A pilot study investigating the effect of pedalling exercise during dialysis on six-minute walking test and hand grip and pinch strength

Manasi Desai MSc, Ahmed Mohamed MD, Andrew Davenport FRCP

UCL Department of Nephrology
Royal Free Hospital
University College London
Rowland Hill Street
London NW3 2PF

Address for correspondence

Manasi Desai	manasi.desai@nhs.net
Ahmed Mohamed	ahmedmahmoud.mohamed@nhs.net
Andrew Davenport	andrewdavenport@nhs.net

contact andrewdavenport@nhs.net orcid 0000-0002-4467-6833
UCL Centre for Nephrology
Royal Free Hospital,
University College London Medical School
Rowland Hill Street,
London NW3 2PF
tel 44-2074726457
fax 44-2073178591

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Abstract

Introduction

Haemodialysis (HD) patients are at increased risk of sarcopenia. Physical inactivity is now recognised as a major cause of muscle wasting in HD patients. It is unclear as to what exercise and how much exercise is required to show benefit. We therefore performed a pilot study of cycling during HD.

Methods

Patients underwent a progressive submaximal individualised cycling-exercise, 3 x week during HD for 4 months using bed-cycle ergometers. Body composition was measured by multifrequency segmental bioimpedance and muscle function by 6-minute walking test (6MWT), and hand grip (HGS) and pinch strength (PS).

Results

56% of patients in a dialysis centre fulfilled exercise study inclusion criteria, and 13 (72.2%) of 18 patients completed the exercise program, mean age 64.0±16.6 years, 76.9% male. 6MWT increased following exercise from 349±105 to 398±94.2 m, $p<0.05$, as did both HGS and PS; 20.4±9.1 vs 23.4±9.9 kg, $p<0.01$ and 4.3±1.8 vs 5.9±2.4 kg, $p<0.05$, respectively. There were no changes in appendicular muscle mass, or other body composition detected with bioimpedance in either the exercise group, or 21 control patients, propensity matched for body composition, co-morbidity and frailty. Muscle strength did not change in the control group. HD sessional Kt/Vurea was greater at the end of the exercise program compared to controls; 1.63±0.63 vs 1.21±0.12, $p<0.01$.

Conclusions

The majority of dialysis centre patients met our exercise study entry criteria and could potentially benefit from cycling during HD. We found that muscle function and strength improved after a four month, thrice weekly cycling exercise program.

Introduction

Patients with chronic kidney disease requiring dialysis treatment are at greater risk of developing sarcopenia, and sarcopenia is associated with increased risk for mortality [1,2]. Although there are many potential causes of muscle wasting in kidney dialysis patients, ranging from restricted diets, to vitamin D deficiency, metabolic acidosis, chronic inflammation, protein losses with dialysis treatment, the effects of co-morbid conditions, it is now recognised that dialysis patients are generally sedentary, with low levels of active energy expenditure [1-5].

Previous studies have demonstrated that increasing physical activity in the elderly and those with pre-existing cardiovascular disease improves survival, reduces the risk of cardiovascular mortality and improves quality of life [6-8]. However, effective strategies to mitigate physical inactivity, such as exercise training, are not routinely prescribed to patients with chronic kidney failure or high-risk patients [9]. Baseline exercise capacity, as assessed by peak oxygen uptake (VO_2) has been shown to both enhance longevity and lower hospitalisation rates in a cohort of haemodialysis patients who had been recruited into a six-month incremental exercise testing program, exercising to a symptomatic maximum [10]. As VO_2 is linked to cardiorespiratory function then these results may be expected, however the over-all mortality in this in-centre haemodialysis exercise group after a mean fellow-up period of 3.5 years was only 13%.

Most haemodialysis patients attend dialysis centres thrice weekly, and spend the session sitting in a specially designed chair, or lying on a bed. As such, haemodialysis therefore enforces regular sedentary behaviour. The key question is how to enrol haemodialysis patients into an exercise program. Patients attend for in-centre dialysis treatments thrice weekly and are therefore somewhat reluctant to attend the centre for a fourth day, and equally most patients feel tired and exhausted at the end of the haemodialysis session. Not surprisingly studies have demonstrated that exercise interventions on non-dialysis days are associated with lower compliance rates [11], whereas intradialytic exercise interventions have demonstrated higher adherence rates [11]. As patients may have large bore needles inserted into their fistula or graft in the arm, then most exercise intervention studies have looked at various forms of leg exercises, such as pedalling during dialysis [12].

Although dialysis patients exercising with bicycle ergometry and resistance training have been reported to increase physical performance [13], others have questioned as to whether there has been any clinically meaningful response to exercise [14]. In view of this uncertainty we wished to undertake a pilot study to determine whether an intra-dialytic pedalling exercise program would benefit patients by improving muscle strength in muscles both involved and not involved in the exercise program and increasing limb muscle mass measured by bioimpedance.

