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An Integrated Outpatient Training Program for Patients with Pulmonary Hypertension - the Munich Pilot Project

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Abstract

Background: The purpose of this study was to examine the effect of an integrated outpatient training program on exercise capacity and health-related quality of life (HRQOL) in patients with pulmonary hypertension (PH).

Methods: 17 patients of our pulmonary hypertension program (World Health Organization clinical classification system "Dana Point 2008" group 1 n=14, group 4 n=3, age 61±13 years, 11 female [65%], body mass index [BMI] 26.7±5.9) on stable disease-targeted medication attended a supervised integrated outpatient training program including breathing exercises, education, strength and endurance training for 1.5 hours once a month for 10 consecutive months. Patients` exercise capacity was evaluated performing a 6 minute walk test (6MWT), and their quality of life was assessed by the standardized "Short Form 36 Health Survey" and the "Cambridge Pulmonary Hypertension Outcome Review" (CAMPHOR), before and after the program. Data analysis was performed using the paired T-test.

Results: All patients completed the outpatient training while medication remained unchanged during the observational period. At baseline 6-minute walk distance was 383 ± 91 m and after 10 months 391 ± 85 m (p=0.157). Both, HRQOL questionnaires, SF-36 and CAMPHOR, tended to improve with a significant signal only in the CAMPHOR activity core (p < 0.023), indicating improved physical capabilities. During the 10 months observation period no adverse events occurred in the study group.

Conclusion: Our data suggest that an integrated outpatient training is safe and may be beneficial as an adjuvant therapeutic option. The best approach for a structured outpatient training for PH patients merits further investigation.

Keywords: Pulmonary hypertension; Exercise capacity; Pulmonary rehabilitation; Quality of life

Introduction

In a cohort of long-term lung transplant survivors, we showed significant improvements of functional outcome and health-related quality of life (HRQOL) achieved by either inpatient or outpatient rehabilitation [1]. In pulmonary arterial hypertension Mereles et al. were the first to show functional improvement with in-patient pulmonary rehabilitation. Based on our experience in lung transplantation we hypothesized that outpatient pulmonary rehabilitation might be of value for PH patients as well. Recently, Fox et al. published their first experiences regarding an ambulatory rehabilitation for PH. The objectives of this study were to investigate the safety of an outpatient supervised comprehensive training program and the effect on HRQOL and exercise capacity in PH patients.

Methods

17 (11 female, 6 male, age 62 ± 13 years, body-mass index 26.7 ± 5.9 kg/m2) patients from the Munich PH center were enrolled in the study according to their willingness and ability to attend the ambulatory training program. Patients were prospectively followed for 10 months, starting in November 2010. For at least 3 months before enrolement only clinically stable patients on optimized targeted PH therapy (prostanoids, phosphodiesterase-5 inhibitors, endothelin receptor antagonists) as well as study medication (riociguat) were included [2,3]. Main inclusion criteria were: minimum age 18 years; confirmed PH diagnosis by our institution according to the standard haemodynamic criteria at right-heart catheterization and World Health Organization functional class (WHO FC) II-III [4]. Exclusion criteria comprised: WHO FC I or IV; ailments associated with a contraindication for physical workout, pulmonary hypertension due to left heart disease and patients with nerves and motor dysfunction as well as with psychological problems [1,4].

The pilot project was performed in accordance with the recommendations of the local ethics committee at the Ludwig Maximilians University of Munich. PH patients attended an integrated outpatient training program at our clinic for 1.5 hours once a month. Moreover, all participants were given printouts to repeat the physical exercises at home. The training program took place in cooperation with the Department of Physical Medicine and Rehabilitation of the University of Munich and was closely supervised by physiotherapists and physicians being present during the training [5-8].

At their baseline and final evaluation visit, patients were assessed using the standardized HRQOL questionnaires and completed a

submaximal physical examination (6 minute walk test) in order to determine physical capacity. Additional clinical data were retrieved from individual charts.

