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Research Article

Analysis of the Efficacy and Safety of Exercise in Hemodialysis

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Abstract

Objectives: This project plans to conduct a randomized controlled trial to investigate whether hemodialysis patients can benefit from cycling during dialysis, and whether it can improve dialysis efficiency and safety.

Methods: One hundred and twenty-five dialysis patients undergoing regular hemodialysis (dialysis for more than 3 months, three times a week, each session lasting 4 hours, with blood flow set between 250 to 350 ml/min, and dialysate flow at 500 ml/min, with dialysate calcium concentration maintained between 1.25 to 1.5 mmol/L) were randomly assigned into three groups. Group A received intensive treatment, aiming for 70% of Maximal Heart Rate (HRmax), and participated in bed cycling exercise during each dialysis session; Group B received treatment with low-intensity exercise targeting 55% of HRR standards; Group C served as the control group undergoing normal dialysis procedures. Participants in the intervention groups exercised three times a week, with each session lasting between 30 to 60 minutes. The weight and blood pressure of all participants were recorded during each session, and fasting blood samples were collected every 3 months for biochemical analyses, including C-Reactive Protein (CRP), Hemoglobin (HGB), serum Intact Parathyroid Hormone (iPTH), ferritin, and urea nitrogen reduction rate. Additionally, blood pressure, dry weight compliance, KT/V, and hemoglobin status were calculated for all three groups. The incidence of serious infections such as pulmonary, urinary tract, and bloodstream infections, as well as the hospitalization rates, were also documented for each group.

Results: Following the intervention, intradialytic hypotension and URR in patients showed significant improvement compared to the control group, with statistically significant differences observed ($P<0.05$). Additionally, the incidence of complications and hospitalization rates markedly decreased, also exhibiting statistically significant differences ($P<0.05$). However, there were no statistically significant differences observed in the remaining indicators ($P>0.05$).

Conclusion: Cycling during dialysis can be beneficial for patients undergoing hemodialysis by enhancing its efficiency and stabilizing blood pressure, thus reducing the occurrence of dialysis hypotension. This practice facilitates adequate dialysis, improves physical function, enhances quality of life, and reduces or delays related complications. Furthermore, its occurrence and development carry economic benefits and social value.

Keywords: Hemodialysis cycling hemodialysis

Introduction

The prevalence of hemodialysis patients is rapidly increasing in my country, accompanied by prolonged survival periods. Nonetheless, disease progression, coupled with restricted physical activity and a high prevalence of cardiovascular and cerebrovascular diseases, contributes to the decline in patients' physical function and quality of life [1-4]. Widespread exercise intolerance exacerbates these challenges. Moreover, inactivity exacerbates the decline in physical function. While physical exercise yields numerous benefits in the general population [5,6], it remains uncertain whether similar effects are observed in hemodialysis patients. Consequently, this project aims to investigate the potential benefits of cycling exercise during dialysis for hemodialysis patients and assess its safety.

Recent advancements in dialysis treatment technology have significantly extended the life expectancy of hemodialysis patients. However, despite these advancements, individuals with chronic kidney disease often experience limited physical activity and a heightened risk of cardiovascular and cerebrovascular diseases, resulting in deteriorating physical fitness and quality of life [2-4]. Additionally, patients undergoing regular dialysis commonly suffer from fatigue, malnutrition, inflammatory reactions, anemia, and vitamin D deficiency, which directly impairs their exercise capacity and peripheral nerves, leading to exercise intolerance. Lack of physical activity further exacerbates declines in bodily function and cardiopulmonary health, impacting oxygen transport and metabolic capabilities. This reduction in oxygen delivery to peripheral skeletal muscles can result in disuse atrophy. Furthermore, factors such as accumulation of circulating toxins, fluid overload, electrolyte imbalances, and nutritional deficiencies contribute to a vicious cycle of both acute and chronic inflammation [7-10].

