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Inspiratory muscle training improves strength and health-related quality of life in hemodialysis patients

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ABSTRACT

Background: Patients undergone hemodialysis (HD) suffer with energy-protein malnutrition, uremic myopathy and protein catabolism reducing their functional capacity, tolerance to exercise and aspects related to quality of life. **Objective:** The aim of this study was to evaluate the effects of the two protocols of inspiratory muscle training (IMT) on muscle strength, pulmonary function and related-health quality of life on male HD patients. **Methods:** Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), peak expiratory flow (PEF), forced expiratory volume in first second (FEV_1), forced vital capacity (FVC) and the FEV_1/FVC ratio and quality of life were evaluated pre and post six months of IMT in HD patients. IMT was performed by one group using a specific training (Power breathe) device (T-IMT, n=19) and by the other with incentive spirometry (I-IMT, n= 15). **Results:** Following the inspiratory training, muscle strength improved in both groups. The group that used incentive spirometry had increments in MIP larger (39.8%, p<0.001) than the group that trained with the specific training device (28.3%, p=0.001). The KDQOL-SF dimensions showed significant difference in the T-IMT group in cognitive function (p=0.03), sexual function (p=0.009) and social function dimensions (p=0.04) and in the I-IMT group in the physical function dimension (p=0.03). **Conclusion:** It was proved that IMT improved muscle strength and I-IMT promoted increments significantly larger in MIP. Aspects of health-related quality of life of HD male patients improved significantly with T-IMT (sexual, social and cognitive functions), while I-IMT ameliorated only physical function.

Key-words: Breathing Exercises, Exercise Therapy, Quality of Life, Hemodialysis.

INTRODUCTION

Several factors, including energy-protein malnutrition, increase in the parathyroid hormone (PTH), abnormalities in vitamin D activity, uremic myopathy and protein catabolism cause impairment in the physical and functional capacity of patients undergoing hemodialysis (HD) treatment[1-8]. Moreover, studies have shown that changes occur in the morphological and histochemical aspects of muscles, such as the reduced cross-sectional area of the fiber, atrophy and reduction in size of fiber type I and type II, infiltration and degeneration of muscle fiber, production of actin fragments of 14kD (kiloDalton) and reduction in the synthesis of mitochondrial proteins and inside the oxidative capacity of muscle cells, further decreasing muscle capillary density[7-9]. As a consequence, respiratory muscle strength, pulmonary function and exercise capacity are affected. However, studies have also demonstrated that inspiratory muscle training (IMT) programs may benefit respiratory (increasing muscle strength) and heart function (increasing cardiac output and oxygen consumption), as well as an improvement in managing everyday activities and the functional capacity of these patients[7,8].

It is known that patients on HD present deficits in muscle strength and pulmonary function[10-12]. Weiner et al. [10] showed that inspiratory muscle performance significantly increased, and was associated with improvement in, functional capacity. Another study performed inspiratory muscle training for eight weeks in 15 patients and found no increase in inspiratory muscle pressure (MIP)[11]. In contrast, the results of a randomized controlled study showed that 10 weeks of IMT improved inspiratory strength and functional performance, but that pulmonary function did not benefit by this training[12]. Thus there is little conclusive evidence in the literature on IMT in HD patients and we hypothesized that six months of IMTcan improve respiratory variables and aspects related to quality of life of HD patients. The aim of this study was to evaluate the effects of the two protocols of IMT on muscle strength, pulmonary function and Health-related quality of life (HRQL) on male HD patients.

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METHODS

Study design

This study was a prospective clinical trial performed by simple randomization.

Patients

The study enrolled from January 2012 to August 2013. One hundred thirteen male patients in HD from two dialysis centers in Goiânia, Goiás, Brazil were evaluated for eligibility of study. Of these 64 held to intervention (figure 1). All patients were submitted to dialysis three times per week for 3-4 hours/day coupled to a dialysis machine (Baxter, USA) by means of an arteriovenous fistula. The dialyzer or capillary filter (Xenium, Japan) had high efficiency and was composed of cellulose diacetate membrane (it has a large number of free hydroxyl groups on the surface) with features of biocompatibility. The inclusion criteria were older than 18 years, treatment time exceeding three months, three times per week for 3-4 hours/day, and exclusion criteria were chronic obstructive pulmonary disease (COPD), uncontrolled cardiac arrhythmia, unstable angina, other severe cardiac disease, decompensated blood pressure (systolic blood pressure > 180 mmHg and diastolic blood pressure > 100 mmHg), diabetes mellitus (serum glucose > 110 mg/dL), subjects with clear inability to use a respiratory device or to collaborate. The study was approved by the Ethics Committee in Research of the Universidade Federal de Goiás (Brazil), under protocol number 294/2011. Those who participated in the study signed an informed consent.

