Acute effects of intradialytic aerobic exercise on solute removal, blood gases and oxidative stress in patients with chronic kidney disease

Efeitos agudos do exercício aeróbio intradialítico sobre a remoção de solutos, gasometria e estresse oxidativo em pacientes com doença renal crônica

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Abstract

Introduction: Hemodialysis contributes to increased oxidative stress and induces transitory hypoxemia. Compartmentalization decreases the supply of solutes to the dialyzer during treatment. The aim of this study was to investigate the acute effects of intradialytic aerobic exercise on solute removal, blood gases and oxidative stress in patients with chronic kidney disease during a single hemodialysis session. **Methods:** Thirty patients were randomized to perform aerobic exercise with cycle ergometer for lower limbs during 30 minutes with intensity between 60-70% of maximal heart rate, or control group (CG). Blood samples were collected prior to and immediately after exercise or the equivalent time in CG. Analysis of blood and dialysate biochemistry as well as blood gases were performed. Mass removal and solute clearance were calculated. Oxidative stress was determined by lipid peroxidation and by the total antioxidant capacity. **Results:** Serum concentrations of solutes increased with exercise, but only phosphorus showed a significant elevation ($p = 0.035$). There were no significant changes in solute removal and in the acid-base balance. Both oxygen partial pressure and saturation increased with exercise ($p = 0.035$ and $p = 0.024$, respectivelly), which did not occur in the CG. The total antioxidant capacity decreased significantly ($p = 0.027$). **Conclusion:** The acute intradialytic aerobic exercise increased phosphorus serum concentration and decreased total antioxidant capacity, reversing hypoxemia resulting from hemodialysis. The intradialytic exercise did not change the blood acid-base balance and the removal of solutes.

Keywords: exercise; oxidative stress; renal dialysis.

Resumo

Introdução: A hemodiálise contribui para aumentar o estresse oxidativo e induz a hipoxemia transitória. A compartimentalização dos solutos diminui sua oferta para o dialisador durante o tratamento. O objetivo deste estudo foi investigar os efeitos agudos do exercício aeróbio intradialítico sobre a remoção de solutos, gasometria e estresse oxidativo em pacientes com doença renal crônica durante uma sessão de hemodiálise. **Métodos:** Trinta pacientes foram randomizados para realizar exercício aeróbio com cicloergômetro para membros inferiores durante 30 minutos com intensidade entre 60-70% da frequência cardíaca máxima, ou grupo controle (GC). Amostras sanguíneas foram coletadas antes e imediatamente após o término do exercício ou no período equivalente no GC. Análises da bioquímica do sangue e dialisato e gasometria foram realizadas. A massa removida e a depuração dos solutos foram calculadas. O estresse oxidativo foi determinado pela peroxidação lipídica e capacidade antioxidante total. **Resultados:** As concentrações séricas dos solutos aumentaram com o exercício, mas somente o fósforo mostrou elevação significativa ($p = 0.035$). Não houve modificações significantes na remoção de solutos e no equilíbrio ácido-básico. A pressão parcial e a saturação de oxigênio aumentaram com o exercício ($p = 0.035$ e $p = 0.024$, respectivamente), o que não ocorreu no GC. A capacidade antioxidante total diminuiu significativamente ($p = 0.027$). **Conclusão:** O exercício aeróbico intradialítico agudo aumentou a concentração sérica de fósforo e diminuiu a capacidade antioxidante total, revertendo a hipoxemia resultante da hemodiálise. O exercício intradialítico não alterou o equilíbrio ácido-básico e a remoção de solutos.

Palavras-chave: estresse oxidativo; exercício; diálise renal.

Introduction

Hemodialysis contributes to increased oxidative stress, producing free radicals and reducing the levels of antioxidant enzymes in patients with end-stage renal disease (ESRD).[1] During hemodialysis, the compartmentalization of solutes reduces its blood levels and dialysis efficiency by decreasing the supply to the dialyzer thus impairing their removal.[2]

Hemodialysis also decreases oxygen partial pressure (PaO_2), increases minute ventilation due to production and excretion of carbon dioxide (CO_2), and increases oxygen consumption as a result of metabolic alkalosis.[3,4] The hypoxemia generated during hemodialysis due to the sequestration of intrapulmonary leukocytes decreases cardiac output and induces microatelectasis as a result of the procedure.[3]

Presently, physical exercise is recommended for hemodialysis patients due to their chronic beneficial effects, which include increased aerobic capacity, muscle strength, production of antioxidants, control of blood pressure and decreased fatigue.[5-9] However, the acute effects of exercise during dialysis have not been adequately studied so far. It is possible that acute exercise could have detrimental effects in the short term, such as increased oxidative stress and decreased production of antioxidant enzymes, aggravating the clinical condition of the patients.[10]

Therefore, the aim of this study was to investigate the acute effects of intradialytic aerobic exercise on solute removal, blood gases and oxidative stress in ESRD using a cycle ergometer for lower limbs during a hemodialysis session.

