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ETIENE CAMPOS DIAS

EXERCÍCIO FÍSICO INTRADIALÍTICO COM RESTRIÇÃO DE FLUXO SANGUÍNEO E ADEQUAÇÃO DA HEMODIÁLISE

Pelotas
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Dissertação apresentada ao Programa de Pós-Graduação em Saúde e Comportamento da Universidade Católica de Pelotas como requisito parcial para obtenção do grau de Mestre em Saúde e Comportamento.

Orientadora: Profª. Drª. Maristela Böhlke

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Conceito final: ________

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RESUMO

INTRODUÇÃO: Hemodiálise (HD) aumenta a sobrevida dos pacientes com doença renal crônica (DRC). Em todo o mundo, dois milhões de pessoas dependem da HD para sobreviver. No entanto, a HD é economicamente dispendiosa e não totalmente eficaz na substituição da função renal. **OBJETIVO:** comparar a adequação da HD entre sessões com exercício intradialítico moderado contínuo com restrição do fluxo sanguíneo (RFS) e exercício físico sem RFS com sessões de controle (sem exercício). **MÉTODOS:** Estudo cruzado, incluindo vinte e dois pacientes adultos com DRC tratados por HD. Os pacientes foram designados para o grupo RFS (n = 11) ou grupo de exercício padrão (n = 11). Durante a intervenção, cada paciente foi submetido a quatro sessões de HD (duas com exercícios e duas sessões de controle). As sessões de exercício de vinte minutos foram realizadas durante as duas primeiras horas de HD. A adequação da HD foi avaliada por Kt / V-ureia equilibrado (eKt / V), *single-pool* Kt / V-ureia (sp-Kt / V), rebote de ureia e fósforo, taxa de redução de ureia (URR) e remoção de ureia e fósforo em dialisado. **RESULTADOS**: O eKt / V e sp-Kt / V foram significativamente maiores nas sessões de HD com exercício (RFS e exercício padrão analisados em conjunto) em comparação com sessões de HD sem exercício (1,28 ± 0,18 vs.1,14 ± 0,29, p <0,05 e 1,48 ± 0,23 vs. 1,31 ± 0,36 p<0,05, respectivamente). A análise estratificada revelou benefícios da RFS em termos de eKt / V e sp-Kt / V (1,32 ± 0,21 vs. 1,10 ± 0,16 para controle, p <0,001 e 1,53 ± 0,26 vs. 1,27 ± 0,19 para controle, p <0,001, respectivamente). A URR foi maior na HD com o exercício (71,86 ± 5,13 vs. 65,94 ± 11,33 para o controle, p <0.02). A análise estratificada mostrou que a RFS melhora a URR (72,51 ± 5,42 vs. 66,14 ± 7,69 para o controle, p <0,001). Rebote de ureia foi menor nas sessões de exercício vs. controle (5,39 ± 25,82 vs. 38,23 ± 15,14, p <0,001), exercício RFS vs. controle (–8,87 ± 9,10 vs. 30,75 ± 12,84, p <0,01) e sessões de exercício convencional vs. controle (13,32 ± 29,05 vs. 42,38 ± 15,35, p <0,01). Não houve diferença no Kt / V, URR ou rebote de fósforo entre sessões de HD com exercício padrão e sessões sem exercício. **CONCLUSÃO:** O exercício intradialítico moderado contínuo com RFS foi mais eficaz do que o exercício convencional no aumento da adequação da HD.

Palavras-chave: Exercício Intradialítico. Restrição Fluxo Sanguíneo. Hemodiálise. Adequação. Dialisato. Ureia. Fósforo.

ABSTRACT

INTRODUCTION: Hemodialysis (HD) increases the life span of patients with chronic kidney disease (CKD). Across the world, two million people depend on HD to survive. However, HD is expensive and partially effective in the replacement of renal function. **OBJECTIVE:** To compare the adequacy of HD between sessions with intradialytic exercise with restriction of blood flow (BRF) and exercise without BRF with control sessions (without exercise). **METHODS:** Cross-sectional study, including twenty-two adult patients with CKD in HD. Patients were assigned to the BRF group (n = 11) or standard exercise group (n = 11). During the intervention, each patient was submitted to four HD sessions (two with exercises and two control sessions). Twenty-minute exercise sessions were performed during the first two hours of HD. The suitability of HD was evaluated by equilibrated Kt / V-urea (eKT/V), single-pool Kt /V-urea (sp-Kt /V), urea and phosphorus rebound, urea reduction rate (URR) and removal of urea and phosphorus in dialysate. **RESULTS:** The eKt / V and sp-Kt / V were significantly higher in HD exercise sessions (BRF and standard exercise analyzed together) compared to HD sessions without exercise (1.28 ± 0.18 vs. 1.14 ± 0.29, p <0.05 and 1.48 ± 0.23 vs. 1.31 ± 0.36 p <0.05, respectively). The stratified analysis revealed benefits of BRF in terms of eKt / V and sp-Kt / V (1.32 ± 0.21 vs 1.10 ± 0.16 for control, p <0.001 and 1.53 ± 0.26 vs 1.27 ± 0.19 for control, p <0.001, respectively). URR was higher in HD with exercise (71.86 ± 5.13 vs 65.94 ± 11.33 for control, p <0.02). Stratified analysis showed that BFR improves URR (72.51 ± 5.42 vs 66.14 ± 7.69 for control, p < 0.001). Urea rebound was lower in exercise vs control sessions (5.39 ± 25.82 vs 38.23 ± 15.14, p < 0.001). BFR exercise vs control sessions (–8.87 ± 9.10 vs 30.75 ± 12.84, p 0.01) and standard exercise vs control sessions (13.32 ± 29.05 vs 42.38 ± 15.35, p 0.01). There was no difference in Kt/V, URR or phosphorus rebound between standard exercise and no-exercise HD sessions. **CONCLUSION:** Intradialytic continuous moderate exercise with BFR was more effective than intradialytic standard exercise to increase hemodialysis adequacy.

Keywords: Intradialytic Exercise. Blood Flow Restriction. Hemodialysis. Adequacy. Dialysate. Urea. Phosphorus.

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APRESENTAÇÃO

A dissertação de Mestrado a seguir é um Estudo Clínico Randomizado, cross-over, realizado no Hospital Universitário São Francisco de Paula, na cidade de Pelotas, no sul do Brasil. Tem como objetivo avaliar o benefício de realizar exercício intradialítico moderado contínuo na adequação do tratamento hemodialítico.

PROJETO

1 IDENTIFICAÇÃO

1.1 TÍTULO

Exercício físico intradialítico com restrição de fluxo sanguíneo e adequação da hemodiálise.

1.2 MESTRANDO

Etiene Campos Dias

1.3 ORIENTADORA

Maristela Böhkle

1.4 INSTITUIÇÃO

Universidade Católica de Pelotas (UCPel)

1.5 CURSO

Mestrado em Saúde e Comportamento

1.6 LINHA DE PESQUISA

Pesquisa Clínica

1.7 DATA

11 de outubro de 2018

2 INTRODUÇÃO

A doença renal crônica (DRC) é um importante problema de saúde pública, não somente no Brasil como no mundo, em função de sua elevada prevalência, impacto negativo na sobrevida e qualidade de vida dos indivíduos por ela acometidos, e do elevado custo financeiro implicado em seu tratamento. As principais causas de DRC são hipertensão e diabetes, doenças com prevalências ao redor de 20% e 10%, respectivamente, nas populações gerais. A DRC também representa importante fator de risco cardiovascular, de forma que a maioria dos indivíduos com estágios mais iniciais da doença morre em decorrência de eventos cardiovasculares, antes de atingir a doença renal crônica em estágio terminal (DRCT), momento em que se torna necessária terapia renal substitutiva (TRS).

A hemodiálise (HD) é a terapia renal substitutiva mais utilizada na maioria dos países. Apesar de desempenhar papel de suma significância na manutenção da vida do paciente portador de DRC, a HD ainda apresenta inúmeras limitações técnicas, o que a torna incapaz de substituir com elevado grau de eficiência as funções renais. Com o objetivo de superar essas limitações, muito aprimoramento técnico tem sido acrescentado aos equipamentos de HD nas últimas décadas. A eficiência da HD está intimamente ligada à capacidade de remover solutos acumulados ou potencialmente tóxicos, além de excesso de água acrescentada aos líquidos corporais. Os métodos atualmente disponíveis para aumentar a eficiência da HD incluem aumento da duração das sessões de diálise, aumento do fluxo do sangue e do dialisato e melhora na permeabilidade do dialisador. Todas essas medidas, porém, aumentam o custo financeiro do tratamento, que já é bastante elevado, sobrecarregando os sistemas públicos e privados de saúde, além de comprometerem ainda mais a qualidade de vida dos pacientes em HD, já bastante reduzida. Aumentar o tempo de cada sessão de HD muitas vezes esbarra na negativa do paciente, comprometendo a adesão ao método. Em função dessas dificuldades, têm-se buscado métodos alternativos, para o aumento da eficiência da HD, que apresentem menores repercussões negativas, tanto em termos econômicos quanto em qualidade de vida.

O exercício físico durante a sessão de HD tem sido descrito como uma medida com potencial impacto na eficiência do tratamento. O exercício físico é capaz de mobilizar solutos de localização predominantemente intracelular para o compartimento intravascular, através do aumento da perfusão sanguínea em áreas normalmente expostas a baixo fluxo arterial durante a HD. O deslocamento dos solutos para a circulação sanguínea favorece a eliminação dos mesmos pela HD, uma vez que o filtro utilizado, o dialisador, somente é capaz de remover solutos plasmáticos. O exercício aeróbico intradialítico envolvendo a musculatura dos membros inferiores promove um aumento do débito cardíaco e do fluxo de sangue para a região, resultando em dilatação capilar e área de superfície mais extensa, para acomodar o maior volume de sangue destinado a essa região. A dilatação capilar leva também a aumento do tamanho dos poros da membrana. Todos esses fatores somados resultam em aumento do coeficiente de transferência de massa inter-compartimental (Kc) e, portanto, a transferência de uma quantidade aumentada de solutos para o compartimento vascular. Estes solutos terão acesso à membrana do dialisador e serão removidos no dialisato, aumentando a eficiência da HD.

A melhora da adequação da HD, através da mobilização de solutos do compartimento intracelular pode ser um benefício adicional dos já bem estabelecidos em termos de saúde cardiovascular e mental para a prática de exercício aeróbico. A partir dessa maior mobilização de solutos, conseguir-se-ia promover uma HD mais eficaz. Dessa forma, a implementação de programas de exercício intradialítico com RFS poderia oferecer uma alternativa acessível, com baixo custo financeiro, para aumentar a eficiência da HD, sem comprometer à adesão do paciente.

O presente estudo tem como objetivo comparar o efeito agudo na adequação da HD do exercício físico aeróbico intradialítico com as sessões de HD sem exercício, estratificando a análise por uso de RFS durante o exercício ou exercício convencional.

3 OBJETIVOS

3.1 GERAL

Analisar o efeito agudo do exercício aeróbico intradialítico convencional e com RFS sobre a adequação da HD, através da avaliação dos parâmetros Kt/V ureia, URR e rebote sérico de ureia, de pacientes com DRCT tratados por HD.

3.2 ESPECÍFICOS

a) Avaliar o efeito do exercício aeróbico intradialítico na eficiência da HD, analisando Kt/V ureia, URR e rebote sérico de ureia, remoção de ureia e fósforo no dialisato e rebote sérico de fósforo;
b) Avaliar o efeito do exercício aeróbico intradialítico com RFS na eficiência da HD, analisando Kt/V ureia, URR e rebote sérico de ureia, remoção de ureia e fósforo no dialisato e rebote sérico de fósforo;
c) Avaliar o efeito do exercício aeróbico intradialítico convencional na eficiência da HD, analisando Kt/V ureia, URR e rebote sérico de ureia, remoção de ureia e fósforo no dialisato e rebote sérico de fósforo.

4 HIPÓTESES

a) O exercício aeróbico intradialítico aumenta a eficiência da HD;
b) O exercício aeróbico intradialítico com RFS aumenta a eficiência da HD;
c) O exercício aeróbico intradialítico convencional aumenta a eficiência da HD, mas com menor poder ou menos parâmetros, do que o exercício aeróbico intradialítico com RFS.

5 REVISÃO DE LITERATURA

A presente revisão buscou encontrar estudos que contemplassem a realização de exercício aeróbico intradialítico e a adequação da HD. Além disso, a análise da qualidade dos estudos, após leitura detalhada, foi utilizada para a inclusão ou exclusão de publicações. Trabalhos com título, resumo ou conteúdo não relacionados ao tema proposto por este estudo foram excluídos. A revisão ainda selecionou artigos considerados relevantes, os quais constavam nas referências dos artigos selecionados, não estando mencionados no quadro de achados da revisão por não terem advindo da busca através de descritores.

A busca foi realizada na base de dados PubMed e foram utilizados os seguintes descritores: ((*"hemodialysis") OR "haemodialysis")) AND ((("exercise") OR "physical activity") OR "aerobic exercise")) AND (((((("solute removal") OR "efficacy") OR "phosphorus removal") OR "urea removal") OR "dialysate"*).

Um resumo dos principais artigos utilizados na revisão pode ser visualizado no quadro abaixo.

Quadro 1: Resumo dos principais artigos utilizados na revisão de literatura.