They were allocated into three groups by simple randomization using sealed envelopes containing the patients' names. The nurse manager randomly selected them and the patients were alternately allocated to each group. One group underwent training using a specific trainer (T-IMT), other group performed two breathing exercises and incentive spirometry (I-IMT) during HD and control group. The respiratory muscle strength and pulmonary function tests were performed on no-dialysis days and at an intermediate session in the week. All tests were performed pre-, mid- (three months) and post-IMT that lasted six months in total. The KDQOL-SF questionnaire was applied pre and post.

Protocols

A record was filled out with information about age, time on HD, body mass, height, medication used and smoking history. The hematocrit, hemoglobin, urea pre- and post-, phosphorus, potassium and the adequacy of dialysis parameters were collected from the patient's medical record in the first week of each month for six month in order to monitor anemia. The adequacy of dialysis (Kt/V) was calculated using the Daugirdas formula[13].

Respiratory muscle strength was measured by MIP and MEP which were held from residual volume and total lung capacity against an occluded airway with a minor air leak (2mm) respectively[15,16]. The maneuvers were explained and demonstrated to each patient. Patients remained seated with the airway occluded by a nose clip and a

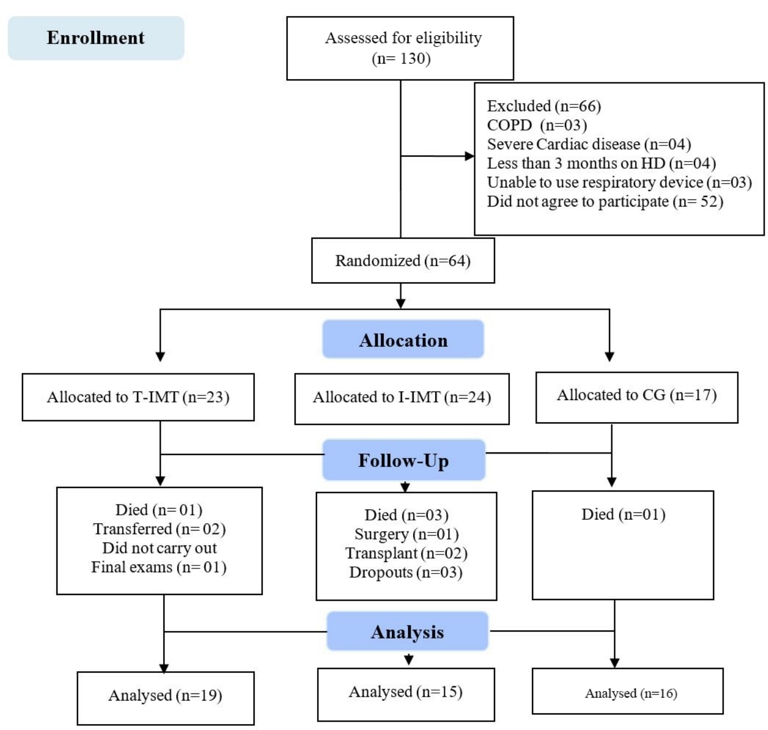

Figure 1- Study design

mouthpiece connected to a manometer (Globalmed, Porto Alegre, Brazil). Inspiratory and expiratory efforts were sustained for one second (s). Three to five acceptable and reproducible maneuvers (difference less than or equal to 10%) were performed and the biggest value was selected. The interval between maneuvers was one minute for all those tested. The predicted values were calculated according to Neder et al.[17].

Spirometrics variables were collected with a computerized spirometer (Micro quark, Cosmed, Rome, Italy). To perform the test and interpretation we used the criteria of the American Thoracic Society[18]. The analyzed variables were peak expiratory flow (PEF), forced expiratory volume in first second (FEV_1), forced vital capacity (FVC) and the FEV_1/FVC ratio.

To evaluate health-self quality of life was used the KDQOL-SF (Kidney Disease Quality of Life – Short Form) questionnaire. The KDQOL-SF was read aloud and the patients followed the printed questionnaire visually, item-by-item. The questionnaire includes SF-36 (Medical Outcomes Study 36) with eight domains about physical and mental health and specific items about kidney disease. This instrument was validated in Brazil by Duarte et al.[14]. The scores range from 0 to 100 and the lower scores correspond to worse health-related quality of life and higher values reflect better quality of life.

