Effects of inspiratory muscle training in hemodialysis patients

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This study was carried out at the Irmandade da Santa Casa de Misericordia de Porto Alegre.

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Abstract

Introduction: Chronic kidney disease associated with hemodialysis treatment can have a variety of musculoskeletal complications, in addition to repercussions in pulmonary function. **Objective:** To evaluate the effects of inspiratory muscle training on inspiratory muscle strength, pulmonary function, and functional capacity in patients with chronic kidney failure undergoing hemodialysis. **Method:** Non-controlled clinical trial, comprising 15 individuals diagnosed with chronic kidney failure and undergoing hemodialysis. Maximum inspiratory (PI_{max}) and expiratory (PE_{max}) pressures were assessed by use of pressure vacuum meter reading. Pulmonary function was assessed by use of spirometry. Functional capacity was assessed by use of walked distance and oxygen consumption obtained in the six-minute walk test (6MWT). For eight weeks, the inspiratory muscle training (IMT) protocol was applied during hemodialysis sessions, with load set to 40% of PI_{max} and weekly frequency of three alternate days. **Results:** A significant increase in the walked distance was observed after training (455.5 ± 98 *versus* 557.8 ± 121.0; $p = 0.003$). No statistically significant difference was observed in the other variables when comparing their pre- and post-training values. **Conclusion:** The study showed no statistically significant difference in respiratory muscle strength, pulmonary function, and oxygen consumption. An increase in the walked distance was observed in the 6MWT.

Keywords: chronic kidney failure, physical therapy (specialty), hospital hemodialysis unit, renal dialysis, respiratory therapy.

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Introduction

Chronic kidney disease (CKD) is the persistent and progressive deterioration of glomerular filtration rate, with consequent uremic syndrome, represented by a set of disorders that affect several body systems.[1] Kidney deterioration can be related to diabetes mellitus, hypertensive nephrosclerosis, smoking habit, acute coronary syndrome, and dyslipidemia.[2] In addition, CKD represents the irreversible stage of kidney failure, which requires dialysis or even kidney transplantation for life maintenance.[3]

The 2009 Dialysis Census of the Brazilian Society of Nephrology estimated in 77,589 the number of dialysis patients in Brazil, of whom 86.7% are treated in the Brazilian Unified Public Health System (SUS). The most recent data have shown a tendency towards a reduction in the CKD growth rate. An explanation for that could be either an actual reduction in the number of dialysis patients in the last year, which is less likely, or, more likely, inaccuracy in the 2008 estimate, due to the low percentage of answers provided by Dialysis Centers (below 50%).[4]

Hemodialysis (HD) partially replaces kidney function, reverses the uremic symptoms, and preserves the life of patients with end-stage CKD, but degenerative alterations, such as malnutrition, which can occur in CKD patients, persist, worsening muscle loss and predisposing to fatigue, with an increase in respiratory rate and work.[5,6,7] The most frequent pulmonary alterations found are obstructive disorders, such as air flow limitation in distal airways[8,9] and reduced pulmonary diffusion capacity.[9,10] In addition, studies of the 1980s have reported a reduced oxygen consumption (VO_2) in CKD patients, similar to that of sedentary individuals.[11-15] However, physiological effects and possible chronic pulmonary alterations due to renal replacement therapy in patients with CKD are not completely known.[9,10,16]

In 2008, Marchesan, Krug, Moreira *et al.*[17] carried out a study with respiratory muscle strength training in CKD patients on HD by use of pressure vacuum meter reading. After 15 weeks of training, a statistically significant ($p < 0.05$) improvement was observed in aerobic resistance, and maximum inspiratory and expiratory pressures (PI_{max} and PE_{max}, respectively) in the experimental group.

This study aimed at assessing the effects of inspiratory muscle training (IMT) on inspiratory muscle strength, pulmonary function, and functional capacity in CKD patients on HD, and at correlating the variables walked distance, PI_{max}, and VO_2.

Method

This is a non-controlled clinical trial with convenience sample comprised by individuals clinically diagnosed with CKD, undergoing HD from April to September 2007 at the Hemodialysis Outpatient Clinic of the Policlínica Santa Clara of the Complexo Hospitalar Santa Casa, in the city of Porto Alegre, state of Rio Grande do Sul.