How to improve the physical condition of dialysis patients is a newly emerging area of research. Subjectively, the ability of these individuals to engage in physical activity is considered unstable, and completing daily tasks (e.g., work, leisure, and household chores) poses challenges. Their exercise capacity may be limited due to various factors including anemia, arteriosclerosis, increased blood volume, ventricular hypertrophy, systemic arterial hypertension, and physical inactivity. Musculoskeletal complications observed in ESRD patients may arise from alterations in calcium and phosphorus metabolism. Muscle atrophy leads to decreased strength, and regular physical exercise can mitigate these conditions.How to improve the physical condition of dialysis patients is a newly emerging area of research. Subjectively, the ability of these individuals to engage in physical activity is considered unstable, and completing daily tasks (e.g., work, leisure, and household chores) poses challenges. Their exercise capacity may be limited due to various factors including anemia, arteriosclerosis, increased blood volume, ventricular hypertrophy, systemic arterial hypertension, and physical inactivity [10-12]. Musculoskeletal complications observed in ESRD patients may arise from alterations in calcium and phosphorus metabolism. Muscle atrophy leads to decreased strength, and regular physical exercise can mitigate these conditions.

Physical exercise is widely recognized for its multitude of health benefits in the general population. Warburton D E R [13] conducted a comprehensive review of the existing literature, presenting a narrative review on the effects of regular physical activity on numerous chronic diseases, including cardiovascular disease, diabetes, cancer, hypertension, obesity, depression, and osteoporosis, demonstrating its efficacy in primary and secondary prevention of premature death. There exists a hierarchical linear relationship between physical activity and health status, with individuals engaging in higher levels of physical activity experiencing the lowest risk of disease. Consequently, the most substantial health improvements are observed among individuals with lower fitness levels who engage in physical activity. Regular exercise offers various advantages, such as enhancing immune function, improving cardiopulmonary function, regulating blood pressure, enhancing mood, reducing anxiety and depression, managing weight, decreasing cardiovascular risk factors, and maintaining musculoskeletal health. Similar benefits are observed in individuals undergoing dialysis [5,6]. Research has indicated [14,15] that exercise therapy can enhance hemodialysis efficiency and completeness. This mechanism may be attributed to increased blood flow in systemic tissues during exercise, acceleration of solute conversion in tissue cells, and enhanced solute clearance during dialysis. Additionally, exercise contributes to a decrease in solute rebound after dialysis by reducing the concentration gradient of solutes in each chamber. Furthermore, exercise improves oxidative stress and inflammatory status among dialysis patients, enhancing immune function [16]. By enhancing the elasticity of blood vessel walls and improving vasoconstriction and relaxation functions, exercise aids in blood pressure regulation [17], while promoting insulin secretion and glucagon consumption, thereby contributing to blood sugar control [18]. Numerous studies have demonstrated that aerobic exercise can modulate the release levels of interleukin IL-6 and interleukin IL-18, thereby improving the depressive symptoms of dialysis patients and enhancing their quality of life [19]. Knap B proposes that aerobic exercise, including resistance exercise, conducted by patients During Hemodialysis (HD), can enhance aerobic metabolism, expedite toxin removal, and improve dialysis efficiency [15,20].