Autor	Desenho	Amostra	Tempo (semanas)	Intervenção	Desfechos	Resultados
Bohm et al., 2017	ECR cross-over	GC:15 GI:15	2	Exercício aeróbico intradialítico	1°) concentração de solutos sérica e no dialisato (Ur,Cr,potássio, fósforo e magnésio) 2°) PaO2, SatO2, estresse oxidativo(séricos!)	Aumentou a concentração sérica de fósforo (p=0,035), PaO2(p=0,037) e SatO2 (p=0,024); reduziu capacidade antioxidante total (p=0,027)
Orcy et al., 2014	ECR cross-over	22	44	Exercício aeróbico intradialítico	1°. concentração de solutos no dialisato (Ur,Cr, potássio e fosfato) 2°. rebotes séricos Ur,Cr, K,fosfato, Kt/V	Aumentou a remoção de fósforo (p=0,04)
Kirkman et al., 2014	ECR Cross-over	11	8	Intervenção 1: aumento de tempo da sessão de HD Intervenção 2:exercício aeróbico intradialítico	1°. Kt/V uréia 2°. redução e rebote Ur,Cr,Fosfato e beta2 microglobulina	Tempo aumentou a depuração de Ur (Kt/V Ur p=0,02; spKt/V Ur p<0,01,Ur p<0,01) e Cr(p=0,02). Exercício aumentou a redução de fosfato sérico (p=0,03)
Farese et al., 2008	ECR Cross-over	9	3	**Intervenção 1:** exercício aeróbico intradialítico **Intervenção 2:** estímulo elétrico intradialítico	PA, eficácia HD: concentração sérica de NA,K, P, Ca,Ur, albumina, Cr e concentração no dialisato de Ur e P	**Exercício**: aumentou a remoção no dialisato de Ur (p<0,001) e fosfato (p=0,002); aumentou a remoção sérica de Ur (p<0,001) e fosfato (p<0,001) por sessão de HD **Estímulo Elétrico:** aumentou concentração no dialisato de

						Ur (p=0,001) e fosfato (p=0,001); aumentou a remoção sérica de Ur (p<0,001) e fosfato (p<0,001) por sessão de HD
Parsons et al., 2008 Parsons et al., 2008	ECR	GC:7 GI:6	20	Exercício aeróbico intradialítico	Eficácia HD (remoção Ur: spKt/V),função física, qualidade de vida	Exercício aumentou a remoção da Ur (spKt/V):p<0,05 ; Melhorou a função física
Vaithilingam et al., 2004	ECR Cross-over	9	2	Aumento do tempo da HD	1°: Remoção semanal fosfato no dialisato 2°: nível sérico fosfato, redução Ur, remoção semanal Ur e	Aumento na remoção semanal de fosfato (p <0,002), aumento no Kt/V (p<0,005)
Vaithilingam et al., 2004	ECR Cross-over	12	3	Exercício aeróbico intradialítico(não considerou o pré dialítico)	1°: Remoção semanal fosfato no dialisato 2°: nível sérico fosfato, redução Ur, remoção semanal Ur, remoção fosfato diário	Aumento na remoção de fosfato quando comparado com ou sem exercício (p=0,02)
Chiew et al., 1999	ECR Cross-over	11	2	Exercício aeróbico intradialítico	Efeito do exercício na remoção sérica de Ur,Cr, K	Diminuição: Ur (p<0,01), Cr (p<0,001), K(p<0,05) Aumento: Kt/V Ur(p=0,001), RR Ur(p<0,001)
Christoforos et al., 2011	ECR Cross-over	10	2	Exercício aeróbico intradialítico	Exercício melhora eficácia da HD	Aumento Kt/V, RR Ur, RR Cr (p<0,05) Diminuiu K sérico (p=0,046)

5.1 DOENÇA RENAL CRÔNICA

A DRC representa importante problema de saúde pública em todo o mundo devido ao número elevado de casos diagnosticados a cada ano, ao impacto prognóstico negativo e ao elevado custo de seu tratamento. A doença caracteriza-se pela perda da função renal de forma progressiva, impedindo a eliminação de resíduos metabólicos e água através dos rins. Seu desenvolvimento ocorre de forma silenciosa podendo ser diagnosticada quando o paciente já se encontra em uma fase avançada da doença, apresentando manifestações clínicas como retenção de líquidos, sonolência, inapetência, dispnéia, fadiga, confusão mental, náuseas e vômitos(1). Dentre os fatores de risco para DRC, as doenças crônicas não transmissíveis (DCNT) como a hipertensão arterial (HA) e a *diabetes mellitus* (DM) são responsáveis por 35% e 29% respectivamente, dos pacientes em terapia dialítica no Brasil, seguidos por glomerulonefrite crônica (11%) e rins policísticos (4%).

Para fins de diagnóstico e tratamento, a DRC é classificada em estágios, podendo variar do estágio 1 ao 5 conforme avaliação da taxa de filtração glomerular (TFG) e de alterações em exames de urina e de imagem dos rins. A TFG em jovens adultos é aproximadamente 125 ±20 ml/min/1,73 m². Com o avanço da idade, a TFG diminui cerca de 10 ml/min/1,73 m² por década e este declínio é superior nos hipertensos, por isso um valor de 60-90 ml/min/1,73 m² pode ser normal, num indivíduo idoso. Um valor inferior a 60 ml/min/1,73 m² é considerado patológico, caracterizando a falha da função renal e consequentemente a presença da DRC, independentemente da presença de eventuais alterações estruturais.

A DRCT é evidenciada quando a TFG estiver abaixo de 15ml/min/1,73 m², passando o paciente a necessitar de alguma modalidade de TRS. A TRS é ofertada aos pacientes com DRCT no estágio 5 dialítico (5-d), contemplando em suas formas a HD, diálise peritoneal (DP) e o transplante renal, este podendo ocorrer com doador vivo ou doador falecido

A HD é a modalidade de terapia dialítica de maior prevalência entre os pacientes portadores de doença renal crônica e também a de maior custo para as organizações de saúde. O tratamento por TRS representa o consumo de grande parte dos recursos globais, devido à sua alta complexidade. O Sistema Único de Saúde (SUS), segundo o Censo Brasileiro de Diálise de 2014, é responsável pelo custeio de aproximadamente 92% das diálises realizadas no país, acarretando em alto custo financeiro.

O tratamento por HD consiste na filtração do sangue através de um capilar acoplado a uma máquina, ocorrendo por meio deste sistema a difusão das substâncias indesejáveis no sangue para o líquido dialisador, eliminando toxinas e o excesso de líquido do organismo. Este procedimento é realizado geralmente três vezes por semana com duração média de 4 horas por sessão().

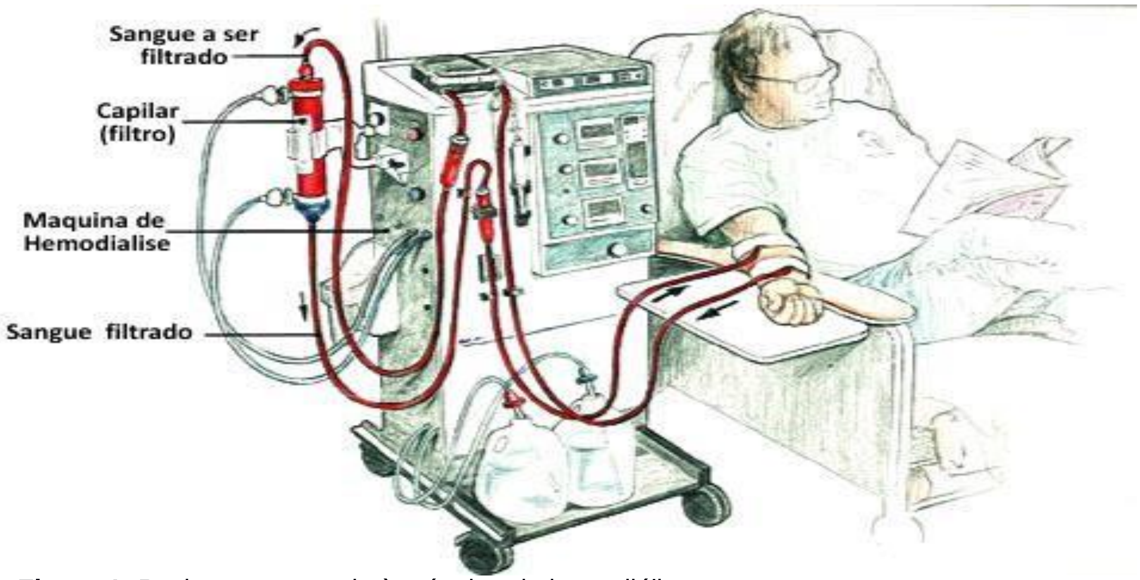

Figura 1: Paciente conectado à máquina de hemodiálise.

5.2 EXERCÍCIO FÍSICO

Exercício físico é definido como uma subcategoria da atividade física, que é planejado, estruturado, repetitivo e intencional, com o objetivo principal de melhorar ou manter a aptidão física. É substancialmente conhecido o impacto positivo do exercício físico regular a uma determinada combinação entre volume e intensidade para a obtenção de um efeito de treinamento (4). Dentre os tipos de exercícios importantes para a promoção da saúde e que geram melhora na aptidão física geral destacam-se os exercícios de força, aeróbicos e de flexibilidade . As melhoras promovidas por um programa de treinamento dependem, dentre outras coisas, da sobrecarga resultante das sessões de treinamento. De maneira geral, sobrecargas maiores proporcionam resultados mais expressivos. Pollock e colaboradores (1990) publicaram a classificação da intensidade do treinamento aeróbico relacionando percentual de intensidade relativa – frequência cardíaca (FC) máxima e consumo máximo de oxigênio ($VO_{2máx}$) – e percepção subjetiva de esforço (PSE) (Tabela 01).

O *American College of Sports Medicine* estabelece as seguintes recomendações de exercício físico para promoção de saúde e melhora da aptidão física para adultos saudáveis:

1) Frequência de treinamento: 3 a 5 vezes por semana;
2) Intensidade de treinamento: 60 a 90% da FC máxima, ou 50 a 85% do $VO_{2máx}$;
3) Duração do treinamento: 20 a 60 minutos de atividade aeróbica contínua, dependendo da intensidade da atividade, ou seja, quanto mais intensa, menos tempo é necessário;
4) Tipo de atividade: qualquer atividade que mobilize grandes grupos musculares, possa ser mantida continuamente e seja de natureza rítmica e aeróbica, como, por exemplo, caminhada, corrida/*jogging*, andar de bicicleta ou exercício no cicloergômetro, esqui *cross-country* (de planície), dançar, pular corda, remar, subir escadas, nadar, patinar e diversas outras atividades lúdicas de *endurance*;
5) Treinamento contra resistência: o treinamento de força de intensidade moderada, suficiente para desenvolver e manter a massa corporal magra deve fazer parte de um programa de aptidão física de um aduto. Uma série de oito a doze repetições de oito a dez exercícios que condicionem os principais grupos musculares pelo menos duas vezes por semana são o mínimo recomendado.Em geral, o exercício físico não aumenta o risco de eventos cardiovasculares em indivíduos saudáveis. No entanto, há um aumento do risco de morte súbita cardíaca e/ou infarto agudo do miocárdio durante a realização de exercícios físicos vigorosos em indivíduos com doenças cardiovasculares (4).

Tabela 1 **–** Classificação da intensidade do exercício de acordo com o *American College of Sports Medicine.*

Intensidade relativa (%)		Índice de percepção de esforço	Classificação de intensidade
$FC_{máx}$	**$VO_{2máx}$**		
< 57%	< 30%	< 9	Muito leve
57-63%	40-59%	9-11	Leve
64-76%	60-89%	12-13	Moderada
77-95%	60-89%	14-17	Pesada
≥ 96%	≥ 90%	≥ 18	Muito pesada

$FC_{máx}$ = frequência cardíaca máxima.
$VO_{2máx}$ = consumo máximo de oxigênio.
Fonte: Tabela extraída de Garber (2011).

5.3 EFEITOS DO EXERCÍCIO INTRADIALÍTICO NA EFICIENCIA DA HEMODIÁLISE

Estudos anteriores têm sugerido que o exercício durante a HD poderiam aumentar a eficácia da remoção de solutos, no entanto esta hipótese não está definitivamente confirmada. Poucos estudos tem sido publicados sobre o assunto. Somente três deles avaliando o efeito em longo prazo (3 a 12 meses), nenhum com grupo controle. O estudo de seguimento mais longo (12 meses) iniciou com uma amostra de 16 pacientes e ao final restavam apenas quatro pacientes. Todos os três usaram como desfecho principal o Kt/V, e dois deles descrevem um aumento do Kt/V após o exercício. Outros estudos tem avaliado o efeito agudo do exercício na eficiência da diálise, a maioria deles com desenho *cross over*, usando de 20 a 60 minutos de exercício com cicloergômetro transdiálise, com amostras entre 10 e 20 pacientes. A maioria utilizou o Kt/V como medida de eficiência, com resultados conflitantes.

A remoção de solutos no dialisato foi avaliada em um pequeno número de estudos com intervenção por exercício. Vaithilingan e cols. compararam a remoção de fósforo em três grupos: um deles com exercício por cicloergômetro antes da HD, outro com exercício intradialitico, e um grupo controle sem exercício. Foi encontrado um aumento significativo na remoção de fósforo com exercício intradialítico quando comparado com o grupo controle (5).Farese e cols. randomizaram 10 pacientes para estimulação elétrica muscular transcutânea durante a HD, movimentos passivos ou controle em um desenho crossover durante nove sessões de HD e encontraram um aumento significativo na remoção de fósforo e ureia nos grupos intervenção em comparação ao controle. Parsons e cols. compararam seis pacientes submetidos a três ciclos de 15 minutos de cicloergômetro transdiálise com sete pacientes submetidos à HD sem exercício, e encontraram um aumento da remoção de ureia no grupo intervenção (6). Bohm e cols. em um estudo controlado crossover, avaliaram 30 pacientes, os quais foram divididos em grupos controle e intervenção. Os pacientes do grupo intervenção foram submetidos a um protocolo de exercício aeróbico intradialítico, com cicloergômetro para membros inferiores, no início da segunda hora do terceiro dia de HD. Foi possível demonstrar que as concentrações séricas de ureia, creatinina, potássio, magnésio e fósforo apresentaram um aumento com o exercício, mas somente o fósforo alcançou significado estatístico (7).

