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Effects of Inspiratory Muscle Training on Respiratory Muscle Strength, Functional Capacity and Health Related Quality of Life of Patients Following Lung Transplantation

Nissan Graur[1,3], Paltiel Weiner[4] and Mordechai Reuven Kramer[1,2]*

[1]Pulmonary Institute, Beilinson Hospital, Petach Tikva, Israel

[2]Department of Medicine, Tel Aviv University, Israel

[3]Department of Physical Therapy, University of Haifa, Israel

[4]Department of Medicine, Technion, Haifa, Israel

Abstract

Lung Transplantation (LTx), which has by now become an established treatment option for patients with a wide variety of end-stage lung diseases, is aimed at improving quality of life and survival. Prior studies illustrated respiratory muscle function impairment in patients who undergone lung transplantation. The objective of this study was to evaluate the effects of an Inspiratory Muscle Training (IMT) program on respiratory muscle strength, functional capacity, physical work capacity and Health-Related Quality of Life (HRQL) of patients following lung transplantation. Four male and one female who had undergone lung transplantation, more than one year prior to the study, participated in a four months inspiratory muscle training program and were evaluated before and after intervention. All of the participants were given instructions for self-management of the power breathe inspiratory muscle trainer (POWER breathe Medic Classic: Gaiam Ltd, Southam, Warwickshire, UK), during the baseline assessment. Participants were instructed to practice IMT daily at home, six times a week (a 15-min session twice a day) at 60% of Maximal Inspiratory Pressure (MIP) value. The results obtained after the IMT program showed an increase in the six-minute walk test and in the maximal inspiratory pressure. There was also an increase in some HRQL domains as shown by the SF-36 questionnaire values. The physical work capacity measured by the peak oxygen consumption (VO_2 peak) and pulmonary function showed no significant change. Therefore, the IMT program in these five patients improved functional capacity, respiratory muscle strength and HRQL.

Keywords: Lung transplantation; Inspiratory muscle training; Maximal inspiratory pressure, 6-Minute walk test

Abbreviation

6-MWT: 6-Min Walk Test; IMT: Inspiratory Muscle Training; MIP: Maximal Inspiratory Pressure; LTx: Lung Transplantation; HRQL: Health-Related Quality of Life

Introduction

Lung Transplantation (LTx) has become an established treatment option for patients with a wide variety of end-stage lung diseases, with the aim to improve quality of life and survival [1]. Nevertheless, exercise intolerance, functional disability, and peripheral muscle weakness often persist following LTx [2,3]. Moreover, prior studies illustrated respiratory muscle function impairment in patients who undergo LT [4,5].

Inspiratory Muscle Training (IMT) has been used for a long time and is defined as any intervention aimed at training the inspiratory muscles [6]. IMT can be carried out with threshold devices, which facilitates the function of the inspiratory muscles [7]. IMT can improve inspiratory muscle strength, endurance, dyspnea, exercise capacity and quality of life and maintaining these benefits requires long term treatment in adults with Chronic Obstructive Pulmonary Disease (COPD) [8-9]. Although most of the research on inspiratory muscle training has focused on adults with COPD [7-8,10-12], some studies have been conducted on patients with asthma [13-15], cystic fibrosis [16-19], postoperative thoracic surgery or upper abdominal surgery [20-23] and in

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***Correspondence:**
Nissan Graur, Department of Physical Therapy, Pulmonary Institute, Beilinson Hospital, University of Haifa, Hazait 84, Sitriyya, 76834, Israel,
E-mail: nisdia62@gmail.com

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critically ill adults [24]. IMT provides additional benefits for patients undergoing a Pulmonary Rehabilitation (PR) program and is even worthwhile for those who have already completed a General Exercise Reconditioning (GER) program [25]. IMT may also provide added benefits together with or without Pulmonary Rehabilitation (PR) for patients following lung transplantation.

The purpose of the present study was to evaluate the effects of an IMT program on respiratory muscle strength, functional capacity, physical work capacity and Health-Related Quality of Life (HRQL) of patients following lung transplantation.

Materials and Methods

Subjects

The present study was characterized as a report of a case series describing five patients, 4 male and 1 female, who had undergone LTx, more than one year prior to the study and were recruited from the outpatient clinic of the Pulmonary Institute, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel. None of the patients was participating in any additional regular exercise or sport activity.

Inclusion criteria: 1) At least one-year post-LTx; 2) Able to perform pulmonary function tests; 3) Clinically stable for at least one month.

Exclusion criteria: 1) Unstable cardiovascular disease; 2) Required supplemental oxygen; 3) Cor pulmonale; 4) Poor compliance.