Patients undergoing at least three HD sessions per week for at least three months were included in this study. The pre-established exclusion criteria were as follows: dialysis by use of a femoral artery catheter or jugular vein catheter; arterial blood pressure (BP) ≥ 220/110 mm Hg or ≤ 100/60 mm Hg; mean arterial blood pressure (MABP) < 60 mm Hg; use of an antihypertensive drug within the hour preceding HD; non-controlled diabetic patients; class III and IV angina; cardiac arrhythmias; mental confusion; comorbidities and osteoarticular or musculoskeletal alterations that limit the six-minute walk test (6MWT) and IMT.

All patients spontaneously signed the written informed consent (WIC).

Of the 102 patients invited to participate in the study, 27 accepted. The other patients refused to participate due to lack of time availability and/or interest. In addition, eight patients were excluded: three due to osteoarticular and musculoskeletal alterations; one due to a right jugular vein catheter; two due to the hypertensive response during pressure vacuum meter reading and spirometry; and two due to comorbidities. Four patients were considered as losses: one due to death; one due to WIC withdrawal; and two due to low protocol adhesion. The final sample comprised 15 patients.

The study was approved by the Committee of Ethics and Research of the Centro Universitário Metodista IPA and of the Complexo Hospitalar Santa Casa de Misericórdia of the city of Porto Alegre, state of Rio Grande do Sul.

The assessment protocol was started after the first contact with patients for signing the WIC and completing the physical therapy assessment datasheet with individual data. Data collected were as follows: identification; clinical aspects [major complaint, etiology and year of chronic kidney failure (CKF) diagnosis, dialysis time, and HD session frequency]; and physical examination (vital signs, cardiac and pulmonary auscultation, chest type, respiratory muscle type, chest mobility, pulmonary expansibility, height, body weight, body mass index, and biotype).

All individuals underwent the same assessment protocol, and the following parameters were measured before and at the end of eight weeks of intervention: PI_{max}, PE_{max}, pulmonary function, and functional capacity. Patients were assessed two hours before HD, with no interference with the patients' weekly routine (Monday, Wednesday, and Friday or, Tuesday, Thursday and Saturday).

Maximum inspiratory and expiratory pressures were measured by use of pressure vacuum meter reading with a digital pressure vacuum meter (Globalmed®, MVD 300 model, Brazil) previously revised and calibrated. The PI_{max} was measured from the residual volume and PE_{max} from the total pulmonary capacity.[18]

Pulmonary function was assessed by use of spirometry with a MR spirometer (Spirodoc model, Italy). The spirometric pulmonary volumes, such as forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and Tiffeneau index (FEV_1/FVC), were measured based on the total pulmonary capacity.[19]

Both tests were performed with patients in the seating position, and followed the recommendations of the Pulmonary Function Tests guidelines.[18,19]

Functional capacity was assessed by calculating indirect $VO_{2\,max}$ (VO_2= -2.344 + 0.044 x distance)[20] based on the 6MWT. Peripheral oxygen saturation (SpO_2) and heart rate (HR) were measured with an oxymeter (Nonin®, 9500 model, USA) positioned on the patient's forefinger. Blood pressure (BP) was measured with an aneroid sphygmomanometer (BIC®, Master 040 model, Brazil) and a stethoscope (BIC®, Standard model, Brazil) with the patient in the seating position and the semiflexed arm supported at heart level.[21]

The 6MWT used the modified Borg scale, a descriptive marker of perceived exertion of breathlessness and lower limb fatigue graded in a 0 to 10 scale.[22] The 6MWT was performed over a 27-meter-long level corridor.

Patients were instructed to walk at their maximum speed, without slowing down, and to complete the highest possible number of laps. At the beginning of the test and immediately after the sixth minute, the following variables were assessed HR; respiratory rate (RR); SpO_2; and breathlessness and lower limb muscle fatigue sensation by use of the modified Borg scale. At the end of the test, the walked distance was recorded.

After assessment, the patients initiated the IMT protocol during dialysis, by using the Threshold Loaded IMT® device. The training lasted eight weeks, with a weekly frequency of three alternate days, with no change in the HD outpatient clinic routine.