Methods

Participants

Thirty patients with clinically stable ESRD who underwent hemodialysis were randomized by the Random Allocation Software 1.0™ (Isfahan University of Medical Sciences, Isfahan, Iran) into intervention group (IG) or control group (CG). Data from medical records and patient history and physical examination were used.

Inclusion criteria were: adults older than 18 years of age, diagnosis of chronic kidney disease (CKD) for at least six months and having hemodialysis treatment for more than three months, physical and clinical stability for performing aerobic exercise, not maintaining regular or having total absence of physical activity, and not having participated in other research related to physical activity in the last six months. As exclusion criteria, presence of acute myocardial infarction three months before the start of the study, unstable angina, hemodialysis vascular access in the lower limbs, hemoglobin level < 10 g/dL, presence of active systemic infection or inflammatory process, or candidate for imminent kidney transplantation with a living donor.

The study protocol was approved by the Research Ethics Committee of the IPA Methodist University Center and Hospital de Clínicas de Porto Alegre, where the study was conducted and performed according to the 1975 Declaration of Helsinki. All participants provided written informed consent prior to enrollment.

Procedures

Dialysis settings

All patients were dialysed with bicarbonate dialysis, thrice weekly for 4 h with a low-flux polysulphone hollow-fiber dialyser (Diacap™ LOPS 20, Laboratórios B.Braun S. A., São Gonçalo, RJ, Brazil). Hemodialysis sessions were performed with single use of dialyzers, and all patients had a native arteriovenous fistula as vascular access. Blood flow rates ranged between 300 and 350 mL/min. The dialysate flow rate was 500 mL/min. The blood flow and dialysate flow rates were kept constant throughout the study period in the individual patient.

Intervention

The intervention was performed in the beginning of the second hour of the third weekly day of hemodialysis. The CG had two blood collections separated by 30-minute interval controlled by the dialysis machine timer on a single hemodialysis session. The IG was compared to the CG and as its own control. The IG was studied contemporaneous with the CG and in the subsequent week, with a blood collection prior to and following 30 minutes of aerobic exercise. The exercise was conducted with a cycle ergometer for lower limbs (Dream EX 150 FLEX®, Dream Indústria e Comércio Ltda., Esteio, RS, Brazil) coupled to the dialysis chair.

Exercise intensity was set between 60-70% of maximal heart rate, calculated using the formula proposed by Karvonen *et al.*,[11] or intensity between 13-14 points on the Borg's Rating of Perceived

Exertion Scale (Borg's RPE Scale). Heart rate was measured using the monitor HR 102 Oregon Scientific™ (Oregon Scientific, São Paulo, SP, Brazil). The interventions were carried out by the same researcher.

Collections and blood samples

Blood samples were drawn from the arterial line of hemodialysis vascular access, after reducing the blood flow pump to 50 mL/minute. A sample (3 mL) was collected in a syringe washed with heparin for blood gases analysis. A second sample (5 mL) was collected in a plain tube for solute measurements. A third sample (5 mL) was collected in a plain tube with EDTA, centrifuged at 1900 rpm for 10 minutes at 4 °C, for plasma separation and storage in conical tubes at -80°C for the analysis of oxidative stress.

Collection of dialysate

The dialysate eliminated by the dialysis equipment during the 30-minute intervention or equivalent time in CG was collected in a container with storage capacity of 20 liters. After homogenization of the content and measurement of the total volume, a sample was separated and aliquoted into two 5-mL collection tubes for analysis. To calculate the clearance of solutes, we used the formula described by Maher.[12]

Biochemical analysis

The analysis of serum creatinine, urea, potassium, phosphorus, magnesium, dialysate and blood gases were performed by automation. For analysis of lipid peroxidation (malondialdehyde, MDA) thiobarbituric acid reactive substances (TBARS) and colorimetric assay at 540 nm (TBARS Assay kit Cayman™, Cayman Chemical Company, Ann Arbor, Michigan, USA) were used. Analysis of the total antioxidant capacity (TAC) of plasma was based on the ability of antioxidants sample to inhibit the oxidation of the compound 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid, ABTS) by metmyoglobin. The amount of ABTS produced was read by a colorimetric assay at 540 nm, and compared with Trolox (Antioxidant Assay kit Cayman™, Cayman Chemical Company, Ann Arbor, Michigan, USA).

