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Combination of Intradialytic Leg Cycling & Upper Limb Range of Motion Exercises on Improving Dialysis Adequacy and Solutes Removal

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ABSTRACT

Background: Dialysis adequacy is an important survival indicator in patients with chronic hemodialysis (HD). Intradialytic exercise in end-stage renal disease (ESRD) patients improve dialysis adequacy.

Objective: This study aimed to evaluate the effect of 2 months combining of intradialytic leg cycling and upper limb range of motion exercises (ROM) on dialysis efficiency for patients with ESRD.

Patients and Methods: Forty six hemodialysis patients of both sexes with ESRD participated in the study. They were randomly assigned into two groups (A & B). Group (A) included 11 males and 12 females where they received 3 sessions per week for 2 months of intradialytic leg cycling and upper limb range of motion exercise. Group (B) included 12 males and 11 females who received only upper limb range of motion exercise. Their mean age were 60.76 ± 3.37 and 60.82 ± 3.41 years old for group A & B respectively.

Results: There was a significant decrease in urea level, K^+ and phosphorus in group A post-treatment compared to their pre-treatment ($p < 0.01$), while there was a significant increase in K t/V, URR and creatinine clearance post-treatment compared to pretreatment ($p < 0.001$). There was no significant change in urea level, URR, creatinine clearance and K^+ in group B ($p > 0.05$), while there was a significant increase in K t/V and a significant decrease in phosphorus post-treatment compared to pre-treatment ($p < 0.01$).

Conclusion: Combination of Intradialytic leg cycling and upper limb range of motion exercises had a significant role in increasing dialysis adequacy (URR & K t/V), creatinine reduction ratio and decreasing phosphorus and potassium for ESRD patients on maintenance hemodialysis.

Keywords: Intradialytic exercise, Cycling exercise, Range of motion, Hemodialysis, ESRD, Chronic kidney disease.

INTRODUCTION

Chronic kidney disease (CKD) is a clinical syndrome secondary to the definitive change in function and/or structure of the kidney. It affects more than 10% of the world population. ESRD is final stage of CKD that is characterized by its irreversibility and slow and progressive evolution and it exits in 8-16% of the population worldwide **Huang *et al.*** [1]. Hemodialysis (HD) represents the main mode for the treatment of chronic kidney disease stage 5 [2]. As replaced part of kidney's function in order to prolong the ESRD patients' survival time to remove waste and extra water from blood [3]**.** Intradialytic aerobic exercise for lower limb in HD patient by cycle-ergometer & ROM for upper limb increase the rate of toxins removal due to vasodilation with increase muscle blood flow and opening of the capillary surface area associated with increased flux of urea and other toxic agents [4, 5]. Intradialytic exercise (IDE) performed during HD has been accepted as a beneficial exercise intervention due to its feasibility and improvements in physical performance and dialysis efficacy [6].

This study was conducted to determine the effect of combining intradialytic leg cycling and upper limb range of motion exercises on dialysis adequacy and solutes removal (creatinine, phosphorus, potassium and urea). According to our knowledge there are limited studies such that.

PATIENTS AND METHODS

Forty six hemodialysis patients of both sexes with ESRD participated in the study. Their ages ranged from 55 to 65 years old. They were randomly assigned into two groups (A & B). Group (A) included 11 males and 12 females who received 3 sessions per week for 2 months of intradialytic lower extremities cycling and upper limb range of motion exercise, while group (B) that included 12 males and 11 females received only upper limb range of motion exercise. All patients in both groups were assessed through blood urea, creatinine, phosphorus, potassium lab tests, urea reduction ratio (URR) and Kt/V dialysis efficiency.

Sample size:

Calculation is performed using G*Power statistical software (version 3.1.9.2; Universitat Kiel, Germany) based on data of Sp Kt/V derived from **Huang *et al.*** [1] and revealed that the required size of each group is 23. The calculations were made using $\alpha = 0.05$, $\beta = 0.2$ and effect size = 0.85 and allocation ratio N2/N1=1.

Inclusion criteria:

Patient's age ranged from 55 to 65 years old from both genders. Patient's body mass index (BMI) ranged from 25 to 34.9. Patients diagnosed with ESRD on hemodialysis more than 3 month. All patients have a vascular access through arteriovenous fistula. They are medically and psychologically stable.

