument S.p.A., Roma, Italy) were used for analysis of HbA_{1c}.

Calculation of estimated average glucose

HbA_{1c} values were translated to average blood glucose accord-

ing to Nathan's regression equation approved by the American Diabetes Association (Nathan et al., 2008), as follows: The estimated average glucose (eAG) in mg/dL = $28.7 \times \text{HbA}_{1c} - 46.7$.

Symptom-limited exercise test

Patients in exercise groups returned on a separate day after blood sampling for performing symptom-limited submaximal exercise test on a treadmill (American motion fitness 8621, made in Taiwan); modified Bruce treadmill protocol was used (Bruce, 1971). The main aim was to measure baseline peak heart rate value for each patient needed for exercise prescription (i.e., determination of the target exercise intensity). The patients performed the test and ended it upon their complaints of exertion, breathlessness, fatigue or discomfort; none of patients experienced symptoms of angina during the test. Peak heart rate (HR_{peak}) value was obtained directly after the end of the test by the use of pulse oximeter (Heal Force, Prince-100B3, Shanghai, China). The treadmill used for exercise test was

Treatment interventions

Supervised exercise training was conducted in Physiotherapy Unit of Ebad Al-Rahman Medical Center in Zawiyat Abu Msallam, Giza. A treadmill was used for exercise training (Vegas 6000, made in China).

The moderate-intensity continuous training (MICT)

Patients in this group performed continuous treadmill walking for about 40 min at intensity of 65%–75% of HR_{peak} three days/week for 8 weeks. The heart rate was continuously monitored by Pulse Oximeter to make sure that it is within the target range.

The high-intensity interval training (HIIT)

According to Tjønnå et al. (2013), patients in this group underwent a warm up at 65%–70% of HR_{peak} , then they walked on a treadmill for 4 intervals of 4 min each at an intensity corresponding to 85%–90% of HR_{peak} with 3 min active recovery in-

terval in between at 65%–75% of HR_{peak} . Finally, a 3-min cool-down period was permitted. The speed and the inclination of the treadmill were adjusted between intervals to ensure that all patients were exercising at the desired target heart rate monitored by Pulse Oximeter.

Statistical analysis

Nonparametric statistics were used due to the small number of the patients. Wilcoxon Signed-Rank Test was used to compare the results within each group before and after intervention. Kruskal-Wallis Test was used to compare results among the three groups before and after the intervention. *Post hoc* paired comparisons after Kruskal-Wallis were done using the Mann-Whitney test and Holm-Bonferroni Method. According to Holm-Bonferroni Method (Holm, 1979): the adjusted *P*-value = Target *P*-value/*n*–rank number of the pair in terms of degree of significance+1; where target *P* = 0.05, *n* = number of paired comparisons, and the rank number of the pair is obtained after ranking *P*-values for all paired comparisons from 1 to *n* in ascending order of size. In this study, since we have three pairs of comparison with 0.05 as the target *P*-value, the adjusted *P*-value for the first-ranked (smallest) *P*-value will equal: $0.05/(3-1+1) = 0.016$. Thus, the most significant of the three *P*-values has to be smaller than 0.016. The adjusted *P*-value for the second-ranked *P*-value equals: $0.05/(3-2+1) = 0.025$. Thus, the second significant *P*-value of the three groups has to be smaller than 0.025. The adjusted *P*-value for the third-ranked *P*-value equals: $0.05/(3-3+1) = 0.05$. Thus, the least significant *P*-value of the three groups has to be smaller than 0.05 (Holm, 1979).

RESULTS

As shown in Table 1, the *P*-value corresponding to Kruskal-Wallis Test was higher than 0.05, suggesting that the baseline characteristics were not significantly different at that level of significance. As shown in Table 2, there were significant reductions

Table 1. Baseline characteristics of patients

Variable	Control group (n = 9)	MICT group (n = 9)	HIIT group (n = 8)	<i>P</i> -value
Age (yr)	45 (41.5–48)	42 (38–43)	44 (35.75–47)	0.056
BMI (kg/m ²)	35.11 (32.2–38)	34.7 (32.85–37.25)	31.62 (28.72–36.45)	0.308
HbA _{1c} (%)	7.1 (6.68–7.95)	8.2 (7.45–8.65)	8.23 (7.94–8.85)	0.055
eAG (mg/dL)	157.07 (145.15–181.46)	188.64 (167.11–201.55)	189.64 (181.18–207.29)	0.056

Values are presented as median (interquartile range).

MICT, moderate intensity continuous training; HIIT, high intensity interval training; BMI, body mass index; HbA_{1c}, glycosylated haemoglobin; eAG, estimated average glucose.