Sample size calculation

The sample estimate was performed using the software G*Power™ version 3.1.9.2 (Department of Psychology, Kiel University, Kiel, Germany). The sample size was calculated based on mean and standard deviation of plasma MDA concentration post-hemodialysis in IG and plasma MDA concentration in CG according to the study of Ozden *et al.*[13] Using a two-tailed test and an effect size of 2.18 obtained in the reference study, it was defined a total of 15 patients in each group to get a power of 80% and a significance level (a) of 5%.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of data distribution. Differences between variables were calculated using nonparametric tests (Wilcoxon or Mann-Whitney) or parametric tests (independent samples t test or paired samples t test), as applicable. Data were expressed as mean ± standard error or median and interquartile range. A $p < 0.05$ was considered statistically significant. The data were analyzed using the program Statistical Package for the Social Sciences™ (SPSS version 19.0, Chicago, Illinois, USA).

Results

The clinical characteristics of the groups are presented in Table 1. In both groups there is a predominance of male and white patients. There were no significant differences between groups with respect to age, Body Mass Index (BMI), duration of hemodialysis treatment, and to Charlson Comorbidity Index (CCI). Five patients underwent previous renal transplantation (4 CG, 1 IG), 17 were former smokers and three patients were active smokers. The predominant etiology of ESRD was *diabetes mellitus*, followed by hypertension and chronic glomerulonephritis. Seven patients had ESRD from unknown etiology. No patient reported discomfort when performing the exercise.

Comparisons between the differences in measures of the groups, before and after an interval of 30 minutes, are shown in Table 2. With the implementation of aerobic exercise, there was a significant increase in the oxygen partial pressure and saturation [4.30 ± 2.15 mmHg *vs*. -6.55 ± 1.90 mmHg, $p = 0.001$ and 1.1% (0.1% to 2%) *vs*. -0.6% (-2.8% to -0.1%), $p = 0.003$, respectively].

Table 3 shows comparisons between the differences of the measures before and after an interval of 30 minutes in the IG, with and without exercise performance. In the hemodialysis session

Table 1 The clinical characteristics of the groups

		CG (n = 15)	IG (n = 15)	*p*-value
Gender (male)		12	11	-
Age (years)		53 ± 3	52 ± 5	0.200
BMI (kg/m²)		27.8 ± 1.2	26.0 ± 1.1	0.104
Duration of treatment (months)		19 (10 - 45)	20 (8 - 64)	0.624
CCI (points)		5.0 ± 0.5	5.0 ± 0.6	0.200
Race (n)	Black	3	2	-
	White	12	13	-
Cause of ESRD (n)	*Diabetes mellitus*	5	4	-
	Hypertension	3	1	-
	Glomerulonephritis	3	1	-
	Unknown	1	6	-
	Others	2	3	-
Smoking (n)	Yes/No	1/4	2/6	-
	Former smoker	10	7	-

Data expressed as mean ± standard error or median (interquartile range). BMI: body mass index; CCI: Charlson comorbidity index; CG: control group; IG: intervention group; ESRD: end-stage renal disease.

with exercise patients showed an increase in serum phosphorous concentration [0.2 mg/dL (-0.3 mg/dL to 0.37 mg/dL) *vs*. -0.2 mg/dL (-0.4 mg/dL to 0 mg/dL), p = 0.035], increased oxygen partial pressure and saturation [2.71 ± 1.81 mmHg *vs*. -0.76 ± 1.17 mmHg, p = 0.037 and 0.3% (-0.3% to 1.1%) *vs*. -0.2% (-0.8% to 0.5%), p = 0.024, respectively] and decreased TAC (-0.165 ± 0.12 mM *vs*. 0.355 ± 0.2 mM, p = 0.027).

Table 4 presents the total dialysate volume, solute concentration measurements, removed mass and solute clearances in the dialysate of 9 individuals of the IG. Compared to baseline, there were no statistically significant differences in any parameter evaluated after the exercise performance.

Discussion

In this study, we found that acute intradialytic aerobic exercise increased serum phosphorus concentration, decreased the total antioxidant capacity, and reversed the hypoxemia resulting from hemodialysis. The oxygen partial pressure and saturation increased with exercise, which did not occur in the control group. However, the intradialytic exercise did not change acutely the blood gas parameters or even increased the removal of solutes.

We showed a significant increase in serum phosphorus after aerobic exercise in the IG. Phosphate is predominantly an intracellular ion, which moves into the cell as the extracellular pH increases.[14] This finding is in line with previous studies that could demonstrate an increase in phosphate removal associated with intradialytic aerobic exercise.[14-17]

Hemodialysis performed with bicarbonate dialysate favors alkalemia, which can hinder phosphate removal. This fact emphasizes the potential of proposed exercise of mobilizing phosphorus from body compartments, increasing its blood concentration. Furthermore, this increase in phosphorus concentration came to accomplish the intervention in the third weekly hemodialysis session where the patient has already shows a reduction in the concentration of solutes due to treatment. Modulation of the intensity and duration of exercise in a hemodialysis session may also be necessary to further promote increases in serum concentration of solutes mediated by a decrease in blood pH induced by the exercise.