Kirkman cols. recrutaram 11 pacientes para participar em ordem aleatória de cada um dos três segmentos do estudo. O primeiro recebeu cuidados tradicionais de HD, o segundo aumento de 30 min na sessão de HD e o terceiro exercício intradialítico. Analisaram os resultados a partir da coleta de sangue antes, no término e 30 minutos após a conclusão da HD, além de amostras de dialisato. Observaram que o exercício intradialítico não foi tão eficaz quanto o aumento do tempo da sessão da HD para melhorar o Kt/V ureia. No entanto, o exercício foi mais eficaz que o tempo para remoção do fosfato. Por esse motivo, o exercício aeróbico intradialítico pode ser um importante adjuvante terapêutico no controle do fosfato sérico (8). Orcy e cols. randomizaram 22 pacientes em um desenho crossover, onde cada paciente em uma sessão de HD era submetido a exercício aeróbico, através do uso de um cicloergômetro durante uma hora, e na sessão seguinte não era desenvolvida atividade física. Foi possível evidenciar aumento estatístico significativo na remoção de fosfato no dialisato (9). Kong e cols. estudaram onze pacientes em sessões de hemodiálise pareadas, uma com exercício aeróbico intradialítico, com cicloergômetro por uma hora, e outra como controle. Analisaram os níveis séricos de ureia, creatinina e potássio no pré, pós e 30 minutos depois do término da HD. Identificaram que o rebote dos três solutos diminuiu significativamente com o exercício, acompanhado de um aumento, também com significância estatística, do Kt/V ureia (10). Giannaki e cols. estudaram 10 pacientes em dois momentos diferentes: um como controle, e outro com exercício aeróbico, num cicloergômetro por três horas. Amostras sanguíneas foram coletadas antes e após o término da sessão de hemodiálise para avaliar a sua eficiência. Evidenciaram que Kt/V ureia, índice de redução de ureia e de creatinina melhoraram significativamente quando realizado exercício prolongado, em comparação com o controle. Os níveis plasmáticos de potássio foram reduzidos, quando comparadas as sessões de hemodiálise com e sem exercício aeróbico (11).

A maioria dos estudos prévios apresentam falhas metodológicas, como tamanhos de amostra insuficiente, medida somente de KtV como desfecho, e mesmo ausência de grupo controle. Os resultados encontrados tem sido heterogêneos mesmo quando são usadas as mesmas medidas de desfecho.

6 METODOLOGIA

6.1 DELINEAMENTO

Ensaio clínico randomizado, controlado, aberto, cruzado, com dois braços.

6.2 PARTICIPANTES (TIPO DE AMOSTRAGEM E CÁLCULO DE TAMANHO DE AMOSTRA)

Os pacientes elegíveis foram alocados no estudo por conveniência. A fase inicial consistiu em exercício físico aeróbico durante as sessões de HD, durante 16 semanas. Em duas sessões consecutivas de HD durante esse período de intervenção foram coletadas amostras do dialisato e de sangue para quantificar a eliminação de ureia e fósforo. Cerca de quatro semanas após o término da intervenção, os mesmos pacientes foram submetidos à nova amostragem do dialisato e de sangue para medida de excreção dos mesmos solutos, constituindo-se esse segundo período na coleta controle (sem exercício intradialítico).

6.2.1 Critérios de inclusão

Pacientes com doença renal crônica tratados para hemodiálise, há mais de três meses; com 18 anos ou mais; em uso de fístula arteriovenosa, como acesso para hemodiálise; com estabilidade clínica e hemodinâmica, no último mês de terapia dialítica aqueles que apresentaram episódios hipotensivos em menos de 15% das sessões; capazes de realizar o protocolo de exercícios físicos propostos; concordaram em participar do estudo.

6.2.2 Critérios de exclusão

Pacientes com eventos cardíacos nos últimos três meses; com diagnóstico atual de infecção ou de neoplasias; história de trombose venosa profunda nos últimos três meses; com pressão arterial sistólica igual ou maior que 180 em repouso; pressão arterial diastólica igual ou maior que 105 em repouso; FC em repouso acima de 120 bpm; alterações cognitivas que impossibilitem a compreensão das instruções dos exercícios; gestantes.

6.3 PROCEDIMENTOS E INSTRUMENTOS

6.3.1 Desfechos primários

Equilibrado e single pool Kt/V ureia, calculado pela equação de segunda geração de Daugirdas; taxa de redução de ureia, medida em percentual, antes, imediatamente após a HD e 30 minutos após cada sessão de HD; rebote sérico de ureia, em percentual, calculado pela equação [(soluto30 - solutof) / solutof] * 100, onde soluto30 é a concentração de soluto plasmático 30 minutos após a sessão de HD e solutof é a concentração de soluto plasmático imediatamente após a sessão de HD***.***

6.3.2 Desfechos secundários

Massa total de ureia e de fósforo no dialisato, medida em gramas, nas amostras contínua e fracionada de dialisato; rebote sérico de fósforo,em percentual, calculado pela equação [(soluto30 - solutof) / solutof] * 100, onde soluto30 é a concentração de soluto plasmático 30 minutos após a sessão de HD e solutof é a concentração de soluto plasmático imediatamente após a sessão de HD.

6.4 ANÁLISE DE DADOS

O cálculo amostral apontou para a necessidade de um mínimo de 16 pacientes, 8 em cada grupo, para atingir um poder de 80%, erro alfa abaixo de 5%, para detectar pelo menos 30% de diferença na sp-Kt / V-ureia (dp ± 0,2) entre sessões de HD com exercício moderado contínuo com RFS e sessões sem exercício e sessões de HD com exercício moderado contínuo padrão e sessões sem exercício.

A distribuição paramétrica foi testada pelo teste de *Skewness and Kurtosis.* Utilizou-se média e desvio padrão (dp) para descrever as variáveis paramétricas e a mediana e IQR para descrever variáveis não paramétricas. As variáveis paramétricas foram comparadas pelo teste t pareado e *Shapiro Wilcoxon* por variáveis não paramétricas. As variáveis de desfecho foram comparadas entre as sessões de exercício (com e sem RFS juntas) e as sessões de controle de HD. A análise estratificada foi realizada avaliando os parâmetros de adequação da HD no exercício RFS moderado contínuo e nas sessões de exercício moderado contínuo padrão, em comparação com as sessões de exercício sem controle. O pacote estatístico *Stata* 15.0 foi utilizado para análise estatística.

6.5 ASPECTOS ÉTICOS

A pesquisa desenvolveu-se após submissão e aprovação do projeto pelo Comitê de Ética e Pesquisa da Universidade Católica de Pelotas, sob número 2.707.365, juntamente a assinatura do Termo de Consentimento Livre e Esclarecido pelos participantes.

Foi assegurado o suporte para possíveis complicações ou dúvidas em decorrência da participação no estudo, bem como o cuidado com o manejo dos dados e confidencialidade. Os pacientes tiveram o direito de deixar de participar do estudo a qualquer momento, sem nenhum prejuízo ao seu tratamento convencional.

6.5.1 Riscos

Os riscos são os mesmos que são propensos os pacientes submetidos à HD, como hipotensão, e não extrapolam os riscos para sujeitos expostos à prática de exercício físico, como suor excessivo e tontura.

6.5.2 Benefícios

Os resultados do estudo proporcionam o desenvolvimento de uma nova metodologia de treinamento para indivíduos com DRC em HD, difundindo uma nova tecnologia. Além disso, os resultados são incorporados ao conhecimento científico e posteriormente a situações de ensino-aprendizagem.

6.6 CRONOGRAMA

CRONOGRAMA	**2017**								**2018**										
	05	**06**	**07**	**08**	**09**	**10**	**11**	**12**	**01**	**02**	**03**	**04**	**05**	**06**	**07**	**08**	**09**	**10**	**11**
Escolha do tema	X																		
Busca de artigos	X	X	X	X	X				X	X	X	X	X	X	X	X	X	X	
Revisão bibliográfica	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Qualificação do projeto							X												
Submissão Comitê Ética				X															
Coleta de dados				X		X													
Transcrição dos dados						X	X												
Análise dos dados							X	X	X										
Análise de resultados										X	X								
Dissertação do artigo												X	X	X	X	X	X		
Defesa do artigo																		X	

6.7 ORÇAMENTO

Despesas de Capital	**Qtd**	**Preço un.**	**Preço Total**
Pipeta monocanal	6	R$ 1.200,00	R$ 7.200,00
Despesas de Custeio	**Qtd**	**Preço un.**	**Preço Total**
Ponteiras 1000uL	3	R$ 30,00	R$ 90,00
Ponteiras 200uL	3	R$ 30,00	R$ 90,00
Microutbo	4	R$ 30,00	R$ 90,00
Seringa (un)	100	R$ 1,20	R$ 120,00
Luvas (cx)	4	R$ 30,00	R$ 120,00
Tubos (un)	1000	R$ 0,40	R$ 400,00
Reagente padrão para kit	1	R$ 500,00	R$ 500,00
Kit ureia (Labtest REF 104)	4	R$ 200,00	R$ 800,00
Kit fósforo (Labtest REF 12)	4	R$ 200,00	R$ 800,00
		Total	**R$ 10.210,00**

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ARTIGO

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Intradialytic Exercise with Blood Flow Restriction: Something to Add to Hemodialysis Adequacy? Findings of a Crossover Trial

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Intradialytic Exercise with Blood Flow Restriction: Something to Add to Hemodialysis Adequacy? Findings of a cross-over trial.

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Abstract

Background Hemodialysis (HD) increases the lifespan of chronic kidney disease (CKD) patients. Around the world, two million people depend on HD for survival. However, HD is expensive and only partially effective in replacing renal function. The aim of this study is to compare HD adequacy between sessions with intradialytic continuous moderate exercise with blood flow restriction (BFR) and physical exercise without BFR with control (no-exercise) sessions. **Methods** A cross-over trial including 22 adult CKD patients on HD. The patients were assigned for BFR group (n=11) or standard exercise group (n=11). During the intervention, each patient was submitted to four HD session (two with exercise and two control sessions). The twenty minutes exercise sessions were performed during the two first HD hours. HD adequacy was assessed by equilibrated Kt/V-urea (eKT/V), single-pool Kt/V-urea (sp-Kt/V), urea and phosphorus rebound, urea reduction rate (URR) and removal of urea and phosphorus in dialysate. **Results** The eKt/V and sp-Kt/V were significantly higher in HD sessions with exercise (BFR and standard exercise analyzed together) in comparison with HD sessions without exercise (1.28 ± 0.18 vs 1.14 ± 0.29, $p<0.05$ and 1.48 ± 0.23 vs 1.31 ± 0.36 $p<0.05$, respectively). Stratified analysis revealed benefits of BFR in terms of eKt/V and sp-Kt/V (1.32 ± 0.21 vs 1.10 ± 0.16 for control, $p<0.001$. and 1.53 ± 0.26 vs 1.27 ± 0.19 for control, $p<0.001$, respectively). URR was higher in HD with exercise (71.86 ± 5.13 vs 65.94 ± 11.33 for control, $p<0.02$). Stratified analysis showed that BFR improves URR (72.51 ± 5.42 vs 66.14 ± 7.69 for control, $p < 0.001$). Urea rebound was lower in exercise vs control sessions (5.39 ± 25.82 vs 38.23 ± 15.14, $p < 0.001$). BFR exercise vs control sessions (–8.87 ± 9.10 vs 30.75 ± 12.84, p 0.01) and standard exercise vs control sessions (13.32 ± 29.05 vs 42.38 ± 15.35, p 0.01). There was no difference in Kt/V, URR or phosphorus rebound between standard exercise and no-exercise HD sessions. **Conclusions** Intradialytic continuous moderate exercise with blood flow restriction was more effective than intradialytic standard exercise to increase hemodialysis adequacy.

Introduction

The last decades have witnessed an important increase in the prevalence of chronic kidney disease (CKD) around the world. The CKD impacts societies with health, social and economic adverse effects. Patients with its most advanced stage, end-stage renal disease (ESRD), need renal replacement therapy (RRT) to survive.[1] The RRT was introduced into clinical practice around 70 years ago, after hemodialysis (HD) machines and proper vascular access creation techniques has been developed.

Since introduction in clinical practice, HD has extended lives of millions of people, but even in these days the procedure has not been capable to exactly substitute normal renal function.[2] The dialysis efficacy is determined by adequate solutes and water removal during each session. Throughout hemodialysis history, efforts have been made to increase its adequacy by giving attention to the changes that occur inside the hemodialyzer, which depends on adequate blood flow, session length and membrane permeability. Despite additional economic burden and low patient acceptance, longer HD sessions have been tried.[3] Hemodialyzer membranes has evolved to synthetic material with high biocompatibility and permeability. Despite these advances, solutes and water still built up in CKD patients. To be filtrated in the dialyzer, the solutes and the water need first to get the intravascular compartment. Solutes mainly located within cells or in interstitial tissue are not available to this filtration process.[4] This notion has redirected attention to the patient microcirculation. The skeletal muscle cell storages great amounts the potassium, phosphorus and other elements that should be eliminated during HD. The constriction of the skeletal muscle circulation, which occur due to cooling, drop of blood volume and electrolytic changes during dialysis, restrain even more the blood flow to these areas.

Trying to circumvent this difficulty, it has been proposed and demonstrated that physical exercise during HD could increase heart stroke volume and lead to muscle vasodilation, exposing the intracellular solutes to circulation. There is already same evidence that intradialytic exercise increases the amounts of phosphorus eliminated in dialysate,[5-9] and increases de Kt/V-urea,[10-12] a parameter of hemodialysis adequacy. However, the best modality and program of physical exercise to improve dialysis adequacy remains unclear.

The blood flow restriction (BFR) physical exercise has been described as a way to increase muscle conditioning with less intense training,[13] leading to a vasodilation that could favor intra and extracellular changes.[14] To the best our knowledge, the effect of this physical exercise modality on dialysis adequacy has not yet been evaluated.

