

Effect of Inspiratory Muscle Training on Health-Related Quality of Life in Patients with Type 2 Diabetes

Ahmad Mahdi Ahmad, Heba Mohammed Ali, Hala Mohammed Abdelsalam

Ahmad Mahdi Ahmad, Department of Physical Therapy for Internal Medicine, Faculty of Physical Therapy, Cairo University, Egypt
Heba Mohammed Ali, Department of Physical Therapy for Internal Medicine, Faculty of Physical Therapy, Beni Suef University, Egypt
Hala Mohammed Abdelsalam, Department of Clinical Pathology, National Nutrition Institute, Cairo, Egypt

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Correspondence to: Ahmad Mahdi Ahmad, Department of Physical Therapy for Internal Medicine, Faculty of Physical Therapy, Cairo University, Egypt.
Email: ahmed.mahdy@pt.cu.edu.eg
Telephone: +200100705664

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ABSTRACT

Patients with type 2 diabetes have poor health-related quality of life due to the disease itself and/or its complications. Pharmacological treatment alone seems to be insufficient to improve quality of life for those patients. Thus, additional interventions are needed to achieve this target. Therefore, the main purpose of this study was to investigate the effect of inspiratory muscle training (IMT) on health-related quality of life as an adjunctive to drug treatment in type 2

diabetics. Twenty eight female patients with type 2 diabetes were equally assigned into two equal groups. The first group was the study group and received supervised IMT at low intensity (30% P_{max}), once daily, 5 days per week, and for 8 weeks plus oral hypoglycemic medications. The second group acted as a control group and received oral hypoglycemic medications only. Health-related quality of life was assessed by the EuroQoL Group's 5-dimension 5-level questionnaire (EQ-5D-5L) and the Short Form-12 (SF-12) Health Survey. Glycosylated haemoglobin (HbA_{1c}) was also measured. Results showed that, IMT induced significant improvement in SF-12 physical functioning and vitality domains with observed non-significant improvements in other SF-12 domains and EQ-5D-5L VAS score. Also, HbA_{1c} was not improved in either group. In addition, there was between-group significant difference in (EQ-5D-5L) VAS score, SF-12 physical functioning, role physical, role emotional, bodily pain, and social functioning domains. Conclusion: Despite having no effect on glycemic control, low intensity inspiratory muscle training still can improve some aspects of health-related quality of life in female patients with type 2 diabetes.

Key words: Inspiratory muscle training; Health-related quality of life; Type 2 diabetes

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INTRODUCTION

Type 2 diabetes is an increasingly growing health problem in Egypt with a significant impact on health-related quality of life (HR-QoL). Patients with type 2 diabetes have deteriorated HR-QoL because of the disease itself and/or its subsequent complications. Women have lower HR-QoL than men, and this becomes even worse when type

2 diabetes coexists with other chronic illness^[1,2]. Thus, quality of life for patients with type 2 diabetes should receive more attention, and improved health-related quality of life in those patients should be the ultimate goal of diabetic management plan.

The routine management plan of type 2 diabetes focuses mainly on pharmacological treatment. However, many patients with type 2 diabetes have poor quality of life despite being on a regular pharmacological therapy. Thus, it seems that medications alone are not enough to produce a remarkable improvement in quality of life for those patients and complementary interventions are needed to produce a noticeable effect.

Inspiratory muscle training (IMT) seems to be an appealing intervention in this regard as it has proved to be effective in improving quality of life in patients with chronic obstructive pulmonary disease^[3-7], in patients with heart failure^[8-10], and in patients with chronic kidney disease^[11]. Nevertheless, in patients with type 2 diabetes, IMT has been studied for outcomes other than health-related quality of life in a number of studies^[12-15]. IMT improved inspiratory muscle function^[12], and acutely reduced blood glucose^[13,14], but failed to induce long term reduction in blood glucose levels or changes in blood lipids^[15]. Thus, it appears that the effect of IMT on health-related quality of life (HR-QoL) still has not been investigated in type 2 diabetes. Therefore, the main purpose of this study was to investigate the effect of IMT, as a complementary intervention to drug therapy; on health-related quality of life (HR-QoL), and glycosylated haemoglobin (HbA_{1c}) as well, in type 2 diabetic females. The results of this study may help efforts directed to improving quality of life for those patients.

