

# Evolution of urea levels with the implementation of an intradialytic physical exercise program

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## ABSTRACT

**Introducción:** The kidneys of patients with chronic kidney disease cannot adequately filter and eliminate urea. High levels of this molecule are harmful to their health. There is evidence that exercise helps eliminate urea during hemodialysis.

**Objective:** To describe the evolution of urea levels over time when performing a low-intensity aerobic physical exercise program in hemodialysis patients.

**Material and Method:** We conducted a longitudinal quasi-experimental study with 10 patients, in whom an aerobic exercise program was applied for 14 weeks. Urea levels were recorded before and after hemodialysis with blood urea nitrogen analysis.

**Results:** A decrease in urea levels from 107.58 down to 79.34 mg/dl (men) and from 82.09 to 56.40 mg/dl (women) was observed in pre-exercise blood urea nitrogen analyses between weeks 0 and 14 of the exercise program ( $p = 0.022$ ).

**Conclusions:** Performing an aerobic physical exercise program while on hemodialysis is related to a decrease in pre- and post-hemodialysis urea levels over time. Therefore, the implementation of aerobic physical exercise could be related to an increase in urea clearance in patients with chronic kidney disease.

**Keywords:** chronic kidney disease; hemodialysis; aerobic exercise; urea.

## RESUMEN

**Evolución de los niveles de urea con la implementación de un programa de ejercicio físico intradiálisis**

**Introducción:** Los riñones de pacientes con enfermedad renal crónica no pueden filtrar y eliminar adecuadamente la urea. Niveles altos de esta molécula son perjudiciales para su salud. Existe evidencia de que el ejercicio ayuda a eliminar la urea durante la hemodiálisis.

**Objetivo:** Describir la evolución de los niveles de urea en el tiempo al realizar un programa de ejercicio físico aeróbico de baja intensidad en pacientes en hemodiálisis.

**Material y Método:** Estudio cuasi experimental longitudinal con 10 pacientes, en quienes se aplicó un programa de ejercicio aeróbico durante 14 semanas. Se registraron los niveles de urea antes y después de la hemodiálisis con análisis de nitrógeno ureico en sangre.

**Resultados:** Se observó una disminución en los niveles de urea de 107,58 a 79,34 mg/dl (hombres) y de 82,09 a 56,40 mg/dl (mujeres) en los análisis de nitrógeno ureico en sangre pre ejercicio entre las semanas 0 y 14 del programa de ejercicio ( $p=0,022$ ).

**Conclusiones:** Realizar un programa de ejercicio físico aeróbico durante la sesión de hemodiálisis se relaciona con una disminución de los niveles de urea pre y post hemodiálisis a lo largo del tiempo. Por tanto, la implementación de ejercicio físico aeróbico podría estar relacionado con un aumento en la depuración de urea en pacientes con enfermedad renal crónica.

**Palabras clave:** enfermedad renal crónica; hemodiálisis; ejercicio aeróbico; urea.

## INTRODUCTION

Chronic kidney disease (CKD) represents a serious health issue worldwide. In Mexico, it has a prevalence of 9,184.9 cases per 100,000 inhabitants, according to the most recent data from 2021<sup>1,2</sup>. This disease poses public health challenges and generates significant economic repercussions due to the high costs associated with treatment for affected patients<sup>3</sup>.

High urea levels in patients with CKD have been shown to be associated with increased mortality, heart problems, and complications such as weakness, anorexia, vomiting, hypothermia, or uremic syndrome<sup>4-6</sup>. Urea levels can be measured through various tests. One of them is the blood urea nitrogen (BUN) test, which is used to assess kidney function by measuring the amount of urea in the blood<sup>7</sup>. Pre-BUN tests are taken before the hemodialysis session, while post-BUN tests are collected afterward to assess treatment effectiveness.

Current evidence suggests that exercising during hemodialysis sessions contributes to the reduction of urea levels. This could be due to the increased blood flow to low-perfusion tissues, such as muscle, which may enhance urea clearance<sup>8</sup>. In fact, combining aerobic and resistance training during hemodialysis has been shown to increase muscular blood flow. This may facilitate the transport of urea and toxins from tissues to the vascular compartment, thereby improving the effectiveness of the hemodialysis process<sup>9</sup>.