The aim of the present study is to compare the effect of regular intradialytic continuous moderate exercise using BFR on parameters of dialysis adequacy in CKD patients treated chronically by HD.

Methods

This is a crossover study that enrolled adult CKD patients on HD in a University Hospital Dialysis Center aiming to compare HD adequacy parameters between intradialytic standard continuous moderate exercise, continuous moderate exercise with blood flow restriction and no-exercise dialysis sessions. The dialysis blood flow was maintained at 350 mL/min, with dialysate flow at 500 mL/min. Fresenius 4008-S machines (Fresenius, Bad Homburg, Germany) were employed to treatment.

The HD adequacy parameters (single-pool and equilibrated Kt/V (sp Kt/V) (eKt/V), urea reduction rate (URR), urea and phosphorus rebound, and mass removal of urea and phosphorus in dialysate) were collected during two HD sessions (each patient) with aerobic BFR exercise and two HD sessions with standard aerobic exercise. After a 60-day washout period, the HD adequacy parameters were collected again, in the same patients, during two HD sessions without exercise.

Patients

The inclusion criteria were to be on HD for longer than three months, 18 years old or more, using an arteriovenous fistula as vascular access, have hemodynamic stability during HD in the last month (less than 15% of the HD sessions with hypotensive episodes), no intercurrent illness cognitive and musculoskeletal ability to perform the physical training. The exclusion criteria were cardiovascular events in the last three months, acute infectious or neoplasm process, pregnancy, inadequate blood pressure (BP) control (systolic BP above 180 mmHg and/or diastolic BP above 105 mmHg) or heart rate above 120 beats per minute (bpm)during HD.

The local Review Board analyzed and approved the crossover study protocol. The trial was registered in the Brazilian Registry of Clinical Trial number RBR- 97 VPJX . All allocated patients signed an informed consent form.

Exercise Training

The participants were submitted to HD while seated in a reclining chair, below which was adapted a cycle ergometer. The cycling exercise was done during the two first hours of HD, lasting 20 minutes. The exercise intensity was guided by perceived effort (moderate intensity, 12-13 Borg scale). The continuous moderate BFR exercise group was submitted to the same training protocol but throughout the exercise practice a 6-cm wide band was fasted in proximal thighs and inflated according to the thigh circumference, as suggested by Loenneke et al.[15]

For safety reasons, heart rate and blood pressure were monitored during all physical exercise session. The criteria for interruption of the training were surpassing 80% of the maximal heart rate (211 – [0,64 x age]) and/or blood pressure above 200/110 mmHg or below 110/50 mmHg, precordial pain, dyspnea, wheezing, muscle cramps, mental confusion, visual disturbances, skin pallor or cyanosis. The exercise training was supervised for properly trained physical education teachers and students.

Hemodialysis Adequacy Parameters

The primary outcomes were equilibrated and single pool Kt/V-urea (e Kt/V and spKt/V), URR and urea rebound. The secondary outcomes were total mass of urea and phosphorus measured in dialysate and phosphorus rebound. The plasma urea and phosphorus concentrations were measured before, immediately after HD and 30 minutes after each HD session. The eKt/V-urea was calculated by Daugirdas second generation equation. Urea and phosphorus rebounds were calculated by the equation [(solute30 – solutef)/solutef] * 100, where solute30 is the plasma solute concentration 30 minutes after HD session and solutef is the plasma solute concentration immediately after the HD session.

The dialysate collection was performed by continuous dialysate sampling (CDS) and fractional dialysate sampling (FDS). The dialysate samples were frozen at

-80°C until biochemical analysis. The dialysate draining tube was connected to a storage recipient with 500 mL volume, where, due to the constant flow, there was continuous renewal of the stored spend dialysate. The CDS was collected from this storage recipient at a 10mL/hour rate by reversed flow infusion bomb into a sample recipient, which stored 40mL after the HD session. The fractional dialysate sampling was obtained by manual collection of 5mL samples from the storage recipient every 20 minutes. The first sample was collected 20 minutes after the HD beginning, and the last one was collected at HD end, with a total of 12 samples at each HD session.

Data Analysis

The sample size calculation pointed to the need of a minimum of 16 patients, 8 in each group, to attain a power of 80%, alfa error below 5%, to detect at least a 30% difference in sp-Kt/V-urea (standard deviation 0.2) between HD sessions with continuous moderate BFR exercise and no-exercise sessions and HD sessions with standard continuous moderate exercise and no-exercise sessions.

The parametric distribution was tested by Skewness and Kurtosis test. Mean and standard deviation (sd) were used to describe parametric variables and median and interquartile range (IQR) to describe non-parametric variables. Parametric variables were compared by paired t test, and Shapiro Wilcoxon was used for non-parametric variables. The outcome variables were compared between exercise sessions (with and without BFR together) and control HD sessions. Stratified analysis was performed evaluating HD adequacy parameters in continuous moderate BFR exercise and standard continuous moderate exercise sessions, compared with their control no-exercise sessions. The statistical package Stata 15.0 was used for statistical analysis.

RESULTS

A total of eleven patients were included in the standard continuous moderate exercise group and eleven in the continuous moderate BFR exercise group. There were three losses during the crossover study, one due to kidney transplantation (BFR group), one for change in HD schedule (BFR group) and one withdraw (standard continuous moderate exercise group), with nineteen patients included in the final analysis. The sample was composed by 12 males, five in the BFR exercise group and seven in the standard exercise group, 27% were diabetics, with mean age of 50.27± 13.80 years (46.64 ± 11.30 in BFR group and 53.90 ± 15.30 the in standard exercise group) (Table 1).

The eKt/V-was significantly higher in HD sessions with physical exercise (BFR and standard exercise analyzed together; $n=19$) when compared with no-exercise HD sessions (1.28 ± 0.18 vs 1.14 ± 0.29, $p<0.05$) (Table 2). In analysis restricted to continuous moderate BFR exercise group ($n=9$), eKt/V was significantly higher in HD sessions with standard continuous moderate exercise (1.32 ± 0.21) compared with control sessions (1.10 ± 0.16, $p<0.001$). eKt/V were not different between HD sessions with standard continuous moderate exercise (1.24 ± 0.16) and control HD sessions (1.17 ± 0.39, $p<0.54$)(Figure 2.B). The same result was found regarding spKt/V, which was significantly higher in HD sessions with exercise (BFR exercise group and standard exercise group together, $n=19$) (1.48 ± 0.23) when compared with no-exercise HD sessions (1.31 ± 0.36, $p<0.05$) (Table 2). In analysis restricted to sessions with BFR ($n=9$), spKt/V were higher in HD sessions with physical exercise (1.53 ± 0.26) than no-exercise HD sessions (1.27 ± 0.19, $p<0.001$). The spKt/V were similar between standard physical exercise HD sessions (1.44 ± 0.20, $n=9$) and no-exercise HD sessions (1.35 ± 0.35. $p<0.54$) (Figure 2.A).

The URR was significantly higher in HD sessions with physical exercise (71.86 ± 5.13) compared with HD sessions without exercise (65.94 ± 11.33. p 0.02) (Table 2). In analysis restricted to BFR, URR was also higher in HD with exercise (72.51 ± 5.42) than no-exercise HD sessions (66.14 ± 7.69. $p < 0.001$). In analysis restricted to standard continuous moderate exercise, there was no difference in URR between exercise sessions (71.27 ± 5.07) and no-exercise sessions (65.75 ± 14.28, $p<0.25$)(Figure 2.C).

The urea rebound was significantly lower in HD sessions including physical exercise (5.39 ± 25.82) than no-exercise sessions (38.23 ± 15.14. $p < 0.001$) (Table 2). The urea rebound was also lower in HD sessions using continuous moderate BRF exercise alone (–8.87 ± 9.10) compared with their HD sessions without exercise (30.75 ± 12.84, $p<0.01$), and in HD session using standard continuous moderate exercise (13.32 ± 29.05) in comparison with no exercise HD sessions (42.38 ± 15.35, $p<0.01$)(Figure 2.D). The phosphate rebound was not significantly different in HD sessions with physical exercise (14.40 ± 19.12 vs 28.43 ± 22.09 in control, $p<0.18$), standard moderate continuous exercise sessions (18.51 ± 18.76 vs 26.58 ± 15.51 in control, $p<0.30$) or continuous moderate BFR sessions (4.83 ± 19.84 vs 32.76 ± 37.88 in control, $p<0.44$).

There was no significant difference in total mass of urea in spent dialysate from HD sessions including exercise (42.20 ± 19.38g) or not including exercise (35.76 ± 12.54g, $p< 0.24$). The urea mass in dialysate was also not different between sessions with continuous moderate BFR exercise alone (42.05 ± 23.05g) and no-exercise sessions (33.56 ± 11.49g, $p<0.32$), or between HD sessions using standard continuous moderate exercise (42.41 ± 14.30g) and no-exercise sessions (38.91 ± 14.19g, $p<0.55$). The total mass of phosphate in spent dialysate was no different between HD sessions with exercise (912.13 ± 360.94g) and without exercise (778.65 ± 245.12g, $p<0.28$), the same when comparing continuous moderate BFR exercise alone (798.09 ± 343.14g) and control (719.41 ± 229.57g, $p<0.71$) or standard continuous moderate exercise alone (1009.89 ± 371.86g) and control (829.44 ± 264.05, $p<0.25$) (Table 2).

There was no registry of adverse event potentially attributed to exercise during the intervention period.

DISCUSSION

This controlled trial has found that intradialytic continuous moderate exercise using BFR was more effective in improving HD adequacy than standard continuous moderate intradialytic exercise. The impact of BFR exercised was significant on different parameters of adequacy – spKt/V, eKt/V, URR and urea rebound.

There is a body of evidence suggesting the positive effect of conventional aerobic and/or resistance intradialytic exercise on HD adequacy.[5-12] Intradialytic exercise increases solutes removal by increasing cardiac output, which associated to the greater metabolic needs of the working muscle, lead to muscle vasodilation.[3] The higher muscle perfusion increases the intercompartment transfer coefficient (Kc), favoring the outward movement of intra-cellular solutes to the vascular system, from where solutes can reach the hemodialyzer, improving HD efficacy.[16]

Exercise with BFR has been described since the 1970s,[13] but only recently this technique has been put under the spotlight.[17] The exercise with BFR allow greater strength and muscle mass gains with lower volume and intensity of exercise, which could be of great interest for frail, sarcopenic and diseased populations, such as CKD patients. The BFR maximize the muscle gains despite lower loads because the muscle fibers work with restricted arterial inflow and venous outflow, which increases the expression of genes related to protein synthesis.

In addition, BFR exercise is followed by a reactive hyperemia.[14] This vasodilation occurs due to the accumulation of wasting products into the hypoxic exercising muscle, most with vasodilating capability, leading to higher Kc and hypothetically to increased HD adequacy. However, to the best our knowledge, it is the first time that the effect of continuous moderate BFR exercise on HD adequacy parameters has been evaluated.

In this crossover analysis, the HD adequacy parameters were measured during two HD sessions in which patients performed standard intradialytic continuous moderate exercise or continuous moderate BFR exercise. After a washout period, the same patients had their HD adequacy parameters measured during two sessions without exercise (control sessions). The eKt/V, sp-Kt/V, URR and urea rebound confirmed better HD adequacy in session with physical exercise when compared with no-exercise hemodialysis sessions. The stratified analysis by exercise condition, with or without BFR, revealed that most HD adequacy parameters had better results than in no-exercise sessions only when exercise with BFR was performed.

The finding is especially interesting for urea rebound, which was significantly lower in dialysis with physical exercise as compared with no-physical exercise sessions. The rebound of solutes, constituted by an increase in solute plasma concentration after HD sessions, is mainly attributed to the rate of dialysis (Kt/V) and the rebalancing between intracellular and plasmatic concentration. The rebalancing degree depends on the amount of blood flow going to low-perfusion high-urea organs, such as skeletal muscle.[18] It is well known that situations leading to significant increases of the fractional flow to these organs, such physical exercise, change the amount of sequestrated urea and phosphorus, having a direct effect on the rebound. The eKt/V estimates the rebound by a predictive equation that do not take into account these extremes in skeletal muscle perfusion.[19] Therefore, eKt/V is considered less accurate in detecting the effect of physical exercise or similar interventions on HD adequacy. The rebound formula, however, since includes the direct measurement of the plasma solute 30 minutes after the HD session could be more sensible to the effects of Kc changes on HD adequacy. Standard intradialytic continuous moderate exercise also increases blood perfusion to muscles, reduces urea sequestration and rebound. What makes continuous moderate BFR exercise different is that it is performed under hypoxic conditions, followed by a burst of vasodilation when the arterial constriction is released, and the reactive hyperemia supervenes.[14] This is the most probable explanation for the even lower urea rebound that occurred in HD sessions with continuous moderate BFR exercise. Among BFR exercise sessions, even negative values for the urea rebound were achieved, which has no biologic plausibility, but was also registered in 20% of the patients followed in HEMO study,[19] being attributed to some degree of measurement error over really tiny rebound values.

Urea and phosphorus mass excretion in dialysate were not statistically different between physical exercise and control groups, which is an unexpected finding. It is possible that this finding could be attributed to insufficient power due to sample size. Despite a marginal higher amount of urea and phosphorus were eliminated in HD sessions with exercise, it was not statistically significant. The measurement of the very small phosphorus concentration on dialysate fluid have been also described as a problem, sometimes reducing the analytic performance.[20]

To the best our knowledge, this is the first study to compare HD adequacy between intradialytic continuous moderate BFR exercise with control HD sessions and standard continuous moderate exercise with control sessions. The study presented a relatively small sample size, was performed using a unique HD prescription, at one hospital-based HD facility. The technique to measure dialysate phosphorus was not the ideal, and the study had no power to detect differences in mass solutes removal in dialysate. The transversal design precludes verify long-term effects of the intervention. Then, longer and properly powered studies are needed to corroborate or dismiss our findings.