Patient characteristics are summarized in Table 1.

Study design

All five patients were assigned to receive IMT for four months. All tests were recorded at baseline before training, and at 4 months, at end of training period. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all subjects.

Tests

Spirometry: Forced Vital Capacity (FVC), Forced Expiratory Volume in One second (FEV1) and Maximum Voluntary Ventilation (MVV) were measured three times on a computerized spirometer according to standard techniques and American Thoracic Society/ European Respiratory Society (ATS/ERS) guidelines (Zan 530: Oberthulba, Wurzburg, Germany) [26-27]. All the measured parameters were presented as the percent of predicted (% pred) values of the European Community for coal and Steel [28]. MVV was presented as L/min.

Cardiopulmonary exercise test (VO_2 peak test): The Cardiopulmonary Exercise Test (CPET) was performed according to established guidelines [29-32]. All tests were supervised by a physician. Patients were instructed to take their usual medications as prescribed. A 10-15 W/min ramp protocol was performed on an electromagnetically braked cycle ergometer (Ergoline -800S) to the patient's maximal subjective exertion level and respiratory exchange ratio (RER ≥ 1.1) [29]. During the test, 12-lead electrocardiogram, blood pressure, pulse oximetry (SpO_2) and breath-by-breath respiratory gas exchange were recorded and monitored (Zan 600, Oberthulba). All peak cardiopulmonary data were calculated and the analysis was based on the average of the last 30s of the test. The anaerobic threshold was determined by the dual methods approach, using the V-slop method combining Ventilatory Equivalents (VE/VO_2 and VE/VCO_2) [20]. Predicted values of peak oxygen consumption (VO_2 peak) were determined according to Jones et al. [33]. Based on prospective data of 100 subjects (50 males and 50 females) from the general population aged 15-71 years.

Six-minute walk test: The 6MWT test was set according to ATS guidelines [34]. The distance the patient was able to walk in 6 min was determined in a measured 35-meter corridor at the pulmonary unit within the hospital. The patients were instructed to walk at their fastest pace and cover the longest possible distance over 6 min under the supervision of a physiotherapist. The test was performed twice, and the best result was recorded.

Respiratory muscle strength: Inspiratory muscle strength was assessed by measuring the Maximal Inspiratory Pressure (MIP) at residual volume and the expiratory muscle strength was assessed by measuring the Maximal Expiratory Pressure (MEP) at total lung capacity, using the technique proposed by Black and Hyatt [35]. Mouth pressures were measured by an electronic pressure transducer (MicroRPM; Micromedical, Kent, UK). Assessments were repeated at least three times (30s recovery between attempts), and the value obtained from the best effort was recorded.

Health-related quality of life (HRQL): Health-related quality of life was measured by the Hebrew Short -Form (SF-36) Questionnaire [36], which has been used widely in many studies and health service institutions. The most popular generic HRQoL instrument is the SF-36. The SF-36 features physical and mental summary scores, and a 4-point change in the SF-36 is considered clinically significant.

The intervention program

The five patients participated in the study for four months. An experienced senior physiotherapist monitored participation in the IMT program and supervised the group.

Inspiratory muscle training (IMT) program: All of the Participants were given instructions for self-management of the Power breathe inspiratory muscle trainer (POWER breathe Medic Classic: Gaiam Ltd, Southam, Warwickshire, UK), during the baseline assessment.

Participants were instructed to practice IMT daily, six times a week (a 15-min session twice a day), for a period of four months. The training was performed using the Power breathe Medic Classic trainer. The participants started breathing at a resistance that required the generation of 15% of their Maximal Inspiratory Mouth Pressure (MIP) for an adaptation period of one week. The load was then increased incrementally for each participant, at a rate of 5% to 10% each session, to reach a generation of 60% of their MIP by the end of the first month. IMT was then continued at 60% of their MIP and adjusted monthly to the newly achieved MIP.

Participants performed IMT at home, and this was verified by phone by the main investigator three times weekly over the four-month period. The purpose of these telephone calls was to answer any questions that the participants might have regarding the performance of their IMT trainer and to remind them to complete the daily IMT training. This is an accepted strategy for controlling clinician contact in clinical trials involving disabled patients with chronic lung disease [37].

Data analysis

All clinical and physiological parameters were presented as mean ± Standard Deviation (SD). Patient's baseline characteristics, all parameters were presented as changes (delta) from baseline to post-

Table 1: Patient characteristics of Training Group (n=5).