Kirkman *et al.*,[17] performing 60 minutes of intradialytic exercise with intensity of 90% of the lactate threshold, showed that this exercise protocol was more effective than the increase in dialysis time for phosphate removal, being an adjuvant therapy for serum phosphorus control. Farese *et al.*[15] also found an increase in the phosphate mass and clearance in dialysate after three exercise sessions lasting 20 minutes at 36 rpm.

In our study, aerobic exercise increased the serum concentration of other solutes (but without reaching statistical significance) but with no absolute

Table 2 Comparisons between the diferences (D) in measures of the groups, before and after an interval of 30 minutes

	IG (n = 15)			CG (n = 15)			*p*-value
	Before	After	D	Before	After	D	
UF rate (mL/h)	643 ± 416		-	700 ± 256		-	0.654
MDA (mM)	9.34 ± 2.92	9.34 ± 2.92	-0.44 ± 3.11	9.77 ± 2.70	11.00 ± 1.89	1.23 ± 2.23	0.666
TAC (mM)	2.65 ± 0.96	2.53 ± 0.86	-0.12 ± 0.15	2.54 ± 0.89	2.89 ± 1.17	0.35 ± 0.26	0.123
Potassium (mEq/L)	3.51 ± 0.12	3.73 ± 0.08	0.22 ± 0.18	4.12 ± 0.15	3.99 ± 0.14	-0.13 ± 0.22	0.087
Urea (mg/dL)	68.60 ± 6.57	71.07 ± 4.97	2.46 ± 6.10	86.79 ± 7.76	84.71 ± 7.20	-2.07 ± 7.74	0.649
Creatinine (mg/dL)	4.70 ± 0.40	4.85 ± 0.26	0.14 ± 0.40	6.21 ± 0.55	6.14 ± 0.52	-0.07 ± 0.58	0.761
Phosphorus (mg/dL)	2.62 ± 0.21	2.80 ± 0.13	0.17 ± 0.21	3.25 ± 0.32	3.10 ± 0.21	-0.14 ± 0.20	0.297
Magnesium (mEq/L)	2.27 ± 0.07	2.25 ± 0.02	-0.02 ± 0.04	2.43 ± 0.14	2.33 ± 0.08	-0.10 ± 0.05	0.370
pH	7.399 ± 0.010	7.413 ± 0.013	0.014 ± 0.007	7.400 ± 0.010	7.399 ± 0.010	-0.001 ± 0.005	0.098
pCO_2 (mmHg)	41.44 ± 0.98	40.94 ± 1.51	-0.50 ± 0.79	42.93 ± 1.08	43.19 ± 0.89	0.26 ± 0.98	0.553
HCO_3 (mmol/L)	25.00 ± 0.46	25.42 ± 0.61	0.42 ± 0.44	25.95 ± 0.46	26.06 ± 0.42	0.11 ± 0.37	0.600
CO_2 total (mmol/L)	26.27 ± 0.47	26.67 ± 0.64	0.40 ± 0.45	27.32 ± 0.49	27.38 ± 0.42	0.06 ± 0.41	0.583
BE (mmol/L)	0.14 ± 0.50	0.82 ± 0.60	0.68 ± 0.42	0.94 ± 0.48	1.01 ± 0.49	0.06 ± 0.27	0.240
pO_2 (mmHg)	67.90 ± 8.16	72.20 ± 9.25	4.30 ± 2.15	87.24 ± 4.94	80.69 ± 5.06	-6.55 ± 1.90	0.001
sO_2 (%)	95.8 (70.6;97.5)	96.4 (71.6;97.9)	1.10 (0.1;2.0)	97.2 (96.2;97.5)	96.6 (95.2;97.1)	-0.60 (-2.8;-0.1)	0.003

Data expressed as mean ± standard error or median (interquartile range). D: measure after 30 minutes less measure before 30 minutes. CG: control group; IG: intervention group; UF: ultrafiltration; MDA: malondialdehyde; TAC: total antioxidant capacity; pCO_2: partial pressure of carbon dioxide; HCO_3: bicarbonate; CO_2: carbon dioxide; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation.

changes in solute clearance. Intradialytic aerobic exercise promotes increased blood flow to the central vasculature and increased vascular permeability, allowing greater area of exchange between the intracellular and intravascular compartments. This favors the solute efflux from muscles of the lower limbs, which usually remain relatively stagnant with collapsed capillaries during hemodialysis.[15,16,18-21]

Orcy *et al.*[16] found an increase in the mass removal and phosphate clearance only in dialysate after three sessions of intradialytic aerobic exercise lasting 40 minutes with an intensity between 13-14 points on the Borg's RPE Scale. Changes in blood concentration of solutes have not been found in this study because the samples were collected prior to and after the hemodialysis procedure. The duration of intradialytic exercise we proposed was sufficient to increase solute blood concentrations, but as the solute removal occurs across the entire time of hemodialysis (four hours in average), it would be necessary to measure them again at the end of dialysis treatment, and not only at the end of the exercise.