Around the world, the lives of more than a million people depend on life-long hemodialysis, an expensive procedure not universally available, especially in lower income countries. Intradialytic continuous moderate exercise with blood flow restriction is a simple intervention that, in addition to other health benefits, could improve dialysis efficacy. The gain in efficacy could led to improve in quality of life or maybe patient lifespan, and allow more democratic access to HD, if confirmed the delivery of the same amount of dialysis in shorter (and less expensive) sessions.

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Table 1 – Characteristics of the sample

	BFR Exercise Group	Standard Exercise Group	p-value*
Male gender (%)	45.45	63.64	p = 0.40
Age (years) (mean/sd)	46.64 ± 11.30	53.90 ±15.31	p = 0.08
Caucasians (%)	54.55	72.73	p = 0.21
Hematocrit (%) (median/IQR)	28.30 (26.30 – 35.10)	30.30 (27.20 – 36.50)	p = 0.41
Diabetes (%)	27.27	27.27	p = 1.00
HD vintage (months) (median/IQR)	63 (48 - 84)	40 (12- 84)	p = 0.14
Estimated dry weight (Kg) (mean/sd)	72.45 ± 9.11	74.27± 16.62	p = 0.76

* t-test or Mann-Whitney for continuous variables, chi-square test for categorical variables.

Table 2: Adequacy Parameters Between HD sessions with and without Intradialytic Exercise and between standard exercise vs. control and BFR exercise vs. control

	Exercise (n=19)	**No-exercise (n=19)**	**p-value**	**Standard Exercise (n=10)**	**No-exercise (n=10)**	**p-value**	**BFR Exercise (n=9)**	**No-exercise (n=9)**	**p-value**
SpKt/V	1.48±0.23	1.31±0.36	p=0.05*	1.44±0.20	1.35±0.35	p=0.54	1.53±0.26	1.27± 0.19	p=0.001*
eKt/V	1.28±0.18	1.14±0.29	p=0.05*	1.24±0.16	1.17±0.39	p=0.54	1.32±0.21	1.10±0.16	p=0.001*
UR (%)	5.39±25.82	38.23±15.14	P<0.001*	13.32±29.05	42.38±15.35	p=0.01*	-8.87±9.10	30.75±12.84	p=0.01*
PR (%)	14.40±19.12	28.43±22.09	p=0.18	18.51±18.76	26.58±15.51	p=0.30	4.83±19.84	32.76±37.88	p=0.44
URR (%)	71.86±5.13	65.94±11.33	p=0.02*	71.27±5.07	65.75±14.28	p=0.25	72.51± 5.42	66.14±7.69	P<0.001*
UD (g)	42.20±19.38	35.76±12.54	p=0.24	42.41±14.30	38.91±14.19	p=0.55	42.05±23.05	33.56±11.49	p=0.32
PD (g)	912.13 ±360.94	778.65 ±245.12	p=0.28	1,009.89 ±371.86	829.44 ±264.05	p=0.25	798.09 ±343.14	719.41 ±229.57	p=0.71

SpKt/V = single pool Kt/V; eKt/V= equilibrated Kt/V; UR = urea rebound; PR = phosphate rebound, URR = urea reduction rate, UD = urea dialysate, PD = phosphate dialysate. *significantly difference

Figure 2

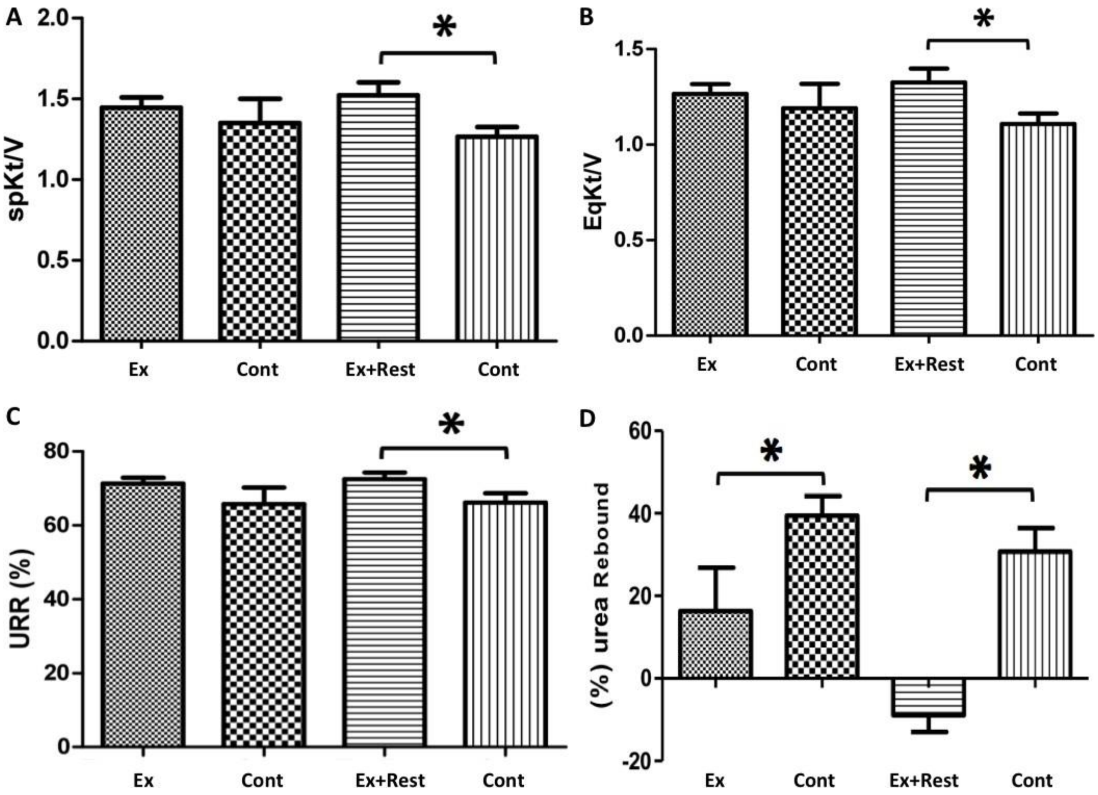

Figure 2- A) the mean of spKt/V was compared between standard exercise (Ex) and no-exercise (Cont) sessions [n=10, p = 0.54] and between exercise with BFR (Ex+Rest) and no-exercise (Cont) [n=9, p= 0.001 (*)]. B) the mean of equilibrated Kt/V (eKt/V) was compared Ex *versus* Cont [n=10, p = 0.54] and Ex+Rest *versus* Cont [n=9, p= 0.001 (*)]. C) the mean of urea reduction rate (URR) was compared Ex *versus* Cont [n=10, p = 0.25] and Ex+Rest *versus* Cont [n=9, p < 0.001 (*)]. D) the mean of urea rebound was compared Ex *versus* Cont [n=9, p = 0.01 (*)] and Ex+Rest *versus* Cont [n=5, p= 0.01 (*)].

CONSIDERAÇÕES FINAIS

Dissertação: Considerações finais (elemento obrigatório) apresentando as modificações do projeto e objetivos não abordados no artigo principal, caso houver e dar um breve fechamento a dissertação.

REVISÃO SISTEMÁTICA

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Does intradialytic exercise improve removal of solutes by hemodialysis? A systematic review and meta-analysis

Journal:	*Physiotherapy Research International*
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Keywords:	Exercise, dialysis efficiency, hemodialysis, solutes
Abstract:	Background: As aerobic intradialytic exercise increases cardiac output and skeletal muscle vasodilation, it is suggested that it could improve the removal of solutes during hemodialysis. Objective: The objective of this paper is to describe a systematic review and meta-analysis to identify if intradialytic exercise improves the removal of solutes and the hemodialysis adequacy. Data sources: A systematic review and meta-analysis of randomized controlled trials (RCT) was performed. The sources were MEDLINE (via PubMed), Web of Science, LILACS and SciELO, from inception until July 2018. Study selection /eligibility criteria: Clinical trials including patients on chronic hemodialysis submitted to the intervention of aerobic intradialytic exercise, and evaluating as outcomes the removal of solutes (creatinine, phosphate and potassium) and/or adequacy parameters (Kt/V-urea). Results: The systematic review included 23 studies (seven evaluating the effect of one exercise session and 16 evaluating the effect of training, lasting from 6 to 25 weeks). Eleven RCT were included in the meta-analyses. It was observed that the aerobic intradialytic exercise increased the Kt/V-urea (0.15, 95% CI 0.08, 0.21) and decreased creatinine (-1.82 mg/dL, 95% CI -2.50, -1.13), despite the high heterogeneity of the analysis. No differences were found in phosphorus and potassium removal. Conclusion: the aerobic intradialytic exercise may be suggested to improve the Kt/V-urea and the creatinine removal during the dialysis. The project was registered in PROSPERO under number CRD42018099016.

Does intradialytic exercise improve removal of solutes by hemodialysis? A systematic review and meta-analysis

Abstract

Background: As aerobic intradialytic exercise increases cardiac output and skeletal muscle vasodilation, it is suggested that it could improve the removal of solutes during hemodialysis. *Objective:* The objective of this paper is to describe a systematic review and meta-analysis to identify if intradialytic exercise improves the removal of solutes and the hemodialysis adequacy. *Data sources:* A systematic review and meta-analysis of randomized controlled trials (RCT) was performed. The sources were MEDLINE (via PubMed), Web of Science, LILACS and SciELO, from inception until July 2018. *Study selection /eligibility criteria:* Clinical trials including patients on chronic hemodialysis submitted to the intervention of aerobic intradialytic exercise, and evaluating as outcomes the removal of solutes (creatinine, phosphate and potassium) and/or adequacy parameters (Kt/V-urea). *Results:* The systematic review included 23 studies (seven evaluating the effect of one exercise session and 16 evaluating the effect of training, lasting from 6 to 25 weeks). Eleven RCT were included in the meta-analyses. It was observed that the aerobic intradialytic exercise increased the Kt/V-urea (0.15, 95% CI 0.08, 0.21) and decreased creatinine (-1.82 mg/dL, 95% CI -2.50, -1.13), despite the high heterogeneity of the analysis. No differences were found in phosphorus and potassium removal. *Conclusion:* the aerobic intradialytic exercise may be suggested to improve the Kt/V-urea and the creatinine removal during the dialysis. The project was registered in **PROSPERO** under number **CRD42018099016**.

Key words: exercise, dialysis efficiency, hemodialysis, removal of solutes.

Introduction

Patients with advanced chronic kidney disease often depend on hemodialysis (HD) treatment (Teruel-Briones et al., 2013). Despite advances in technology and equipment in recent years, alternatives to increase solute removal and dialysis efficiency continue to be tested to improve survival of patients and quality of life. Improved solute removal and dialysis adequacy is classically dependent on increased length or frequency of HD sessions. However, additional increases in dialysis time are associated with a higher cost and poor patient adhesion (GUÉRY et al., 2014).

Removal of solutes located in the intracellular compartment, such as potassium, creatinine, urea and phosphate, are often reduced by constriction of the peripheral circulation during dialysis (Choi & Ha, 2013). It is suggested that the aerobic intradialytic exercise for the lower extremities may promote an increase in cardiac output and blood flow to the periphery, resulting in vasodilation and greater surface area facilitating inter-compartmental mass transfer and, therefore, removal of solutes for the vascular compartment and dialysate (BENNETT et al., 2013; KIRKMAN et al., 2014a; PARSONS, TOFFELMIRE, & KING-VANVLACK, 2006; RIBEIRO et al., 2013).

The aim of this paper is to perform a systematic review and meta-analysis to identify if aerobic intradialytic exercise may improve the removal of solutes and hemodialysis adequacy in chronic kidney disease patients.

Materials and Methods

Design and search strategy

This systematic review was reported according to PRISMA Statement and the AMSTAR 2 (LIBERATI et al., 2009; SHEA et al., 2017) registered under number **CRD42018099016**. The search for English, Portuguese or Spanish papers was conducted in the following electronic databases: MEDLINE (via PubMed), Web of Science, LILACS and SciELO, until July 2018. The MeSH terms and their synonyms were used searching the terms in all fields. The search strategy used in PubMed is shown in Table 1.

Eligibility criteria, intervention and participants

According to PICOS principles, we consider the following criteria: Participants who presented chronic disease patients on hemodialysis; Intervention as aerobic intradialytic exercise; Control group for patients on hemodialysis without intradialytic exercise; Outcomes, removed of blood solutes and dialysis adequacy parameters; and Study design, clinical trials. Inclusion criteria were papers that describe the exercise programs and analyzed parameters related to our pre-specified aims. Exclusion criteria were studies in which the exercise was not performed during the dialysis, reviews, protocols or studies published in a languages other than English, Spanish or Portuguese.

Study selection and data extraction

Full texts of the papers selected after screening the titles and abstracts were assessed and data extracted. The extracted data included the author/s name and year of the publication, country, type of the study, types of exercise, outcomes reported and results.

Two independently researchers performed the literature search, screening titles and abstracts, full-paper reviews, study quality assessment, and data extraction. When there were disagreements, there were referred to a third author.

Assessment of risk of bias

The assessment of risk of bias was analyzed descriptively, according to the method proposed by the PRISMA Statement (Liberati et al., 2009) and the AMSTAR 2 (SHEA et al., 2017), considering generation of the random sequence, concealed allocation, blinding of investigators and outcome assessors, intention to treat analysis (was considered as all randomized patients were analyzed at the end of the study), and description of losses and exclusions.

Data analysis

Effect size was calculated using the difference between the mean of Kt/V-urea, and plasma creatinine, phosphorus and potassium, comparing the training of intradialytic exercise and control group (pre and post intervention) in Randomized Clinical Trials. Statistical heterogeneity was assessed using the Q test and the inconsistency test (I_2), where values above 60% were considered indicative of high heterogeneity. An alpha value ≤.05 and a confidence interval of 95% (95% CI) were considered statistically significant. All analyses used Stata 13.0 and Review Manager 5.3.

