Effect of resistance exercise intradialytic in renal patients chronic in hemodialysis

Authors
Ronaldo Ribeiro[1,4]
Gustavo L. Coutinho[2]
Anderson Iuras[3]
Ana Maria Barbosa[4]
José Adilson Camargo de Souza[2]
Denise Pará Diniz[5]
Nestor Schor[1]

[1] Federal University of São Paulo - UNIFESP.
[2] Nephrology Institute of Taubaté.
[3] School of Health Sciences, University of the State of Amazonas.
[4] Faculty of Anhanguera of Taubaté.
[5] Department of Nephrology Psychology, Federal University of São Paulo - UNIFESP.

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Correspondence to:
Nestor Schor.
Disciplina de Nefrologia, Departamento de Medicina, Escola Paulista de Medicina - UNIFESP.
Rua Botucatu, nº 740, São Paulo, SP, Brazil. CEP: 04023-900.
E-mail: nestor@nefro.epm.br
Tel.: (011) 5904-1699.
Fax: (011) 5904-1684.

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Abstract

Introduction: Patients with chronic kidney disease (CKD) when subjected to resistance exercise (RE) show substantial improvements in many functions, especially those related to the cardiovascular system, respiratory, muscular and quality of life (QOL). There are no evaluations of the impact of exercise simple and feasible in patients with CKD associated with Diabetes Mellitus (DM) during the intradialytic period. Thus, patients with CKD and submit to the DM + RE during hemodialysis. **Objective:** To study the role of resistance exercise in the treatment and quality of life in patients undergoing chronic hemodialysis (HD). **Methods:** 15 patients in each group: 1: DM with CKD and RE; 2: DM + CKD sedentary; 3: CKD + RE and 4: DRC sedentary. They were evaluated during eight weeks, with RE three times a week. Parameters: Laboratory assessments, muscle strength testing (FM) and QV (SF-36). **Results:** RE induced improvement in glucose and FM with subtle but significant changes in urea, or even in the K ($p < 0.0001$). It was an improvement in the impact assessment of QOL parameters ($p < 0.001$) with the RE, such as Functional Capacity, Physical Aspect, Reduction of Pain (in general), General Health, Vitality, Social Function, Emotional State and Mental Health. **Conclusion:** The RE program (simple and feasible) during intradialytic clinical parameters changed FM and a significant improvement in QOL assessment were observed. The impact on QOL was important for the patient, including those involving improvement in level of family and social relationships when subjected to RE.

Keywords: diabetes mellitus, type 2, dialysis, exercise, renal insufficiency, chronic.

Introduction

Chronic kidney disease (CKD) limits functional capacity, leading to cardiovascular complications, and endocrine-metabolic, musculoskeletal, and other disorders that affect the quality of life (QOL).[1] An exercise protocol could lead to improvements in many functions, such as blood pressure, heart function (especially ventricular function in hemodialysis [HD] patients), muscle strength, and respiratory capacity, and reduce muscle atrophy, with excellent results for the QOL.[2]

Conversely, lack of exercise, even in the healthy, albeit sedentary population, leads to changes in the QOL and a significant increase in early mortality.[3] It has also been considered one of the main factors that negatively affect health and QOL,[4] favoring the onset of chronic diseases such as diabetes, heart disease, and hypertension, which increases morbimortality rates.[5]

Resistance exercise (RE) training is important in the non-pharmacological treatment of diabetes mellitus (DM), along with proper diet and medications when needed. Although the treatment of DM is mainly based on hypoglycemic drug therapy and diet, a program of regular physical activity is important to obtain additional metabolic stability, preventing or minimizing many of the more frequent complications.[6-9]

According to systematic studies, patients who performed RE showed improvements in physical and psychological fitness, improving QOL in patients with

CKD, and those who exercise while undergoing HD showed improvement in their uremic condition.[9-11] The results of the studies showed that exercise performed for 6 months during dialysis increased urea removal by 20%.[11-13]