Analyzing the results of blood gases post-exercise, we observed a statistically significant increase in the oxygen partial pressure and saturation, reversing hypoxemia induced by hemodialysis. Meyring-Wösten *et al.*[22] described a significant association between hypoxemia and adverse clinical outcomes, most notably all-cause of hospitalization and mortality.

Table 3 Comparisons between the diferences (D) in measures before and after an interval of 30 minutes, with and without exercise performance, in intervention group (n = 15)

	With exercise			Without exercise			*p*-value
	Before	After	D	Before	After	D	
UF rate (mL/h)	643 ± 416		-	576 ± 410		-	0.660
MDA (mM)	5.17 (3.54;10.05)	8.20 (5.24;12.68)	2.23 (-0.6;7.83)	8.33 (3.00;14.68)	10.42 (4.90;17.21)	0.54 (-5.04;6.5)	1.000
TAC (mM)	2.69 ± 0.85	2.52 ± 0.87	-0.16 ± 0.12	2.49 ± 0.90	2.84 ± 0.99	0.35 ± 0.20	0.027
Potassium (mEq/L)	3.7 (3.4;4.0)	3.9 (3.5;4.4)	0.1 (-0.2;0.3)	3.8 (3.5;4.1)	3.7 (3.4;3.9)	-0.1 (-0.2;0)	0.116
Urea (mg/dL)	70 (55.25;97.00)	75 (63.25;96.50)	-6 (-10;3.25)	80 (70.25;90.50)	73 (54.25;94.50)	-10 (-12;-5.75)	0.052
Creatinine (mg/dL)	5.13 (4.12;5.97)	5.24 (4.13;6.31)	-0.51 (-0.71;0.19)	5.95 (4.49;6.37)	5.33 (4.23;6.31)	-0.62 (-0.78;-0.35)	0.338
Phosphorus (mg/dL)	2.9 (2.2;3.5)	2.9 (2.5;3.4)	0.2 (-0.3;0.37)	3.0 (2.6;3.3)	2.9 (2.5;3.0)	-0.2 (-0.4;0)	0.035
Magnesium (mEq/L)	2.36 ± 0.23	2.33 ± 0.21	-0.02 ± 0.02	2.31 ± 0.24	2.17 ± 0.39	-0.14 ± 0.08	0.244
pH	7.400 ± 0.041	7.416 ± 0.049	0.016 ± 0.004	7.397 ± 0.042	7.405 ± 0.043	0.007 ± 0.004	0.297
pCO_2 (mmHg)	40.50 ± 4.0	40.06 ± 5.60	-0.43 ± 0.55	41.99 ± 4.45	41.60 ± 4.78	-0.38 ± 0.51	0.946
HCO_3 (mmol/L)	24.5 (23.6;25.8)	25.0 (23.8;26.1)	0.9 (-0.6;1.7)	25.3 (24.2;26.0)	25.4 (24.0;26.6)	0.3 (-0.4;1.2)	0.543
CO_2 total (mmol/L)	25.71 ± 1.82	26.30 ± 2.41	0.59 ± 0.32	26.49 ± 1.55	26.67 ± 1.67	0.18 ± 0.26	0.370
BE (mmol/L)	0.5 (-1.8;0.8)	0.3 (-0.8;1.7)	1.1 (-0.5;1.9)	0.3 (-0.8;1.6)	0.6 (-0.6;1.9)	0.6 (0.2;1.2)	0.330
pO_2 (mmHg)	75.03 ± 29.78	77.75 ± 32.37	2.71 ± 1.81	75.37 ± 28.68	74.60 ± 28.74	-0.76 ± 1.17	0.037
sO_2 (%)	96.5 (80.9;97.5)	97.3 (80.5;97.8)	0.3 (-0.3;1.1)	96.7 (78.4;97.6)	96.8 (75.3;97.4)	-0.2 (-0.8;0.5)	0.024

Data expressed as mean ± standard error or median (interquartile range). D: measure after 30 minutes less measure before 30 minutes. UF: ultrafiltration; MDA: malondialdehyde; TAC: total antioxidant capacity; pCO_2: partial pressure of carbon dioxide; HCO_3: bicarbonate; CO_2: carbon dioxide; BE: base excess; pO_2: partial pressure of oxygen; sO_2: oxygen saturation.