SUBJECTS AND METHODS

Ethical considerations

The protocol of this study was approved by the Ethics Committee of Scientific Research at the Faculty of Physical Therapy, Cairo University. Written consents were obtained from patients before the beginning of the study.

SUBJECTS

Twenty eight female patients with type 2 diabetes were recruited for this research by referral from the Outpatient Clinic of Diabetes in Omm El Misryeen Hospital, Giza, Egypt. Inclusion criteria included type 2 diabetics, female patients, patients from 30- 55 years old, overweight (BMI > 25 Kg/m²) and obese (BMI > 30 Kg/m²) patients, and type 2 diabetic patients on regular oral hypoglycemic medications. Inclusion criteria also comprised patients with controlled HbA_{1c} (i.e. < 7%), and patients with uncontrolled HbA_{1c} (i.e. 7-10%) but still being on their medications. Exclusion criteria included type 1 diabetes, male patients, female smokers, type 2 diabetic patients under current insulin therapy, pregnancy, pre-diabetics, patients with other metabolic or hormonal disorder, patients with pulmonary disease, patients with heart failure, or patients with chronic kidney disease. Eligible patients were equally divided into two groups; an IMT group (*n* = 14), and a control group (*n* = 14). IMT group received routine pharmacological treatment plus IMT; twelve patients underwent supervised IMT program, while two patients received unsupervised IMT at home. The compliance of patients to the home IMT was checked by telephone calls. The control group received the routine pharmacological treatment only. Twenty six patients completed the study as two patients had dropped out from IMT group.

METHODS

1. Measurements

1.1 Demographic and anthropometric measures

Patients' ages were obtained. Body weight (BW) and height were measured by weight and height scale. Body mass index (BMI) was calculated according to this formula: BMI (Kg/m²) = BW/ height in meter squared^[16].

1.2 Maximal Inspiratory Pressure (Pimax)

Pimax was simply measured by an aneroid manometer gauge connected to a tube. A nose clip was used and the patient was instructed to seal the lips tightly around the tube, and to breathe in as deeply as possible. The manometer recorded the negative pressure generated which represented the maximal inspiratory pressure for the patient^[17-20].

1.3 Health-related quality of life (primary outcome)

Health-related quality of life (HRQoL) was assessed by two questionnaires.

1.3.1 The EuroQoL Group's 5-dimension 5-level questionnaire (EQ-5D-5L)

The EuroQol five-dimension questionnaire (EQ-5D) is a standardized questionnaire produced by the EuroQol Group to provide an easy, uncomplicated and collective assessment of health for clinical evaluation. The Arabic version of EQ-5D-5L was obtained from the author (i.e. the EuroQol Group)^[21].

The EQ-5D-5L comprises two pages: one page contains five dimensions with five answer levels, and the other page contains visual analog scale (VAS) of the patient's overall health. The VAS is a continuous response scale that ranges from 0 (worst state) to 100 (best state). All patients reported their perception of their general health state before and after the intervention by selecting a point on this scale^[22].

1.3.2 The Short Form-12 (SF-12) Health Survey

The SF-12® Health Survey is a 12-item short questionnaire developed from the widely used SF-36 and covers the same domains of health outcomes as SF-36 but with answer choices that cover wider range of health states. The Arabic SF-12 version was used^[23], and reversed scoring was done for four items so that all SF-12 domains are scored that a higher score indicates a better health state^[24,25]. For all measurements, scores were transformed linearly to scales ranging from 0 to 100, with 0 indicating maximal impairment and 100 indicating no impairment^[26]. The SF-12 was administered to the patients before and after the intervention to assess patient's physical, emotional, and social aspects; mental health, bodily pain and vitality from the patient's perspective.

