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Case Series

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Inspiratory Muscle Training Effects on Respiratory Muscle Strength, Functional Capacity, Physical Work Capacity and Health-Related Quality of Life of Cystic Fibrosis Patients Following Lung Transplantation: A Three Case Series Report

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Abstract

Lung transplantation, 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 undergo lung transplantation. The objective of this study was to evaluate the effects of an inspiratory muscle training program on respiratory muscle strength, functional capacity, physical work capacity and health-related quality of life of cystic fibrosis patients following lung transplantation. Three male subjects with cystic fibrosis, who had undergone lung transplantation, 15-17 months 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 inspiratory muscle training daily at home, six times a week (a 15 min session twice a day) at 60% of maximal inspiratory pressure value. The results obtained after the inspiratory muscle training program showed an increase in the six-minute walk test and in the maximal inspiratory pressure. There was also an increase in some health-related quality of life domains as shown by the SF-36 questionnaire values. The physical work capacity measured by the peak oxygen consumption (VO2 peak) and pulmonary function showed no significant change. Therefore, the inspiratory muscle training program in these three patients improved functional capacity, respiratory muscle strength and health-related quality of life.

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

Abbreviation: 6MWT: 6-Minute Walk Test; IMT: Inspiratory Muscle Training; MIP: Maximal Inspiratory Pressure; LT: Lung Transplantation; HRQL: Health-Related Quality of Life; CF: Cystic Fibrosis; MEP: Maximal Expiratory Pressure

Introduction

Lung Transplantation (LT) is an established therapy for patients with end-stage Cystic Fibrosis (CF). CF is the commonest indication for those aged <50 years of age needing LT. CF LT is associated with a 45% 10-year survival, according to the world's largest registry [1,2]. Nevertheless, exercise intolerance, functional disability, and peripheral muscle weakness often persist following LT [2-8]. Prior studies illustrated respiratory muscle function impairment in patients who undergo LT [9-11].

Inspiratory Muscle Training (IMT) is defined as any intervention aimed at training the inspiratory muscles. IMT can be carried out with a threshold inspiratory trainer, which facilitates the function of the inspiratory muscles [12,13]. IMT can improve inspiratory muscle strength, endurance, dyspnea and exercise capacity in adults with Chronic Obstructive Pulmonary Disease (COPD) [14]. Although most of the research on inspiratory muscle training has focused on adults with COPD [13,15-19], some studies have been conducted on patients with asthma [20,21], cystic fibrosis [22-25] and postoperative thoracic surgery [23-25]. 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 [26]. IMT may also provide added benefits (together with or without PR) for patients following lung transplantation.

The purpose of the present case series report was to evaluate the possible benefits of an IMT program on respiratory muscle strength, functional capacity, physical work capacity and health-related quality of life (HRQL) of three cystic fibrosis patients following lung transplantation.

Case Presentation

The present study was characterized as a report of a case series describing the physical therapy management using an IMT protocol of three young male subjects with CF, who had undergone double lung transplantation (DLT), 15-17 months prior to the study. They were recruited from the outpatient clinic of the medical center (Pulmonary Institute, Rabin Medical Center, Beilinson Hospital, Petach Tikva,

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Israel). None of the patients were performing additional regular exercise or sport activity during participation the study. There were at least four months post-LT, able to perform pulmonary function tests and clinically stable for at least one month.

Initial evaluation

Their characteristics are summarized in Table 1.

All tests were performed before, and 4 months, after starting the training period. A group of three patients assigned to receive IMT for four months.

All the data were collected by the same investigator. The study protocol was approved by the institutional ethics committee, and informed consent was obtained from all the subjects.

Outcomes

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) [27-28]. All the measured parameters were presented as the percent of predicted (%pred) values of the European Community for coal and Steel [29]. MVV was presented as L/min.

Cardiopulmonary exercise test (VO2 peak test): A Cardiopulmonary Exercise Test (CPET) was performed according to established guidelines [30-33]. 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) [30]. During the test, 12-lead electrocardiogram, blood pressure, pulse oximetry (SpO2) 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 30 s of the test. The anaerobic threshold was determined by the dual methods approach, using the V-slope method combining ventilatory equivalents (VE/VO2 and VE/VCO2) [30]. Predicted values of peak oxygen consumption (VO2 peak) were determined according to Jones et al. [34], 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 6 MWT test was performed according to ATS guidelines [35]. The distance the patient was able to walk in 6 minutes was determined in a measured 35 metre 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 minutes under the supervision of a physiotherapist. The test was performed twice, and the best result is reported.