Hemodialysis with bicarbonate lowers the PaO_2 in its initial minutes and reaches the nadir between 30 and 60 minutes, remaining at this level throughout the dialysis procedure and after its completion.[3,23] Several mechanisms have been proposed to explain this reduction: an increase in the oxyhemoglobin dissociation curve (Bohr Effect) caused by increased pH, depression of the respiratory center due to alkalosis, reduced oxygen diffusion, imbalance in the ventilation-perfusion ratio due to the accumulation of leukocytes in small pulmonary vessels caused by blood contact with the dialyzer membrane, and alveolar hypoventilation caused by excretion of CO_2 via dialysate during the alkalization of blood.[4,23-25]

Moore *et al.*[26] performed five minutes of intradialytic aerobic exercise in each hour of treatment with intensity at 60% of maximal oxygen consumption (VO_{2max}) to assess the hourly PaO_2. These authors did not observe changes in the PaO_2 probably because the training volume was low. Burke *et al.*[27] conducted a moderate intensity exercise protocol during hemodialysis treatment, and Germain *et al.*[28] prescribed aerobic exercise of low intensity for three hours during dialysis. Both groups found an increase in PaO_2 and increased alveolar oxygen pressure during exercise. The intensity and duration of exercise that we applied generated enough hyperventilation to increase the diffusion of oxygen, but this did not decrease the alkalinization of blood, because the partial pressure of CO_2 remained unchanged.

The ability of the body to resist oxidative changes depends on the levels of antioxidant enzymes such as

Table 4 Total volume, concentration measurements, removed mass and clearance of solutes in the dialysate in intervention group (n = 9)

	With exercise	Without exercise	*p*-value
UF rate (mL/h)	623 ± 387	582 ± 364	0.192
Volume (liters)	14.70 (14.32 - 19.94)	14.81 (14.24 - 23.27)	0.594
[Cr] (mg/dL)	1.68 ± 0.21	1.64 ± 0.24	0.561
mCr (mg)	272.98 ± 31.46	272.24 ± 30.07	0.895
cCr (ml/minute)	151.28 ± 5.77	153.06 ± 10.00	0.878
[U] (mg/dL)	32.00 ± 4.09	34.11 ± 5.17	0.352
mU (mg)	5189.22 ± 560.71	5558.71 ± 561.01	0.262
cU (ml/minute)	227.51 ± 10.44	226.26 ± 15.31	0.933
[P] (mg/dL)	0.70 (0.60 - 0.95)	0.70 (0.55 - 0.80)	0.777
mP (mg)	132.30 (93.77 - 165.10)	118.48 (102.94 - 153.46)	0.678
cP (ml/minute)	147.30 ± 10.25	163.84 ± 16.13	0.437
[K] (mEq/L)	2.5 (2.4 - 2.6)	2.4 (2.3 - 2.6)	0.365
mK (mEq)	39.03 (35.39 - 48.50)	40.17 (35.17 - 49.86)	0.859
cK (ml/minute)	304.83 (296.91 - 458.12)	336.36 (309.24 - 446.49)	0.161
[Mg] (mg/dL)	1.36 ± 0.04	1.37 ± 0.06	0.826
mMg (mg)	234.17 ± 23.72	245.59 ± 22.85	0.577
cMg (ml/minute)	341.24 ± 35.24	383.52 ± 27.78	0.228

Data expressed as mean ± standard error or median (interquartile range). UF: ultrafiltration; [Cr]: creatinine concentration; mCr: mass of creatinine; cCr: creatinine clearance; [U]: urea concentration; um: mass of urea; cU: urea clearance; [P]: phosphorus concentration; mP: mass of phosphorus; cP: phosphorus clearance; [K]: potassium concentration; mK: mass of potassium; cK: potassium clearance; [Mg]: magnesium concentration; mMg: mass of magnesium; cMg: magnesium clearance.

superoxide dismutase, glutathione peroxidase, and catalase, as well as of nonenzymatic antioxidants. TAC is a valuable tool for understanding the ability of the biological system to oppose oxidative stress.[29]

In our study, we observed a statistically significant reduction in TAC after the exercise. Previous studies performed without exercise[29-31] showed significant reduction in TAC after a hemodialysis session that was attributed in large part to a correlation of their elimination with a decrease in uric acid concentration and antioxidant vitamins removed by dialysis. Furthermore, additional loss of antioxidants is frequent and caused by the removal of water soluble antioxidants due to their low molecular weight.[30] The increased blood flow promoted by aerobic exercise may have contributed to the additional loss of antioxidants.

This study has limitations, including the small number of patients in each comparison group. Moreover, for better assessment of maximal heart rate training to adjust exercise prescription it would be appropriate to implement a standardized exercise stress test. The analysis of uric acid concentration could have been carried out in order to verify its parallel relationship with the reduction of TAC. Finally, to verify the effectiveness of hemodialysis on solute removal and the influence of exercise on the outcome of the dialysis process, it would be necessary to perform blood and dialysate collection at the end of hemodialysis session, in addition to the end of exercise.

In conclusion, moderate intradialytic aerobic exercise acutely reversed hypoxemia induced by hemodialysis and increased serum phosphorus levels. Despite this, no changes occurred on solute removal. The exercise did not promote acute changes in the acid-base balance, but decreased the total antioxidant capacity of these patients.