The Threshold Loaded IMT® device is an inspiratory pressure load device in which the patient uses a nasal clip and breathes through a mouthpiece with resistance in the inspiratory branch.[23,24]

Patients underwent the IMT in the seating position, with an established load of 40% of the PI_{max} measured on the assessment day. The maneuvers were performed in a set of five repetitions, at one-minute intervals, in a total of 15 minutes of training in the first four weeks. The IMT duration was increased until the exercise sessions completed 30 minutes in the last four weeks, according to the adapted Riedemann's protocol (2005).[25]

Statistical analysis

Data used for the statistical analysis were stored in a Microsoft Excel 2003 datasheet as mean and standard deviation (X ± SD). For the continuous variables with normal distribution, *t* test was used for paired samples, and Wilcoxon test was used for the continuous variables with abnormal distribution. To assess the existence of correlation between two or more variables, Pearson correlation test was used. The SPSS (Statiscal Package for the Social Sciences) software, version 15.0, was used for the analyses. The significance level adopted was $p < 0.05$.

Results

The study sample comprised 15 CKD individuals (eight males, 53.3%; age range, 21 to 73 years; mean age, 45.0 ± 13.7 years) undergoing HD three times a week for 61.4 ± 32.3 months. Table 1 shows the characteristics of the group studied.

Table 1 Sample characteristics

	Sample variables (n = 15)
Sex	
Male n (%)	8 (53.3)
Female n (%)	7 (46.7)
Color	
White n (%)	9 (60.0)
Black n (%)	6 (40.0)
Age (years)*	45.0 ± 13.7
Weight (kg)*	69.0 ± 11.0
Height (m)*	1.68 ± 0.1
BMI (kg/m²)*	20.4 ± 3.0
HD time (months)*	61.40 ± 32.3

HD: hemodialysis; BMI: body mass index; *: data shown as mean ± standard deviation.

The most common causes of CKD in the sample studied were as follows: polycystic kidney disease (33.3%); systemic arterial hypertension (20%); chronic glomerulonephritis (13.3%); chronic glomerulonephritis (6.6%); diabetes mellitus (6.6%); obstructive uropathy (6.6%); and unknown etiology (13.3%).

No significant variation in hemoglobin levels after training was observed (before training, 11.3 ± 1.3 g/dl; after 11.1 ± 1.6 g/dl; p = 0.44) (Table 1).

Table 2 shows the results of pressure vacuum meter reading and spirometry before and after training. None of the variables showed any statistically significant difference after training.

Table 3 shows the data obtained in the 6MWT before and after IMT. No statistically significant differences were observed in the variables RR, HR, SpO_2, lower limb muscle fatigue sensation, and VO_{2max} after training. However, a statistically significant improvement was observed in the breathlessness sensation (p = 0.046) and walked distance (p = 0.003).

Figure 1 shows a statistically significant correlation between walked distance and PI_{max} before training (r = 0.578; p = 0.024). Two months after the intervention, a positive correlation (r = 0.741; p = 0.002) was observed between the same variables, as shown in Figure 2. A significant correlation between VO_{2max} and PI_{max} was observed before and after the intervention (r = 0.578 and p = 0.024; r = 0.603 and p = 0.017, respectively).

Table 2 PRESSURE VACUUM METER READING AND SPIROMETRY VARIABLES

	Pre-training	Post-training	p*
$PI_{máx}$ (cmH_2O)	69.7 ± 30.3	119.8 ± 114.7	0.074
$PE_{máx}$ (cmH_2O)	96.4 ± 36.4	101 ± 40.3	0.320
FVC (L)	4.0 ± 0.9	4.0 ± 1.2	0.825
FEV_1 (L)	2.4 ± 0.8	2.6 ± 0.9	0.284
FEV_1/FVC	60.9 ± 19.2	64.3 ± 26.5	0.664

Variables are shown as mean ± standard deviation; *: t paired test for normal distribution samples. Statistically significant test when $p < 0.05$. PI_{max}: Maximum Inspiratory Pressure; PE_{max}: Maximum Expiratory Pressure; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in one second; FEV1/FVC (%): Tiffeneau index.