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 [36]. Mouth pressures were measured by an electronic pressure transducer (MicroRPM; Micromedical, Kent, UK). Assessments were repeated at least three times (30 s recovery between attempts) and the value obtained from the best effort was used.

Health-Related Quality of Life (HRQL): Health-related quality of life was measured by the Hebrew Short–Form (SF-36) Questionnaire [37], which has been used widely in many studies and health service institutions. The most popular generic HRQL 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.

Intervention program

The three 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-minute session twice a day), for a period of four months. The training was performed using the Power breathe trainer. The participants started breathing at a resistance that required the generation of 15% of their maximal inspiratory mouth pressure for an adaptation period of one week. The load was then increased incrementally for each participant, at a rate of 5-10% 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 [38].

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.

	Participant 1	Participant 2	Participant 3
Age (years)	23	29	29
Time from Transplantation (months)	16	15	17
BMI (index)	19.9	16.7	19.7
Weight (Kg)	48	58	64
Height (cm)	155	186	180
Abbreviations: BMI: Body Mass Index. All Measures are presented as Frequencies.			

Table 1: Demographic and characteristics of the three male transplant patients.

Spirometry and VO2 peak

After 4 months IMT, there was no significant change in FEV1, FVC and VO2 peak values. There was a significant change in MVV values in participant 1 and participant 2 (Table 2).

Respiratory muscle strength

After 4 months of training, there was a significant increase in MIP values in all participants, but MEP values were unchanged (Table 3).

6-Minute Walk Test (6MWT)

After 4 months of training, there was a significant increase in the 6MWT distance only in participant 2 and participant 3 (Table 3).

Health-related quality of life (HRQL)

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

Participant 1 achieved more than a 4-point increase in the following domains: Emotional well-being (4 point change), social functioning (12.5 point change), pain (10 point change) and general health (5 point change).

Participant 2 achieved more than a 4-point increase in the following domains: energy/fatigue (10 point change), social functioning (12.5 point change). Participant 3 achieved more than a 4-point increase in the following domains: physical functioning (10 point change), energy/fatigue (25 point change), emotional well-being (24 point change), social functioning (12.5 point change), pain (10 point change) and general health (15 point change). Only participant 3 had an increase in the physical functioning domain, which can be classified as all most no difficulties with mobility and the activities of daily living (walking down the street, up the stairs, shopping, bathing, and dressing without any assistance). In participants 1 and 3 there was an increase in the emotional well-being domain, which can be classified as almost no problems with situations where the mental and health condition do not limit social life and activity.

In all three participants, there was an increase in the social functioning domain, which can be classified as no problems in social activities and obstacles arise due to health and emotional problems (with family, friends and at work). In participants 1 and 3, there was an increase in the pain domain, which can be classified as almost no problems indicating the presence of pain. In participants 1 and 3, there was an increase in the general health domain, which can be classified as mild problems with general feeling of health. In participants 2 and 3, there was an increase in the energy/fatigue domain, which can be classified as all most mild problems in participant 2 and no problems in participant 3 with feeling of exhaustion and fatigue, pessimism, but experienced energy and happiness.

Discussion

In the present case series report, we examined the possible benefits of a 4-month IMT program, on inspiratory muscle strength, functional capacity, HRQL, predicted values of peak oxygen consumption (VO2 peak) and pulmonary function in three cystic fibrosis patient's post-lung transplantation. The participants were more than one-year (15-17 months) post lung transplantation. The IMT program was well tolerated by all three participants.

The results of our case series report show that in post lung transplantation cystic fibrosis patients, even more than one year after the 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), MVV values and improved HRQL, but with no improvement in pulmonary function and physical work capacity (VO2 peak).