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References

1. Koca T, Berber A, Koca HB, Demir TA, Koken T. Effects of hemodialysis period on levels of blood trace elements and oxidative stress. Clin Exp Nephrol 2010;14:463-8. DOI: http://dx.doi.org/10.1007/s10157-010-0310-3
2. Schneditz D, Daugirdas JT. Compartment effects in hemodialysis. Semin Dial 2001;14:271-7. DOI: http://dx.doi.org/10.1046/j.1525-139X.2001.00066.x
3. Symreng T, Flanigan MJ, Lim VS. Ventilatory and metabolic changes during high efficiency hemodialysis. Kidney Int 1992;41:1064-9. DOI: http://dx.doi.org/10.1038/ki.1992.162
4. Sherlock J, Ledwith J, Letteri J. Determinants of oxygenation during hemodialysis and related procedures: A report of data acquired under varying conditions and a review of the literature. Am J Nephrol 1984;4:158-68. DOI: http://dx.doi.org/10.1159/000166797
5. Smart N, McFarlane J, Cornelissen V. The Effect of Exercise Therapy on Physical Function, Biochemistry and Dialysis Adequacy in Haemodialysis Patients: A Systematic Review and Meta-Analysis. Open J Nephol 2013;3:25-36. DOI: http://dx.doi.org/10.4236/ojneph.2013.31005
6. Storer TW, Casaburi R, Sawelson S, Kopple JD. Endurance exercise training during haemodialysis improves strength, power, fatigability and physical performance in maintenance haemodialysis patients. Nephrol Dial Transplant 2005;20:1429-37. DOI: http://dx.doi.org/10.1093/ndt/gfh784
7. Ouzouni S, Kouidi E, Sioulis A, Grekas D, Deligiannis A. Effects of intradialytic exercise training on health-related quality of life indices in hemodialysis patients. Clin Rehabil 2009;23:53-63. DOI: http://dx.doi.org/10.1177/0269215508096760
8. Chang Y, Cheng SY, Lin M, Gau FY, Chao YF. The effectiveness of intradialytic leg ergometry exercise for improving sedentary life style and fatigue among patients with chronic kidney disease: a randomized clinical trial. Int J Nurs Stud 2010;47:1383-8. DOI: http://dx.doi.org/10.1016/j.ijnurstu.2010.05.002
9. Schneider CD, Oliveira AR. Radicais livres de oxigênio e exercício: mecanismos de formação e adaptação ao treinamento físico. Rev Bras Med Esporte 2004;10:308-13. DOI: http://dx.doi.org/10.1590/S1517-86922004000400008
10. Fatouros IG, Pasadakis P, Sovatzidis A, Chatzinikolaou A, Panagoutsos S, Sivridis D, et al. Acute exercise may exacerbate oxidative stress response in hemodialysis patients. Nephron Clin Pract 2008;109:c55-64. PMID: 18560239 DOI: http://dx.doi.org/10.1159/000139990
11. Karvonen MJ, Kentala E, Mustala O. The effects of training on heart rate: a longitudinal study. Ann Med Exper Fenn 1957;35:307-15.
12. Henderson LW. Biophysics of Ultrafiltration and Hemofiltration. In: Maher JF, ed. Replacement of Renal Function by Dialysis. 4th ed. Dordrecht: Springer Netherlands; 1989. p. 300-26.
13. Ozden M, Maral H, Akaydin D, Cetinalp P, Kalender B. Erythrocyte glutathione peroxidase activity, plasma malondialdehyde and erythrocyte glutathione levels in hemodialysis and CAPD patients. Clin Biochem 2002;35:269-73. DOI: http://dx.doi.org/10.1016/S0009-9120(02)00307-7
14. Vaithilingam I, Polkinghorne KR, Atkins RC, Kerr PG. Time and exercise improve phosphate removal in hemodialysis patients. Am J Kidney Dis 2004;43:85-9. DOI: http://dx.doi.org/10.1053/j.ajkd.2003.09.016
15. Farese S, Budmiger R, Aregger F, Bergmann I, Frey FJ, Uehlinger DE. Effect of transcutaneous electrical muscle stimulation and passive cycling movements on blood pressure and removal of urea and phosphate during hemodialysis. Am J Kidney Dis 2008;52:745-52. PMID: 18487001 DOI: http://dx.doi.org/10.1053/j.ajkd.2008.03.017
16. Orcy R, Antunes MF, Schiller T, Seus T, Böhlke M. Aerobic exercise increases phosphate removal during hemodialysis: a controlled trial. Hemodial Int 2014;18:450-8. DOI: http://dx.doi.org/10.1111/hdi.12123