Health related quality of life

HRQOL data were assessed using two questionnaires: the „Short Form 36 Health Survey" (SF-36) as a generic instrument and the „Cambridge Pulmonary Hypertension Outcome Review" (CAMPHOR) as a PH specific questionnaire [9-11].

Short form 36 health survey

The SF-36 is a multipurpose, short form health questionnaire with 36 items. It measures three aspects of health quantified by eight multi item variables: functional ability (physical functioning, social functioning, role limitations attributed to physical problems, role limitations attributed to emotional problems), well-being (mental health, energy and fatigue, pain) and overall health (general medical health). For each variable, the item scores are coded, added up and transformed into a scale from 0 (worst possible health) to 100 (best health) [9]. The German validated version 1.0 of the SF36 was used [9,10].

Cambridge pulmonary hypertension outcome review

The CAMPHOR is a disease specific outcome measure to assess the impact of PH and its treatment on quality of life and health-related quality of life [11]. It consists of three sections on the basis of 65 items (the first two address HRQOL issues): 1 symptom (impairment) score, 2 activity (disability) score; and 3 quality of life. Each statement on the CAMPHOR "symptom" and "quality of life" sections is given a score of "1" or "0" and are added up to provide a total score that ranges from 0 (good) to 25 (poor); the activity section is scored "0", "1" and "2" with a score ranging from 0 (good) to 30 (poor), respectively [11].

6 Minute walk test

The 6 minute walk test (6MWT) measures the distance that a patient can walk quickly on a flat, hard surface over a period of 6 minutes monitored by a supervisor. Oxygen saturation, pulse and blood pressure are measured at the beginning and the end of the test. The 6 minute walk test was performed according to the guidelines of the American Thoracic Society [12].

Comprehensive training program

The patients participated in an exercise program once a month for 90 minutes at low workloads (10 to 60 W) that was supervised by physical therapists (one-by-one) and a physician. The training consisted of 30 minutes breathing exercises for improvement of diffusion capacity and the musculoskeletal system of the respiratory pump, 30 minutes moderate strengthening exercises and very moderate endurance training of orthostatic leg muscles with general coordination movements as well as 30 minutes of education.

Education sessions were aimed at promoting self-management to improve patients perception of their individual physical abilities and limits to keep physical exercise safe even in demanding situations and were facilitated by various members of the multidisciplinary team including physiotherapists, physicians, a dietician, a pharmacist and a nurse. Topics included e.g. activities of daily living (personal hygiene and household tasks), PH specific medication, maintaining and improving physical function, a balanced nutrition and awareness of coordination of breath and physical activity in order to avoid right-heart strain.

The training intensity was increased (e.g., up to 30 W) with respect to the individual tolerability and improvement. Training intensity was limited by peak heart rate (no more than additional 30 bpm after exercise), oxygen saturation >85%, and subjective physical exertion. Furthermore, subjective rating of dyspnea and physical exertion according to Borg Scale (no more than a rating of 6 out of 10) were used to adjust the training intensity [13].

Respiratory therapy intended to enhance oxygen uptake by utilization of whole lung capacity and comprised of slowing down and deepening of breath, airway clearance (gentle cough technics and strategies to suppress the need to cough), stretching and breathing techniques such as pursed lip breathing to prevent valsalva maneuver during demanding exercises, body perception, modified Yoga, and strengthening of respiratory muscles.

Physical activity involved functional training: (a) upper and lower limb strength training consisting of three to five individual exercises (e.g. step-ups, squats, adjusted and individualized technic for climbing stairs) with three sets 5 repetitions (concentric- and eccentric muscle tension for 2 seconds, respectively) with progression of the training load based on the patient's tolerance (b) stretches of major muscle groups including biceps, muscles of the shoulder and the trunk and (c) range of motion exercises of the vertebra, shoulder girdle, trunk and thorax.