Materials and Methods

Adult haemodialysis patients with established end-stage kidney disease in a dialysis centre under the care of a university hospital were asked to participate in the study, atients with unstable angina and uncontrolled hypertension (pre-dialysis blood pressure >180/100 mmHg), lower-limb amputees, those who were blind, or had terminal illnesses, or emergency admissions to hospital within the previous 3 months, or with severe cognitive impairment were excluded. Study patients were assessed at every dialysis session for their suitability to pedal, and exercised provided that they did not have symptomatic hypotension, hypoglycaemia, or in symptomatic pulmonary oedema

The intra-dialytic exercise prescription was based on current, the American College of Sports Medicine guidelines [15], which recommend that haemodialysis patients should perform aerobic exercise training at mild-moderate levels for 20-60 minutes/day, 3-5 days/week. The exercise intervention programme was administered through a progressive submaximal individualised cycling-exercise, which was performed by patients at each dialysis session three times per week for a period of 4 months using bed-cycle ergometers which were positioned in front the patient's dialysis chair. Depending upon the design of the dialysis chair we used both the MSD Delux pedal exerciser (MSD Europe, Tisselt, Belgium) and the SBI MedBike (MedBike, Hamme, Belgium). Each exercise session consisted of three phases: warm up, conditioning, and cooling down. The warm up phase consisted of low-load aerobic cycling at an intensity of 8-9 on the rate of perceived exertion scale (RPE) scale [16]. In the conditioning phase, the patients were asked to cycle optimally aiming for their RPE between 13 and 15 which corresponds to moderate intensity, and exercise intensity was monitored every five minutes. During the cooling down phase the participants performed light cycling with no load or resistance at an intensity of 8-9 on the RPE scale. We then matched the exercise group with a comparator group of haemodialysis patients from one of our other satellite dialysis centres, controlled for body composition, co-morbidity and frailty.

Muscle strength was measured using the hand grip-D strength dynamometer (Takei Scientific Instruments Co, Nigata, Japan) and a pinch gauge (Jamar digital plus, Lafayette Instrument, Lafayette, USA) [17,18]. Patients were instructed and shown how to use the hand grip and pinch gauges, and measurements made following the manufacturer's recommendations. Patients were encouraged to make their maximal voluntary effort, and three measurements were made using their dominant arm, and the maximum strength recorded. Physical function for the exercise group was determined using the 6-minute walk test (6MWT). Patients were advised to walk as far as they could in 6 minutes carrying a trundle wheel which measured the distance.

Body composition, including muscle mass was measured post mid-week dialysis by multifrequency segmental bio-impedance (MFBIA) (In Body S720, Seoul, South Korea), using a standardised protocol [19,20]. Patient frailty was assessed using the 7-point Canadian clinical frailty scale clinical [21] and patient co-morbidity with the Stoke-Davies co-morbidity grading system [22].

All patients were dialysed with high flux dialysers (Elisio series, Nipro, Osaka, Japan), and were anticoagulated with a single bolus dose of tinzaparin (Leo

Laboratories, Prices Risborough, UK), median dose 2500 (2500-2500) IU, and used ultrapure dialysis water [23,24].

Patients had standing height measured and weighed pre-and post-dialysis. Routine biochemical tests were obtained from the mid-week dialysis session using hospital computerised records and dialysis session adequacy (Kt/Vurea) and nitrogen appearance rate normalised for body weight (nPNA) calculated by standard methods [25].

Statistical analysis

Results of our pilot study are expressed as mean ± standard deviation, or median and interquartile range, or percentage. We used standard statistical analysis D'Agostino & Pearson normality test, paired t test, Wilcoxon rank sum pair test, anova or Kruskal Wallis were used for parametric and nonparametric data respectively, with appropriate correction for multiple analyses where appropriate, and Chi square testing with correction for small numbers. Statistical analysis was performed using Graph Pad Prism (version 7.0, Graph Pad, San Diego, CA, USA) and Statistical Package for Social Science version 24.0 (IBM Corporation, Armonk, New York, USA). Statistical significance was taken at or below the 5% level.

Ethics

This pilot study was approved by the London City and East National Research Ethics Committee (IRAS 210888), and all patients provided written informed consent. This study complied with the Helsinki declaration., and all patient data was anonymised.

Results

34 patients out of a possible 60 patients (56.7%) met the study entry criteria and 18 (52.9%) patients were recruited into the exercise group. The reasons given for not entering the study included uncertainty about the exercise program, wishing to relax on dialysis and taking exercise on non-dialysis days. These patients were then propensity matched for base-line muscle mass, frailty and co-morbidity with 21 control patients dialuysing in a separate dialysis centre, acting as cluster controls (tables 1 and 2). Although the mean age of control group was greater and weight were lower, age and weight were not significantly different (tables 1 and 2).