Table 2. Results of each group before and after treatment

Variable	Control group (n=9)		MICT group (n=9)		HIIT group (n=8)	
	Pre	Post	Pre	Post	Pre	Post
HbA _{1c} (%)	7.1 (6.68–7.95)	7.4 (6.9–8.6)	8.2 (7.45–8.65)	6.9 (6.6–7.15)*	8.23 (7.94–8.85)	6.25 (6.1–6.89)*
eAG (mg/dL)	157.07 (145.15–181.46)	165.68 (151.33–200.12)	188.64 (167.11–201.55)	151.33 (142.72–158.50)*	189.64 (181.18–207.29)	136.69 (128.37–151.04)*

Values are presented as median (interquartile range).

MICT, moderate intensity continuous training; HIIT, high intensity interval training; HbA_{1c}, Glycylated haemoglobin; eAG, estimated average glucose.

*Significant *P*-value from Wilcoxon signed rank test.

Table 3. Comparison between the three groups after the intervention with post hoc analysis

Variable	Control group (n=9)	MICT group (n=9)	HIIT group (n=8)	<i>P</i> -value ^{a)}	Treatment pairs	<i>P</i> -value ^{b)}	<i>P</i> -value ^{c)}
HbA _{1c} (%)	7.4 (6.9–8.6)	6.9 (6.6–7.15)	6.25 (6.1–6.89)	0.0070*	HIIT vs. Control	0.007	<0.016*
					MICT vs. Control	0.042	<0.025
					MICT vs. HIIT	0.083	>0.05
eAG (mg/dL)	165.68 (151.33–200.12)	151.33 (142.72–158.50)	136.69 (128.37–151.04)	0.0102*	HIIT vs. Control	0.009	<0.016*
					MICT vs. Control	0.042	>0.025
					MICT vs. HIIT	0.123	>0.05

Values are presented as median (interquartile range).

MICT, moderate intensity continuous training; HIIT, high intensity interval training; HbA_{1c}, Glycylated haemoglobin; eAG, estimated average glucose.

*Significant *P*-value from Wilcoxon signed rank test. ^{a)}Kruskal–Wallis test. ^{b)}Mann–Whitney. ^{c)}Holm–Bonferroni adjusted.

in HbA_{1c} and eAG in both exercise training groups with nonsignificant changes found in the control group. As shown in Table 3, *P*-value from Kruskal–Wallis Test was lower than 0.05, suggesting that at least one pair was significantly different. *Post hoc* paired comparisons were needed to detect possible significant difference between each pair. *Post hoc* paired comparisons after Kruskal–Wallis were done using the Mann–Whitney test and Holm–Bonferroni Method. Since *P*-values of the treatment pair (HIIT vs. control) for HbA_{1c} and eAG were 0.007 and 0.009 respectively (i.e., <0.016), the null hypothesis was rejected for this individual comparison and *P*-value was the most significant value. Since *P*-value of the treatment pair (MICT vs. control) for HbA_{1c} and eAG was 0.042 (i.e., >0.025), the null hypothesis was not rejected for this individual comparison and *P*-value was not significant. Since, the adjusted *P*-value for the second comparison was nonsignificant, we did not have to proceed to the subsequent comparison.

DISCUSSION

The purpose of this study is to investigate whether moderate-intensity continuous exercise could be as good as the high-intensity exercise training with regard to average blood glucose and glycemic control in female patients with type 2 diabetes. The key findings in this study are: (a) Both MICT and HIIT showed statistically significant (*P* < 0.05) reductions in HbA_{1c} and eAG con-

centrations compared to baseline values, with no improvement in the control group. (b) The statistically significant (*P* < 0.05) reductions in HbA_{1c} in both exercise groups were clinically significant as well because all HbA_{1c} values were under control (i.e., HbA_{1c} < 7%) after the study. (c) Compared to the control group, only HIIT showed a statistically significant difference in the measured variables. (d) HIIT has failed to show a statistically significant difference in the same variables when compared to MICT. These observations provided an answer to the research question suggesting that, the less physically demanding MICT can be equally as, just as HIIT in reducing blood glucose concentrations in type 2 diabetes.

