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# Effect of nutritional supplement taken with and without exercise on muscle condition in adults on hemodialysis: A randomized controlled trial

**Submission date**
19/02/2019

**Recruitment status**
No longer recruiting

**Registration date**
27/02/2019

**Overall study status**
Completed

**Last Edited**
28/03/2023

**Condition category**
Urological and Genital Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Patients on hemodialysis have a loss of muscle quantity and quality due to the procedure as well as the inability to perform activities of daily living, so they have low physical function and are characterized by being physically inactive. Studies conducted by our group have shown that nutritional supplementation alone or in combination with exercise and performed during hemodialysis sessions, have a positive effect on muscle mass and physical function.
Although both interventions have been shown to be beneficial for the patients, until now we have not been able to observe the potential added effect of exercise when combined with the oral nutritional supplementation, which may be due to the fact that our patient population is young and physically active, or the follow-up time has not been enough.
For this reason, we intend to know the effect of an exercise program performed for 1 year, which combines exercise with oral nutritional supplementation.

Who can participate?
Anyone aged 18 - 60 years who is undergoing dialysis 2 times or more every week at the Hospital General de México "Dr. Eduardo Liceaga" can participate in this trial.

What does the study involve?
Participants are going to be randomly allocated to receive one of two treatments two times per week for 24 weeks: either intradialytic oral nutritional supplement without exercise or oral nutritional supplement in combination with an exercise program (Aerobic and resistance exercise). At baseline and the end of the study participants' body measurements, blood test results, physical function, quality of life, intramuscular lipid infiltrations and mid-thigh cross-sectional area measured with computed tomography are going to be assessed. These measurements are going to be taken after the hemodialysis treatment at Hospital General de México "Dr. Eduardo Liceaga".

What are the possible benefits and risks of participating?
Is has been shown that oral nutritional supplements and exercise, improved the muscle mass, quality of life and the physical function of hemodialysis patients, although it has been

documented that those patients with normal physical function have better survival than those with worse physical function.
Exercise and oral nutritional supplements are safe and beneficial. Low blood pressure and symptoms such as diarrhoea and nausea have been associated with oral nutritional supplements, but there is a lack of evidence supporting this.

Where is the study run from?
Hospital General de México "Dr. Eduardo Liceaga", Dr. Balmis 148 Cuauhtémoc Doctores, Mexico City, Mexico.

When is the study starting and how long is it expected to run for?
March 2019 to May 2020.

Who is funding the study?
Hospital General de México "Dr. Eduardo Liceaga"

Who is the main contact?
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# Additional identifiers

**EudraCT/CTIS number**
Nil known

**IRAS number**

**ClinicalTrials.gov number**
Nil known

**Secondary identifying numbers**
DI/18/105-B/04/021

# Study information

**Scientific Title**
Oral nutritional supplementation alone compared to oral nutritional supplementation with exercise on the skeletal muscle quantity and quality of adult hemodialysis patients

## Study objectives
The combination of exercise with oral nutritional supplementation will have a larger effect size on the skeletal muscle quantity and quality than those patients that receive the same supplement without exercise.

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 28/04/2018, Hospital General de México, Dr. Eduardo Liceaga ethics committee (Dr. Balmis 148, Doctores, 06720, Ciudad de México, Mexico, +52(55) 50 04 38 42 Ext: 1164), ref: DI /18/105-B/04/021

## Study design
Parallel Single-centre Randomized Controlled Trial

## Primary study design
Interventional

## Secondary study design
Randomised parallel trial

## Study setting(s)
Hospital

## Study type(s)
Treatment

## Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

## Health condition(s) or problem(s) studied
Adult hemodialysis patients

## Interventions
We are going to randomize our patients to one of the two groups using a blocked design in the Research Randomizer program (www. randomizer.org). The intervention is during the hemodialysis treatment (intradialytic) two times a week for 24 weeks. Patients need to visit the hospital the day they are going to receive the hemodialysis treatment and we are going to the measurements on these days.

Intervention group: The exercise program will consist of resistance plus endurance exercise, patients will be trained for 16 months.
In the warm-up and cool-down phase, patients will cycle the bike for 10 minutes without resistance, the rating perceived exertion of the patients will be very light.
In the conditioning phase, patients will first cycle the bike, patients will exercise at a moderate intensity during the first two hours of the HD session. The optimal exercise time will be established during the first session and then it will be gradually increased to reach 30 minutes.
After endurance training, patients will start the resistance exercise routine. For the resistance exercise, patients will be trained according to an adaptation of the program ‘Exercise: A Guide