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Exclusion criteria:

Uncontrolled arterial hypertension [7]. Severe uncontrolled diabetes. Acute myocardial infarction or unstable angina within the past 12 months. Current heart disease, severe COPD or liver disease. Acute infectious or other inflammatory illness. Inability to comprehend and to follow instructions (mental disability- speech problems). Musculoskeletal disorder (paralysis-amputation in one of lower limb).

Procedure:

Written sheet was taken (name, age, address and associated diseases), vital signs measurement (blood pressure, temperature - pulse &respiratory rate), Measurement of weight and height to record body mass index (weight Kg/ height m^2). Detect any limitation of ROM for free arm due to muscle spasm or stiff. Joint. Laboratory investigations included blood urea (BU), serum creatinine and measurement of the blood level of potassium and phosphorus. Measuring dialysis adequacy (URR-K t/V).

Treatment procedure:

All subjects were instructed to keep the same scheme of training throughout the trial. Subjects were familiar with the equipment and the appropriate exercise technique before starting the study. Subjects were assigned randomly as block randomization scheme was created using a computer generated random to allocate subjects to one of the two treatment groups.

Patients in group A:

They performed 30 minutes intradialytic (cycling exercise for lower limbs by cycle ergometer – ROM exercise for free arm). The session was done as the follows: Aerobic leg cycling exercises Warm-up phase, 5 minutes low intensity at low speed, Active phase for 20 minutes at 9 – 11 Borg scale. Cooling down phase for 5 minutes cycling exercise for lower limbs at low speed with cooling down to prevent pooling of blood and orthostatic hypotension [8]. At the same time, they did ROM of exercises for free arm, which included close and open the hand, rotating wrist (clockwise and counter-clockwise), wrist flexion and extension and elbow joint full flexion and extension. The exercise included 3 sets every set from 8-10 repetition [3].

Patient in group B:

They did ROM of exercise for free arm, which included (close and open the hand), rotating wrist (clockwise and counter-clockwise), wrist flexion and extension and elbow joint flexion & extension).

Duration: Each training session consisted of 30 minutes at the first 2 hours from the dialysis session.

Frequency: 3 sessions per week for 8 weeks.

Mode: Continuous cycling leg pedaling exercise in semi-supine position using leg ergometer and ROM exercise for free arm (moves slowly, gently, and smoothly). Avoid fast or jerky motions, stop if patient feel pain. **Criteria for interruption** of the exercise include intense physical exhaustion, (articular, retrosternal and muscular) pain, nausea, dizziness, malaise, fatigue and muscle cramp [9].

Intensity: The prescription of exercise intensity is based on:

1) Borg's Perceived Exertion Scale, which corresponds to an exercise from fairly light (9) to moderate intensity (11) in this scale.
2) Heart rate according to Karvonen formula (Target heart rate from 40% - 60% of MHR)
   THR Karvonen = (HRmax - HRrest) X k + HRrest. HRmax = 220-age.

   Where k is constant number of exercise intensity and is the coefficient determined by K= 0.24. In this study apply Karvonen formula only to patients not undergoing beta-blocker therapy [10].

Ethical consent:

This study was approved by The Research Ethics Committee, Cairo University (No. P. T.REC/012/003338). Participation was voluntary. Each participant signed written informed consent prior to be enrolled in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Unpaired t-test was used for comparison of subject characteristics between groups. Chi- square test was used for comparison of sex distribution between groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levine's test for homogeneity of variances was used to ensure the homogeneity between groups. Mixed design (MANOVA) was used to compare within and between groups effects on urea level, creatinine clearance, K^+, phosphorus, K t/V and URR. Post-hoc tests and the Bonferroni correction were carried out for subsequent multiple comparison. The level of significance for all statistical tests was set at $p \leq 0.05$. All statistical analysis was conducted through the statistical package for social sciences (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

RESULTS

Demographic Data:

Table (1) showed the subject characteristics of group A and B. There was no significant difference between groups in the mean age, weight, height, BMI and duration of illness ($p > 0.05$). Also, there was no significant difference in the distribution of sex between groups ($p > 0.05$).

Table (1): Basic characteristics of participants

	Group A	Group B	p-value
	Mean ± SD	Mean ± SD	
Age (years)	60.76 ± 3.37	60.82 ± 3.41	0.94
Weight (kg)	81.26 ± 14.36	80.33 ± 13.46	0.82
Height (cm)	163.82 ± 6.82	164.78 ± 6.88	0.63
BMI (kg/m²)	30.21 ± 3.35	29.39 ± 3.15	0.39
Years of dialysis	2.1 ± 0.72	2.28 ± 0.63	0.35
Sex			
Females	12 (52%)	11 (48%)	0.76
Males	11 (48%)	12 (52%)	

Effect of treatment on urea level, creatinine clearance, K^+, phosphorus, Kt/V and URR:

Mixed MANOVA revealed that there was a significant interaction of treatment and time ($F = 3.93$, $p = 0.004$). There was a significant main effect of time ($F = 18.78$, $p = 0.001$). There was no significant main effect of treatment ($F = 0.51$, $p = 0.79$).

