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Research Article

THE EFFECTS OF PHYSICAL EXERCISE IN CHRONIC END-STAGE KIDNEY FAILURE PATIENTS ON HAEMODIALYSIS

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ABSTRACT
Physical exercise is known to have beneficial effects on healthy individuals, but there are insufficient data concerning the effects of physical exercise in chronic end-stage kidney failure patients on haemodialysis. The aim of this study is to assess the effects of a regular moderate physical exercise programme on body composition, nutritional status, cardiovascular risk factors, and haemodialysis (HD) treatment in chronic end-stage kidney failure (CESKF) patients on haemodialysis. Twenty-nine HD patients on a 6-month physical exercise programme and who were non-randomly assigned to an experimental or control group in two hospitals in Spain (Jaén and Úbeda Hospital) underwent whole body composition analysis (body fat, muscle, bone, body fluids, and mass regionalization) using non-invasive, reliable, valid, standardized, low-cost, easily transportable methods, i.e., bioelectrical impedance (BIA) and anthropometric analysis, to gather pre-physical exercise and post-physical exercise haemodialysis data.

Key words: Physical exercise, kidney failure, haemodialysis, anthropometry, bioimpedance, impedance spectroscopy.

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INTRODUCTION

Though the beneficial effects of physical exercise on healthy individuals has been well documented in the literature, there are insufficient data regarding the effects of physical exercise in chronic end-stage kidney failure patients on haemodialysis. Multi-organic disorders associated to chronic end-stage kidney failure (CESKF) are contributing factors to several complications that may diminish the patient's quality of life and may eventually jeopardize it. The patient's health may be further compromised by complications derived from haemodialysis leading to further complications, both real and potential. Identifying risk factors and lifestyles may improve the patient's quality of life. The reasons underlining the physical inactivity characteristic of sedentary HD patients are multifactorial, i.e., biological and/or psycho-social factors. Approximately 50 to 60 % of CESKF mortality is associated to cardiovascular disorders. The aim of this study is to assess the effects of a regular, moderate physical exercise programme on nutritional status, cardiovascular risk factors, and haemodialysis (HD) treatment in chronic end-stage kidney failure (CESKF) patients on haemodialysis.

Cardiovascular Risk Factors

The cardiovascular risk factors under study were as follows:

- Arterial hypertension
- High-flow internal arteriovenous fistula (IAVF)
- Left ventricular hypertrophy (LVH) and ventricular enlargement
- Dyslipidemia (hypertrigliceridemia and hypercholesterolemia)
- Obesity and CESKF insulin resistance leading to atherogenesis
- Diabetes
- Smoking status
- High lipoprotein A
- Hypercaliemia, and sedentary life style.

The precise relationship between HD and arteriosclerosis is not entirely understood. Along with the aforementioned risk factors, uraemic toxins and high parathyroid hormone (PTH) levels have been reported to damage vascular endothelium.

Neurological disorders associated to HD include fatigue, irritability, depression and peripheral encephalopathy. Haematological disorders include anaemia. Respiratory disorders are characteristic of uraemia (to compensate for acidosis) or arise from the retention of body fluids and may be further aggravated by smoking. Muscular-skeletal disorders range from cramps to calcifications due to alterations in the calcium-phosphorus metabolism and primarily as a consequence of renal osteodystrophy. Endocrine-metabolic disorders include malnutrition and obesity, the latter being associated to cardiovascular risk factors such as high blood pressure, high total cholesterol and LDL-cholesterol, and low HDL-cholesterol, which in turn are major risk-factors triggering diabetes in adults.

 ISSN 1988-5202

The regional distribution of body fat is a significant risk-factor with android obesity (distribution of fat in the upper portion of the body) posing a greater health risk than gynoid obesity (greater accumulation of fat in the thighs and buttocks).