Furthermore, patients received a training manual and were asked to repeat respiratory and exercise training at home once daily for a total of 15 to 30 minutes for 5 days a week. The amount of training at home was supervised by written form and was discussed with physiotherapists and physicians at the next training session. During the home-based respiratory and exercise training, all patients were asked to keep in close phone contact with the physiotherapists and physicians of the training program as needed.

Statistics

Data analysis was performed using Microsoft Excel 2010 (Microsoft® Office Professional, Microsoft Corporation, San Francisco) and SPSS version 19.0 (SPSS Inc., Chicago, IL). Differences in HRQOL as well as 6MWT data before and after the training period were analyzed using the paired t-test. All values are listed as arithmetic mean with standard deviation. A p-value of <0.05 was considered significant.

Results

Table 1 shows the baseline characteristics of the study population. 17 consecutive patients with PH (35% WHO FC II and 65% WHO FC III) were assessed. Seven patients received supplemental oxygen at rest. All participants completed all parts of the training and were included in the evaluation.

PH Patients	N [%]
Age [years ± SD]	62 ± 13
Min	23
Max	73

Gender [n/%]	
Male	6 [35]
Female	11 [65]
Body-Mass-Index [kg/m2]	26.7 ± 5.9
Min	15
Max	343.25]ars ndex [kg/m2]iod; EOS,.2
WHO Functional Class [n]	
1	-
2	6 [35]
3	11 [65]
4	-
Cardiac Catheterization	
mPAP [mm Hg]	40.8 ± 15.7
PVR [dyn*s*cm -5]	7 ± 3.8
CI [L * min -1 * m-2]	2.7 ± 0.6
RAP [mm Hg]	6 ± 3
Medication [n]	
ERA	8
PDE5i	5
Prostanoids [inh.]	2
Investigational product (riociguat)	2
Monotherapy	12 [71]
Combination therapy	5 [29]

Table 1: Baseline characteristics of the study population. PH: Pulmonary Hypertension; WHO: World Health Organisation; mPAP: mean Pulmonary Artery Pressure; PVR: Pulmonary Vascular Resistance; CI: Cardiac Index; RAP: Right Atrial Pressure; ERA: Endothelin Receptor Antagonist; PDE5i: Phosphodiesterase-5-Inhibitor; values are mean ± SD.

Health-related quality of life

Regarding the SF-36 health questionnaire, the 10 months training program did not result in significant improvements (Figure 1).

There was a trend towards improved scores for physical domains, without reaching statistical significance. In contrast, the disease specific CAMPHOR showed a significantly enhanced "activity" score (p=0.023) in comparison to the baseline value (Figure 2).

Exercise capacity

With respect to exercise performance, the study group as a whole improved by a mean of 9 m of six-minute walking distance after completion of the exercise program, but this effect did not reach statistical significance (383 ± 91 m vs. 392 ± 85 m; p=0.157; Figure 3).

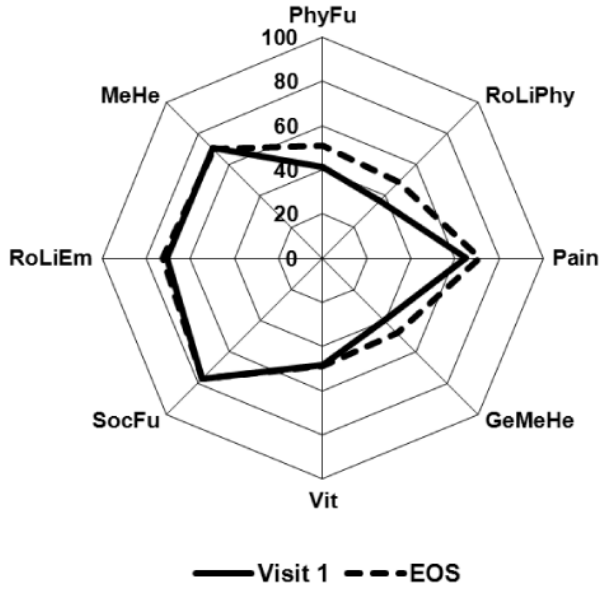

Figure 1: Results from the Short-Form 36 Health Questionnaire. Visit 1, before the training period; EOS: End-Of-Study; PhyFu: Physical Functioning; RoLiPhy: Role Limitations Attributed to Physical Problems; GeMeHe: General Medical Health; Vit: Vitality; SocFu: Social Functioning; RoLiEm: Role Limitations Emotional; MeHe: Mental Health. p>0.05.