Mild to moderate-intensity intradialytic RE enhances treatment efficiency and helps in the recovery of CKD patients since it increases functional capacity, strength, muscular hypertrophy, and power.[14,15] RE improves overall health and physical fitness, and it is recommended for all adults to perform at least 2 days of exercise per week to reduce the risk of degenerative and cardiovascular diseases.[16]

In patients with DM, when initiating muscle contraction, RE causes the mobilization of glycogen reserves to meet the new energy requirements, increasing the uptake of circulating glucose, which increases glucose transport, resulting in a reduction of hyperglycemia. When performed regularly, exercise also induces an increase in the sensitivity of insulin receptors and in the number of insulin-dependent glucose transporters (GLUT4), with increased glucose uptake and efficiency in the selection and use of energy sources by activating mitochondrial enzymes.[17-20]

The effects of RE has not been reported in patients with CKD and DM, and this is the main focus of this study since DM is a leading cause of CKD requiring renal replacement therapy.

For these reasons and given the increasing cases of CKD associated with DM, it becomes important to evaluate the improvement of the QOL of DM patients undergoing HD. The objective of this research was to study the role of RE in the treatment and QOL of patients undergoing chronic HD.

Methods

Study Protocol

The sample population consisted of 60 adult volunteer patients, from the Institute of Nephrology of Taubaté-São Paulo. All procedures were submitted for approval by the Ethics Committee of the Federal University of São Paulo (UNIFESP), number 580/09. Only patients who agreed to be volunteers and signed an informed consent form participated in this study.

Patients were selected according to the following criteria: patients with CKD and DM type 2 (DM2) on dialysis, with > 6 months of dialysis and ages between 40 and 75 years for both sexes. Exclusion criteria were adopted to homogenize the samples, and individuals with the following features were excluded: limb amputation, congestive heart failure, intermittent claudication, angina, sequelae of cerebrovascular accident, peripheral neuropathies, patients with kyphosis, and patients who had already been performing RE.

To observe the effect of RE, patients were distributed as follows:

- Group 1: Patients with DM2 and CKD on dialysis. This group underwent a protocol of RE for 8 weeks (DM + CKD + RE, n = 15).
- Group 2: Patients with DM2 and CKD on dialysis. This group was not subjected to RE and are therefore sedentary (DM2 + CKD + S, n = 15).
- Group 3: Patients without DM2 but with CKD of other etiologies on dialysis. This group was also subjected to the protocol of 8 weeks of RE (CKD + RE, n = 15).
- Group 4: Patients without DM2 but with CKD of other etiologies on dialysis. This group was not subjected to RE (sedentary) (CKD + S, n = 15).

At the beginning and end of the protocol, the following variables were analyzed: creatinine, urea, potassium, and fasting glucose levels, as well as the efficiency of dialysis by the Kt/V index, analysis of quadriceps muscle strength with manual strength testing, and QOL by using the questionnaire "Medical Outcomes Study 36 (SF36)", validated for the Brazilian population.[21]

After initial evaluations, the subjects underwent 8 weeks of monitored RE training, intended and adapted for the physical reality of each patient. The exercises were conducted at the Institute of Nephrology of Taubaté (INEFRO).

The intervention was a program of resistance training during HD sessions, 3 times per week for a period of 8 weeks. The RE program consisted of a phase of passive stretching of the lower limbs, REs in major muscle groups, and a relaxing phase. The series of RE was composed of 8 exercises, 3 sets of 12 repetitions working the muscles of the quadriceps, hamstrings, adductors and abductors of the lower limbs, abdomen, biceps, and shoulder. The load was stipulated in accordance with the test result of manual strength, and load evolution was according to the method of linear progression, increasing the load by 10% after every 6 exercise sessions.

The pre and postexercise blood glucose measurements per session were performed by finger prick. Diabetic patients who were in a state of hyperglycemia (blood glucose ≥ 250 mg/dL), confirmed by testing before the exercise session, were subjected only to the relaxing activity. The values of creatinine, urea, potassium, glucose, and Kt/V were analyzed by testing in the clinical laboratories of INEFRO.