Age (years)	**39.4** ± **17.7**
Male/Female	04-Jan
Time from Transplantation (months)	15 ± 3.5
Disease	
Basic lung disease	
• Cystic Fibrosis	3
• Emphysema	2
Type of Transplantation	
• SLT	2
• DLT	3
BMI (index)	20 ± 4.8
Weight (kg)	57.6 ± 8.1
Height (cm)	171.2 ± 15

Abbreviations: IMT: Inspiratory Muscle Training; BMI: Body Mass Index; DLT: Double Lung Transplantation; SLT: Single Lung Transplantation

Data presented as means and standard deviations at the following measures: Age, Time from transplantation, BMI, Weight, and Height. All other measures are presented as frequencies

Table 2: Comparison of pulmonary function and VO2 peak pre- and Post-Inspiratory Muscle Training (IMT).

Pulmonary Function Tests	Pre-IMT(T0)	Post-IMT (ΔT1-T0)
FVC% predicted	76.6 ± 7.9	2.6 ± 13.6
FEV1% predicted	68.4 ± 20	2 ± 22
MVV (L/Min)	81.2 ± 42.6	12.8 ± 43.3
VO_2 peak % predicted	44.4 ± 9.6	3.6 ± 11.5

Abbreviations: MVV: Maximal Voluntary Ventilation; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in 1 sec; VO_2 peak, Values of peak Oxygen Consumption; T0 - Baseline; T1, after 4 months of intervention. Data presented as means and standard deviations

intervention.

Results

No adverse events were observed during the IMT program. The participants did not practice any other exercise training or sports activity at home while participating in the study and none of the participants was hospitalized.

Spirometry and VO_2 peak

After 4 months of training, there was no significant change in FEV1, FVC, MVV and VO_2 peak values (Table 2).

Respiratory muscle strength

After 4 months of training, there was a significant increase in MIP values in all participants, but there was no significant change in MEP values (Table 3).

6 Minutes' walk test (6 MWT)

After 4 months of training, there was a significant increase in the 6MWT distance in all participants (Table 3).

Health-related quality of life

A summary of the SF-36 questionnaire results and comparisons pre- and post-IMT are shown in Table 4.

In the physical health domain of the SF-36, the difference in the HRQL values between pre-IMT and post-IMT was 15 ± 44.7. It can be classified as an improvement with work or activities. In the vitality (energy/fatigue) domain of the SF-36, the difference in the HRQoL values between pre-IMT and post-IMT was 6 ± 16.7. It can be classified as no feelings of exhaustion and fatigue. In the mental health (emotional well-being) domain of the SF-36, the difference in the HRQoL values between pre-IMT and post-IMT was 8.8 ± 11.4. It can be classified as no limitations in social activities due to mental health problems. In the social functioning domain of the SF-36, the difference in the HRQL values between pre-IMT and post-IMT was 17.5 ± 20.5. It can be classified as an improvement with social activities due to health and emotional health.

Table 3: Comparison of respiratory muscle strength and functional capacity pre- and post- inspiratory muscle training (IMT).

	Pre-IMT (T0)	Post-IMT (ΔT1-T0)
MIP (cm H_2O)	104.2 ± 14.5	31.8 ± 14.6
MEP (cm H_2O)	121.4 ± 37.9	6.6 ± 30.6
6 MWT (m)	540.4 ± 74.8	48.8 ± 71

Abbreviations: MIP: Maximal Inspiratory Pressure; MEP: Maximal Expiratory Pressure; 6-MWT: 6-Minutes-Walk Test; T0, Baseline; T1 - After 4 Months of Intervention. Data presented as means and standard deviations

Table 4: Summary of the SF-36 questionnaire average scores pre- and post-Inspiratory Muscle Training (IMT) in post LT patients.

SF-36 Domains	Pre-Inspiratory Muscle Training (IMT)	The difference in the HRQL values between pre-IMT and post-IMT (ΔT1-T0)
Physical Functioning	81 ± 15.2	-3 ± 21.7
Physical Health	**65** ± **48.7**	**15** ± **44.7**
Emotional Health	80 ± 44.7	0 ± 44.7
Vitality- Energy/Fatigue	**45** ± **11.7**	**6** ± **16.7**
Mental Health/Emotional Well-Being	**68.8** ± **16.3**	**8.8** ± **14.3**
Social Functioning	**67.5** ± **25.9**	**17.5** ± **20.5**
Pain	67 ± 21.8	2 ± 25.9
General Health	55 ± 3.5	0 ± 18.4

T0 - Baseline; T1- After 4 Months of Intervention

Categories with the highest difference in the quality of life between pre- and post-Pulmonary Rehabilitation (PR) in post LT patients are in bold. Data presented as means and standard deviations

Discussion

In the present study, we examined the before and after training effects of a 4-month IMT program on inspiratory muscle strength, functional capacity, physical work capacity and HRQL in post-LTx patients. To the best of our knowledge, no previous study of IMT programs in patients following LTx have investigated respiratory muscle strength, before and after training. The participants were more than one year (15 ± 3.5 months) post-LTx. The IMT program was well tolerated by all patients.