Inspiratory Muscle Training

The IMT was carried out for six months, three times per week during the first two hours of hemodialysis. Patients remained seated or on the reclining hemodialysis' chair at 45º. Before the beginning of each exercise session, the clinical signs such as blood pressure, heart rate, breathing pattern and oxygen saturation were checked.

The T-IMT group trained with one specific trainer (Power Breathe, Southam, UK), and the I-IMT group with the incentive spirometer (Respiron, NCS, São Paulo, Brazil). Patients began training using 30.0% of MIP and performing three sets of 10 maximal inspirations with 60 seconds of rest time between them. The adjustment of the load, number of inspirations and number of series was changed each 30 days The mean time to execute the training was 11 minutes. The incentive spirometer (I-IMT) training group performed two breathing exercises, diaphragmatic breathing [20] (for breath control) and inspiration in times (to increase tidal volume)[20,21]. The control group underwent the same assessments as the others groups without any intervention.

Data analysis

Data are expressed as frequencies, mean, standard deviation (SD), percentage or graphs. The Shapiro-Wilk test was used to verify normality. The differences between the two groups (T-IMT and I-IMT) were analyzed by t-Student non-paired for continuous variables and Chi-square for categorical variables. The effects of interventions on continuous variables were compared by ANOVA for repeated measures with Bonferroni adjustments. The t-student assessed the difference between the dimensions of the KDQOL-SF questionnaire. The data were processed and analyzed using the Statistical Package Social Sciences (SPSS, Chicago, US). Significance was accepted when the probability was < 0.05.

RESULTS

The baseline characteristics are shown in Table 1. Of 47 patients enrolled, 13 did not complete the study (Figure 1). However, 34 male patients were studied with an average age of 51.3 (13.2) years (ranging from 19 to 75 years). 36.8% and 5.3% of the IMT-T group and 33.3% and 26.7% of the IMT-I group were classified as pre-obese and obese I, respectively. The etiology of renal disease (p = 0.47) and a history of smoking (p = 0.07) were not significantly associated with the type of intervention. The main cause of chronic kidney disease was hypertensive nephrosclerosis in the T-IMT group (42.0%) and the I-IMT group (40.0%) which were related to the use of anti-inflammatory hormones and infections.

Table 1. Clinical baseline characteristics of patients randomized to T-IMT, I-IMT and CG.

	T -IMT (n=19)	I-IMT (n=15)	CG (n=16)
Age (years)	54.7 (10.4)	49.5 (13.2)	49.3 (16.3)
Body mass (kg)	71.3 (10.9)	74.6 (12.7)	68.8 (14.9)
Dry weight (kg)	70.3 (10.9)	73.5 (12.9)	67.2 (14.2)
Height (m)	1.7 (0.04)	1.7 (0.08)	1.7 (0.09)
BMI (kg/m²)	24.1 (3.1)	25.8 (4.4)	24.3 (4.2)
Time on HD (months)	44.16 (47.3)	57.3 (42.1)	55.1 (57.7)
Hemoglobin (mg/dl)	11.2 (1.1)	11.5 (1.2)	10.7 (1.5)
Hematocrit (%)	33.2 (6.8)	35.6 (3.1)	32.9 (4.6)
Urea-pre (mg/dl)	172.4 (56.8)	170.1 (47.4)	147.1 (33.3)
Urea-post (mg/dl)	47.1 (21.5)	42.7 (16.8)	45.8 (17.2)
Potassium (mg/dl)	5.7 (1.0)	5.4 (1.0)	5.3 (0.6)
Phosphorus (mg/dl)	5.4 (1.5)	5.6 (1.8)	5.8 (1.6)
Kt/V	1.7 (0.4)	1.8 (0.3)	1.5 (0.4)
Etiology of CKD – n (%)			
SAH	08 (42.0)	05 (33.4)	07 (43.8)
DM	04 (21.1)	02 (13.3)	01 (6.3)
CGN	03 (15.8)	02 (13.3)	06 (37.5)
Others	04 (21.1)	06 (40.0)	02 (12.5)
Smoking – n (%)			
Former smokers	15 (78.9)	06 (40.0)	11 (68.8)
Never smoked	04 (21.1)	09 (60.0)	05 (31.3)

Note: Data presented as mean (SD), frequencies and percentages (%). BMI= body mass index; HD = hemodialysis; Kt/V= dialysis adequacy; SAH = systemic arterial hypertension; DM = diabetes mellitus; CGN = Chronic glomerulonephritis.