Pulmonary Function Tests	Participant 1 Pre (T0)	Post (ΔT1-T0)	Participant 2 Pre (T0)	Post (ΔT1-T0)	Participant 3 Pre (T0)	Post (ΔT1-T0)e
FVC% predicted	78	-1	75	7	76	4
FEV1%predicted	88	1	87	3	69	4
MVV(L/Min)	58	30	57	14	72	5
VO2 peak % predicted	40	4	39	2	59	5
Abbreviations: MVV: Maximal Voluntary Ventilation; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in 1 sec; VO2 peak: Values of Peak Oxygen Consumption; T0: baseline; T1: After 4 months of intervention.						

Table 2: Comparison of pulmonary function and VO2 peak pre and post-IMT.

	Participant 1 Pre (T0)	Post (ΔT1-T0)	Participant 2 pre (T0)	Post (ΔT1-T0)	Participant 3 Pre (T0)	Post (ΔT1-T0)
MIP (cmH_2O)	98	17	100	26	87	30
MEP (cmH_2O)	85	2	88	3	80	7
6MWT(m)	545	17	592	33	630	61
Abbreviations: MIP: Maximal Inspiratory Pressure; MEP: Maximal Expiratory Pressure; 6MWT: 6 Minute Walk Test; T0: baseline; T1: After 4 months of intervention.						

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

SF-36 Domains	Participant 1 Pre (T0)	Post (ΔT1-T0)	Participant 2 pre (T0)	Post (ΔT1-T0)	Participant 3 Pre(T0)	Post (ΔT1-T0)
Physical functioning	90	0	100	0	80	**10**
Physical health	100	0	100	0	100	0
Emotional health	100	0	100	0	100	0
Energy/fatigue	55	-5	30	**10**	55	**25**
Emotional Well being	88	**4**	72	0	64	**24**
Social functioning	87.5	**12.5**	75	**12.5**	87.5	**12.5**
Pain	90	**10**	80	0	67.5	**10**
General health	55	**5**	55	0	60	**15**
Categories with the highest difference in the quality of life between pre and post-IMT are in **bold.**						

Table 4: Summary of the SF-36 questionnaire results comparison between pre and post-IMT.

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 [15].

Prior studies illustrated respiratory muscle function impairment in patients who undergo lung transplantation [9-11]. 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]. In seven patients with DLT for cystic fibrosis or bronchiectasis, Reynaud-Gaubert et al. [47] reported substantial improvements in endurance time to sustained inspiratory efforts performed after, compared with before, surgery; they also noted that endurance time continued to increase. 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. According to the summary of the results of the SF-36 questionnaire, our three patients exhibited the best results in the quality of life in the following domains: emotional well-being, social functioning, pain, general health, energy/fatigue and physical functioning (Table 4).

Our study group included three CF patients after lung transplantation aged 23,29,29 years old. For this age group, the problems generated will probably be due to the intervention of lung transplantation, debilitating disease prior to transplantation including nutritional abnormalities and peripheral muscle weakness which are prevalent in adult and children with CF, most likely related to CF itself and respiratory failure, rather than to old age as in other lung diseases (COPD, pulmonary fibrosis, etc. Lung transplantation (LT), 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 [1]. Improvement in HRQL is an important objective of the lung transplant procedure. It has even been suggested that for diseases such as COPD, improving HRQL is the primary goal of the lung transplant procedure [9]. Yet there is a paucity of studies of HRQL in post-LT patients, because both the incidence of the procedure and recipients' survival rates are limited.

The study of Anyanwu et al. [49] was one of the first to address the important issue of potential differences in HRQL according to the type of LT procedure, comparing HRQL in SLT, DLT and HLT recipients. They conducted a cross-sectional study of 87 pre-transplant and 255 post-transplant patients and found a greater rate of HRQL improvement among the DLT and HLT recipients, relative to the SLT recipients.

In summary, although the reports about HRQL in post-LT patients are favorable [50], more research is needed to better understand the specific causative factors affecting HRQL in LT recipients.

To the best of our knowledge, the present case series report is the first IMT program which studied its effects in patients who have undergone lung transplantation. It is the first case study to show significant improvements in MIP, 6MWT, MVV values 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, MVV values 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.

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 (6MWT distance), MVV values and HRQL after the IMT program. Future studies should identify a cutoff MIP value that requires IMT during a PR program or alone in post lung transplantation patients.

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