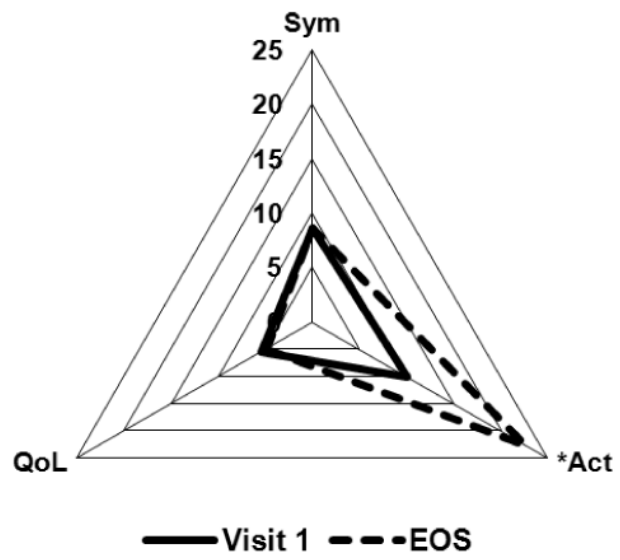

Figure 2: Results from the Cambridge Pulmonary Hypertension Outcome Review. Visit 1, before the training period; EOS: End-Of-Study; Sym: Symptoms; Act: Activity; QoL: Quality of Life. *p <0.05 for Visit 1 vs EOS.

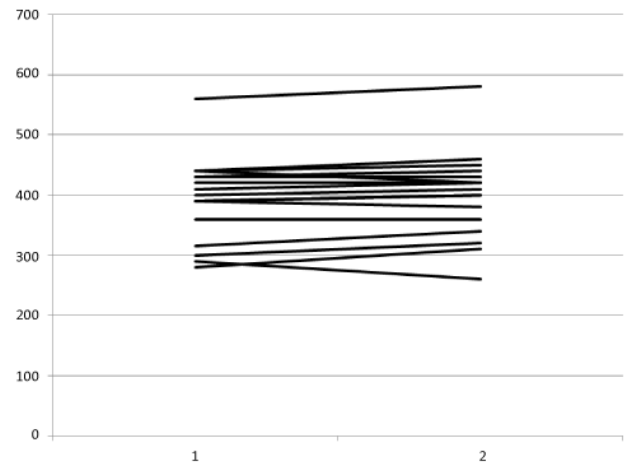

Figure 3: Individual Rresults from the 6- Minute Walk Test, n=17. 1, 6- minute walking distance before the training period; 2, 6-minute walking distance after the training period. (mean value 383±91 m vs. 391 ± 85 m, p=0.157).

Safety

All patients tolerated the exercise training well and experienced no adverse events due to physical activity at our institution along with exercise training at home. There were no changes in PH medication during the observation period, no deterioration of PH, no PH-related hospitalizations and no deaths.

Discussion

This study addresses the safety of an integrated outpatient training program for PH patients and its effect on HRQOL and exercise capacity. Within this study, patients were prospectively followed over a period of 10 months. The main findings were as follows: [1] no adverse events occurred during the training period; [2] there was no statistical significance before and after the exercise program for 6MWD and SF-36, except CAMPHOR activity core ($p < 0.023$), indicating improved physical capabilities.