DISCUSSION

Patients undergoing HD have many abnormalities, possibly due to cell adaptations to inner environment changes, such as changes in capillaries, enzymes, and contractile proteins,[9,26] and also mitochondrial abnormalities.[9,27] In addition, HD patients can show a reduction in physical function and fitness, [2,9,28-30] with a decrease in peripheral muscle strength.[9,31-33] Thus, muscle weakness present in CKD patients on HD can result from muscle atrophy. This interferes with the normal musculoskeletal fiber functioning and structure.[9,31]

The potential mechanisms through which CKD can negatively interfere with skeletal muscles are multifactorial and complex, and can result from alterations in muscle perfusion, substrate transferences, and intermediate catabolism by factors, such as metabolic acidosis, corticosteroid use, and release of pro-inflammatory cytokines.[9,27]

Respiratory function alterations are one of the most frequent conditions in such patients.[8,9,10] However, despite CKD pulmonary repercussions, the physiological effects and possible pulmonary alterations of patients undergoing renal replacement therapy are not yet well known.[9,10,16]

In 1991, Bush and Gabriel assessed patients with different CKF stages undergoing HD for 2.1 years and compared them to patients not undergoing dialysis. Those authors reported pulmonary diffusion capacity abnormalities in 70% of the patients undergoing renal replacement therapy.[9,16]

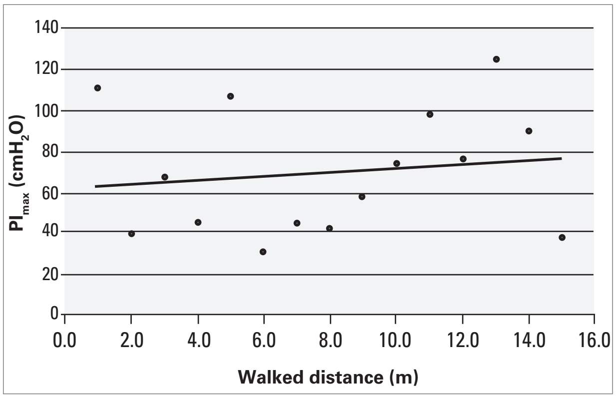
In 2008, Schardong, Lukrafka and Garcia assessed the pulmonary function, respiratory muscle strength, and quality of life of 30 CKD patients undergoing HD. Those authors reported that pulmonary function values were reduced, PI_{max} values were below those predicted, and no patient achieved normal PE_{max} values.[9] In the present study, pulmonary function showed no statistically significant difference when comparing values before and after IMT, which is probably due to the fact that IMT is aimed at improving inspiratory strength and not pulmonary volumes and capacities.

Table 3 SIX-MINUTE WALK TEST VARIABLES

	Variables Pre-training		Post-training		
	Beginning	End	Beginning	End	p
RR	20.3 ± 3.1	24.1 ± 3.6	19.8 ± 2.8	24.2 ± 4.6	0.947
HR	84.6 ± 11.0	98.9 ± 26.2	82.0 ± 9.3	91.6 ± 24.7	0.438
SpO_2	95.8 ± 4.8	95.4 ± 3.3	98.2 ± 0.7	96.6 ± 2.6	0.278
Borg dyspnea	0.6 ± 1.0	1.0 ± 1.4	0.2 ± 0.5	0.2 ± 0.5	0.046
Borg LL	0.4 ± 1.0	2.2 ± 2.2	1.3 ± 2.3	1.6 ± 2.0	0.461
SBP (mm Hg)	155.3 ± 18.0	162.0 ± 22.7	154.6 ± 26.1	150.0 ± 37.0	0.293
DBP (mm Hg)	95.3 ± 27.2	96.0 ± 26.4	90 ± 10.6	93.3 ± 16.3	0.738
Walked distance (m)	455.5 ± 98.8		557.8 ± 121.0		0.003
$VO_{2\ max}$ (mL.kg.min)	1087.9 ± 236.1		1149.1 ± 454.1		0.592