Physical activity also leads to greater diffusion of urea from tissue to plasma and thus increases the effectiveness of hemodialysis. It has also been suggested that maintaining high blood flow to low-perfusion tissues at the end of dialysis eliminates urea during the post-dialysis recovery period<sup>8</sup>.

Although hemodialysis alone plays a key role in urea elimination, the inclusion of intradialytic exercise presents itself as a comprehensive complement, as suggested by the available evidence. However, some studies were unable to confirm that exercise helps eliminate urea<sup>10</sup>.

Given that high urea concentrations are harmful in patients with CKD, and there is no consensus on the benefits of exercise, it is important to investigate the impact of exercise on the evolution of urea levels in these patients.

The objective of this study is to describe the evolution of urea levels over time when implementing a low-intensity aerobic physical exercise program in hemodialysis patients.

## MATERIALS AND METHODS

### Study design

We conducted a quasi-experimental longitudinal study at the Renal Replacement Therapy Unit of *Centro Médico Naval* (CEMENA). It consisted of implementing an exercise program for CKD patients during hemodialysis sessions in May, June, and July of 2023.

### Population and sample

The study population included CKD patients on hemodialysis at CEMENA's Renal Replacement Therapy Unit. A non-probability convenience sampling was used, including all individuals who met the inclusion criteria: **a)** patients of both sexes; **b)** older than 20 years; **c)** on hemodialysis therapy (at least, 3 months); **d)** on hemodialysis 3 times/week; **e)** having a functioning vascular access; and **f)** having signed the informed consent form.

Exclusion criteria included: **a)** patients with a recurrent history of complications while on hemodialysis (hypotension, tachycardia) over the past 2 months; **b)** diagnosis of myocardial infarction in the past 6 months; **c)** diagnosis of stroke; **d)** diagnosis of arrhythmia; **e)** lower limb amputation; **f)** musculoskeletal or respiratory conditions worsened by exercise; **g)** patients who voluntarily dropped out of the program; **h)** 3 absences from the physical exercise sessions; **i)** physical complications during hemodialysis sessions; and **j)** recurrent hospitalizations.

### Study variables

To characterize the sample, sociodemographic variables were collected: age (in completed years), sex (male or female), and occupation (active military, retired military, or beneficiary). The independent variable was aerobic physical exercise measured in three phases: warm-up, intense, and cool-down (in minutes), and the dependent variable was the evolution of urea levels (mg/dl).

### Data collection instrument

A data collection instrument was designed consisting of two sections: the first for sociodemographic variables and the second for aerobic physical exercise and the evolution of urea levels. For the latter, measurements were recorded at weeks 0, 6, 10, 14, and 16, and BUN pre and post-exercise samples were taken at the start and end of each hemodialysis session, respectively.

### Procedure

Upon admission to the hemodialysis service, the following routine data were collected: current body weight (to verify dry weight) and vital signs. These were not study variables. The hemodialysis machine was programmed, and the patient was connected. Ten minutes after starting treatment, a BUN pre-exercise blood sample was collected.

From the first hour of the hemodialysis session, patients began performing seated aerobic exercise using only their feet on a stationary pedal machine made of steel and rubber, measuring 37 cm × 49.5 cm × 23.5 cm and weighing 2.2 kg. The device has a digital display with five functions: time, counter, revolutions, calories, and scan.

The exercise program was divided into 3 phases: warm-up (10 minutes), intense (30 minutes), and cool-down (10 minutes). At the end of the hemodialysis session, a BUN post-exercise blood sample was taken.

The exercise program was conducted 3 times per week during hemodialysis sessions, with a duration of 50 minutes. Participants were organized into 2 groups on different days: Group 1 attended on Mondays, Wednesdays, and Fridays, while Group 2 attended on Tuesdays, Thursdays, and Saturdays.