Table 2- Variables of respiratory muscle strength and pulmonary function for the two groups pre-, mid- and post-IMT.

Variables	T-IMT (n=19)			I-IMT (n=15)			CG (n=16)		
	Pre	Mid	Post	Pre	Mid	Post	Pre	Mid	Post
MIP (cmH2O)	67.2 (27.7)	79.4 (24.4)*	86.2 (26.8)†	71.7 (27.8)	94.0 (28.0)*	100.3 (25.9)†	77.2 (26.0)	84.8 (28.5)	88.4 (26.3)
MEP (cmH2O)	83.4 (29.3)	90.1 (25.1)	93.0 (26.6)	97.5 (34.1)	92.5 (28.4)	95.5 (25.4)	85.6 (38.6)	85.8 (34.3)	75.8 (18.4)
PEF (L/s)	6.0 (2.3)	6.5 (2.6)	7.0 (2.1)	6.1 (2.4)	6.5 (2.2)	6.8 (2.0)	5.6 (2.1)	6.3 (2.3)	6.6 (2.2)
FEV1 (L)	2.8 (0.6)	2.8 (0.6)	2.9 (0.7)	3.0 (0.8)	2.9 (0.7)	2.9 (0.7)	2.9 (0.7)	3.0 (0.7)	3.0 (0.7)
FVC (L)	3.5 (0.6)	3.4 (0.7)	3.6 (0.7)	3.6 (0.8)	3.6 (0.7)	3.6 (0.8)	3.7 (0.6)	3.8 (0.8)	3.7 (0.8)
FEV_1/FVC (%)	80.0 (0.1)	81.2 (0.1)	80.1 (0.1)	81.7 (0.1)	81.7 (0.1)	82.0 (0.1)	78.0 (0.1)	81.2 (0.1)	81.0 (0.1)

Note: Data presented as mean ± SD. T-IMT = trainer – inspiratory muscle training; I-IMT = incentive – inspiratory muscle training; MIP = maximal inspiratory pressure; MEP = maximal expiratory pressure; PEF = peak expiratory flow; FEV1 = forced expiratory volume in first second; FCV = forced capacity vital. *Difference between pre-mid; † difference between pre-post. Values of *p* obtained to p<0.05.

The variables related to respiratory muscle strength and pulmonary function pre-, mid-, and post-intervention protocols are shown in Table 2. The MIP improved during and after in both T-IMT and I-IMT groups. The MIP values in the T-IMT group increased by 18.1% ($p = 0.008$) and 28.3% ($p = 0.001$) following three and six months of training respectively. In the I-IMT group, the increments were higher, attaining 31.0% ($p = 0.01$) and 39.8% ($p < 0.001$) after three and six months of inspiratory training respectively. Two patients in the T-IMT group and one in the I-IMT group had MIP predicted before the intervention. At the end of inspiratory training nine patients in T-IMT and seven in I-IMT had MIP values within the expected range for age and sex. I-IMT induced a significantly larger increase in MIP ($p = 0.02$) when compared to T-IMT. In contrast, no significant differences were found to MEP in either group. In addition, peak expiratory flow was the only variable of pulmonary function that showed differences pre- and post-training for T-IMT ($p = 0.02$).

The aspects related to HRQL assessed by KDQOL-SF showed significant differences in social function (p=0.004), sexual function (p=0.009) and cognitive function (p=0.03) dimensions in the T-IMT group, and in physical role (p=0.03) in the I-IMT group (Table 3). The general health dimension was significantly reduced in the I-TMT group (p=0.04). And, before the intervention the mean score of the burden of kidney disease and work dimensions remained below 50 points.

DISCUSSION

In this study, we showed that HD patients had reduced respiratory muscle strength and lung function when compared with the predicted values (Table 1). Following IMT, inspiratory muscle strength improved in both groups. Moreover, the group that used incentive spirometry showed a greater increase in strength than the T-IMT group. The scores of the aspects related to quality of life presented significant differences in the T-IMT group in cognitive function, sexual function and social function dimensions. In the I-IMT group, the physical function dimension and general health were the only that showed a significant difference after the intervention.