Malnutrition is highly prevalent in HD patients (an estimated 30% of patients are malnourished whereas 33% have a higher than normal body mass index BMI), which increases morbidity and mortality. Though the assessment of nutritional status is a key factor for improving quality of life and clinical outcome, no single test is entirely comprehensive and reliable for evaluating the nutritional status of HD patients, and range of data concerning the patient's condition must be assessed. The malnutrition parameters assayed were: albumin, prealbumin, transferrin, retinol-bound and iron-bound proteins (a deficiency in either of the latter two stimulates prealbumin) as well as the muscle protein and visceral protein status.

Changes in body weight should be regularly monitored as they are indicators of alterations in the body fluid balance. Monitoring the uraemic condition of HD patients will further the understanding of real or potential alterations. Body composition is vital for diagnosing nutritional deficiencies or excesses, predicting potential risk factors, assessing calorie and fat intake of individuals of stature, i.e., low, medium, and large musculature, and for determining fat reserves.

Correct body weight does not imply healthy fat or muscle ratios, particularly in HD patients. Hence, it is essential to determine body composition, i.e., profiles to evaluate the mass of body fat, muscle, bone, fluids and their regional distribution. The method must be non-invasive, low-cost, easily transportable, precise, reliable, valid, and standardized. The most widely used are double indirect methods which are based on the measurement of physical parameters on the principle of which components can be calculated by a statistical equation or by a predetermined relationship between the component and the physical property. The following methods employed in this study:

- Anthropometry
- Bioelectrical impedance spectroscopy (BIS)

Standard anthropometric analysis involves assessing body weight, height, and subcutaneous fat by measuring body circumference and skin flaps.

Bioelectrical Impedance Analysis

Bioelectrical impedance analysis (BIA) is a relatively simple, quick, and non-invasive method widely used for estimating body mass composition in a variety of clinical conditions. BIA determines the electrical impedance of body tissues by measuring the flow of a harmless electrical current through the body and provides an estimate of total body water (TBW). The more fat the greater the resistance to the flow of the electrical current through the body, conversely, the less fat the greater the flow of the electrical current through the body. By measuring the electrical current, one can estimate body fat percentage.

 ISSN 1988-5202

The method is simple, practical and safe given that it:

1. Indirectly estimates body composition and the basal metabolic rate.
2. Evaluates nutritional status by measuring low electrolyte resistance through the body.
3. Determines the percentages of body fat, fat-free tissue and water.

Body impedance analysis provides a direct estimate of total body fluids, muscle mass and lean tissue mass.

The method is precise for estimating body fluids and fat-free tissue in stable patients and healthy subjects given that there are predictive equations based on the general population that serve as a standard.

In contrast, HD patients are unstable, and few studies have been undertaken to design charts to predict or to establish standards in these patients.

This is in part due to the fact that this method is not widely used given that it is somewhat cumbersome requiring the attachment of electrodes (distal, proximal or segmental) in antecubital fossa, popliteal fossa and/or on the upper/lower limbs. Thus, further analysis using this method involves repeating the same procedure in the same areas, using the same explorer under the same conditions. Consequently, it has restricted and limited the use of this technique.

Hence, being able to perform the analysis repeatedly and with ease in all of the patients was one of the main achievements of this study. The use of the body mass analyzer (resembling a body weight scale), which is easily transportable, inexpensive, simple and easy to use, reliable, and valid, has not only enabled the assessment of the patients under study, but also allows assessing the general population by providing tables that may in the future serve as a reference for patients exhibiting such particular characteristics.

The aim of this study is to assess the effects of a regular moderate physical exercise programme on the nutritional status, cardiovascular risk factors, and haemodialysis (HD) treatment in chronic end-stage kidney failure (CESKF) patients on haemodialysis by bioimpedance impedance and anthropometric analysis. We hypothesised that regular moderate physical exercise improves the nutritional status of HD patients, and reduces the risk of cardiovascular disorders without increasing the need for dialysis in CESKF patients

A sedentary lifestyle is associated to cardiovascular disease whereas physical exercise is considered to have a beneficial effect by:

- Reducing anxiety and hostility
- Reducing blood pressure, and the release of stress-related serum catecholamine norepinephrine that increase fatty acid levels and accelerate atherosclerosis.
- Produces fibrolysis that reduces the growth of arteriosclerotic lesions.
- Reduces Lipoprotein A.
- Regulates glucose homeostasis.