Results

Flow of studies

The initial search identified 366 papers. After screening the titles and abstracts, 33 papers were selected for full-text evaluation. Of these, 23 papers were included in the systematic review (Figure 1).

Descriptions of studies

Table 2 shows the summary of the included studies. Seven studies evaluated the acute effect of exercise on the removal of solutes and/or dialysis adequacy. Another 16 studies evaluated the effect of training, with lengths of intervention ranging from 6 to 25 weeks.

Acute effect of exercise

Regarding the found studies that evaluated the acute effect of the exercise, the first one that evaluated the removal of solutes and the adequacy of dialysis was Kong *et al.* (KONG, TATTERSALL, GREENWOOD, & FARRINGTON, 1999). After a 60 minutes intervention (two sets of 20 minutes in a submaximal capacity + 10 minutes in rest), was observed a decrease in the rebound of urea (from 12.4 to 10.9%) and potassium (from 62 to 44%), and the Kt/V-urea significant increased from 1.0 to 1.15.

Vaithilingam *et al.* applied an exercise intervention for 30 to 60 minutes on a stationary bicycle and showed that phosphate removal increased in the intervention group (Vaithilingam, Polkinghorne, Atkins, & Kerr, 2004). Similar to these findings, Orcy *et al.* performed a cross-over study, with an intervention of 60 minutes of cycling (20 minutes of pedaling and 10 minutes of rest, alternating) and observed that the removal of phosphate in the dialysate during HD sessions with exercise was significantly greater than in HD sessions without exercise. However, exercise did not modify the removal of urea, creatinine and potassium (ORCY, ANTUNES, SCHILLER, SEUS, & BOHLKE, 2014).

Kirkman *et al.* also performed a cross-over study with a intervention of 60 minutes at an intensity relative to 90% of the anaerobic threshold (compared to baseline and with a 30-minute increase in hemodialysis time), and observed that exercise was not as effective as the increased hemodialysis time for improve equilibrated Kt/V. However, exercise was more effective for the rate of phosphate reduction (KIRKMAN et al., 2014b). Another cross-over study was Giannaki *et al.*, who showed that patients cycling for 3 hours at 40% of maximum capacity showed an improvement in Kt/V (20%), in the urea reduction ratio (11%) and in the creatinine reduction rate (26%), in addition to a reduction in serum potassium levels of 77.5% (GIANNAKI et al., 2011).

Bohm *et al.* randomized 30 patients to perform exercise or control, using an acute cycloergometer intervention at a moderate intensity, and found no difference in the removal of potassium, urea, creatinine and phosphorus between groups. However, the intervention group had greater removal of phosphorus during exercise compared to hemodialysis at rest (BÖHM, MONTEIRO, ANDRADE, VERONESE, & THOMÉ, 2017).

Brown *et al*. evaluated two different intensities of aerobic exercise controlled by maximum heart rate (55% and 70%) and observed that Kt/V-urea was higher in patients who exercised for 30 min at 55% intensity compared to control. In addition, there were greater removals of urea in both groups of exercise compared with control group (BROWN, ROWED, SHEARER, MACRAE, & PARKER, 2018).

Chronic effect of training

Regarding to training and chronic effects, Parsons *et al.* performed a 20-week intradialytic exercise program on a stationary bicycle and found that single-pool Kt/V increased 11% after the first month and remained elevated at 4^{th} (19%) and 5^{th} months (18%) during the program (PARSONS et al., 2006). The study of Afshar *et al.* compared the aerobic and resistance exercise to a control group for 8 weeks, and observed that both exercises reduced serum creatinine, with a greater effect of the aerobic exercise. However, the exercise did not change Kt/V-urea and plasma urea concentration (SANAVI, AFSHAR, SHEGARFY, & SHAVANDI, 2010). Kopple *et al.* and Chigira *et al.*, after 18 weeks and a 3-month exercise intervention, respectively, also found no change in Kt/V-urea (CHIGIRA, ODA, IZUMI, & YOSHIMURA, 2017;

KOPPLE et al., 2007). Also van Vilsteren *et al.* proposed a low to moderate intensity program for 12 weeks on a stationary bicycle and observed an increase in Kt/V after the intervention period (VAN VILSTEREN, DE GREEF, & HUISMAN, 2005). In addition to this study, Reboredo *et al.* performed a 12-week intervention with aerobic exercise and found improvement in Kt/V-urea values in the exercise group (REBOREDO et al., 2010), as well as Dobsak *et al.* (DOBSAK et al., 2012), and after Giannaki *et al.* (GIANNAKI et al., 2013), who evaluated exercise with 60-65% of the maximum capacity of the individuals, and also found that Kt/V improved significantly in the exercise group compared to baseline values (1.10 ± 0.0 baseline versus 1.25 ± 0.1 post exercise). In a retrospective study, Freire *et al.* (FREIRE et al., 2013) also found improvement in Kt/V after intervention with isotonic exercise.

Makhlough *et al.* applied an 8-week intervention and found a decrease in serum phosphate and potassium levels (MAKHLOUGH, ILALI, MOHSENI, & SHAHMOHAMMADI, 2012), while Paglialonga *et al.* with a 12-week intervention showed a reduction in creatinine levels (PAGLIALONGA et al., 2014).

The Groussard *et al.* (GROUSSARD et al., 2015) exercise protocol showed no difference in the creatinine levels, but Liao *et al.* (LIAO et al., 2016) indicated that three-month intradialytic exercise might decrease blood creatinine. This data was corroborated one year later, when Adam *et al.* showed decrease by 17% in blood creatinine after a 6-month intervention (ADAM, MTECH, & SBN, 2017).

Mohseni *et al.* showed an increase in urea removal rate - URR (11%) and also an improvement in Kt/V after 8 weeks of intradialytic exercise program (MOHSENI et al., 2013). Musavian *et al.*, comparing active exercises and passive movements showed that exercise can decrease phosphorus and potassium plasma levels (MUSAVIAN, SOLEIMANI, MASOUDI ALAVI, BASERI, & SAVARI, 2015).

Risk of bias

Of the 23 studies included, 11 are Randomized Controlled Trials. Of these, all described that it was performed adequate sequence generation, six studies reported the method used for randomization and the studies with loss and exclusions presented the reasons. Only two indicated that the sample was blinded, this was the main difficulty to applying the intervention. These data are present in Table 3.

Another 9 studies used a cross-over design, with patients themselves acting as their controls at different times, this order being randomized in 6 of these studies. Three studies did not have a control group, and only performed a pre and post intervention evaluation. The studies that are not Randomized Controlled Trials with control group were not included in the analysis.

Effects of intradialytic exercise

The RCT metanalysis was performed for the variables: Kt/V-urea (adequacy of dialysis); and plasma creatinine, phosphorus and potassium concentration (removal of solutes) to evaluate the effect of intradialytic aerobic training.

Kt/V-urea: 10 analyzes were performed, totaling 346 patients (171 in exercise and 175 in control groups). It was observed that the intradialytic exercise increased the Kt/V by 0.15 (95% CI 0.08, 0.21) (I^2: 99%) (Figure 2). Creatinine: Five analyzes, totaling 128 patients (63 exercise and 65 control). It was observed that the intradialytic exercise decreased creatinine by -1.82 mg/dL (95% CI -2.50, -1.13, I^2: 99%) (Figure 3). The results should be analyzed with caution, because there is a high heterogeneity.

Plasma Phosphorus and potassium concentrations were evaluated in two and three studies, including 69 and 103 patients, respectively. No differences were found between the groups exercised and controls. Phosphorus -1.06 mg/dL (CI:-2.72, 0.60) and potassium -0.07 mg/dL (CI: -0.68, 0.55) (Figure 4 and 5, respectively).

Discussion

Summary of evidence

In this systematic review with a meta-analysis of RCTs was observed that the aerobic intradialytic exercise increased Kt/V-urea and decreased blood creatinine concentration in patients undergoing hemodialysis, but with no change in the plasma phosphate and potassium concentration.

Aerobic exercise performed during HD has been reported as beneficial as traditional exercise, improving cardiorespiratory fitness, maximal oxygen consumption, lower limb muscle strength, nutricional parameters, quality of life and functional capacity (ORCY, DIAS, SEUS, BARCELLOS, & BOHLKE, 2012; RIBEIRO et al., 2013; SHENG et al., 2014). In addition to the usual advantages, performing the exercises during the HD session reduces the monotony of the dialysis process and facilitates medical follow-up. Despite the documented benefits, intradialytic exercise still considered as intervention rather than a routine care (BENNETT et al., 2013; MAHESHWARI et al., 2012).

However, some studies indicate that this intervention may increase the rate of toxin removal during HD due to its physiological effects, but these mechanisms should be better understood. Parsons *at al.* have suggested that exercise with cycloergometer increases vasodilation and blood flow to the lower extremities, it increases the surface area and transfer of more solutes to the vascular compartment, and subsequent removal to the dialysate (PARSONS et al., 2006). An other possible effect of exercise is the rise of body core temperature which will probably further dilate the vasculature (KALOUSOVÁ et al., 2006). These two effects can change the resistance of endothelial and cell membranes to exchange toxins. Maheshwari *et al.* described that this effects could be explained because in the rest state, approximately 80% of total body fluid are in organs with low perfusion, like skeletal muscles, skin and bones that receive only about 15% of cardiac output, but its represent a body compartment that retains a large concentration of uremic toxins. In exercise state these organs are better perfused and increase the toxin exchange between compartments and probably decreasing the rebound effect of uremic toxins (MAHESHWARI et al., 2012; MAHESHWARI, SAMAVEDHAM, & RANGAIAH, 2011).

Because of the effect of acute exercise on peripheral vasodilation and of angiogenesis as a consequence of aerobic training, we believe that physical exercise may contribute in addition to blood pressure control, increased strength and muscle endurance, also to improve toxin removal and dialysis adequacy (BASTOS, BREGMAN, & KIRSZTAJN, 2010).

Our data showed that aerobic training increased Kt/V-urea and decreased creatinine concentration in the blood. We found no difference in the removal of phosphorus and potassium, but we emphasize that only two and three studies analyzed the effect of training on the removal of these variables, respectively.

Strengths and limitations of the review

The main limitation of our analysis is that only half of the selected studies are Randomized Clinical Trials (meta-analysis) and the others usually have a small sample size. In addition, analyzes presented high heterogeneity and the studies have moderate quality, especially without blinding. As a positive aspect, we were able to include in the systematic review studies with acute and chronic effects of exercise and analyzing different markers to evaluate removal of solutes and dialysis adequacy, thus encouraging the intervention with intradialytic exercise, as it was a safe intervention (GIANNAKI et al., 2013), and that suggest to be beneficial in the efficiency of solute removal in the dialysis.

Compared with other systematic review

A comparison with other similar systematic review is with the paper by Sheng, which evaluated the effects of intradialytic exercise on Kt/V-urea, and in physical and mental function. Although this study did not aim to evaluate removal of solutes, it showed a significantly increase by 0.27 in Kt/V-urea, as well as improve in peak oxygen consumption and physical performance in the exercise group. Besides, it showed no difference in mental function (SHENG et al., 2014). Our review confirm the finding of increased of Kt/V-urea and adds an analysis of blood creatinine, phosphorus and potassium concentrations.

In summary, we concluded that the intradialytic exercise may be suggested as a complementary intervention in the treatment of patients on hemodialysis, contributing by increase the blood flow to improve the Kt/V-urea and the creatinine removal during the dialysis.

Implications for Physiotherapy Practice

We suggest that intradialytic aerobic exercise should be an additional alternative applied by the physiotherapist in the dialysis treatment units, in order to reduce monotony, increase cardiac output and that may potentiate solute removal and dialysis adequacy.

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Table 1. Literature search strategy used for the PubMed database.

#1	"dialysis efficiency" OR "dialysis efficacy" OR "hemodialysis efficiency" OR "hemodialysis efficacy" OR “hemodialysis adequacy” OR "kt/v" OR "solute removal efficiency" OR "urea" OR "creatinine" OR "microglobulin" OR "phosphate" OR “potassium”
#2	renal dialysis OR renal replacement therapy OR hemodialysis OR hemodialyses OR dialysis OR dialyses
#3	exertion, physical OR exercise OR exercise therapy OR physical activity OR physical fitness OR aerobic exercise OR exercise training OR aerobic training OR aerobic program OR endurance exercise OR endurance training OR endurance program OR physical activities) OR physical rehabilitation) OR intradialytic exercise
#4	#1 AND #2 AND #3

Table 2. Summary of the studies.