Currently, Intradialysis Exercise (IDE) is widely recognized [14-22]. In comparison with hospital rehabilitation training and home exercise on non-dialysis days, Konstantinidou E [23] found that although exercise on non-dialysis days has been proven effective and safe, the high dropout rate from training in rehabilitation centers due to time constraints and transportation issues, and the inability to control exercise frequency and intensity during home training without supervision pose challenges. Consequently, IDE is more recommended for individuals with End-Stage Renal Disease (ESRD) facing time or transportation constraints. However, the efficacy of IDE remains inconclusive. This study examined Urea Clearance (UUR) before and after dialysis and found IDE to be effective compared to patients without IDE. Nevertheless, at varying exercise intensities, including moderate and low-intensity exercise (maximum heart rate HRmax of 55% and 70%, respectively), no significant difference was observed ($P>0.01$), suggesting that higher intensity IDE did not confer additional benefits on urea clearance. Similar results were obtained by Brown P D S in a previous study [24]. Additionally, this study observed that IDE reduced the frequency of intradialytic hypotension and maintained systolic blood pressure in patients experiencing intradialytic hypotension, while no similar effect was observed for intradialytic hypertension. Numerous studies have demonstrated that physical exercise can also alleviate anxiety and depression symptoms in dialysis patients [25,26], indicating its potential benefits for individuals with ESRD.This study reveals that intradialytic exercise significantly reduces post-dialysis urea nitrogen levels and increases UUR, thereby enhancing dialysis efficiency. The mechanism underlying this improvement involves increased oxygen consumption, accelerated metabolism, and enhanced clearance of creatinine during exercise. Consequently, intradialytic exercise emerges as an economical and effective intervention for patients in developed areas. Furthermore, it mitigates the likelihood of intradialytic hypotension, ameliorating symptoms in patients prone to this condition and averting hemodynamic instability, thus reducing the risk of cardiovascular and cerebrovascular events and enhancing dialysis safety. Notably, exercising within a specific intensity range (maximum heart rate HRmax of 55% and 70%, respectively) does not heighten the risk of serious infection or hospitalization frequency, and it aids in bolstering physical fitness and improving immunity [27]. However, it is essential to acknowledge that while this study observed changes in dry weight, blood pressure, Kt/V, and other biochemical markers (hemoglobin (HGB), homocysteine, albumin, C-Reactive Protein (CRP), serum Intact Parathyroid Hormone (iPTH)), these alterations did not reach statistical significance ($p<0.05$).

The Current Report is as Follows

General: A total of 125 patients were recruited from the blood purification center of our hospital for this study. Among them, 75 were males and 50 were females, with ages ranging from 25 to 60 years and disease durations spanning from 6 to 72 months.

- **Inclusion criteria:** Meet the diagnostic criteria for End-Stage Renal Disease (ESRD), with dialysis time >3 months; dialysis occurring 3 times a week, each session lasting 4 hours, with blood flow set at 250~350ml/min; dialysate flow at 500ml/min, and dialysate calcium concentration ranging from 1.25 1.5mmol/L, with sodium concentration between 135~145mmol/L.
- **Exclusion criteria:** Case exclusion criteria: ① Infection within 1 month before enrollment; ② Acute cardiovascular and cerebrovascular events, uncontrolled hypertension, and diabetes within 6 months before enrollment; ③ Use of hormones or immunosuppressants; ④ Diagnosis of malignancy, mental illness, or pregnancy; ⑤ Individuals with physical disabilities.

Teatment method: Approved by the Hospital Clinical Trial Ethics Committee (Approval number: 201926) and registered on the international RCT official website with the registration code ChiCTR2000029125: All patients signed an informed consent.

The random sequence generated by SPSS was divided into 3 groups [7-9]. Group A was the intensive treatment group (n=41) (70% of maximal heart rate, HRmax). Bed cycling exercise was added to each dialysis session. The main exercise intensity was based on the maximum heart Rate Reserve Percentage (HRR), with the implemented medium intensity set at 70% of the HRR standard. Group B was the treatment group (n=42) (70% of maximal heart rate, HRmax), and also added bed cycling exercise during each dialysis, with the implemented low intensity set at 55% of the HRR standard. Group C served as the control group with normal dialysis (n=42). Before starting exercise, each patient completed all physical tests and a physical activity questionnaire. They warmed up for 5 minutes before each exercise and cooled down for 5 minutes after exercise. Additionally, the exercise is performed during the first half of the dialysis session. The experimental group exercised up to three times a week during dialysis, with each exercise lasting between 30 and 60 minutes. During training, it is important to note that patients aged >50 years old should not have their heart rate exceed 120 beats/min during exercise. Once symptoms such as dizziness, headache, chest tightness, and pain occur, the exercise needs to be stopped immediately and observed. Patients are permitted to stop and rest midway or continue to a tolerable level, and their performance on the bicycle is summarized and recorded.