Compared to previous studies examining the effect of a physical training on exercise capacity in PH patients, our findings are modest [5-7]. Mereles et al. evaluated 30 PH patients randomly assigned into normal physical activity and intensive inpatient rehabilitation for 3 weeks followed by a home exercise program for 12 weeks [5]. Rehabilitation group patients experienced substantial improvements of averaging 96 meters (22%) in their 6 minute walking distance (6MWD) [5]. Fox et al. assessed 22 patients who were allocated to outpatient rehabilitation (n=11) or to the control group [8]. The rehabilitation group underwent 24 1-hour sessions of exercise training over 12 weeks. After the training, the 6MWD improved significantly by 32 meters and the control group decreased by 26 meters [8]. In contrast, we could only achieve an accrual of 9 meters without reaching statistical significance. One reason for this most likely involves the frequency of our outpatient training. We performed a monthly training of 1.5 hours of breathing exercises, education, strength and endurance training. This rather low training frequency might be insufficient to generate a more pronounced increase in 6MWD. Moreover, training not only comprised of endurance training which might be reflected in an enhancement of 6MWD, but pursued a holistic approach, especially designed for real-life conditions. Mereles et al. focused on interval bicycle ergometer training with an increase of the training intensity with respect to the individual tolerability and improvement [5]. Furthermore, 60 minutes of walking was performed 5 days a week and consisted of flat-ground and uphill walking. This approach of a dose-response strategy of endurance training and exercise capacity resulted in an impressive increase in 6MWD (85 ± 56m).

The mechanism by which rehabilitation improves exercise capacity is not entirely clear. In fact, the reasons for exercise intolerance in PH patients are multifactorial, comprising a decreased oxygen supply in peripheral muscles, impaired skeletal muscle function (loss of slow-twitch fibers and mitochondrial aerobic enzyme deficits) and deconditioning [14-17].

While Fox et al. reported positive effects of an outpatient supervised exercise program on exercise capacity in individuals with PH. However, they did not analyze the impact of improved physical activity on quality of life [8]. In our study we investigated not only changes in exercise performance but also in HRQOL of patients undergoing an outpatient physiotherapy program. Physical activity is directly associated with improved health in patients with chronic cardiopulmonary diseases [17]. Mereles et al. demonstrated that respiratory and exercise training was associated with a significant improvement in 5 of 8 SF-36 scales, with respect to the physical domain, compared to control group patients following inpatient rehabilitation [5]. Except of a statistically significant signal from CAMPHOR "activity" score, we found trends of improved values for physical domains of HRQOL according to SF-36. On the other hand our patient group did not deteriorate during a 10 months period which is in contrast to the otherwise relentlessly progressive course of PH, even in mild disease. The optimal intensity of an outpatient training program remains to be elucidated. There are some limitations to our study. The absence of a control group precludes definite conclusions from our pilot study. Moreover, exercise capacity and HRQOL were measured only twice, before and after the ten months study period and do not allow any conclusions regarding the endurance of the effects observed.

It was the purpose of our study to evaluate an integrated outpatient training for assistance in everyday life offered by a local PH center as an add-on to medical therapy. Inpatient rehabilitation is challenging in terms of high costs as well as the geographic availability. In our opinion in- and outpatient rehabilitation for PH patients are potentially synergistic elements, enhancing physical performance and self-confidence in daily life of PH patients and should be integrated as a regular part of best-practice management.

The results of this pilot study are in line with findings from previous studies and demonstrated the feasibility and safety of our approach. The optimal frequency of training sessions remains to be established and will be subject of future studies.

Conclusion

In pulmonary hypertension, physiotherapy is safe and effective if patients are stable on medical therapy and a close supervision is provided. A comprehensive physiotherapy program provides important and underutilized opportunities to improve the integrated care of people with PH. Existing pulmonary physiotherapy programs

can easily be adapted to specific needs of these patients, in particular the non-exercising parts to avoid the potentially life-threatening right heart burden. Nevertheless, physiotherapists and physicians need to become aware of the positive effects of this non-pharmacological intervention to increase referral rates and, in turn, improve the integrated care of people with pulmonary hypertension.

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