Author, year, Country	**Type of study**	**Intervention**	**Sample**	**Protocol**	**Outcomes**	**Features**
Kong, 1999, United Kingdom	Controlled clinical trial: cross-over	Acute	11 Patients	Cycle ergometer for 5-20 min at submaximal load followed by 10 min rest (two sets - total of 60 min). All patients were studied on two dialysis sessions (exercise	Serum urea, creatinine and potassium. Post dialysis rebound (%rebound) and reduction ratios (RR) of solutes and Kt/V-urea.	The rebound effect of all evaluated solutes decreased. The rebound effect of urea decreases from 12.4 to 10.9%. Potassium decreased from 62 to 44%. Kt/V-urea increased from 1.0 to 1.15. The Kt/V-creatinine increased from 0.71 to 0.84. RR creatinine from 0.51 to 0.57.

				and control) on the same day of consectuive weeks.		
Vaithilingam, 2004, Australia	Controlled clinical trial: cross-over	Acute	12 Patients	Randomly assigned to 1 week of exercise immediately before dialysis, 1 week of no exercise, and 1 week of exercise intradialytic. Cycle ergometer for 30 to 60 minutes.	Serum urea, creatinine, phosphate, calcium and albumin.	The urea reduction rate was not different between the groups, however, phosphate removal significantly improved with exercise intradialytic.
Giannaki, 2011, Greece	Controlled clinical trial: cross-over	Acute	10 Patients	In two consecutive weeks, first: usual HD session (Control). After: bicycle in the supine position for 3 hours in an intensity of 40% of the patient's maximal exercise capacity.	Kt/V, creatinine, potassium and urea and urea reduction ratio (URR).	Kt/V, URRe and creatinine reduction rate improved significantly by 20%, 11% and 26% respectively. Plasma potassium levels were reduced by 77.5%.
Kirkman, 2014, Germany	Controlled clinical trial: cross-over	Acute	11 Patients	Each patient three moments in a randomized order: Control, increased HD time of 30 min, and intradialytic exercise for 60 min	Urea, creatinine, β 2 – microglobulin and phosphate.	The exercise was not as effective as HD time to increasing Kt/V. Exercise was less effective at improving of urea and creatinine reduction rates. However, exercise was more effective than increasing the dialysis time for the phosphate

				of cycling at 90% of the lactate threshold.		reduction rate.
Orcy, 2014, Brazil	Controlled clinical trial: cross-over	Acute	22 Patients	Randomly assigned to 1 week of exercise and 1 week of control. Training on a cycle ergometer. Total exercise time of 60 minutes (2 sets of exercise of 20 minutes + 10 minutes of rest). Controlled for 13–14 in Borg scale.	The dialysate concentration of urea, creatinine potassium and phosphate; Kt/V.	The removal of phosphate in the dialysate during intervention sessions was significantly greater than the control sessions. The exercise did not modify the removal of urea, creatinine and potassium.
Bohm, 2017, Brazil	Controlled clinical trial: cross-over	Acute	15 Patients. Moderate intensity aerobic training/ cross over rest (n=15), and control (n=15)	Cycle ergometer in an intensity of 60-70% of the patient's maximal exercise capacity (13-14 Borg scale).	Urea, creatinine potassium and phosphate.	No difference between control and exercise. The intervention group had greater removal of phosphorus during exercise compared to hemodialysis at rest.
Brown, 2018, Canada	Controlled clinical trial: cross-over	Acute	17 Patients	Randomized to three different protocols during the mid-week HD treatment over three	Urea kinetics and Kt/V.	Kt/V was significantly higher during the 55% session compared to the control. There was no difference in urea clearance between exercise intensities (55% group and 70%

				consecutive weeks: no exercise, 30-minutes of exercise at 55% of age-predicted maximal heart rate (HRmax) and 30-minutes of exercise at 70% HRmax.		HRmax group). A significant increase in urea clearance was observed during intradialytic exercise compared with dialysis at rest (5.5 ± 1.9% and 12.4 ± 2.6% increase at 55 and 70%, respectively).
van Vilsteren, 2005, Netherlands	Randomized controlled trial	Training (12 weeks)	96 Patients. Randomized: exercise group (n=53) and control group (n=43)	Exercise programme: Cycling controlled for 12–16 according to the rate of perceived exertion (RPE).	Kt/V	The exercise group increased the Kt/V.
Parsons, 2006, Canada	Quasi-experimental study	Training (5 months)	13 Patients	Intradialytic exercise program: 3 times a week (cycle ergometer for 30 minutes with hydraulic resistance).	Creatinine, Potassium, Urea, Kt/V.	Serum urea clearance increased (KT/V) 11% after the first month of the training program and remained elevated at 4 (19%) and 5 months (18%). No control group.
Kopple, 2007, USA	Randomized controlled trial	Training (18 weeks)	51 Patients: Endurance training (ET) = 10, strength training	First: 50% of peak oxygen consumption and 20 min, after four weeks, exercise was advanced to 40 min and intensity was	Kt/V and IGF signaling	Training increases muscle IGF-I protein (protein anabolism). No changes in Kt/V.

			(ST)= 15, endurance plus strength training (EST)= 12 or no training (NT)= 14	increased as tolerated.		
Afshar, 2010, Iran	Randomized controlled trial	Training (8 weeks)	21 Patients. Resistance training (n=7), Moderate intensity aerobic training (n=7), and control (n=7)	Aerobic: cycling at an intensity of 12–16 of Borg scale (65–85%). Resistence: training of the lower extremities with weights for knee extension, flexion and hip abduction-flexion at an intensity of 15–17 of Borg scale. Training started at 60% of 3RM for two sets of eight repetitions and increased to three sets as tolerated.	Serum urea, creatinine, Kt/V.	Aerobic and resistance exercises were correlated with reduced serum creatinine, and aerobic exercise induced more reduction. These exercises did not influence Kt/V and serum urea.
Reboredo, 2010, Brazil	Randomized controlled trial	Training (12 weeks)	22 Patients. Randomized: exercise group (n=11) and control group (n=11)	Control group: regular HD. Exercise Group: Three weekly sessions of aerobic exercise.	Kt/V, creatinine, phosphorus, potassium and calcium.	Analyzes of potassium, creatinine and albumin were not clinically relevant. Improvement of KT/V in the exercise group (Kt/V baseline 1.6 ± 0.2, final 2.0 ± 0.8) compared to control (baseline 1.6 ± 0.3, final

						1.8 ± 0.7).
Dobsak, 2012, Czech Republic	Randomized controlled trial	Training (20 weeks)	32 Patients. exercise group (n=11), electro-stimulation (EMS) of leg extensors group (n= 11); and control group (n=10)	Cycling at an intensity of 60% of peak oxygen consumption first for 20 min, and after 5 weeks for 2X20 min.	Kt/V, URR.	Increased urea clearance (Kt/V and URR) was found in the 6th, 14th and 20 weeks in the exercise group in relation to the control.
Makhlough, 2012, Iran	Randomized controlled trial	Training (8 weeks)	48 Patients Randomized: exercise group(n=25) and control group(n=23)	Intradialytic exercise program consisting of 15 minutes of low-intensity exercise, 3 times a week.	Phophate, Calcium, Potassium	Significant improvements were observed in serum phosphate levels (decreased by 1.84 mg/dL) and serum potassium levels (decreased by 0.69 mg/dL). Serum calcium levels did not change significantly in the exercise group.
Giannaki, 2013, Greece	Randomized controlled trial	Training (6 weeks)	24 Patients. Randomized: exercise group(n=12) and control exercise with no resistance group(n=12)	Exercise training programme: Cycling at an intensity of 60–65% of the patient's maximal exercise capacity for 45 min, 3 times/week for a 6-month period. Control: the same	Kt/V	Kt/V improved significantly in the exercise group compared to baseline. (1.10 ± 0.0 baseline versus 1.25 ± 0.1 post exercise). In contrast, no differences were found in Kt/V in the control group.

				protocol without resistance.		
Freire, 2013, Brazil	Retrospective study (medical records)	Training (3 months)	15 Patients	A protocol of low intensity isotonic exercises of upper and lower limbs with duration of 30 minutes was applied.	Kt/V	The mean Kt/V values in the three months without exercise was 1.13±0.11 and after the application of the training program was 1.29±0.12 (p <0.05)
Paglialonga, 2014, Italy	Quasi-experimental study	Training (3 months)	10 Patients	Exercise program: 30min using a cyclo ergometer two to three times a week for 3 months. Intensity adjusted on the basis of heart rate and subjective tolerance, as Borg scale of 3 (0-10).	Creatinine, Potassium, Calcium, Phosphate, spKT/V	Creatinine levels improved significantly post-intervention. Other variables without change. No control group.
Mohseni, 2013, Iran	Randomized Controlled Trial	Training (8 weeks)	50 Patients. Randomized: exercise group (n=25) and the control group (n=25).	Aerobic exercise: 15 min/day, three times a week, during dialysis sessions for the intervention group.	Kt/V, URR.	There was an overall 11% increase in URR and 38% improvement in Kt/V after 8 weeks of intradialytic exercise program. Control group had no change.
Musavian, 2015, Iran	Controlled clinical trial: cross-over	Training (8 weeks)	16 Patient	The first 8 weeks: considered as the control period. After:	Kt/V, URR, phosphorus, potassium and	No significant change was observed in serum potassium, phosphorus and calcium levels at

				8 weeks of passive intra-dialytic exercise and another 8 weeks of washout, and finally 8 weeks of active intradialytic pedal exercise for 30 minutes.	calcium.	the end of the passive exercise program compared to the baseline. However, potassium and phosphorus levels were significantly decreased in the active exercise program.
Groussard, 2015, France	Randomized controlled trial	Training (3 months)	20 Patients. Randomized: exercise group (n=10) and the control group (n=10).	Intradialytic aerobic cycling training: 3 days/week for 30 min at a constant pedal frequency of 50 r/min.	Creatinine, Kt/V	Solute removal: no differences were found between blood creatinine and Kt/V between groups.
Liao, 2016, Taiwan	Randomized controlled trial	Training (3 months)	20 Patients. Randomized: exercise group (n=10) and the control group (n=10).	20 minutes of cycling at the desired workload, during 3 sessions/week.	Creatinine, Kt/V	Exercise group decreased blood creatinine after the intervention. No change in Kt/V.
Chigira, 2017, Japan	Quasi-experimental study	Training (3 months)	7 Patients	Bicycle 20 minutes. Intensity for Karvonen method (75% of HRmax) and based on the Borg Scale (between 11 and 13)	Kt/V	Significant differences were not observed in Kt/V values. However, according to the authors, the result was favorable because in the individual patients the values indicate conditions maintained or improved. No control group.

				+ resistence training (ankle flexion/dorsiflexion and stepping) and lower-limb muscle strength training.		
Adam, 2017, South Africa	Randomized controlled trial	Training (6 months)	34 Patients. Randomized: exercise group (n=17) and the control group (n=17).	Exercise group: cycling for 15 min every hour (total of 60 min of exercise over a dialysis session). Intensity: heart rate at 100 beats per minute.	Potassium, creatinine, blood urea nitrogen (BUN) and urea-Kt/V.	Exercise group: reduction in the serum urea clearance by 30% (p<0.001) and in the creatinine levels by 17% (p=0.01) as compared to that of the baseline. The Kt/V-urea increased from 1.2 to 1.4 after 6 months of cycling (p=0.5). The potassium levels dropped by 8% in both groups.

Table 3. Assessment of risk of bias of Randomized Controlled Trial.

Study	Adequate Sequence Generation	Allocation Concealment	Blinding of sample	Blinding of outcome assessors	Description of losses and exclusions	Intention to treat analysis
Adam, 2017	Yes	Yes	No	No	not applicable	Yes
Liao, 2016	Yes	unclear	unclear	unclear	not applicable	Yes
Groussard, 2015	Yes	unclear	No	No	Yes	No
Giannaki, 2013	Yes	Yes	Yes	No	not applicable	Yes
Mohseni, 2013	Yes	Yes	No	No	Yes	No
Makhlough, 2012	Yes	Yes	Yes	No	not applicable	Yes
Dobsak, 2011	Yes	unclear	unclear	unclear	not applicable	Yes
Afshar, 2010	Yes	unclear	unclear	unclear	Not applicable	Yes
Reboredo, 2010	Yes	unclear	No	No	Yes	No
Kopple, 2007	Yes	Yes	unclear	unclear	Yes	No
van Vilsteren, 2004	Yes	Yes	unclear	unclear	Yes	No

not applicable: there were no losses or exclusion

Figure legends

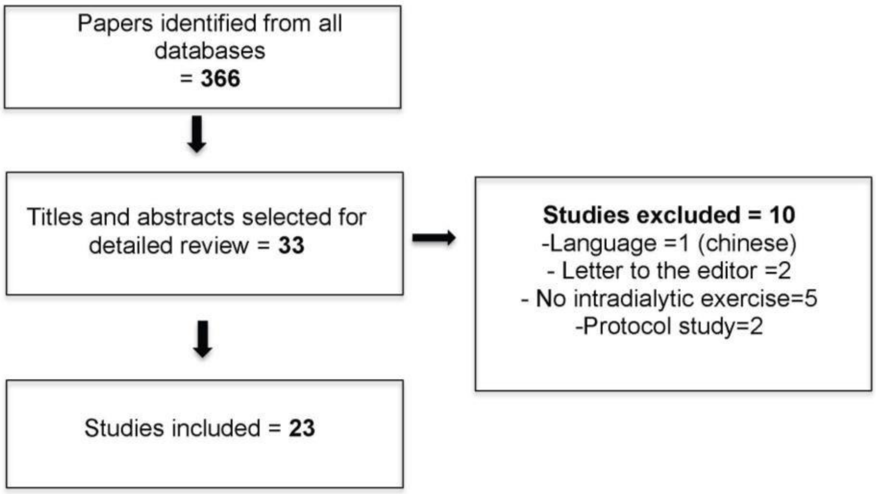

Figure 1. The flow diagram of studies included in the systematic review

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Adam 2017	0.2	0.02	17	0.001	0.001	17	12.3%	0.20 [0.19, 0.21]
Afshar 2010	0.001	0.02	7	0.01	0.01	7	12.2%	−0.01 [−0.03, 0.01]
Dobsak 2011	0.15	0.01	10	−0.1	0.15	11	10.2%	0.25 [0.16, 0.34]
Giannaki 2013	0.15	0.001	12	0.001	0.3	12	7.1%	0.15 [−0.02, 0.32]
Groussard 2015	0.11	0.001	8	−0.15	0.04	10	12.1%	0.26 [0.24, 0.28]
Kopple 2007	0.25	0.17	10	0.13	0.05	20	9.5%	0.12 [0.01, 0.23]
Liao 2016	0.02	0.01	20	−0.03	0.07	20	12.0%	0.05 [0.02, 0.08]
Mohseni 2013	0.3	0.2	23	0.05	0.1	24	10.1%	0.25 [0.16, 0.34]
Reboredo 2010	0.4	0.6	11	0.2	0.4	11	2.2%	0.20 [−0.23, 0.63]
van Vilsteren 2004	0.06	0.02	53	0.001	0.02	43	12.3%	0.06 [0.05, 0.07]
Total (95% CI)			**171**			**175**	**100.0%**	**0.15 [0.08, 0.21]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 862.32$, $df = 9$ ($P < 0.00001$); $I^2 = 99\%$
Test for overall effect: $Z = 4.10$ ($P < 0.0001$)