Provide nutritional support and symptomatic treatment during treatment. Regarding nutritional support: Dietary guidance for renal failure should include protein intake for hemodialysis patients at 1.0~1.2g (kg·d), while ensuring sufficient energy supply to meet the body's needs. Dialysis patients often suffer from depression, anxiety, insomnia, anorexia, and other discomforts, and are also at risk of complications such as hypertension, hyperglycemia, bone pain, hyperphosphatemia, and renal anemia. Targeted guidance and treatment should be given according to the patient's specific situation. Healthcare providers should choose appropriate drugs and auxiliary facilities to improve quality of life, strengthen care, and prevent various complications.

Observation Indicators: The weight, abdominal circumference, and blood pressure of the three groups of patients were recorded before and after each dialysis session. Fasting blood samples were drawn at baseline (0th month), 3rd month, and 6th month to assess various parameters including blood routine, homocysteine, albumin, biochemistry, blood lipids, C-Reactive Protein (CRP), ferritin, serum Intact Parathyroid Hormone (iPTH), and urea nitrogen decline rate. Additionally, measurements of blood pressure and dry weight compliance were recorded for each patient, along with calculations of URR and KT/V. Simultaneously, the incidence of serious infections such as pulmonary, urinary tract, and bloodstream infections, as well as the hospitalization rate, were documented for the three groups of patients. The observation period spanned 6 months.

Statistical Methods: SPSSPRO statistical software was used. Measurement data were expressed as mean ± standard deviation ($x\pm s$), and variables between groups were tested for normal distribution. If the overall distribution is normal, the t-test is used; if the distribution is skewed, the Mann-Whitney U test is used. Count data were analyzed using the chi-square test.

Result

item	figures
(Gender) Male: Female	1.27:1
Age (years)	46.55±12.30
Weight (kg)	57.61±11.44
Body surface area (kg/m^2)	1.57±4.01
Disease duration (months)	25.73±17.51
Smoking history	37
complication	
Diabetes	60
hypertension	97
Chronic ischemic heart disease	18
chronic heart failure	10
ESRD etiology	
Diabetes nephropathy	50
Glomerular disease	46
hypertension	12
Obstructive nephropathy	7
other	10
Hemoglobin (g/dl)	109.13±18.77
Pre dialysis creatinine (mmol/L)	900.11±15.15
Pre dialysis urea nitrogen (mmol/L)	26.91±7.12
Potassium (mmmol/L)	5.2±0.84
PTH（pg/L）	378.17±52.49
Calcium (mg/dl)	2.29±0.26
Phosphorus (mg/dl)	0.68±0.38
Albumin (g/dl)	38.37±3.90

Note: The values are expressed as mean ± standard deviation (x ± s).

Table 1: General information of patients before enrollment (n=125).

A total of 121 patients completed the entire trial this time (41 in Group A, 40 in Group B, and 40 in Group C), and 4 patients withdrew from the trial. Reasons for withdrawal included factors such as pulmonary infection (n = 2), bloodstream infection (n = 1), and voluntary discontinuation (n = 1). None of these reasons are related to the sport itself. During exercise, some patients complain of body pain in the legs (especially knee joints), cramps, fatigue, and weakness, but this does not affect the exercise process. After 6 months of intradialytic exercise, several changes were noted compared to baseline data (0 months). First, the equipment used for exercise is low-cost, efficient, space-saving, and easy to manage. Additionally, decompensation of heart failure, especially hypotension, can be prevented by exercising within half an hour before hemodialysis. Furthermore, there were no common dangerous adverse events caused by exercise, including musculoskeletal injuries, serious cardiovascular and cerebrovascular complications such as ischemic heart disease, acute heart failure, and arrhythmia. Only mild discomfort symptoms of physical pain in the legs were reported. Through intradialysis exercise, patients generally report that it is helpful in improving physical function, increasing muscle strength, and enhancing activity tolerance to a certain extent.