 ISSN 1988-5202

- Increases HDL.
- Lowers heart rate during rest and improves myocardial oxygenation.

MATERIALS AND METHODS

Subjects

A total of 55 CESKF patients on HD from Ciudad de Jaén Hospital (8 patients), and Úbeda Hospital (47 patients) located in the province of Jaen (Spain), were selected for study from January to September, 2003. The study was approved by the Institutional Ethics Committee an informed consent was obtained from every patient. Patients were informed of the type of study as well as the aims, method, and equipment to be used. Furthermore, patients were given a detailed explanation as to the working of the equipment in order to assure them that it was harmless and painless.

Criteria for inclusion were:

1. HD for at least 6 months.
2. Agreed to participate in the study and comply with the procedures.
3. No vascular accesses in lower limbs (neither Gore-Tex nor catheters).
4. No amputated limbs.
5. No previously diagnosed cardiovascular or osteomuscular disorders.
6. Undergoing dialysis 3 times weekly.

Experimental Design

The sample was non-randomized, i.e., the patients chose to be assigned to the experimental group (29 patients who underwent the physical exercise programme) or the control group (26 patients who decided not to undergo the physical exercise programme) after reading the informed consent form.

The physical exercise programme involved walking for a minimum of 20 minutes a day (the maximum walking time was determined by each patient according to their own judgement concerning their physical effort), and a pedometer was used to record the time and count the number of steps. If patients felt tired, they were instructed they could stop until they had recovered or to cease exercising. As expected, patients exercised more during pre-dialysis than post-dialysis when they complained of fatigue and were less keen on exercising.

Patients who did not undertake physical exercise throughout the entire six-month period were not informed that they had been withdrawn from the study though follow-up was continued. Other patients on the physical exercise programme who became keen on sport and stopped walking to take up other sports such as swimming, cycling, etc, were also excluded from the study though follow-up was continued.

Patients underwent BIA and anthropometric analysis on the second day of HD, and the blood samples taken regularly by the HD units of the hospitals were used for experimental assay.

 ISSN 1988-5202

Materials

- A portable bioimpedance body fat analyzer (TANITA TBF-300, Bio Logica, Japan).
- Lipometer Holtain LTD, Crymych, Dyfed, Wales, UK).
- Pedometer "Van Allen 32763".
- Laboratory screens: ADVIAS 120, HITACHI 917, and AXYM (Abbot) for biochemical determinations.
- Borg Rating of Perceived Exertion Scale.
- Nursing records.
- Non-extendible measuring tape.
- Thermometer for ambiance air temperature.

The analyser, which is similar in appearance to a household bathroom scale, has an operating frequency of 50 Khz, and 4 electrodes in the foot sensor pads send a low, safe signal through the body. The analyzer measures fat mass ranging from 1-75% and quantifies muscle mass, lean tissue mass, and total body water at 100 gram intervals. The analyzer must be programmed with the patient's input data, such as body weight, height, age, and sport done or not.

Bearing in mind the type of study and the characteristics of the patients, the measurements should not be considered as absolute values but rather as references for assessing variations.

The Holtain lipometer maintains a steady contact surface pressure of 10 mgrs/mm^2, a range of 0-45 mm, and the display increments at 0.7 mm intervals. The Lipometer can measure a margin of error of 0.1

Timing and Stages

The study was subdivided into six stages (i.e., preliminary, data gathering, the commencement of the intervention, and the three controls) from January to September, 2003.

Preliminary Stage

In the preliminary stage, subjects who had not been diagnosed for any previous pathology were assessed during a trial period with the intention of allowing researchers to familiarise themselves with the devices and overcome any problems that arose. In addition, different areas were explored to determine if they were detected by the system or influenced in any way.