Similarly to our results, two recent meta-analysis studies (De Nardi et al., 2018; Jelleyman et al., 2015), have concluded that the traditional MICT is not inferior to HIIT for improving blood glucose and HbA_{1c}. In addition, several studies reported that both MICT and HIIT have induced similar reductions in blood glucose and HbA_{1c} in patients with type 2 diabetes (Hollekim-Strand et al., 2014; Karstoft et al., 2013; Maillard et al., 2016; Mitranun et al., 2014; Terada et al., 2013). Contrary to our results, a meta-analysis by Liubaoerjijin et al. (2016), has reported that higher-intensity exercise led to more reduction in HbA_{1c} compared to the lower-intensity exercise. However, that study does have some limitations including limited sample size, lack of analysis of two recent studies (i.e., Hollekim-Strand et al., 2014; Maillard et al.,

2016), and narrowed inclusion criteria. Thus, the results of that meta-analysis were not conclusive enough.

Explanations for exercise-induced reductions in baseline values of HbA_{1c} and eAG, in both MICT and HIIT groups could be based on several mechanisms: (a) the first mechanism is an insulin-independent stimulus of exercise itself (Colberg et al., 2010; Hawley and Lessard, 2008; Shepherd and Kahn, 1999). (b) The second mechanism is exercise-induced enhanced insulin sensitivity (Braun et al., 1995; Hood et al., 2011; Horton, 1986; Koivisto et al., 1986; Mikines et al., 1988; O'Donovan et al., 2005; Tjønnå et al., 2008; Winnick et al., 2008). (c) The third mechanism is a synergistic effect of insulin and exercised muscle contractions (Santos et al., 2008). (d) The fourth mechanism is exercise-induced improvement in peak VO₂ (Boulé et al., 2003; Larose et al., 2011; Nojima et al., 2017). The first mechanism is exercise independent effect for inducing reductions in HbA_{1c} and average blood glucose. Although insulin is the chief acute physiologic stimulus of glucose disposal, exercise itself has an insulin-like effect. Muscle contractions during exercise have the capability to increase membrane permeability to glucose, and facilitate muscle glucose uptake through activation of intracellular translocation of isoform-4 of glucose transporter (GLUT4) to the cell membrane (American Diabetes Association, 2004). Accordingly, even in the face of insulin resistance, exercise training enhances muscle glucose uptake by a pathway that is not dependent on insulin (Colberg et al., 2010). Both MICT and HIIT can lead to similar improvements in muscle oxidative capacity (Gibala, 2007). The second mechanism is exercise-enhanced insulin sensitivity. Although we did not measure insulin resistance, improved blood glucose concentrations following both types of exercise training could be attributed to improved peripheral insulin sensitivity (Hood et al., 2011; O'Donovan et al., 2005; Winnick et al., 2008). Exercise can enhance insulin sensitivity regardless of exercise intensity (Braun et al., 1995). In patients with insulin resistance, HIIT may seem to produce more improvement in peripheral insulin sensitivity compared to MICT (Jelleyman et al., 2015). However, in sedentary men, moderate-intensity exercise has been found to be as effective as high-intensity exercise in improving insulin sensitivity (O'Donovan et al., 2005). The third mechanism explaining exercise-induced improvement in average blood glucose and HbA_{1c} is a synergistic effect of insulin and muscle contraction, which stimulates the redistribution of GLUT4 from the cytoplasmic vesicles through the sarcolemma, allowing more muscular uptake of glucose (Santos et al., 2008). The fourth potential mechanism is exercise-induced improvement in peak VO₂. De-

spite being not measured in the present study, peak VO₂ was reported to be increased after aerobic exercises (Boulé et al., 2003), which has been found to be correlated with reductions in HbA_{1c} (Larose et al., 2011; Nojima et al., 2017). Based on this evidence, we can assume that an improvement in peak VO₂ did occur after both types of exercise training, which could ultimately improve glucose utilization and glycemic control.

Limitations of this study include the relatively small number of patients per group and lack of male patients, which could affect the generalisability of the findings. Moreover, neither insulin sensitivity nor peak VO₂ was measured. Nevertheless, this study does have strengths as well; in the present study, the determination of the target heart rate and/or the intensity of exercise for each patient were accurately made according to the actual values of peak heart rate obtained from treadmill sub-maximal exercise test. We did not use predicted or estimated equations to predict or estimate peak heart rate values.

In conclusion, this study was conducted as an additional research work in the field of exercise training in type 2 diabetes, in an attempt to resolve inconsistency in the results among the earlier studies which have compared the glycemic outcomes between MICT and the HIIT. The major findings in the present study are that both MICT and HIIT similarly have delivered statistically and clinically significant reductions in HbA_{1c} and eAG compared to baseline values with no significant difference between the two exercise training types. Accordingly, to achieve glycemic control in type 2 diabetes, the easily practiced MICT can substitute for the more physically demanding HIIT. Additional studies are needed to confirm our findings, and further research work directed to the field of exercise training in diabetes is recommended.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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