1.4 Glycosylated haemoglobin (HbA_{1c}) (Secondary outcome)

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

2. Treatment intervention

The treatment sessions were conducted in the Outpatient Diabetes Clinic at Omm El-Misryeen Hospital, Giza, Egypt. Inspiratory muscle exercise training (IMT) protocol was the same as the previously published data^[15]. Threshold inspiratory muscle training device was used (Threshold IMT®, Koninklijke Philips Electronics

N.V., China). The intensity of inspiratory exercises was set at 30% Pimax. IMT duration was 10-15 min/session in the first two weeks, 15-20 min/session for the next three weeks, and for 20-25 min/session till the end of the study. The IMT session comprised 5-8 sets with 20-30 breaths per set and 2 min rest inbetween. IMT was practiced once daily, 5 days/ week, and for 8 weeks. IMT was supervised for all patients in the study group except for two patients who were practicing IMT at home and were followed up by telephone calls. The patients were instructed to perform IMT through deep breathing^[27].

3. Statistical analysis

First, the normal distribution of data was assessed by Shapiro-Wilk normality test^[28]. In regard with age, body weight, BMI, and duration of diabetes; unpaired t test was used to compare their values between the two groups at baseline. In regard with HbA_{1c}, EQ-5D-5L (VAS) score, and SF-12 domains; Mann-Whitney U test was used to statistically compare data between the two groups at baseline and after the intervention. Wilcoxon Signed-Rank test was used to statistically analyze the data before and after the intervention within each group. For all tests, values of *p* < 0.05 were considered as statistically significant. Statistical analysis was done using Statistical Social Science and Graph Pad Prism software.

RESULTS

As shown in table 1, there was no significant difference between the two groups in any of the measured variables at baseline. As

shown in table 2, there was within-group significant difference in SF-12 physical functioning and vitality domains in the study group and a significant increase of HbA_{1c} in the control group after the intervention. In addition, there was between-group significant difference in EQ-5D-5L VAS score, SF-12 physical functioning, role physical, role emotional, bodily pain, and social function domains.

DISCUSSION

To our knowledge, this study is the first study that investigates the effect of IMT on health –related quality of life (HR-QoL) in type 2 diabetic patients. The main findings in this research are that IMT had induced significant improvement in SF-12 physical functioning and vitality domains, as well as observed improvements in EQ-5D-5L VAS score, SF-12 role physical, bodily pain, role emotional, and social functioning domains in female patients with type 2 diabetes. Upon comparison between the two groups, the observed improvements in these variables in the study group had succeeded to be significantly different from those in the control group. These observations may pay attention to a new role of IMT in type 2 diabetes patients’ population, aiding efforts that seek a better healthy life for those patients.

In regard with HR-QoL, similarly to our results; Dall’Ago *et al*^[8], have demonstrated that IMT (at 30% Pimax for 12 weeks) induced a significant improvement in quality of life in patients with heart failure compared to the control group. Also, Soares *et al*^[29], have shown that inspiratory muscle training at 30% of Pimax had improved quality of life (QoL) in patients receiving haemodialysis.

Table 1 Baseline patients' characteristics.

Variable	Control group (n = 14)	Study group (n = 14)	P value
Age (Years)	44.00 ± 6.97	42.36 ± 5.58	‡ 0.497
Body weight (Kg)	89.21 ± 12.98	84.57 ± 13.07	‡ 0.354
BMI (Kg/m ²)	37.10 ± 5.22	34.55 ± 4.61	‡ 0.182
Duration of DM (yrs)	2.9 ± 3.36	3.9 ± 3	‡ 0.386
HbA _{1c} (%)	6.63 (5.7 - 7.3)	6.68 (5.9 - 7.2)	¶ 0.802
EQ-5D-5L Health State VAS Score (%)	65 (50 - 80)	75 (57.5 - 86.25)	¶ 0.190
SF-12 Physical Function Scale (%)	25 (0 - 56.25)	50 (18.75 - 50)	¶ 0.303
SF-12 Role Physical Scale (%)	0 (0 - 100)	12.5 (0 - 100)	¶ 0.522
SF-12 Role Emotional Scale (%)	0 (0 - 12.5)	50 (0 - 100)	¶ 0.136
SF-12 Bodily Pain Scale (%)	50 (43.75 - 50)	50 (43.75 - 56.25)	¶ 0.779
SF-12 Mental Health Scale (%)	40 (27.5 - 60)	50 (47.5 - 80)	¶ 0.207
SF-12 Vitality scale (%)	20 (0 - 45)	40 (20 - 45)	¶ 0.368
SF-12 Social Function Scale (%)	25 (25 - 75)	62.5 (25 - 100)	¶ 0.167