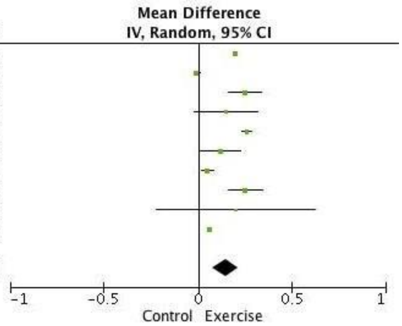

Figure 2: Analysis of Kt/v comparing the intradialytic exercise group and control group. SD: standard deviation, CI: confidence interval, I^2: Inconsistency Test.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Adam 2017	−7.13	1.8	17	−5.24	1.28	17	14.7%	−1.89 [−2.94, −0.84]
Afshar 2010	−7.28	0.82	7	0.11	0.13	7	19.0%	−7.39 [−8.01, −6.77]
Groussard 2015	−0.01	0.001	8	−0.1	0.05	10	22.4%	0.09 [0.06, 0.12]
Liao 2016	−0.33	0.15	20	−0.11	0.1	20	22.4%	−0.22 [−0.30, −0.14]
Reboredo 2010	0.7	0.4	11	1.2	0.3	11	21.5%	−0.50 [−0.80, −0.20]
Total (95% CI)			**63**			**65**	**100.0%**	**−1.82 [−2.50, −1.13]**

Heterogeneity: $Tau^2 = 0.54$; $Chi^2 = 637.09$, $df = 4$ ($P < 0.00001$); $I^2 = 99\%$
Test for overall effect: $Z = 5.21$ ($P < 0.00001$)

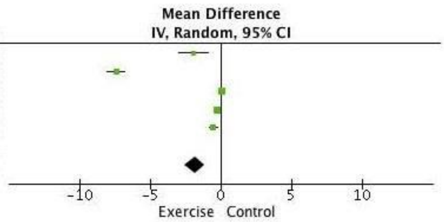

Figure 3: Analysis of blood creatinine comparing the intradialytic exercise group and control group. SD: standard deviation, CI: confidence interval, I^2: Inconsistency Test.

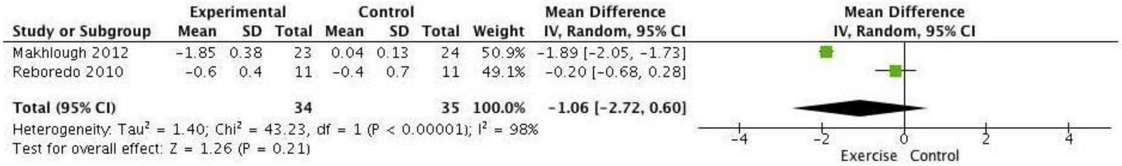

Figure 4: Analysis of blood phosphorus comparing the intradialytic exercise group and control group. SD: standard deviation, CI: confidence interval, I²: Inconsistency Test.

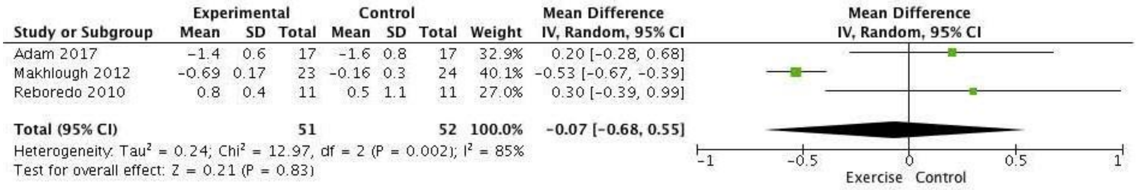

Figure 5: Analysis of blood potassium comparing the intradialytic exercise group and control group. SD: standard deviation, CI: confidence interval, I²: Inconsistency Test.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Report on pag
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1,2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4, tabl
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4,5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5,6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Report on pag
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7, fig.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 7-10
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10,11, table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	table 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11,12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13,14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14,15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e100
doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

ANEXOS

Anexo A

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

UNIVERSIDADE CATÓLICA DE PELOTAS

PROGRAMA DE PÓS-GRADUAÇÃO EM SAÚDE E COMPORTAMENTO

Pesquisador responsável: Etiene Campos Dias
Instituição: Programa de Pós Graduação Saúde e Comportamento da Universidade Católica de Pelotas
Endereço: Rua Gonçalves Chaves, 373, Centro, Pelotas -RS
Telefone: (53) 2128-8243

Concordo em participar do **“** *Exercício físico aeróbico intradialítico e a eficiência da hemodiálise “*

Estou ciente de que estou sendo convidado a participar voluntariamente do mesmo.

PROCEDIMENTOS: Fui informado de que o objetivo geral será comparar as respostas de remoção de moléculas do sangue, com e sem exercício físico aeróbico durante a hemodiálise, cujos resultados serão mantidos em sigilo e somente serão usados para fins de pesquisa. Estou ciente de que a minha participação envolverá coletas de sangue intravenosa, do dialisato; e realizar três sessões de exercício aeróbio na bicicleta ergométrica.

RISCOS E POSSÍVEIS REAÇÕES: Fui informado de que os riscos são normais para sujeitos expostos à prática de exercício físico, como suor excessivo e tontura.

BENEFÍCIOS: O benefício de participar da pesquisa relaciona-se ao fato que os resultados do estudo podem proporcionar o desenvolvimento de uma nova metodologia de treinamento para indivíduos com doença renal crônica em hemodiálise, com o difundindo uma nova tecnologia. Além disso, os resultados serão incorporados ao conhecimento científico e posteriormente a situações de ensino-aprendizagem.

PARTICIPAÇÃO VOLUNTÁRIA: Como já me foi dito, minha participação neste estudo será voluntária e poderei interrompê-la a qualquer momento.

DESPESAS: Eu não terei que pagar por nenhum dos procedimentos, nem receberei compensações financeiras.

CONFIDENCIALIDADE: Estou ciente que a minha identidade permanecerá confidencial durante todas as etapas do estudo.

CONSENTIMENTO: Recebi claras explicações sobre o estudo, todas registradas neste formulário de consentimento. Os investigadores do estudo responderam e responderão, em qualquer etapa do estudo, a todas as minhas perguntas, até a minha completa satisfação. Portanto, estou de acordo em participar do estudo. Este Formulário de Consentimento Informado será assinado por mim e arquivado na instituição responsável pela pesquisa.

Nome do participante: ___________________________

Identidade: ____________________________________

ASSINATURA: ___________________________________

DATA:_____/_____/ _______

DECLARAÇÃO DE RESPONSABILIDADE DO INVESTIGADOR: Expliquei a natureza, objetivos, riscos e benefícios deste estudo. Coloquei-me à disposição para perguntas. O participante compreendeu minha explicação e aceitou, sem imposições, assinar este consentimento. Tenho como compromisso utilizar os dados e o material coletado para a publicação de relatórios e artigos científicos referentes a essa pesquisa. Se o participante tiver alguma consideração ou dúvida sobre a ética da pesquisa, pode entrar em contato com o pesquisador pelo celular: 53 991562521

____

Etiene Campos Dias

Pesquisador responsável

Anexo B

CARTA DE APROVAÇÃO DO COMITÊ DE ÉTICA EM PESQUISA

UNIVERSIDADE CATÓLICA DE PELOTAS - UCPEL

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Efeitos do treinamento físico com restrição parcial do fluxo sanguíneo na eficiência da remoção de solutos por hemodiálise

Pesquisador: Rafael Bueno Orcy

Área Temática:

Versão: 2

CAAE: 70236317.2.0000.5339

Instituição Proponente: Universidade Católica de Pelotas - UCPel

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.707.365

Apresentação do Projeto:

Trata-se de um tipo de pesquisa classificado como outros vinculado a Unidade de Nefrologia.

Objetivo da Pesquisa:

Objetivo Geral:

Avaliar o efeito agudo do exercício físico contínuo e do exercício com restrição parcial do fluxo sanguíneo, ambos intradialítico, sobre a dinâmica da remoção de moléculas pequenas e médias em pacientes com insuficiência renal crônica.

Objetivo Específico:

• Avaliar o efeito do exercício físico intradialítico e do exercício com restrição de fluxo na eficiência da hemodiálise na remoção de moléculas pequenas: uréia, creatinina, potássio e fósforo.

• Avaliar o efeito do exercício físico intradialítico e do exercício com restrição de fluxo na eficiência da hemodiálise na remoção de moléculas médias: beta 2 microglobulina.

• Realizar uma curva temporal para quantificar a remoção das moléculas ao longo do período de diálise

UNIVERSIDADE CATÓLICA DE PELOTAS - UCPEL

Continuação do Parecer: 2.707.365

Avaliação dos Riscos e Benefícios:

Riscos: Há apenas pequenos riscos de hipotensão leve ou tontura advindo do exercício. Para isso terá um profissional habilitado que estará com o paciente durante todo o período da intervenção, observando os sinais vitais.

Benefícios:

os pacientes poderão realizar sessões de exercício durante a diálise e realizarão exames dos solutos. Caso comprovado o benefício do exercício e do exercício com restrição de fluxo sanguíneo, poderá ser um tratamento adjuvante para esta população potencializando os efeitos da hemodiálise.

Comentários e Considerações sobre a Pesquisa:

Adequado

Considerações sobre os Termos de apresentação obrigatória:

Apresentados

Conclusões ou Pendências e Lista de Inadequações:

Aprovar

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_948783.pdf	06/06/2018 14:39:20		Aceito
Recurso Anexado pelo Pesquisador	AutorizLocal.pdf	06/06/2018 14:33:25	Rafael Bueno Orcy	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.pdf	06/06/2018 14:18:36	Rafael Bueno Orcy	Aceito
Projeto Detalhado / Brochura Investigador	Atividade_fisica__renal_cronica.pdf	06/06/2018 13:57:39	Rafael Bueno Orcy	Aceito
Outros	local.pdf	26/06/2017 15:52:51	Rafael Bueno Orcy	Aceito
Outros	curriculoFranklin.pdf	23/06/2017 19:56:49	Rafael Bueno Orcy	Aceito
Outros	curriculojean.pdf	23/06/2017 19:52:04	Rafael Bueno Orcy	Aceito

Endereço: Rua Felix da Cunha, 412
Bairro: Centro **CEP:** 96.010-000
UF: RS **Município:** PELOTAS
Telefone: (53)2128-8404 **Fax:** (53)2128-8298 **E-mail:** cep@ucpel.tche.br

UNIVERSIDADE CATÓLICA DE PELOTAS - UCPEL

Continuação do Parecer: 2.707.365

Outros	CurriculoMaristela.pdf	23/06/2017 19:51:46	Rafael Bueno Orcy	Aceito
Outros	CurriculoRafael.pdf	23/06/2017 19:51:11	Rafael Bueno Orcy	Aceito
Outros	CurriculoGustavo.pdf	23/06/2017 19:50:49	Rafael Bueno Orcy	Aceito
Outros	instrumentoprontuario.pdf	23/06/2017 19:50:10	Rafael Bueno Orcy	Aceito
Declaração de Pesquisadores	cartaapresentacaoprojeto.pdf	23/06/2017 19:34:19	Rafael Bueno Orcy	Aceito
Folha de Rosto	folhaderosto.pdf	22/06/2017 21:15:25	Rafael Bueno Orcy	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

PELOTAS, 12 de Junho de 2018

Assinado por:
Luciana de Avila Quevedo
(Coordenador)

Anexo C

QUESTIONÁRIO SOCIODEMOGRÁFICO E CLÍNICO

QUESTIONÁRIO SOCIODEMOGRÁFICO E CLÍNICO

Número do Questionário: |_ _ _|

Data da avaliação: |_ _ / _ _ /_____ |

Data de nascimento: |_ _ / _ _ / _____ |

Sexo: (_) 0 – masculino (_) 1 – feminino

Estado civil: (_) 0 – solteiro (_) 1 – casado (_) 2 – divorciado (_) 3 – viúvo (_) 4 – vive com companheiro

Cidade onde reside: (_) 0 – Pelotas (_) 1 – outra

Profissão:

____

Recebe algum benefício, qual/quais?

____

Tipo de moradia: (_) 0 – própria (_) 1 – alugada (_) 2 – mora com familiares

Há quanto tempo faz hemodiálise _ _ anos e _ _ meses

Outras doenças: Hipertensão/ Diabetes/ Doença cardiovascular/ Doença Renal Policística____

Faz uso de medicações, quais?

____

Qual o seu grau de instrução?	
1	Analfabeto/ Fundamental I Incompleto
2	Fundamental I Completo/ Fundamental II Incompleto
3	Fundamental II Completo/ Ensino Médio Incompleto
4	Ensino médio completo/ Superior Incompleto
5	Superior completo

Itens de conforto	Quantos possui				
	0	1	2	3	4+
Carro de passeio exclusivo para uso particular					
Empregados mensalistas, que trabalham pelo menos 5 dias por semana					
Possui máquina de lavar roupa, excluindo tanquinho					
Quantos banheiros tem a sua casa					
Possui DVD, qualquer dispositivo que leia DVD, sem contar o do carro.					
Possui quantas geladeiras					
Possui quantos freezers, sem contar a geladeira duplex					
Possui computadores de mesa, laptops, notebook ou netbooks, desconsiderando tablets, palms ou smartphones					
Quantidade de lava louças					
Quantidade de fornos de micro-ondas					
Quantidade de motocicletas, desconsiderando as usadas exclusivamente para uso profissional					
Quantidade de maquinas secadoras de roupa, considerando lava e seca					

A água utilizada em sua casa é proveniente de?	
1	Rede geral de distribuição
2	Poço ou nascente
3	Outro meio

Considerando o trecho da rua da sua casa, você diria que a sua rua é:	
1	Asfaltada/ pavimentada
2	Terra/ cascalho