

Effects of Intradialytic Aerobic Training on Sleep Quality in Hemodialysis Patients

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Introduction. Sleep disorders are common in hemodialysis patients. They can affect their quality of life. The purpose of this study was to evaluate the effects of aerobic training on sleep quality, inflammatory status, and serum leptin levels in hemodialysis patients.

Materials and Methods. Twenty-eight men in the age range of 28 to 74 years who were on maintenance hemodialysis and had sleep problems were enrolled in this study. They were randomly assigned into control and training groups (14 patients in each group). Patients in the training group performed a 10- to 30-minute stationary cycling, 3 times a week, during the 1st two hours of every dialysis session, for 8 weeks. The Pittsburgh Sleep Quality Index and the Baecke questionnaire on physical activity were filled out for all participants. To assess serum leptin and C-reactive protein levels, blood samples were drawn before the beginning and at the end of the eighth week.

Results. At the end of the study, serum leptin and C-reactive protein levels were significantly reduced ($P < .001$ and $P < .001$, respectively). Furthermore, the Pittsburgh Sleep Quality Index scores of the training group declined significantly after 8 weeks ($P < .001$). There was a positive correlation between sleep quality and serum levels of leptin and C-reactive protein ($P = .03$ and $P = .04$, respectively).

Conclusions. Aerobic exercise with moderate intensity during the first two hours of a dialysis session could improve sleep quality and inflammatory status of hemodialysis patients, which predicts morbidity, mortality, and quality of life. However, additional research is needed to confirm these effects.

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INTRODUCTION

Sleep-related complaints are prevalent in end-stage renal disease (ESRD) patients, including insomnia, delayed sleep onset, frequent arousals, and apnea. They may be attributed to the dialysis-induced cytokine production, the cooling mechanism activation that follows rising body temperature, disequilibrium syndrome, and paradoxical acidosis.¹⁻³ Early identification of

sleep disturbances, specifically sleep-disordered breathing is important to give its association with cardiovascular morbidity.^{4,5}

Inflammatory cytokines and leptin have incriminated in the pathogenesis of daytime sleepiness associated with sleep-disordered breathing.^{6,7} Leptin is a small peptide hormone mainly produced by adipocytes (white fat cells). It acts on the hypothalamus to reduce appetite, and

its circulating level reflects the amount of body fat.^{8,9} Leptin is freely filtered by the glomeruli, and perhaps it is taken up by the proximal tubule.⁸ Despite a low body fat composition, dialysis patients have elevated serum leptin levels due to reduced glomerular filtration rate and increased secretion of leptin in a uremic milieu.^{7,9} On the other hand, ESRD patients have a mild chronic inflammation which is attributed to decreased cytokine excretion, uremia, acidosis, oxidative stress, bio-incompatibility of dialyzer membrane, and frequent episodes of infections.^{10,11} Inflammation stimulates further leptin secretion and leptin per se increases production of pro-inflammatory cytokines.¹²

Patients with ESRD have diminished physical activity, which is associated with increased risk of cardiovascular diseases. Exercise improves hypertension, endothelial dysfunction, insulin resistance, dyslipidemia, inflammation, and oxidative stress in this population.¹³ Thus, it is postulated that exercise may have a positive influence on the sleep quality of hemodialysis patients. Aerobic exercise is an exercise that improves oxygen consumption by the body. There are many types of aerobic exercise, which exert useful effects by performing them at the moderate levels of intensity for extended periods of time.¹⁴ Physical exercise has beneficial effects on functional capacity, quality of life, cardiovascular risk factors, anemia, serum lipid levels, endothelial function, inflammation, type 2 diabetes mellitus, and psychosocial problems in ESRD patients.¹⁵ On the other hand, exercise capacity and physical performance of ESRD patients are severely impaired, which can be ameliorated by exercise training.^{16,17} This study was carried out to determine the effects of intradialytic aerobic training on sleep quality, serum leptin, and inflammatory status, which is reflected by serum C-reactive protein (CRP) levels.