The program lasted for 3 consecutive months (May, June, and July 2023). BUN blood tests were conducted at 5 points (weeks 0, 6, 10, 14, and 16). The exercise program started in week 1 and ended in week 15. During weeks 0 and 16, BUN pre and post tests were conducted without exercise.

The lead researcher and clinical advisor were responsible for training patients and supervising the exercise program.

### Statistical analysis

Data analysis was conducted using Excel. Quantitative variables were expressed as mean and standard deviation (SD), and qualitative variables as percentages and frequencies. BUN pre and post-exercise values were compared across different weeks using the Wilcoxon signed-rank test, with  $p \leq 0.05$  considered statistically significant.

### Ethical considerations

The entire study followed the ethical guidelines of CEMENAV's Research Ethics Committee and the Declaration of Helsinki, to protect participant integrity, rights, and privacy. All participants provided written informed consent. The study was approved by both the Research Committee and the Research Ethics Committee of CEMENAV.

## RESULTS

Although the initial study population included 50 adult patients from CEMENAV's hemodialysis unit, only 13 (26%) met the inclusion criteria, signed the informed consent, and started the exercise program. However, three patients withdrew in week four, leaving only 10 participants (20%).

Of the 10 participants, 50% (n=5) were men and 50% (n=5) women. Age distribution showed that 10% (n=1) were 21–30 years old; 40% (n=4), 41–50; 20% (n=2), 51–60; and 30% (n=3) were older than 60. Regarding occupation, 10% (n=1) were active military; 20% (n=2) retired military; and 70% (n=7) beneficiaries.

The highest mean BUN pre-exercise value in men was recorded in week 0: 107.58 mg/dl (SD, 10.87); the mean post-exercise BUN was 37.62 mg/dl (SD, 9.10) that same week. In women, the highest mean BUN pre-exercise was also in week 0: 82.09 mg/dl (SD, 12.17), with a post-exercise value of 28.93 mg/dl (SD, 6.91).

The lowest BUN pre and post values in both men and women were recorded in week 14. BUN pre in men was 79.34 mg/dl (SD, 13.46) and in women 56.40 mg/dl (SD, 7.78). BUN post in men was 32.33 mg/dl (SD, 8.69) and in women, 16.71 mg/dl (SD, 5.47).

On week 16, when the exercise program had been suspended, BUN pre and post means increased vs week 14, but remained lower vs week 0. Complete BUN values are shown in **table 1**.

BUN pre and post values were compared using the Wilcoxon signed-rank test. First, the test revealed a significant difference in BUN pre levels between week 0 (no exercise) and week 16 (also without exercise), with a p-value of 0.017.

Comparing BUN pre levels from week 0 to week 14 yielded a p-value of 0.005; comparing BUN post levels between those same weeks gave a p-value of 0.022. Finally, when comparing week 14 (last week with exercise) and week 16 (no exercise), the Wilcoxon test showed p-values of 0.007 (pre) and 0.005 (post), indicating a significant difference. Of note, by week 16 the exercise program had been discontinued (**tables 2 and 3**).

**Table 1.** Mean and standard deviation of BUN with and without aerobic physical exercise (weeks 0–16), expressed in milligrams per deciliter (mg/dl).

Week		Men		Women	
		Mean	Standard deviation	Mean	Standard deviation
Week 0 (W/O Ex)*	BUN pre	107.58	10.87	82.09	12.17
	BUN post	37.62	9.10	28.93	6.91
Week 6 (W/ Ex)**	BUN pre	102.29	26.71	76.80	6.83
	BUN post	40.00	14.99	27.23	7.23
Week 10 (W/ Ex)	BUN pre	90.30	15.64	79.92	18.43
	BUN post	33.48	16.25	25.32	5.32
Week 14 (W/ Ex)	BUN pre	79.34	13.46	56.40	7.78
	BUN post	32.33	8.69	16.71	5.47
Week 16 (W/O Ex)	BUN pre	92.56	12.66	72.77	9.49
	BUN post	41.71	10.98	26.79	7.38

\*W/O Ex= without exercise. \*\*W/ Ex= with exercise.