In this study, intradialytic hypotension (IDH) was defined as a minimal intradialytic systolic blood pressure (<90 mmHg, nadir 90) or any hypotension-related symptoms requiring nursing intervention. The occurrence of IDH was checked during every dialysis session, and the total number of IDH episodes was recorded at the 0, 3, and 6-month time points.

	Before penetration BUN	After penetration BUN	URR	KT/V	Dry weight	IDH (Number of cases)	IDH (probability)
0□□	26.62±7.12	8.16±6.7	72.91±7.89	1.38±2.89	57.11±11.21	7	5.8
3□□	26.39±7.15	7.28±5.23	73.84±8.80	1.37±2.80	57.62±11.38	4	0.09
6□□	26.84±6.53	7.19±5.91	73.31±7.29	1.26±2.29	57.47±11.73	3	0.07
P□	>0.05	<0.05	<0.05	>0.01	>0.01		<0.01

Note: BUN is the abbreviation for urea nitrogen (unit: mmol/L). URR stands for urea reduction rate or urea clearance rate, calculated as URR = (urea nitrogen before dialysis - urea nitrogen after dialysis)/urea nitrogen before dialysis. The KT/V value refers to KT, which denotes the ratio of the urea removal amount to the volume of the dialyzer within a certain dialysis time. The formula for Kt/V is given by $Kt/V= -In(R-0.008t+4-3.5R)*UF/W$, where K represents the clearance rate, t denotes the treatment time, V stands for the urea distribution volume, R signifies the ratio of urea nitrogen before dialysis to after dialysis, UF represents the ultrafiltration rate (l/s), and W represents the dry body weight (kg). Values are expressed as mean ± standard deviation (x ± s).

Table 2 Comparison of numerical values before and after dialysis among patients in Group A (n=41)

The BUN and URR of patients in group A exhibited a downward trend at 0, 3, and 6 months after dialysis, which was statistically significant (P<0.05). Similarly, the probability of IDT attack decreased significantly at 0, 3, and 6 months, with a decreasing trend that was statistically significant (P<0.01).

	Before penetration BUN	After penetration BUN	URR	KT/V	Dry weight	IDH(Number of cases)	IDH(probability)
0□□	27.58±8.21	8.87±6.7	73.22±8.80	1.22±2.89	58.89±13.54	6	1.5
3□□	27.49±8.45	8.36±5.23	74.51±8.77	1.24±2.42	58.58±13.41	3	0.07
6□□	27.79±7.584	7.89±5.91	74.38±7.93	1.26±2.63	58.72±13.75	3	0.07
P□	＞0.05	＜0.05	＜0.05	＞0.01	＞0.01		＜0.01

Table 3: Comparison of numerical values before and after dialysis for patients in Group B (n=40).

In group B patients, both BUN and URR exhibited a downward trend at 0, 3, and 6 months after dialysis, which was statistically significant (P<0.05). Similarly, the probability of IDT attack decreased at 0, 3, and 6 months, showing a decreasing trend with statistical significance (P<0.01).

	systolic pressure			diastolic pressure		
	Beafore During After			Beafore During After		
Group A	156.31±10.37	130.45±9.29	148.87±9.24	91.40±7.51	73.04±6.56	80.23±6.09
Group B	154.24±10.47	124.32±9.23	145.33±10.23	88.81±7.54	72.81±6.64	85.83±6.54
Group C	153.24±11.01	122.33±10.30	146.65±12.22	87.91±8.33	70.61±6.81	84.28±7.70
P	＞0.05	＞0.05	＞0.05	＞0.05	＞0.05	＞0.05

Notes:1mmHg□0.133 3kPa

Table 4: For the comparison of blood pressure levels among the three groups of patients before, during, and after dialysis in the 6th month (mean ± standard deviation, mmHg).