The data are expressed as means ± SD and medians and 25th-75th percentiles. ‡= P value from Unpaired t-test. ¶ = P value from Mann-Whitney U test. MI = Body mass index; HbA_{1c} = Glycosylated haemoglobin; EQ-5D-5L = The EuroQoL Group's 5-dimension 5-level questionnaire, VAS=Visual analogue scale. SF-12: The short form-12 questionnaire.

Table 2 Comparisons within each group & between the two groups after the intervention.

Variables	Control group (n = 14)			Study group (n = 12)		
	Pre	Post	Δ	Pre	Post	Δ
HBA _{1c} %	6.63 (5.7 - 7.3)	7.2 (6.4 - 8.16)*	↑0.78 ± 1.43	7.03 (5.7 - 7.26)	7.65 (6.85 - 8.5)	↑0.93 ± 1.77
EQ-5D-5L Health state VA Score %	65 (50 - 80)	60 (50 - 72.5)	↑0.71 ± 14.78	75 (52.5 - 88.75)	80 (71.9 - 83.75) §	↑6.89 ± 18.11
SF-12 physical Function Scale (%)	25 (0 - 56.25)	12.5 (0 - 25)	↓7.14 ± 20.63	50 (25 - 50)	72.72 (50 - 93.75)* §	↑28.78 ± 20.99
SF-12 Role Physica Scale (%)	0 (0 - 100)	0 (0 - 0)	↓17.85 ± 37.24	12.5 (0 - 100)	100 (18.18 - 100) §	↑28.97 ± 14.11
SF-12 Role Emotional Scale (%)	0 (0 - 12.5)	0 (0 - 0)	↓7.14 ± 18.15	25 (0 - 100)	50 (0 - 100) §	↑8.33 ± 46.87
SF-12 Bodily Pain Scale (%)	50 (43.75 - 50)	37.5 (0 - 50)	↓12.5 ± 23.51	50 (50 - 68.75)	56.81 (50 - 75) §	↑11.55 ± 22.27
SF-12 Mental Health Scale (%)	40 (27.5 - 60)	50 (20 - 55)	↓2.14 ± 18.88	50 (42.5 - 80)	55 (50 - 75.22)	↑2.57 ± 24.56
SF-12 Vitality Scale (%)	20 (0 - 45)	40 (20 - 60)	↑8.57 ± 23.15	40 (20 - 40)	40 (40 - 75)*	↑15.90 ± 21.41
SF-12 Social Function Scale (%)	25 (25 - 75)	25 (18.75 - 50)	↓3.57 ± 27.48	62.5 (31.25 - 100)	75 (75 - 100) §	↑14.95 ± 34.02

The data are expressed as medians and 25th-75th percentiles as well as means ± SD. * *p* < 0.05 significant difference within each group (Wilcoxon Signed-Rank Test). § *p* < 0.05 significant difference between study and control group (Mann-Whitney U test). Δ= Absolute (total) change, ↑ = increased, ↓= decreased. HBA_{1c} = Glycosylated haemoglobin; EQ-5D-5L = The EuroQoL Group's 5-dimension 5-level questionnaire, VAS=Visual analogue scale. SF-12: The short form-12 questionnaire.