MATERIALS AND METHODS

This is a descriptive cross-sectional case control study that was performed in a hemodialysis unit in Tehran, Iran, in 2009. Of 65 patients who were on conventional maintenance hemodialysis for 9 hours to 12 hours per week, 36 (55%) with sleep disturbances (in regular sleeping time at night) volunteered to participate in this study. Of the 36 volunteered patients, 28 men were enrolled (all women refused to participate). All participants were

informed of the study purposes and signed a consent form. The studied patients had to meet the following inclusion criteria: maintenance hemodialysis more than 3 months, age higher than 20 years, and good compliance with dialysis treatment (not missing more than 2 dialysis sessions in the prior month). The exclusion criteria were as follows: presence of active infection or inflammation, autoimmune disorders, malignancy, presence of psychiatric diseases, severe musculoskeletal disorders, poor controlled diabetes, uncontrolled heart failure or pulmonary diseases, hospitalization during the prior month, using drugs that influence serum cytokines levels, vascular access in the lower extremity, and a body mass index (BMI) higher than 25 kg/m².

The participants were randomly divided into the training group and the control group (n = 14 in each group). The Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality. It has been developed to measure sleep quality during the previous month and to discriminate between good and poor sleepers. Sleep quality is a complex phenomenon that involves several dimensions, each of which is covered by the PSQI. The covered domains include subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction due to sleepiness. The PSQI is composed of 19 self-rated questions. The self-administered scale contains 15 multiple-choice items that inquire about frequency of sleep disturbances and subjective sleep quality and 4 written items that inquire about typical bedtime, time to wake up, sleep latency, and sleep duration. All items are brief and easy for adolescents and adults to understand. The range of each component score is from zero (no difficulty) to 3 (severe difficulty). The component scores are summed to obtain a global score (range, 0 to 21). A PSQI global score of 5 and higher is considered to be suggestive of significant sleep disturbance.¹⁸ The global PSQI score was calculated at baseline and at the end of the study (after the 8th week).

Participants in the training group were assigned to perform a regular aerobic training which consisted of 5 minutes of warm-up and 10 to 30 minutes of stationary cycling (Medi-Bike Medical Exercise Peddler 3000, Medi-Bike, Taiwan; Figure). They cycled during the 1st two hours of each dialysis session (3 sessions per week) in a recumbent position



Medi-Bike Medical Exercise Peddler 3000.

for 3 weeks. According to the primary results of the Baecke questionnaire on participants' physical activities at baseline, patients were asked to cycle at an intensity of 12 to 15 of 20 at the rate of perceived exertion of Borg scale, so that intensity involved 65% to 85% of an individual's maximal capacity, a level at which cardiovascular health can be obtained.

Blood pressure and heart rate of the participants were monitored each 5 minutes, during the exercise. Fasting blood samples were obtained from the patients before midweek dialysis session at baseline and after the 8th week. Serum leptin levels (reference range, 2 ng/mL to 6 ng/mL) were assayed by an enzyme-linked immunosorbent assay. Serum CRP levels were measured by turbidometric technique (reference range, < 10 mg/L).

All data analyses were carried out using the SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc, Chicago, Ill, USA). The Kolmogorov-Smirnov test, *t* test, and Pearson correlation test were used for test of normal distribution, between-group comparisons, and test of associations, respectively. Continuous variables were shown as mean \pm standard deviation, if normally distributed. A *P* less than .05 was considered significant.

RESULTS

The age range of the training and control groups were from 28 to 74 years and 32 to 74 years, respectively. Diabetes mellitus and hypertension were the most frequent underlying diseases. The participants' characteristics are shown in Table 1.

Serum leptin and CRP levels significantly decreased after 8 weeks of the aerobic training course in the training group ($P < .001$ and $P < .001$, respectively), while such alterations were not observed in the control group. In addition, sleep quality improved and the PSQI scores declined in the training group at the end of the study course ($P < .001$), but not in the control group. Table 2 illustrates the details of these alterations in the two studied groups. Each of serum leptin and CRP levels had a positive correlation with sleep

Table 1. Demographic Data of Patients With and Without Intradialytic Training

Parameter	Training Group A	Control Group B	<i>P</i>
Body mass index, kg/m ²	02.98 \pm 22.71	02.18 \pm 22.30	.10
Age, y	21.06 \pm 50.71	19.40 \pm 53.00	.08
Hemodialysis duration, mo	07.61 \pm 25.71	15.44 \pm 24.86	.95
Underlying disease, %			
Diabetes mellitus	40	40	
Hypertension	40	40	
Renal disease	20	20	.10

Table 2. Serum Leptin, C-Reactive Protein (CRP), and Pittsburgh Sleep Quality Index (PSQI) Score at Baseline and After 8 Weeks