Within group comparison:

There was a significant decrease in urea level, K^+ and phosphorus in the group A post treatment compared to pre-treatment ($p < 0.01$), while there was a significant increase in K t/V, URR and creatinine clearance post-treatment compared with pre-treatment ($p < 0.001$).

There was no significant change in urea level, URR, creatinine clearance and K^+ in group B ($p > 0.05$), while there was a significant increase in K t/V and a significant decrease in phosphorus post treatment compared to pretreatment ($p < 0.01$) (Table 2-3).

Between groups' comparison:

There was no significant difference between groups pre-treatment ($p > 0.05$). There was a significant increase in K t/V, URR and creatinine clearance and a significant decrease in K^+ of group A compared to group B post-treatment ($p < 0.01$). However, there was no significant difference in urea and phosphorus ($p > 0.05$). (Table 2-3)

Table (2): Mean urea, Kt/V and URR pre and post treatment of the group A and B

	Pre	Post	MD	% of change	p value
	Mean ± SD	Mean ± SD			
Urea (mg/dl)					
Group A	55.39 ± 7.79	42.61 ± 1.49	12.78	23.07	0.001
Group B	51.21 ± 3.63	48.82 ± 5.26	2.39	4.67	0.51
Mean difference	4.18	-6.21			
	p = 0.5	***p = 0.12***			
Kt/V					
Group A	1.09 ± 0.14	1.31 ± 0.13	-0.22	20.18	0.001
Group B	1.1 ± 0.24	1.18 ± 0.25	-0.08	7.27	0.006
Mean difference	-0.01	0.13			
	p = 0.88	***p = 0.004***			
URR (%)					
Group A	60.02 ± 4.75	66.96 ± 3.72	-6.94	11.56	0.001
Group B	60.77 ± 8.11	62.01 ± 7.08	-1.24	2.04	0.17
Mean difference	-0.75	4.95			
	p = 0.71	***p = 0.005***			

Table (3): Mean creatinine clearance, K^+ and phosphorus pre and post-treatment of the group A and B

	Pre	Post	MD	% of change	p value
	Mean ± SD	Mean ± SD			
Creatinine clearance (%)					
Group A	53.26 ± 6.77	60.03 ± 5.21	-6.77	12.71	0.001
Group B	53.22 ± 10.98	55.26 ± 6.98	-2.04	3.83	0.21
Mean difference	0.04	4.77			
	p = 0.98	***p = 0.01***			
K^+ (mmol/L)					
Group A	3.98 ± 0.54	3.62 ± 0.34	0.36	9.05	0.001
Group B	3.94 ± 0.38	3.91 ± 0.38	0.03	0.76	0.69
Mean difference	0.04	-0.29			
	p = 0.78	***p = 0.001***			
Phosphorus (mg/dl)					
Group A	5.39 ± 1.41	4 .7 ± 0.28	0.69	12.8	0.003
Group B	5.46 ± 1.55	4.44 ± 0.18	1.02	18.68	0.001
Mean difference	-0.07	0.26			
	p = 0.88	***p = 0.48***			

DISCUSSION

The current study was done to draw the effect of combining intradialytic lower extremities cycling & upper limb range of motion exercise in the same time of session on dialysis adequacy, blood urea, creatinine, phosphorus and potassium among patients on maintenance hemodialysis (MHD). Intradialytic leg cycling exercise was performed using cycle ergometer.

Forty six adult patients of both sexes with age ranged from 55 to 65 years old who didn't receive any physical therapy program before participating in the study, subjects were selected from hemodialysis unit of Al-Galaa Military Hospital, Cairo, Egypt. They were randomly assigned into two groups of equal numbers group (A and B). **Group (A**) included 23 patient (11 males 12 females) who followed a program of intradialytic leg cycling and upper limb range of motion exercise for free arm 3 times per week for 8 weeks and **Group (B)** included 23 patient (12 males 11 females) who received upper limb range of motion exercise during the same period.

Intradialytic leg cycling exercise was made on moderate **intensity** based on Borg's perceived exertion scale that represented nearly a score ranged from 9 (light) to 11 (moderate) intensity [11].