for People on Dialysis. One week prior to the clinical study, patients will perform the physical conditioning exercise routine without any extra weight; afterwards, each subject will be asked to use 500 g ankle weights and TheraBand Latex Resistance Bands® will be used to individualize the exercise. Patients will perform four types of resistance exercise during the second hour of their HD session (four sets of 30 repetitions). For the first exercise (lower leg extension), patients sit with their feet on the floor. This exercise consists of slowly raising one leg up to waist height, slowly returning it to the floor and repeating the same movement with the other leg. For the second exercise (arm extension), the patients will use resistance bands. This exercise consisted of slowly pulling the resistance band up to their shoulders and slowly returning them to their original position. The patients who had a fistula performed this exercise with one hand; patients with a catheter performed the exercise with both hands. For the third exercise, patients will recline in a semi-recumbent position with their arms at the sides of the reclining chair (to maintain body balance). In this position, they slowly will raise one leg up to head height without bending their knee and count to five and then slowly returned the leg to its original position to repeat the exercise with the other leg. Finally, patients bent their knees one after another, taking them to their chest as if they were marching in the air.
The Borg scale of rating perceived exertion (RPE) (6-20) will be used to establish the intensity of the exercise (moderate intensity, 12-13) and the exercise will be individualized with the FITT principle (frequency, intensity, time, and type) ; the weight, the resistance of the bands and the time of the endurance exercise will increase if the patient´s RPE is less than target.
Patients will receive two cans of a specialized oral nutritional supplement for maintenance dialysis patients that consist of 434 kcal, 19.2 g protein and 22.8 g lipids (Nepro with Carb Steady, Abbott Nutrition). Nepro is low in vitamins A and D and high in folates and vitamin B6, and it includes high-oleic safflower oil, corn syrup solids and fructooligosaccharides (FOSs). They will drink one can before the exercise and the other before the exercise program to ensure the muscle mass gain.

Control group: During the HD sessions, the patients will receive two cans of a specialized oral nutritional supplement for maintenance dialysis patients that consist of 434 kcal, 19.2 g protein and 22.8 g lipids (Nepro with Carb Steady, Abbott Nutrition). Nepro is low in vitamins A and D and high in folates and vitamin B6, and it includes high-oleic safflower oil, corn syrup solids and fructooligosaccharides (FOSs)

## Intervention Type
Mixed

## Primary outcome measure
Quantity of muscle mass:
1. Indicators of muscle mass using anthropometry, measured at baseline, 3-months, and 6-months:
1.1 Mid-arm muscle circumference:
mid-arm circumference – (π x triceps skinfold thickness)
1.2 Bone-free arms muscle area:
males = [(midarm circumference (cm) - π x triceps (cm)]2/4 π) – 10
females = [(midarm circumference (cm) - π x triceps (cm)]2/4 π) - 6.5
2. Mid-thigh cross-sectional area of muscle mass measured with computed tomography.

Quality of muscle mass:
3. Intramuscular lipid infiltration with computed tomography, measured at baseline and at six months.
4. Physical function tests, measured at baseline, 3-months, and 6-months:

4.1 Sit to stand test: To move from a sitting position to a standing position on a 42cm high chair as quick as possible, for five times.
4.2 Time up and go test: measures the time in seconds for a patient to rise from a standard armchair, walk 3 meters, turn around, and return and sit down again.
4.3 Six-minute walk test: To walk back and forth along a 22 m course (two 10-m straight lines connected by two 1-m curves) in a corridor for 6 min. We are going to use the protocol of the American Thoracic Society. Subjects are allowed to rest in case of fatigue or pain, and to resume when possible

### Secondary outcome measures
1. Serum concentrations of myostatin by ELISA, measured at baseline and at six months.
2. Quality of life of patients using the SF-36 KDQOL scale, measured at baseline and at six months.
3. Biochemical indicators of nutritional status (albumin, creatinine, total lymphocyte count and cholesterol) before and after the intervention, measured at baseline and at six months.
4. Dietary indicators of nutritional status (protein and energy intake) before and after the intervention, measured at baseline and at six months.
5. Percentage of patients with protein-energy wasting before and after the intervention

### Overall study start date
01/01/2018

### Completion date
01/05/2020

## Eligibility

### Key inclusion criteria
1. Hemodialysis two or three times a week
2. Age > 18 years
3. No previous exercise program participation

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
50

### Total final enrolment
37

### Key exclusion criteria
1. Limb amputation
2. Hospitalization in the last 3 months
3. One or less hemodialysis session a week
4. Severe effort angina (CC3) or stage 4 of the New York Heart Association (NYHA) classification scale of heart failure
5. Pregnancy
6. Severe dyspnoea
7. Femoral fistula
8. Arrhythmias
9. Precordial pain
10. Orthopaedic or neurological compromises or cognitive alterations affecting study participation.

### Date of first enrolment
01/03/2019

### Date of final enrolment
31/05/2019

## Locations

### Countries of recruitment
Mexico

### Study participating centre
**Hospital General de México "Dr. Eduardo Liceaga"**
Dr. Balmis 148 Cuauhtémoc Doctores
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## Sponsor information

### Organisation
Hospital General de México, Dr Eduardo Liceaga

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### Sponsor type
Hospital/treatment centre

### ROR
https://ror.org/01php1d31

## Funder(s)

### Funder type
Hospital/treatment centre

### Funder Name
Hospital General de México Dr. Eduardo Liceaga

## Results and Publications

### Publication and dissemination plan
Planned publication in a high-impact journal, such as Journal of the American Society of Nephrology in 2021.

### Intention to publish date
01/06/2021

### Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Basic results | | 11/06/2021 | 14/06/2021 | No | No |
| Results article | | 19/07/2022 | 28/03/2023 | Yes | No |