Statistical Analysis

Results are expressed as mean ± standard deviation. To compare groups with regard to the difference between the pre- and postclinical variables and SF-36 domains, we used analysis of variance (ANOVA). When the assertions of the ANOVA model were not satisfactory, we employed the nonparametric Mann-Whitney test. A significance level of 5% ($p \leq 0.05$) was also used.

Results

We compared the results of CKD patients with respect to the studied variables, analyzing the differences between the pre and post-training and comparing the differences between the groups.

Of the 60 patients studied, 46 (76.7%) were men with a mean age of 57.8 ± 8.0 years and 14 were women (23.3%) with a mean age of 57.8 years. The family income was less than twice the minimum wage for 90% of patients. The time in school was < 8 years, which corresponds to elementary school for 46.70% of the participants. We found that 98% were retired owing to disability. The length of time on dialysis maintenance ranged from > 6 months to 5 years. We found that 30 patients (50%) had DM2 as the main comorbidity.

As expected and shown in Table 1, 2 and 3 we observed a slight but significant increase in creatinine in the groups submitted to RE, suggesting, although not directly measured, that physical activity was effective in increasing muscle mass.

We observed a discrete reduction in urea as measured in predialysis before and after the RE protocol (Table 4). The same was observed when postdialysis urea was measured (Table 5).

Table 1 Initial and final mean clinical parameters (mg/dL) of the DM + CKD groups with (RE) and without (S) resistance exercise

Variables	Initial	At 8 weeks
Creatinine	8.4 ± 0.2	8.9 ± 0.6
Predialysis urea	126.3 ± 1.3	125.0 ± 2.5
Postdialysis urea	40.7 ± 0.7	41.9 ± 1.7
Potassium	5.4 ± 0.4	5.3 ± 0.4
KT/V	1.4 ± 0.01	1.3 ± 0.01
Glucose	160.2 ± 5.5	140.5 ± 8.5
Hemoglobin	12.7 ± 2.1	12.7 ± 2.2

Table 2 Smoking history in DM + CKD groups with (RE) and without (S) resistance exercise

Smoker	15 (14.94%)
Ex-smoker	6 (10.00%)
Non-smoker	39 (65.00%)

We observed reductions in blood glucose as measured in predialysis, before and after the RE protocol (Table 6), when compared with sedentary groups.

We observed an improvement in muscle strength after the RE protocol (Table 7).

We also observed significant improvements in QOL variables (Table 8).

Discussion

The protocol of 8 weeks of RE during HD resulted in significant, although slight, alterations in biochemical parameters. However, they showed no clinically important impact on dialysis. There was an expected elevation of creatinine with RE, interpreted as increased muscle mass, which was not directly measured. Blood glucose decreased mainly in patients with DM; however, it was not enough to modify drug therapy as they were no longer undergoing insulin treatment. Discrete (but significant) reduction in urea and potassium were observed but with no biological impact.

We chose the 8-week protocol because we were studying patients with CKD on HD and who also have DM2. As these patients have a high degree of limitations, some of them could have been lost with a longer protocol.

Table 3 Initial and final serum creatinine (mg/dL) in the DM + CKD groups with (RE) and without (S) resistance exercise

Groups	DM + CKD + RE	CKD + RE	DM + CKD + S	CKD + S
Initial	8.5 ± 0.1	8.4 ± 0.1	8.6 ± 0.2	8.3 ± 0.04
Final	9.4 ± 0.2*	9.4 ± 0.2*	8.3 ± 0.2	8.2 ± 0.10

Values represent mean ± standard error. * Final *vs.* Initial, $p < 0.0001$.