The involvement of the respiratory system in the clinical manifestations of CKD and its treatment is very complex but exercise training can help ameliorate the respiratory conditions of these patients. When evaluated before IMT, the MIP and MEP values of patients in the T-IMT group were 5.3% and 15.8%, respectively, of the values predicted for age and in the I-IMT group, the values were 6.7% and 13.3% for MIP and MEP, respectively. After IMT, the percentage of patients with MIP predicted for age in the T-IMT group increased to 21.1% and in the I-IMT group to 40%. These results tie in with several studies showing a reduction in respiratory muscle strength and changes in lung function of patients on HD compared with the predicted values for age or healthy subjects[22-24]. Other studies have evaluated the acute effects of HD on strength and lung function and showed that the weight gained between dialysis sessions has deleterious effects on respiratory function[25,26].

In the present study, we performed IMT for six months during HD sessions, with three sets of 10 inspirations (30% MIP) initially and then with three sets of 14 inspirations (50-60% of MIP) at the end; our results were satisfactory for both groups. To obtain findings for the effects of resistance training on the respiratory muscles, beyond the Principle of Overload, the specificity (inspirations of high intensity and short duration) was taken into consideration [27]. In the literature, three published studies have evaluated the effects of IMT on patients receiving HD[10-12] only one study was randomized and controlled (10 weeks of treatment, three sets of 15 inspirations, three times per week and during hemodialysis) and showed a significant increase in respiratory muscle strength and in aspects related to quality of life[12]. The improvement in respiratory strength in this study was probably owing to adaptations by the inspiratory muscles linked to the type of training (moderate load) that promotes hypertrophy (increase in muscle strength), increases the proportion of type I fiber, reduces type II fiber and increases

Table 3- Generic and specific dimensions of the Kidney Disease Quality of Life-Short Form pre- and post-inspiratory muscle training.

Dimensions (nº of items)	T-IMT (n=19)		I-IMT (n=15)		IH-IMT (n=16)	
	Pre	Post	Pre	Post	Pre	Post
Physical functioning (10)	70.3 (24.4)	69.0 (24.9)	72.3 (25.5)	72.7 (29.5)	71.2 (29.0)	71.8 (31.3)
Physical role (4)	75.8 (38.3)	85.5 (34.7)	57.0 (46.5)	83.3 (32.3)*	78.0 (41.3)	70.6 (42.6)
Pain (2)	74.4 (29.9)	77.6 (30.0)	89.6 (19.8)	77.5 (23.0)	74.4 (24.9)	90.7 (12.6)
Health general (5)	63.2 (26.6)	56.6 (29.6)	70.1 (19.8)	59.7 (22.6)*	64.4 (29.5)	59.7 (30.6)
Emotional wellbeing (5)	75.4 (28.1)	77.3 (26.1)	78.8 (18.8)	81.9 (17.9)	72.9 (17.7)	85.9 (15.2)
Emotional role (3)	60.2 (44.8)	78.9 (37.2)	78.7 (32.4)	86.7 (27.6)	86.3 (33.5)	84.3 (35.6)
Social function (2)	73.8 (26.7)	88.2 (19.3)*	85.3 (25.0)	83.7 (23.3)	76.6 (27.3)	86.7 (22.6)
Energy/fatigue (4)	66.3 (23.8)	68.7 (27.7)	69.7 (21.7)	68.8 (21.2)	64.4 (22.6)	72.6 (19.0)
List of sintoms/problems (12)	87.1 (13.2)	90.8 (10.4)	84.8 (14.4)	87.4 (11.3)	87.5 (13.7)	87.6 (13.0)
Effects of kidney desease (8)	65.0 (25.5)	64.6 (27.4)	71.9 (18.3)	71.7 (16.8)	78.1 (14.4)	74.3 (19.3)
Burden of kidney desease (4)	41.8 (30.3)	42.4 (32.2)	45.8 (28.1)	52.5 (27.6)	50.0 (34.3)	55.1 (27.7)
Work (2)	39.5 (39.4)	36.8 (36.8)	40.0 (43.1)	50.0 (46.3)	35.3 (38.6)	44.1 (46.4)
Cognitive function (3)	82.5 (19.7)	90.5 (15.8)*	89.3 (10.3)	88.9 (13.7)	91.4 (14.3)	96.1 (5.8)
Social interaction (3)	85.3 (15.6)	87.0 (17.0)	95.1 (7.3)	93.8 (7.8)	90.6 (17.6)	91.0 (12.5)
Sexual function (2)	36.2 (46.6)	61.2 (44.1)*	54.2 (46.7)	58.3 (45.2)	36.0 (47.6)	35.3 (46.8)
Sleep (4)	74.6 (23.9)	73.8 (26.4)	77.0 (14.7)	80.1 (18.3)	74.1 (22.7)	77.6 (28.2)
Social support (2)	89.5 (15.9)	90.2 (25.6)	75.6 (30.1)	74.4 (41.2)	84.3 (26.7)	85.3 (23.5)
Dialysis staff (2)	92.8 (17.8)	86.8 (26.5)	95.8 (13.1)	96.7 (12.9)	87.5 (17.1)	93.4 (16.6)
Patient satisfaction (1)	78.1 (18.5)	72.8 (20.9)	72.2 (19.6)	74.4 (17.7)	70.1 (18.0)	82.4 (18.1)