Primary outcomes: Pre- and post-measuring blood urea, creatinine, potassium, phosphorus (through virtoz (350-450) dry analysis system) and dialysis efficiency (URR – K t/v) were performed.

Secondary outcome: Short form health survey (QoL SF-36 and sleep scale) were applied for each patient in the 2 groups.

The result of study showed that there was a significant increase (p=0.0001) by percent of change within group (A) as follows: dialysis adequacy (Kt/V) by 20.18%, URR by 11.56%, creatinine reduction ratio by 12.71%, while there was significant decrease in potassium by 9.05% and phosphorus by 12.8%. Regarding group (B), there was significant increase (p=0.01) in Kt/V by 7.27% and significant decrease in phosphorus by 18.68%, while there was no significant difference in URR, K^+, creatinine reduction ratio and urea level.

As shown by the result of this study that intradialytic leg cycling when added to upper limb ROM exercise for 8 weeks improved significantly post treatment dialytic adequacy (Kt/V) in group (A) compared to group (B). This agrees with **Ferreira *et al.*** [4] who concluded in their systemic review of 23 studies that intradialytic exercise for 4-16 weeks showed change of Kt/V where there was increase by 11% at end of 4 weeks &19% at end of 16 weeks. Similarly A recent study by **Bogataj *et al.*** [6] where they conducted the first functional exercise training before each HD session with additional intradialytic cycling exercise in the first 8 weeks and demonstrated a significant increase of dialysis adequacy from 0.15 to 0.24 mean difference. Also, this was revealed by **Huang *et al.*** [13] who investigated 24 weeks combined exercise (leg cycling-resistance) that was evaluated every 4 weeks. They showed gradual improvement in Kt/V, which improved QoL mainly in physical health. In addition, **Cho *et al.*** [14] conducted 8 week of intradialytic ROM exercise for upper & lower limb 15 min/day with low intensity. They found that the efficacy of dialysis (Kt/V) was increased at the end of first month by 38 % (P=0.001) with increase in URR by 11%. **Kirkman *et al.*** [15] conducted a systematic review that include 7 studies with intradialytic cycling as common modality of exercise. They showed a statistically significant increase of phosphate and potassium clearance. Moreover, a study by **Hung *et al.*** [1] where they investigated 24 weeks combined exercise (leg cycling-resistance) that was evaluated every 4 weeks. The exercise was divided into 2 stages: first stage consisted of 20 min aerobic cycling and 10 min resistance ex, then second stage that was consisted of 15 min AE and 10 min RE. They showed gradual improvement in Kt/V. **Salhab *et al.*** [5] had 12 studies 5 of them showed that IDE had no significant effect on Kt/V.

Similar with this study, **Al Rashedi *et al.*** [8] showed no significant difference in urea due to inadequate nutrition rather than sufficient dialytic urea removal. Subsequently IDE did not affect urea and creatinine clearance. Parallel to this study, **Pellizzaro *et al.*** [7] reported that receiving intradialytic ROM exercise and tai chi showed that there was significant effect on increasing dialysis adequacy after the intervention (1.67-1.73) and between groups. Results of **Mohseni *et al.*** [16] the study group performed ROM intradialytic exercise and showed that, there were no significant changes in serum urea between groups and there was no significant changes in creatinine reduction. Also, **Huang *et al.*** [13] conducted exercise training that consisted of aerobic-resistance-combined training for minimum 8 week. They showed that exercise training did not affect urea clearance and dialysis adequacy.

Secondary outcomes: MHD patients had very low daily physical activity (DPA), poor quality of life (QoL) and sleep quality (SQ) that could be improved with intradialytic exercise. **Yabe *et al.*** [17] in their study revealed improving sleep quality where some patients mentioned that their sleep periods increased from 3 h to 5h. With regard to improvement of QoL, many patients in group (A) reported changing in their functional status (climbing stairs from 5 to 8 and walking outside the house large distance than before the exercise).

In the light of this study, combining the two types of exercise together helped in increasing dialysis adequacy (Kt/V and URR) and creatinine reduction ratio with significant decrease of potassium and phosphorus clearance.

CONCLUSION

We concluded that combination of the intradialytic leg cycling & ROM exercises when performed at the same time in a session might be suggested as a complementary intervention in the treatment of patients on HD, contributing by increase the blood flow to improve dialysis adequacy (K t/V and URR) and solute removal (urea, creatinine, phosphorus and potassium).

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