Table 4 Initial and final predialysis urea (mg/dL) in the DM + CKD groups with (RE) and without (S) resistance exercise

Groups	DM + CKD + RE	CKD + RE	DM + CKD + S	CKD + S
Initial	126.7 ± 0.9	125.3 ± 1.1	127.0 ± 1.31	126.05 ± 0.99
Final	124.1 ± 1.2*	122.1 ± 1.2*	127.2 ± 1.78	126.60 ± 1.24

Values represent mean ± standard error. * Final *vs.* Initial, $p < 0.0001$.

Table 5 Initial and final increase in postdialysis urea (mg/dL) in the DM + CKD groups with (RE) and without (S) resistance exercise

Groups	DM + CKD + RE	CKD + RE	DM + CKD + S	CKD + S
Initial	40.7 ± 0.9	40.8 ± 0.6	40.8 ± 0.84	40.6 ± 0.5
Final	42.8 ± 1.5*	43.6 ± 1.1*	40.7 ± 0.81	40.4 ± 0.5

Values represent mean ± standard error. * Final *vs.* Initial, $p < 0.0001$.

Table 6 Initial and final glycemia (mg/dL) in the DM + CKD groups with (RE) and without (S) resistance exercise

Groups	DM + CKD + RE	CKD + RE	DM + CKD + S	CKD + S
Initial	166.6 ± 1.0	113.0 ± 3.6	162.3 ± 3.7	114 ± 1.9
Final	136.0 ± 4.6*	104.0 ± 5.5*	151.3 ± 7.9	108 ± 3.9

Values represent mean ± standard error. * Final *vs.* Initial, $p < 0.0001$.

Table 7 Initial and final muscle strength, in degrees, in the DM + CKD groups with (RE) and without (S) resistance exercise

Groups	DM + CKD + RE	CKD + RE	DM + CKD + S	CKD + S
Initial	2.3 ± 0.5	2.4 ± 0.5	2.3 ± 0.5	2.3 ± 0.5
Final	3.5 ± 0.6*	3.5 ± 0.6	2.3 ± 0.5	2.3 ± 0.5

Values represent mean ± standard error. * Final *vs.* Initial, $p < 0.0001$.

Table 8 Initial and final quality of life (mean of improvement) in the DM + CKD and CKD with resistance exercise (RE) groups

Variables	DM + CKD + RE initial	DM + CKD + RE post-training	CKD + RE initial	CKD + RE post-training
FC	70.61 ± 5.23	84.00 ± 4.50*	72.07 ± 3.54	84.90 ± 7.57*
PA	76.13 ± 3.48	91.47 ± 4.47*	75.60 ± 2.75	84.07 ± 6.51*
PP	52.87 ± 3.07	76.53 ± 12.1*	53.13 ± 4.24	78.07 ± 5.60*
GH	53.07 ± 2.62	62.89 ± 6.43*	54.55 ± 2.83	64.47 ± 6.83*
VIT	69.40 ± 4.60	74.27 ± 5.35*	50.4 ± 3.16	66.07 ± 4.76*
SF	62.73 ± 2.17	72.53 ± 3.52*	50.27 ± 3.26	61.13 ± 4.81*
ES	62.13 ± 2.88	79.33 ± 3.60*	61.29 ± 3.15	80.80 ± 5.91*
MH	72.00 ± 2.98	83.01 ± 4.32*	59.67 ± 4.47	70.13 ± 4.81*

Values represent mean ± standard error. * Final *vs.* Initial, $p < 0.0001$. FC: Functional capacity; PA: Physical appearance; PP: Pain perception; GH: General health; VIT: Vitality; SF: Social function; ES: Emotional state; MH: Mental health.