Following four months of IMT we found significant increase in MIP and 6MWT but there was no significant change in FEV1, FVC, MVV, MEP and VO_2 peak values.

The results of our study show that in post lung transplantation patients, even more than one year after the lung transplantation, inspiratory muscles can be trained with improvement of muscle strength (MIP values). The improvement in the inspiratory muscle strength is associated with improved exercise performance (6MWT distance), and improved HRQL, but with no improvement in pulmonary function and physical work capacity (VO_2 peak).

The results of our basic IMT program were in agreement with previously published studies in which significantly increased inspiratory muscle performance was associated with improved exercise tolerance [38].

Prior studies illustrated respiratory muscle function impairment in patients who undergone lung transplantation [4,5].

A number of studies have assessed inspiratory muscle strength after lung transplantation. Their results are somewhat inconsistent (differences methods used to assess respiratory muscle strength and differences in patients' characteristics). Studies in patients with Heart-Lung Transplantation (HLT) reported decreased Maximal Inspiratory Pressure (MIP) [39,40], but in other studies in recipients of HLT or DLT found MIP values within normal or slightly reduced [41-48].

The positive effect of the IMT program on physiological and clinical outcomes in our patients following lung transplantation can be explained by several mechanisms. It is possible that repetitive stimulus of high ventilator demands during inspiratory muscle sessions, chest expansion during deep breathing while exercising with the inspiratory muscle trainer device -all of which were used in the present study, resulted in a more efficient breathing pattern, and improved the respiratory muscle strength and performance.

An evidence-informed clinical approach article [49], reported that MIP and Maximal Expiratory Pressure (MEP) values, lower-extremity muscle force, and 6MWT distance continued to improve at 12 and 18 months after the LTx procedure. The VO_2 peak test value, however, reached its highest predicted value at 6 months after the LTx procedure and did not change at 12 or 18 months after the LT procedure.

It is likely that the baseline level of respiratory muscle performance before admission to LTx may be a factor conditioning the change after training. Thus, despite the interesting results of our study, lack of such data is a drawback.

The results of our study consequently emphasize the importance for routine screening for weakness of inspiratory muscles in patients who are candidates for LTx, particularly in patients who have a history of chronic respiratory illness as COPD, with well-established respiratory muscle weakness.

According to the summary of the results of the SF-36 questionnaire, we found that our five patients exhibited significantly higher ratings differences in HRQL values between pre-IMT and post-IMT in 4 of the 8 health domains: physical health (higher score by 15 ± 44.7 points), emotional well-being (higher score by 8.8 ± 14.3 points), social functioning (higher score by 17.5 ± 20.5 points) and energy/fatigue (higher score by 6 ± 16.7 points). Together, these results could indicate positive improvement following participation in an IMT program in patients post LTx (Table 4).

It is the first case series report to show significant improvements in MIP, 6MWT, and HRQL after participating in an IMT program in this population. To date, the prognostic value of IMT alone in patients following lung transplantation is unknown. We think that an IMT program could have an additional benefit for patients following lung transplantation, given that significant improvements were detected in MIP, 6MWT, and HRQL following these interventions. Enhancement in these parameters may increase physiological reserves, delay the clinical course, and slow the progression and the decline of the general condition. This issue needs to be further ascertained through long-term studies.

The first limitation of this case series study was the small number of participants combined with the variability between patients following LTx who participated in this IMT program.

Second, although MIP values reflect the respiratory muscle strength better than MEP, no studies to date have been conducted to determine a cutoff value for MIP that requires Inspiratory Muscle Training (IMT) in patients following LTx. Therefore, future studies should identify a cutoff MIP value that requires IMT program in this population.

In conclusion, in our small case series report population the participants were more than one year after the lung transplantation. There was a significant increase in respiratory muscle strength (MIP values), functional capacity (6 MWT distance), and HRQL after the IMT program. The HRQL in our LTx patients was higher in the following domains of the SF-36 questionnaire: Emotional well-being, social functioning, energy/fatigue and physical health.

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