Note: T-IMT = trainer – inspiratory muscle training; I-IMT = incentive – inspiratory muscle training. Values of *p* obtained to p<0.05.

the cross-sectional area in the diaphragm[7,8]. These changes are reflected in an increase in inspiratory muscle strength as assessed by MIP.

With respect to the spirometrics variables, we found no significant difference after IMT, except to PEF in the T-IMT group (Table 3). Studies have shown that IMT does not influence spirometrics variables and perhaps the application of endurance training may have effects on lung function, since exercises are performed in high flows and tidal volumes[11,12]. The fluid overload between HD sessions and abnormal permeability of the pulmonary microcirculation have been cited as causes of acute pulmonary edema (noncardiogenic) and pleural effusion [28] that can reduce volumes and lung capacity over time. This respiratory complication changes the ventilation/perfusion relationship (with or without the presence of anemia), reduces gas exchange, tissue oxygenation, and, consequently, functional capacity (activities of daily living) and exercise tolerance [29-31].

In the present study, significant improvements in the dimensions of the SF-KDQOL showed that IMT contributed to an increase in the scores of cognitive and social function. Scores for the dimensions of sexual function in the T-IMT group and physical function in the I-IMT group also increased after training (Table 3). Sexual function is particularly impaired in HD patients due to physical factors (intermittent uremia, continuous anemia, hormonal and gonadal dysfunction and spermatogenesis damage in the case of males), psychological factors (depression and anxiety reduce interest and ability in daily activities, including sex) and drug interactions (use of antihypertensive drugs, which leads to reduced libido and impotence in men) which interfere with sexual activity[14,32-33]. However, studies have demonstrated that these factors can be influenced by a training program (resistance exercises, aerobic training and flexibility) which can improve the health-related quality of life of HD patients. [12,34,35] The training program should not be neglected in health care because it has a positive effect on mental health and well-being, reducing depression and anxiety and improving cognitive functioning[36].

Some aspects about the relevance of this study should be highlighted. First, there has been no mention in the literature of IMT in HD patients for a long time (six months)[10,12]. Secondly, the increase in inspiratory muscle strength in these patients may make them less susceptible to respiratory complications caused by the kidney disease itself (general muscle mass loss, respiratory included) and the weight gained between dialysis sessions that commonly increases the number of admissions of these patients into hospital (acute pulmonary edema and pleural effusion). It has been possible to show that the least expensive device (incentive spirometer) for performing IMT was also the one that offered the most increments of muscle strength after training.

Although IMT showed significant increases in inspiratory muscle strength, our study had some limitations: the small number of patients allocated to each group (reduced adhesion of patients), the large number of co-morbidities that were inclusion criteria for the study and the loss of patients during the study due to several factors (transfer unit, death, surgery and dropouts). Other aspects should also be considered, such as the lack of a control group in all stages of intervention and the lack of females included in the study. In addition, the device used to train the T-IMT group is costly and its use is impractical in clinical care. In the present study, it was not possible to evaluate specific biochemical parameters (CPK and albumin) to check muscle breakdown and the availability of fatty acids as a source of substrate for exercising muscle evaluated by albumin. Further studies are suggested with IMT (interventions longer than six months) and associated resistive or aerobic training to verify the benefits of exercise in reducing respiratory complications, to enhance functional capacity and quality of life in HD patients.

CONCLUSION

In conclusion, the study showed that respiratory muscle strength and pulmonary function are reduced in male patients receiving hemodialysis. However, it was proved that at least three months of IMT, with the use of different types of apparatus, is able to improve inspiratory muscle strength in both groups as measured by MIP. Also, I-IMT promoted increments significantly larger in MIP. Furthermore, it was demonstrated that T-IMT significantly improved health-related quality of life aspects (sexual, social and cognitive function), while I-IMT ameliorated the physical function of male HD patients.

AUTHOR DETAILS

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