The different health centres were contacted and authorisation for undertaking the experiment was obtained from the director of each centre. Patients were explained the study in terms of the objectives, method, and devices and equipment to be used. Thereafter, the patient's consent was obtained prior to requesting patients to specify the degree to which they wished to collaborate in the experiment.

Patients were given a detailed explanation and demonstration of the devices to be used to assure them that the equipment was not aggressive, i.e., neither produced pain nor discomfort.

 ISSN 1988-5202

Patients were given an appointment to begin the patient's measurements and to ensure that the measurements were taken on the intermediate day to the three blood sampling days in each centre.

Second Stage: Data Gathering.
Measurements were taken on each of the three days in which the patients underwent dialysis, i.e, during pre-dialysis and post-dialysis. Care was taken to avoid interrupting either the renal unit's work schedule or delaying patient care or transport. BI and anthropometry analysis were done on each of the three days a week in which the patient attended the HD unit.

Third Stage
In the third stage, each of the patients who participated in the control and experimental groups was provided with the same model of pedometer. Individually, the patients were instructed on the handling of the pedometer, and care was taken to double-check they understood the procedure. Patients were given a one-week trial period to become familiar with the device and to answer any queries or concerns. Prior to HD, each patient was double-checked to ensure they knew how to function their pedometer correctly.

Neither the first session of HD was considered to be representative of the patient's physical condition (given that there had been a three-day lapse without dialysis, i.e., a very "heavy load" both in terms of water and uraemic toxins) nor the third day of dialysis (the patient was heavily dialyzed to supplement three concurrent days without HD, which is not the average physical condition). Consequently, assays were carried out during the second HD session for three reasons:

- Firstly, statistically there were no significant differences in the values obtained on the second day of HD and the average values.
- Secondly, the patient is most stable on the second day of HD.
- Thirdly, on Wednesday, i.e., the day blood samples were taken for biochemical analysis, the values obtained would be in the same condition as those of the said analysis, thus, comparisons can be undertaken without the need for controlling a further odd variable. The fact that some patients had fasted (overnight food abstinence) and others had not was controlled by taking into account their appointment time.

The first control was undertaken in the two situations that the patients presented: pre-dialysis and post-dialysis and the 2nd and 3rd with the same characteristics.

Variables
Undoubtedly, there are a number of variables to control, the following were checked and controlled during the trial period with the analyzer:

- Barefoot (or a thin stocking),
- Sweat.
- Foot time.
- Posture during the session.
- Patient's body and room temperature.
- Do not carry mobile phones or batteries (pacemakers).

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- Corns or rough skin on feet.
- Pes valgus foot.
- No vibration.
- Empty bladder.
- Unchanged situation as regards food and liquid intake.
- Ovulation.
- Caffeine.
- Alcohol.
- Diuretics.
- Sleep.
- Awake State.

The Independent Variable
The independent variable under study was physical exercise.

Biochemical and Dialysis Data
The variables for the atherogenic lipid profile were: cholesterol, triglycerides, HDL, LDL, lipoprotein A, homocysteine as well as waist and hip circumference.

Variables of nutritional status were glucose, total proteins, albumin, muscle mass, forearm circumference, tricipital and scapular skinfold.

The variables for the efficacy of dialysis in relation to anaemia were haematies, haematocrit (Hto.), haemoglobin (Hb), iron, and ferritin.

Variables of protein metabolism: urea, creatinine, uric acid as well as variables related to sodium electrolytes, potassium, calcium, phosphorus.

Other variables assessed were: sex, age, patient's condition, season of year, environmental conditions, dialysis parameters (type of dialyzer, bath, medication), and the time of blood sampling, i.e., pre-dialysis or post-dialysis.

Method
Biochemical assays were carried out in the Laboratory of the Ciudad de Jaén Hospital.

The experimental conditions for BIA were maintained constant, i.e., the same body mass analyzer, hour and day of blood sampling, patient's body temperature, location, room temperature (23º), and the same trained investigator performed BIA and anthropometry measurements in all subjects.

The patient's position during the session was not controlled because the discomfort caused did not influence the results obtained as they were the same as when the patient remained seated for 5 minutes in the room used for taking measurements.