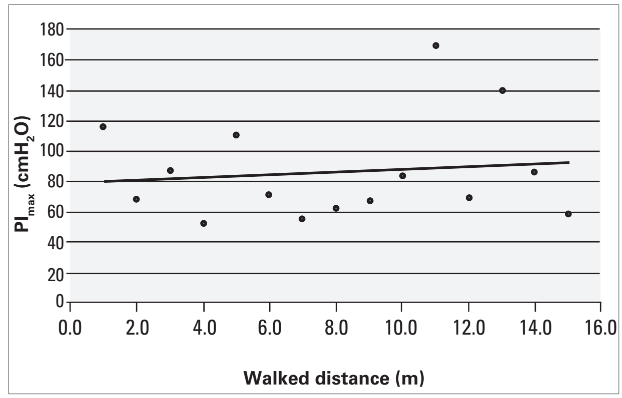
Variables are shown as mean ± standard deviation; RR: respiratory rate; HR: heart rate; SpO2: peripheral oxygen saturation; SBP: systolic blood pressure; DBP: diastolic blood pressure; VO2: oxygen consumption; LL: lower limbs. t paired test for normal distribution samples. Statistically significant test when $p < 0.05$.

Figure 1. Correlation between PI_{max} and walked distance before training



Pearson correlation test; r = 0.578; p = 0.024.

Figure 2. Correlation between PI_{max} and walked distance after training



Pearson correlation test; r = 0.741; p = 0.002.

Despite the scarcity of studies assessing IMT in CKF patients, the effectiveness of that approach has already been well documented in patients with chronic obstructive pulmonary disease (COPD), who, similarly to CKD patients, have systemic alterations that predispose to muscle weakness.[25,34-38]

In 2008, Marchesan *et al*. studied 11 CKF patients on HD in the city of Cruz Alta, state of Rio Grande do Sul. Of the 11 patients, six comprised the control group (CG) and five the experimental group (EG). The EG underwent respiratory muscle training with a pressure vacuum meter and operational threshold ranging from +300 cmH$_2$O to -300 cmH$_2$O. This was prescribed based on the individual values obtained in the pressure vacuum meter reading. The intensity increased at every 15 training sessions, initiating with 50% of the maximum load (ML), passing to 55% until the 30th session, and from the 31st to 45th session, 60% of the ML was used. Similarly to the present study, training was also performed during HD. The study was carried out for 15 weeks, during which the patients performed 30 inspiratory maneuvers (PI_{max}) and 30 expiratory maneuvers (PE_{max}), three times a week, with duration of approximately 20 minutes. The authors reported a significant increase in PI_{max} ($p = 0.04$) in the EG as compared with the CG. The intragroup comparison showed a significant increase ($p < 0.05$) in PI_{max} and PE_{max} and aerobic resistance only for the EG by use of pressure vacuum meter reading and 6MWT, respectively.[17]

In the present study, the mean PI_{max} for training was 27.0 ± 11.6 cmH$_2$O. Two months after the intervention, an increase, although not statistically significant, in PI_{max} was observed. A significant increase was observed in the walked distance in the 6MWT, and that performance improvement could not be justified by changes in anemia control, because the hemoglobin level remained constant between both assessment occasions. The positive and significant correlation between the walked distance and PI_{max} after training suggests that inspiratory muscle strength contributes to exercise tolerance and functional capacity.

The morphological and functional adaptations resulting from physical training increase the body's capacity to respond to that stress.[39] The increase in cardiac output, proportional to exercise intensity, is essential to provide large amounts of oxygen and other nutrients necessary to active muscles.[40] Although this study showed no significant alterations in VO_{2max}, a positive and significant correlation between that variable and PI_{max} was observed. This fact can be associated with the cardiovascular conditions of the population studied, who can still increase cardiac output, and, thus, oxygen offer to peripheral tissues.

Further studies should be carried out with direct cardiac output and oxygen arteriovenous difference measurements, aiming at better investigating the IMT effects on those variables of CKD patients on HD. Studies assessing the pulmonary function of those patients by use of respiratory physical therapeutic techniques to improve pulmonary volumes and capacities are also required.

Study limitation

Several patients refused to participate in this study because of the long follow-up, jeopardizing the sample size. Another relevant factor for the study would be the use of a control group and the selection of young patients with less comorbidity than the average HD population. In addition, the study could have assessed the nutritional status and inflammatory response of those individuals.

Conclusion

Inspiratory muscle training for eight weeks provided a significant increase in the walked distance in the 6MWT of HD patients, but no alteration was observed in the other parameters assessed.[3]

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