**Table 2.** Differences in pre-dialysis BUN (comparison between weeks).

Weeks Compared	Average BUN (mg/dl)	p-value
Week 0 vs. Week 16	94.83 → 82.67	0.017
Week 0 vs. Week 14	94.83 → 67.87	0.005
Week 10 vs. Week 14	85.11 → 67.87	0.017
Week 14 vs. Week 16	67.87 → 82.67	0.007
Week 0 vs. Week 10	94.83 → 89.54	0.333

**Table 3.** Differences in post-dialysis BUN (comparison between weeks).

Weeks Compared	Average BUN (mg/dl)	p-value
Week 0 vs. Week 6	33.27 → 33.61	0.799
Week 0 vs. Week 14	33.27 → 24.52	0.022
Week 10 vs. Week 14	29.40 → 24.52	0.047
Week 14 vs. Week 16	24.52 → 34.25	0.005

## DISCUSSION

This study implemented an intradialytic exercise program in CKD patients on hemodialysis for 3 months. The results suggest a significant reduction in blood urea levels during the exercise program.

These findings are consistent with previous studies such as those by Alonso et al.<sup>9</sup> and Paluchamy et al.<sup>10</sup>, who examined the effects of exercise during dialysis sessions. Alonso et al.<sup>11</sup> conducted a before-and-after study with 29 patients using a combination of aerobic and resistance training. Like in this study, a pedal machine was used for aerobic activity. They also employed resistance bands for quadriceps, foot dorsiflexors, and glutes. Sessions lasted 30–60 minutes.

The results of Alonso et al.<sup>9</sup> indicate that the incorporation of exercise during dialysis led to improvements in dialysis efficiency, with an increase in solute clearance, including urea. This result aligns with the evolution of urea levels observed in the present study, as pre- and post-dialysis BUN analyses showed that urea values decreased in patients over time when the exercise program was implemented. Notably, urea levels increased after the program was discontinued (82.67 mg/dl on week 16), although they did not return to the levels recorded before the program began (94.83 mg/dl on week 0).

Similar results were obtained in the experimental study by Paluchamy et al.<sup>11</sup>. That study reported improvements in parameters such as Kt/V, blood urea, serum creatinine, serum potassium, phosphorus, and quality of life in 20 patients who participated in an intradialytic exercise program within the first 2 hours on dialysis. The finding of reduced blood urea specifically is consistent with that of the present study. It was inferred that the exercise program is complementary, a conclusion also drawn in this study.

Previous studies reinforce the idea that aerobic physical exercise helps eliminate urea during hemodialysis—a conclusion also reached in the present research, as the progression of urea levels suggests a reduction in blood urea, at least during the period in which the exercise program was implemented.

Compared to previous studies, it is evident that few have examined a physical activity profile similar to that used in this

study. The aspects evaluated in those studies that resemble the present one include the duration of the program (12 weeks), the timing of exercise during the dialysis session (after the first hour of treatment), and the duration of low-intensity aerobic exercise using stationary pedals (50 minutes).

The limitations of the present study were that the results cannot be extrapolated to other populations, since the study population is Mexican; it was not possible to form a control group to compare the impact of the exercise program with the results obtained here; and finally, the sample size is small, which also limits generalizability.

Based on the results obtained, it is possible to conclude that performing an aerobic physical exercise program during hemodialysis sessions is associated with a decrease in pre- and post-dialysis urea levels over time. Based on the data obtained, it can be stated that implementing the aerobic exercise program may increase urea clearance during the period it was carried out in combination with hemodialysis treatment. However, it is not possible to affirm that a sustained reduction in urea would continue if the program were to be maintained.

As a recommendation, the possibility of implementing the program during hemodialysis sessions in hospital centers is proposed to maintain control of blood urea levels and prevent future complications in patients with CKD. However, follow-up studies with larger populations are necessary to assess the feasibility, acceptability, and effectiveness of the program.

## Conflicts of interest

The authors declare no conflicts of interest related to the research, authorship, and/or publication of this manuscript.

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