The significant improvement in SF-12 physical functioning domain within IMT group and the significant between-group difference in SF-12 role physical domain and 5D-5L VAS score function could be attributed to; (1) decrease in breathlessness perception during daily physical activities. As IMT has consistently been found to reduce exertional dyspnea either in healthy or patients population^[30], (2) Another possible explanation could be improvements in inspiratory muscles strength and endurance with resultant improved performance of these muscles. This explanation can be supported by several studies^[8,29,31-33]. The results of these studies showed that low intensity IMT (at 30% Pimax) increased inspiratory muscle strength and function in patients with heart failure^[8], in patients receiving haemodialysis^[29], in patients with metabolic syndrome^[31], in patients with COPD^[32], and in patients atrial fibrillation^[33]. (3) Furthermore, a possible improvement in physical activity tolerance after IMT could represent additional explanation for our results. This could result in reduction in patients' difficulties and discomforts while performing activities of daily living. This explanation can also be supported by a number of studies^[27,32-33]. These studies reported that IMT at low inspiratory loading had induced the following benefits: an increase in walking ability and 6 minutes walking distance compared to the control group in patients with sub-acute stroke^[27], an increase in exercise tolerance measured by 12-minute walking test in patients with COPD^[32], and an increase in 6-minute walking distance in patients with atrial fibrillation^[33].

The physiological mechanism beyond these explanations may be an enhanced O₂ delivery to the working muscles of the patients during daily life physical activities with more recruitment of aerobic metabolism within the muscles. This in turn reduces skeletal muscle fatigability and increases patients' tolerance to physical activities. It has been reported that, IMT can induce enhancement in pulmonary oxygen uptake (VO₂) dynamics as a consequence of reduction in inspiratory muscle fatigue and improvements in alveolar ventilation and diffusion^[34]. Enhanced pulmonary oxygen uptake rate was found to be linked with concomitant improvements in oxygen delivery and utilization in skeletal muscles during physical activities via the cardiovascular system and transport processes within muscle tissue^[35]. Thus, the net result would be more utilization of aerobic system with reduction in the fatigability of the limb muscles and increase time to exhaustion during patient's physical movements. This ultimately would lead to more easiness and comfort in performing daily living and social activities.

In regard with glycemic control, it has been proved that an earlier review of HbA_{1c} after 8 weeks was highly correlated and strongly predictive of 12-weeks HbA_{1c} levels^[36]. Thus, analysis of HbA_{1c} after our 8-weeks intervention was of sufficient accuracy to explore glycemic control either in the control or in the study group. Our study has showed that, in the control group; there was a statistically significant elevation in HbA_{1c} after the intervention which indicated worse glycemic control of patients in this group. In the study group, there was also poor glycemic control after the intervention but did not reach statistically significant level; IMT was not able to reverse the hyperglycemia in type 2 diabetic women in this group as well. This finding was in accordance with what was reported by Ahmad *et al*^[15], who have shown that low intensity IMT was not able to reduce blood glucose levels in female patients with type 2 diabetes. Also, similarly to this finding, Feriani *et al*^[31], have also shown that IMT at 30% Pimax failed to reduce hyperglycemia in older women with metabolic syndrome. Furthermore, Silva *et al*^[37], have found that two months of IMT at 40% Pimax did not induce any significant improvement in glycemic control in older adults. Although IMT

could not improve glycemic control in our study, it is not surprising that IMT was able to improve some aspects of health-related quality of life for patients with type 2 diabetes despite their poor glycemic control. Because there is no evidence that an increased HbA_{1c} value is accordingly associated with a reduced quality of life in type 2 diabetic patients, and therefore a cause- effect relationship between a poor glycemic control and a low quality of life cannot be established. There are several studies investigated this issue^[38-42], all of which have reported no association between glycemic control and quality of life. That is, patients with poor glycemic control do not accordingly have a concomitant worse HR-QoL and vice versa. For example, Lau *et al*^[41], had conducted their research for 12 months and finally they concluded that a good glycemic control did not lead to a better physical HR-QoL. Furthermore, Riaz *et al*^[42], had reported that mental and physical aspects of SF-12 health survey were independent of glycemic control status in patients with diabetes.

In conclusion, our study was the first one to shed light on a new and favorite role of the IMT, as a complementary intervention to drug therapy, in improving health-related quality of life in female patients with type 2 diabetics. Low intensity IMT can improve some aspects of health- related QoL independently from improvement in glycemic control. Being simply taught and easily practiced either supervised or unsupervised at home, IMT can be recommended to be a part of diabetic management plan for type 2 diabetics, particularly for female patients who could have personnel, social, cultural, or physical barriers to traditional physical exercise training. Future studies with larger sample size may be needed to confirm our results.

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