 ISSN 1988-5202

The following assays were carried out:

- Basal metabolic rate.
- Impedance.
- Fat mass (%).
- Fat mass (kilos).
- Muscle mass (kilos).
- Total water.

Anthropometric variables.
Anthropometric measurements were taken from the lateral and subscapular skinfold. The following measurements were taken: The forearm, waist, hip circumference, and tricipital and subscapular skinfold thickness. Care was taken to ensure patients were comfortable to avoid orthostatic hypotension (particularly during post-dialysis). Iliac skinfold thickness was not measured to avoid traumatising the patient due to the difficulty in undressing the patient during post-dialysis. Measurements were undertaken in accordance with the recommendations of the International Working Group on Kinanthropometry as they are regarded to be the most standardized method.

Statistical analysis
Data analysis were carried out using the statistical package SPSS 10.1 version for Windows. Standard deviation was used to calculate the mean and the dispersion in the distribution. The comparison between groups was undertaken by Student t test, and variance analysis for more than two groups.

RESULTS
In all probability, the heterogeneity of patient profiles observed in both the inter-group and intra-group comparisons of the experimental and control groups was due to the non-randomized distribution of patients into experimental and control groups.

As the initial data analysis revealed considerable differences in the amount of physical exercise undertaken by patients in the experimental group, this group was further subdivided into three subgroups according to the patient's level of physical exercise, which further reduced the sample size of the experimental group:

1. Level 1 patients walked 1,000 meters daily.
2. Level 2 patients walked 1,000 to 5,000 meters daily.
3. Level 3 patients walked 5,000 meters a day or more.

As for the cardiovascular risk factors in the control group, cholesterol, LDL and triglyceride levels increased though HDL also increased, which reduced glucose and water levels. In comparison, considerable data inconsistency were observed in the experimental group i.e., in level 1 patients, cholesterol, triglycerides, glucose and water levels decreased, but LDL levels increased and HDL decreased; in level 2, cholesterol, LDL, and water levels decreased, but triglycerides and glucose levels rose, and HDL levels fell; and in level 3 the highest cardiovascular risk factors were observed with a fall in LDL levels but a rise in cholesterol,

 ISSN 1988-5202

triglycerides, glucose, and water levels and a fall in HDL levels. On the whole, the cardiovascular risk factors in levels 1 and 2 improved.

In terms of nutritional parameters, the values of the control group remained practically unchanged, whereas protein totals increased in all three experimental subgroups, and albumine levels fell in levels 1 and 3.

It is worth noting that the parameters for the efficacy of dialysis exhibited the same tendency in the control group and in the three experimental subgroups. Similarly, in terms of the haematological parameter, anaemia, iron levels fell in all groups.

The results for protein metabolism showed increased creatinine levels in all of groups.

As for electrolytic alterations, no levels remained unchanged, and phosphorous levels fell in all groups.

On the whole, body fat increased in the control group and in the level 2 experimental group, whereas body fat decreased in experimental level 1 and 3 groups and lean mass increased.

DISCUSSION

The modifications brought about by physical exercise on the population under study in relation to the assessment of the body composition of renal failure patients cannot be referred to since this is a highly complex issue.

Due to the considerable short, medium, and long-term instability of CESKF patients on HD, one should be cautious in attempting to establish common criteria for all patients in order to assess their "normality". In these patients one can neither rely on absolute values nor "variations in their health status".

The only studies that consider these variations are the cohorts of Piccoli et al., (2002) with 1,116 patients, and Pillou et al., (1996, 1999) with 3,000; however, as they only undertook post-dialysis measurements to determine body water levels in the former, and haemodialysis in relation to survival in the latter, these studies are of limited value for our purposes. As for other BIA studies, our sample is one of the largest to our knowledge (Barril, 2003: 30 patients; Cigarran 2005: 55 patients; Andersen, 2004: 19 patients; Zhu, 1988: 15 patients, and in Spain, Rodríguez, 1998: 21 patients, and Hernández, 1993: 30 patients). Though this study was undertaken in the aforementioned population, our current sample undergoing research consists of 136 patients.