13 (72.2%) of patients completed the exercise program. One patient with a colostomy found pedalling during dialysis uncomfortable and discontinued the exercise program, as did one other patient who suffered from chronic hip pain due to arthritis. Two other patients did not complete the exercise program due to increasing frailty, unrelated to the exercise program. The final patient was withdrawn due to persistent pre-dialysis hypotension. The mean duration of cycling achieved at the end of the programme was 20.4±6.1 minutes per session, with a mean distance travelled of 7.93±2.93 km, and with a mean energy expenditure of 45.6±22.4 kcal achieved for each exercise session

Following the exercise program there were no statistically significant changes in weight, haemoglobin or standard biochemistries. Estimated dietary protein derived by nitrogen appearance rate did not increase, sessional dialysis urea clearance (Kt/Vurea) increased, but was not significantly different from pre-exercise, but post-exercise sessional Kt/Vurea was greater than that of the controls (table 2). There were no differences in body composition at the start of the exercise program, or on follow-up (table 2). However, muscle strength, both hand grip strength (HGS) and pinch strength (PS) increased (Figure 1). Similarly testing function with the 6MWT, then distances increased from 349±105 to 398±94.2 m, $p<0.05$, following exercise. There was a significant improvement in frailty grade for those completing the exercise program ($p=0.046$).

Discussion

We recruited patients into a pilot thrice weekly cycling exercise study conducted during haemodialysis, and found that muscle function and strength increased for both muscles involved in the exercise program, as evidenced by the increased 6-minute walking test, but also for muscles not directly involved in the exercise, with improved hand grip and pinch strength. Although overall function improved with a reduction in frailty score, we found no change in lower or upper limb muscle mass. In the cluster centre controls, there were no corresponding changes in frailty scores, muscle strength or body composition.

If exercise programs are to benefit patients, then ideally all patients should participate. In our pilot study only 56% of our dialysis centre population met the study entry criteria and then just over half took part in the study. Although our patients benefited from exercise, it must be remembered that less than 30% took part. Our findings are in keeping with previous studies which have reported that patients are reluctant to attend exercise programs on non-dialysis days at the dialysis centre [11], and even more simple exercise programs, such as encouraging walking on non-dialysis days at home reported that around 30% only completed 10% or less of the scheduled number of exercise sessions [26].

On the positive side, the majority of our patients (72.2%) completed the exercise program. Two patients discontinued the exercise program, as pedalling during dialysis exacerbated pre-existing medical problems; arthritic hip pain, and pressure on a stoma bag. Other studies have also reported that patients who take part in exercise programs during dialysis are more likely to continue with exercise [13,14].

Although some studies have also reported benefits from exercise programs [13], this has not been universal [14]. Meta-analysis of published studies has reported that exercise programs have differed markedly in type, frequency and duration of the exercise program, but overall did not improve walking test times [27], including two cycling programs similar to our study [28,29]. Although our study was of similar duration to most of those previously published, we noted a significant improvement in physical functioning with an increase in the 6-minute walking test and over-all frailty score, which supports the findings of a recent study which recruited both haemodialysis and peritoneal dialysis patients to a walking exercise program [26].

Whereas a small number of studies have reported an increase mid-thigh muscle mass measured by computerised tomography [27], we found no change in total skeletal muscle mass, appendicular lean mass, or individual lean limb mass, despite finding an increase in muscle strength in muscles not directly involved in the exercise program. However, this may have been due to the small number of patients studied, using an aerobic rather than a resistance exercise program, and the relatively short exercise period. In addition, previous studies have reported a variable relationship between muscle strength and muscle mass in dialysis patients, which may be due to an increased fat and water content of the muscle in patients with chronic kidney failure [30,31]. In terms of potential side-effects of exercise during dialysis we did not find that cycling during the first two hours of the dialysis session led to a fall in blood pressure or other adverse events. Whereas previous studies which have suggested that exercise can lower blood pressure, we found no such effect [27].

We chose a control group of patients based on muscle mass and frailty in another of our dialysis centres, as we have previously found that recruiting patients in the same dialysis centre can lead to the control group being influenced by the active study group [32]. Although the control group was marginally older, there were no significant baseline differences, and repeated measurements of muscle strength and body composition did not significantly change. Previous studies have shown that the reported benefits of exercise are independent of age [13,14]. Dialysis urea clearance did not change in the control group, whereas sessional Kt/Vurea increased in the exercise group. Previous reports have suggested that by maintaining muscle blood flow during dialysis with exercise allows greater urea clearance from muscle during the dialysis session, as normally muscle blood flow falls during the session [12].

Although there are many potential causes for loss of muscle mass in dialysis patients [1,2], physical inactivity is now recognised as a major cause [33]. As such dialysis patients would potentially benefit from exercise. The key question is how best to encourage dialysis patients to exercise, and patients are more likely to exercise whilst dialysing than on non-dialysis days. In this pilot study we found that around 50%

of patients could potentially take part in a pedalling program during the dialysis session, with around 70% completing the exercise program. We found that muscle function improved with exercise, in terms of distance walked and pinch and hand grip strength, and over-all frailty score. There were no direct complications of exercise, although in 11% exercise exacerbated pre-existing conditions and these patients discontinued exercise.

This pilot study was submitted as a MSc project to Univeristy of London and archived in the medical library St George's Univeristy Hospital.

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Figure 1. Hand grip strength (HGS) and Pinch strength (PS) measured prior to starting and after completion of the exercise program and in control group. *$p<0.05$ and **$p<0.01$ vs pre- measurement.