17. Kirkman DL, Roberts LD, Kelm M, Wagner J, Jibani MM, Macdonald JH. Interaction between intradialytic exercise and hemodialysis adequacy. Am J Nephrol 2013;38:475-82. DOI: http://dx.doi.org/10.1159/000356340
18. Kong CH, Tattersall JE, Greenwood RN, Farrington K. The effect of exercise during haemodialysis on solute removal. Nephrol Dial Transplant 1999;14:2927-2931. DOI: http://dx.doi.org/10.1093/ndt/14.12.2927
19. Giannaki CD, Stefanidis I, Karatzaferi C, Liakos N, Roka V, Ntente I, et al. The effect of prolonged intradialytic exercise in hemodialysis efficiency indices. ASAIO J 2011;57:213-8. PMID: 21412149 DOI: http://dx.doi.org/10.1097/MAT.0b013e318215dc9e
20. Mohseni R, Emami Zeydi A, Ilali E, Adib-Hajbaghery M, Makhlough A. The effect of intradialytic aerobic exercise on dialysis efficacy in hemodialysis patients: a randomized controlled trial. Oman Med J 2013;28:345-9. DOI: http://dx.doi.org/10.5001/omj.2013.99
21. Parsons TL, Toffelmire EB, King-VanVlack CE. Exercise training during hemodialysis improves dialysis efficacy and physical performance. Arch Phys Med Rehabil 2006;87:680-7. PMID: 16635631 DOI: http://dx.doi.org/10.1016/j.apmr.2005.12.044
22. Meyring-Wösten A, Zhang H, Ye X, Fuertinger DH, Chan L, Kappel F, et al. Intradialytic Hypoxemia and Clinical Outcomes in Patients on Hemodialysis. Clin J Am Soc Nephrol 2016;11:616-25. DOI: http://dx.doi.org/10.2215/CJN.08510815
23. Abdalla ME, AbdElgawad M, Alnahal A. Evaluation of pulmonary function in renal transplant recipients and chronic renal failure patients undergoing maintenance hemodialysis. Egypt J Chest Dis Tuberc 2013;62:145-50. DOI: http://dx.doi.org/10.1016/j.ejcdt.2013.04.012
24. Blanchet F, Kanfer A, Cramer E, Benyahia A, Georges R, Méry JP, et al. Relative contribution of intrinsic lung dysfunction and hypoventilation to hypoxemia during hemodialysis. Kidney Int 1984;26:430-5. DOI: http://dx.doi.org/10.1038/ki.1984.192
25. Cardoso M, Vinay P, Vinet B, Léveillée M, Prud'homme M, Téjédor A, et al. Hypoxemia during hemodialysis: a critical review of the facts. Am J Kidney Dis 1988;11:281-97. PMID: 3128109 DOI: http://dx.doi.org/10.1016/S0272-6386(88)80133-1
26. Moore GE, Painter PL, Brinker KR, Stray-Gundersen J, Mitchell JH. Cardiovascular response to submaximal stationary cycling during hemodialysis. Am J Kidney Dis 1998;31:631-7. DOI: http://dx.doi.org/10.1053/ajkd.1998.v31.pm9531179
27. Burke EJ, Germain MJ, Braden GL, Fitzgibbons JP. Mild Steady-State Exercise During Hemodialysis Treatment. Phys Sportsmed 1984;12:153-7. DOI: http://dx.doi.org/10.1080/00913847.1984.11701880
28. Germain MJ, Burke EJ, Braden GL, Fitzgibbons JP. Amelioration of hemodialysis-induced fall in PaO_2 with exercise. Am J Nephrol 1985;5:351-4. DOI: http://dx.doi.org/10.1159/000166961
29. Montazerifar F, Hashemi M, Karajibani M, Dikshit M. Hemodialysis alters lipid profiles, total antioxidant capacity, and vitamins A, E, and C concentrations in humans. J Med Food 2010;13:1490-3. DOI: http://dx.doi.org/10.1089/jmf.2010.1074

30. Bianchi PDA, Barp J, Thomé FS, Belló-Klein A. Efeito de uma sessão de hemodiálise sobre o estresse oxidativo sistêmico de pacientes renais crônicos terminais. J Bras Nefrol 2009;31:175-82. DOI: http://dx.doi.org/10.1590/S0101-28002009000300002

31. Clermont G, Lecour S, Lahet J, Siohan P, Vergely C, Chevet D, et al. Alteration in plasma antioxidant capacities in chronic renal failure and hemodialysis patients: a possible explanation for the increased cardiovascular risk in these patients. Cardiovasc Res 2000;47:618-23. PMID: 10963735 DOI: http://dx.doi.org/10.1016/S0008-6363(00)00117-6

Erratum

In the Original Article "Acute effects of intradialytic aerobic exercise on solute removal, blood gases and oxidative stress in patients with chronic kidney disease", published in the Brazilian Journal of Nephrology 2017; 39(2): 172-180, please be aware that the correct spelling for Francisco Veronese is Francisco Veríssimo Veronese.