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As shown in Table 4, there was no statistically significant difference in blood pressure among the three groups of patients before, during, and after dialysis at the 6th month (P>0.05).

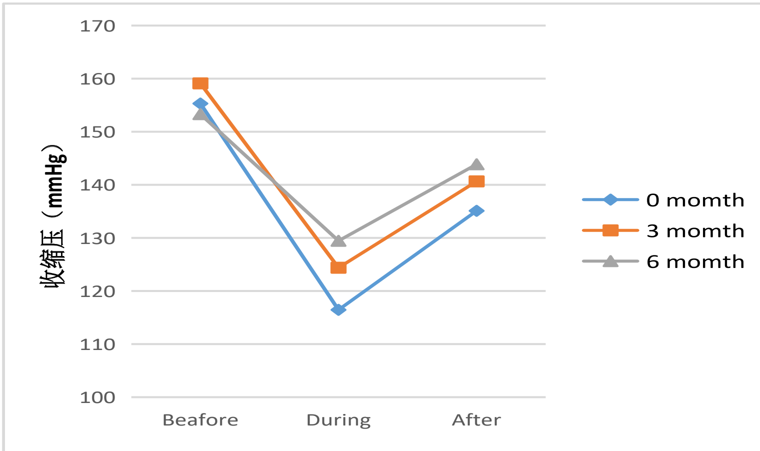

Figure 1: Comparison of average systolic blood pressure of patients in Group A from 0 to 6 months.

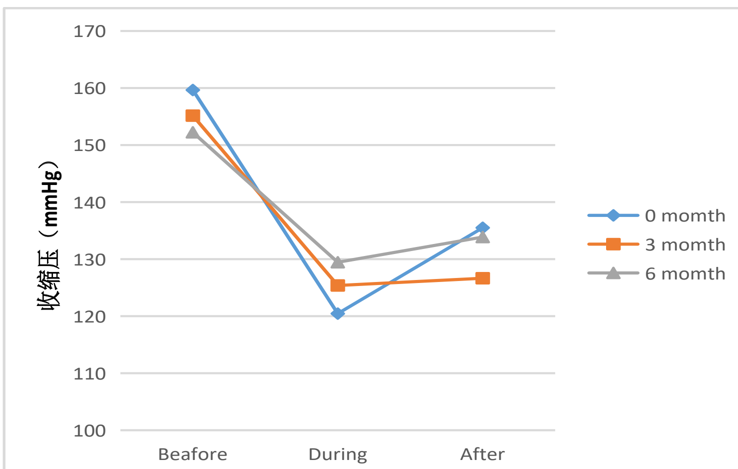

Figure 2: Comparison of average systolic blood pressure of patients in group B from 0 to 6 months.

	pulmonary infection	Urinary tract infection	hematogenous infection	hospitalization rate
Group A	0	0	0	0
Group B	1	0	0	2.5%
Group C	1	0	1	5%

Table 5: Incidence rates of infection and hospitalization rates among the three groups of patients.

This study also compared Hemoglobin (HGB), homocysteine, albumin, C-Reactive Protein (CRP), and serum Intact Parathyroid Hormone (iPTH) levels between groups both before and after the test, and no statistically significant differences were found (P >0.05). However, this article still has shortcomings. Firstly, intradialytic exercise may not be suitable for all dialysis patients, particularly frail individuals who cannot tolerate exercise, especially those with underlying heart disease. Additionally, the efficacy of exercise on non-dialysis days remains to be explored for comparable outcomes. Furthermore, while this study focused on bed cycling as a form of aerobic exercise, there exist other aerobic and anaerobic exercises that warrant investigation in future research endeavors.

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Conflict of Interest: No potential conflict of interest was reported by the authors.

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