As previously stated, the bioimpedance values obtained for these patients were scarce and difficult to obtain, causing discomfort to the patient (as well as for the researchers). For this reason, our method enables the undertaking of large quantities and under different circumstances to obtain standard values in order to establish criteria of "normality" for these highly unstable patients. Furthermore, measurements should be carried out under all possible circumstances to determine the profiles. As the method is so simple, it facilitates this goal. This systematic evaluation coupled with the others will provide renewed parameters for adjusting haemodialysis to improve the quality of life of these patients. Moreover, they can be quite useful to determine total changes in body composition in terms of water, lean body mass, and fat mass, as well as correlating these with other biochemical parameters.

 ISSN 1988-5202

In the future we aim to use this technique in these patients to: estimate body liquids (by determining dry weight), apply the urea kinetic model and its distribution in the body, as well as the ionic and nutritional changes and predict risk factors.

Thus, from the very onset of the disorder and throughout the treatment, the goal of care programmes for renal patients should be to include regular, moderate, systematic, supervised physical exercise. Our findings slightly disagree with the findings of Triolo (2000) in terms of the fall in triglyceride levels, and with Cham (1995) in relation to the overall increase in HDL. Our findings agree with Stenvinkel (2000) observation that physical exercise not only improves, but also prevents the deterioration of the HD patient's condition. Likewise, our data agrees with Kutner (2000), Fitts (1999), and Koudi et al., (1997) that physical exercise improves muscle strength and resistance and walking ability, which in turn increases mobility and improves functionality as well as reducing symptoms such as depression, insomnia, high blood pressure. It increases appetite, feelings of well-being and control over the disease. Hence, the increase in physical ability is translated into psychological benefits.

Throughout this study we have borne in mind the following limitations: The instability of the patients under study has hindered the determination of body composition parameters using BIA, thus, we have been unable to determine absolute values and have only determined the variations in the said parameters. A further drawback is the lack of available standards by which to draw comparisons, and this underscores one of the main aims of the study, i.e., to set standards as a reference guide for further research.

We have been unable to determine the degree of physical exercise to be undertaken in each particular case as this is determined by the patient's subjective impressions and not by objective data that would have permitted the individual assessment of quantity and intensity, but our sample size was small and the duration of the study short in comparison to the length of time these patients are on HD), and it was the patients themselves who freely chose if they wanted to be assigned to the experimental group. In addition, the schedule for dialysis, collective transport, and the time they remained in the HD units thwarted the implementation of alternative methods or experimental designs particularly since the HD units did not have the resources or funding required. Moreover, the large quantity of medication and changes in drug regime must be borne in mind in the interpretation of the data.

CONCLUSIONS

1. Physical exercise was undertaken by the population under study but restricted to the activities of daily life.

2. A slight fall in cardiovascular risk-factors (cholesterol, triglycerides, and LDL) was observed in the experimental group.

3. A comprehensive estimate of nutritional status was undertaken using anthropometric and BIA analysis.

4. We have pointed out the need for tables and indexes (none are currently available) for comparing the parameters of body mass analysis in CESKF patients on HD given that this would involve the need to establish a new criteria for "normality" in these patients. For future undertakings, they are being devised.

 ISSN 1988-5202

5. The results show a deficient relationship between biochemical indicators and body composition highlighting the need to assess a range of criteria (cardiovascular, nutritional) in order to evaluate the effects of a physical exercise programme in CESKF patients.

6. Physical exercise was not found to increase the CESKF patient's HD needs, though an increase in food intake was observed.

7. Though a moderate physical exercise programme for CESKF patients on HD did not improve the physical fitness of these patients, they personally did report being more keen on physical exercise as well as feeling healthier and physically fitter.

8. Due to their "good physical condition" (none of the transplanted CESKF patients (8) in the experimental group had post-transplant complications), this finding demonstrates the benefits of a moderate physical exercise programme for CESKF on HD.

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