The results of this RE protocol were different from those of another study that evaluated 16 patients who underwent 1 h of exercise a day for 12 weeks. Eleven of those patients who were undergoing chronic HD showed a significant improvement in arterial stiffness. This effect was transient (i.e., arterial stiffness values returned to baseline levels after 1 month of detraining), which was interpreted as being due to a better supply/demand myocardial balance with improved mechanical stress of the large arteries.[22,23]

In another study assessing intradialytic training, using a training cycle with ergometers in the first 2h of each dialysis session, 3 times a week for 6 months, the subjects showed improvement in physical function and blood pressure and a reduction in blood glucose, which demonstrate the effectiveness of a continuous intradialytic exercise program for 6 months with regard to the improvement of a dialysis patient.[24]

In another study in patients undergoing 12 weeks of intradialytic training, statistically significant improvements in muscle strength of the quadriceps and biceps were observed, improving physical function and vitality and the QOL domains.[25] Longer-duration protocols were used in these surveys, which may explain some differences observed when compared with the present protocol.

Although it is widely accepted that exercise is beneficial in patients with CKD, improving physical functioning in general, including maximal oxygen uptake, muscle strength, nutritional and hematologic status, inflammatory cytokines, and QOL, it is unclear whether the benefits of exercise are limited to a group of dialysis patients with no DM. Therefore, the effects of individualized exercise programs for elderly patients or patients with comorbidities must be evaluated.[26,27]

Leehey[27] studied the effect of exercise for 24 weeks on medical treatment in patients with DM2, obesity (body mass index, > 30 kg/m^2), and CKD. These patients performed exercise 3 times a week. The exercise training resulted in an increase in physical and functional capacity of the patients, accompanied by a slight but insignificant decrease in systolic blood pressure at rest, and increased muscle strength as assessed by static and dynamic resistance. The exercise did not alter the rate of glomerular filtration.[28]

Our study used intradialytic RE, which facilitated adherence, besides screening the patients through the assistance of various health professionals, such as doctors, nurses, nutritionists, and psychologists. An RE program would also be beneficial in relation to the acceptance and well-being of the patient regarding the treatment, for HD limits, and among other things, for the patient's social and family life, as quite often a person undergoing HD develops a derogatory self-perception accompanied by depression. It was clear from the observations that exercise induced an overall psychological improvement, including the "will to live", leading to positive expectations about the return to a productive life. These subjective observations were confirmed in the application of the SF36.

Moreover, it has been suggested that high-intensity RE would require consumption of contractile proteins and calcium, and therefore this type of exercise would not be recommendable because it could potentially compromise recovery. As the basal metabolic rate is increased in this situation, this requires greater functional reserve. This effect can cause the patient to present clinical symptoms of anemia, bleeding, increased blood pressure, cramps, excitation of the autonomic nervous system, and osteodystrophy.[29,30]

We also observed a substantial improvement in QOL in all evaluated parameters, such as functional ability, physical appearance, perception of pain, general health, vitality, social function, emotional status, and mental health. These results indicated that the RE program during HD was reliable in demonstrating an improved QOL.

The RE program was of low intensity, with low loads, and 40% of the maximum resistance, which facilitated its realization. For example, patient A.G., a 51-year-old man, started training with a 500 g anklet on each leg, which is a reduced load for healthy men 50 years of age. He gradually gained fitness and muscle strength with exercise and could train with a 2 kg anklet (4-fold increase!) at the end of 8 weeks, a fact that surprised the patient, raising his self-esteem. Patient J.A., a 58-year-old man, was able to return to daily living activities that he thought to be untenable, such as playing a musical instrument and meeting with friends over the weekend, activities that had been curbed after he started HD.

It is striking that, despite this protocol not showing an improvement in biochemical parameters, an RE program of only 8 weeks was enough to induce a significant improvement in QOL, indicating that the exercise protocol, by its simplicity and adherence, makes it feasible in any environment where patients undergo dialysis sessions.

Conclusion

This assessment suggests that low-intensity RE, 3 times a week, with 40% of the maximum force, is an adjuvant therapy to complement medical and dietary treatment in terminal CKD patients. The intradialytic RE program was proved easy to implement by the different professional exercise specialists working in the HD clinic, and its impact on QOL was much higher than expected on the basis of the load required, evaluation time, and simplicity.

We therefore suggest that simple and feasible exercise programs be developed for patients with CKD, including those with DM.

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