Parameter	Baseline	End of Study	Mean Difference	<i>P</i>
Serum CRP, mg/L				
Training group	5.55 \pm 2.54	0.93 \pm 0.66	4.62 \pm 1.96	< .001
Control group	4.05 \pm 3.97	4.10 \pm 03.90	0.88 \pm 0.05	.07
Serum leptin, ng/mL				
Training group	25.60 \pm 11.08	20.50 \pm 10.70	5.10 \pm 1.87	< .001
Control group	25.90 \pm 11.73	33.47 \pm 11.12	-7.57 \pm 1.44	< .001
PSQI score				
Training group	12.14 \pm 3.89	6.29 \pm 2.92	5.85 \pm 2.61	< .001
Control group	11.00 \pm 3.51	12.00 \pm 03.78	-1.00 \pm 1.00	.04

quality scores ($P = .03$, $r = 0.58$ and $P = .04$, $r = 0.55$; respectively).

DISCUSSION

Many studies of aerobic training in different levels of intensity have been performed among hemodialysis patients. However, few studies have been focused on exercise effects on inflammatory markers, and some revealed a significant reduction of inflammation after training programs.¹⁹ Regarding the relation between the inflammation and serum leptin levels also their roles in sleep disturbances of hemodialysis patients, we showed that exercise might have a beneficial effect on sleep quality in hemodialysis patients, an effect that must be further investigated. In a similar study, Sakkas and colleagues reported that sleep quality and functional capacity are closely related in hemodialysis patients and improvement in exercise capacity has been also related to the improved sleep quality and quantity.²⁰ It is possible that exercise can improve solute removal during dialysis by increasing blood flow to the skeletal muscles, which leads to greater efflux of uremic toxins into the vascular compartment where they can be removed.²¹⁻²³ However, these benefits must be balanced by the possibility of reduced exercise tolerance during dialysis due to fluid and electrolyte shifts and the possibility that exercise could exacerbate dialysis-associated hypotension. Nevertheless, the 30-minute moderate-intensity aerobic activity relative to an individual's level of fitness rather than on an absolute scale is well tolerated during the first two hours of dialysis sessions.^{24,25}

In our training program, all the patients safely completed the training course, because of considering patients' Baecke questionnaire results (habitual activity) and applying of Borg scale in a gradually increasing rate up to 85% maximal heart rate achievement. However, due to the high prevalence of cardiac disease in hemodialysis patients, the risks of cardiac events are higher than in the healthy general population.²⁶ Unfortunately, few studies correspond to our study. Most of them investigated a relationship between sleep quality and inflammation or effects of exercise on inflammatory cytokines, physical performance, solute removal, and quality of life in hemodialysis patients.^{13,15,16,21-25,27} In one study, the benefits of self-reported exercise on sleep quality was reported.²⁸

The association between poor physical function and an elevated CRP level with poor sleep quality in hemodialysis population has been shown.²⁹ We preferred to choose CRP as an inflammatory marker which reflects the pro-inflammatory cytokine activity (interleukin-6, tumor necrosis factor- α , and interleukin-1 β). In comparison to interleukin-6 levels, CRP has a more stable daily concentration, and it is more reliable than other inflammatory markers in ESRD patients due to its less diurnal variability.^{30,31} Exercise effects on the sleep quality of the elderly who complained of sleep disturbances were investigated by polysomnography and the PSQI.³² It was revealed that exercise improved some subjective and objective dimensions of sleep to a modest degree. To our knowledge, our study is the first to evaluate the effects of aerobic training on sleep quality and its regulatory factors, particularly leptin in hemodialysis patients.

Although, we reached good results with aerobic exercise prescription in hemodialysis patients but our study population was small and was limited to men. Prevalence studies of hemodialysis patients report that 50% to 80% of patients have one or more sleep complaints (in our study 55%), and more than 50% of them, who studied in a sleep disorders laboratory had a sleep disorder objectively documented by polysomnography.³³ With regard to the high prevalence of poor sleep quality in hemodialysis population and its complications, which eventually result in impaired quality of life, we recommend further studies with large sample sizes, in different gender groups and wide age range to improve physical activity, sleep quality, inflammatory status, and quality of life. It is important to consider the role of inflammation in cardiovascular mortality of hemodialysis patients.³⁴ These measures may contribute in decreasing cardiovascular mortality.

CONFLICT OF INTEREST

None declared.

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