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IMPACT OF AIROGYM EXERCISE ON SOLUTE REMOVAL AND OEDEMA ON END-STAGE KIDNEY DISEASE PATIENTS: A RANDOMISED CONTROLLED TRIAL

JK Adam¹ PhD | S Singh² MTech | M Nasr³ PhD | SBN Krishna¹ PhD

¹Department of Biomedical & Clinical Technology, M L Sultan Campus, Durban, South Africa

²Ethekwini Kidney and Dialysis Centre, Newlands East, Durban, South Africa

³Sanitary Engineering Department, Faculty of Engineering, Alexandria University, Alexandria, Egypt

Corresponding author: Dr SBN Krishna | tel: +27 (31) 373 3093 | email: Sureshk@dut.ac.za

ABSTRACT

It is well established that end-stage renal disease patients often have other health problems that can be improved by participation in regular exercise programmes. In addition, the reduced physical functioning that is experienced by patients who are on dialysis is potentially addressable through exercise interventions. Very few studies are undertaken to investigate the effect of exercise on solute removal and oedema in patients undergoing hemodialysis in South Africa. In this study, a sample of thirty four patients (17 in the intervention group aged between 25 and 60; 17 in the control group aged between 18 and 60) performed airogym exercises on a cushion for fifteen minutes every hour to achieve a total of sixty minutes of exercise over a four-hour dialysis session, for period of nine months. Results showed there was a significant reduction in the mean serum urea clearance of 30% ($p < 0.001$) during post hemodialysis over a six month period as compared to pre hemodialysis. A significant reduction was also seen in the creatinine levels post hemodialysis of 17% ($p = 0.01$) as compared to that of the baseline. The serum urea Kt/V mean values increased from 1.2 at baseline to 1.4 after six months of exercising, suggesting 17% increase in serum urea ($p = 0.5$). Furthermore, the potassium levels during pre and post hemodialysis dropped by 8% between April and September in both the intervention and control groups. The airogym exercise programme improves the wellbeing and quality of life (QoL) of dialysis patients and can be integrated into a hemodialysis routine with a high long-term adherence.

KEYWORDS

Airogym exercise, end-stage kidney patients, oedema, intervention, urea

INTRODUCTION

Sub-Saharan Africa geographically, is a vast and heterogeneous region of roughly 24 million km² that includes 47 countries and more than 900 million people.^[1] By 2030, more than 70% of patients with end-stage kidney disease (ESKD) are estimated to be living in low-income countries, such as those in sub-Saharan Africa, where the gross domestic product per person is on average, less than US \$1500 per year.^[2] There are many potential causes of chronic kidney diseases (CKD) in sub-Saharan Africa, making kidney disease devastatingly burdensome for the region. In addition to non-communicable diseases; communicable diseases such as infectious glomerulonephritis, schistosomiasis, leishmaniasis, and HIV infection are common and can cause CKD. Because more than 22 million people in sub-Saharan Africa have HIV, the potential for the devastating burden of CKD in the region is high.^[3]

Less than 5% of all patients with ESKD in sub-Saharan Africa receive dialysis and patients in several of these countries having no access to dialysis at all.^[4,5]

The most commonly reported causes of ESKD in South Africa are glomerulonephritis (36.5%) hypertensive renal disease (31.7%), diabetic nephropathy (11.8%) uncertain or not stated

(8.6%) and cystic kidney disease (3.1%).^[6,7] Patients with ESKD are known to be inactive and have a high burden of disease (particularly cardiovascular comorbidities) that affects QoL, and dramatically reduces their life expectancy.^[8] Some of these include; reduced effort tolerance and muscle strength caused by anaemia, cardiovascular and pulmonary disease, altered skeletal muscle metabolism, myopathy changes associated with chronic renal failure per se, malnutrition and overall physical conditioning.^[9-12]

The positive influence of regular exercise on QoL, muscle strength, social and professional eminence and this regular exercise should be encouraged in patients with CKD.^[13,14] Furthermore, many trials emphasise the benefits of exercise training to support ESKD patients during dialysis. These benefits include: improved peak VO₂^[15], QoL^[16], cardiac function^[17] and reduced sympatho-adrenal activity.^[12] In addition, exercise training improves cardiovascular risk factors such as blood pressure^[18], lipid profiles^[19] as well as dialysis efficacy.^[20] Despite these proven benefits, a structured physical exercise programme (SPEP) for patients with dialysis is rarely performed on a routine basis. This is surprising, as this approach offers a supervised setting for patients. This is time sparing, as patients will not have to attend additional exercise sessions which improves dialysis efficacy. Lack

of widespread awareness of exercise in hemodialysis literature may be contributing to these shortcomings in clinical practice.

Our present study focuses in establishing the impact of airogym exercise during hemodialysis on solute removal and oedema in ESKD patients. Though, similar experiments have been conducted with success, this is the first time that such a study was undertaken in dialysis units in South Africa. The results of this study will help to establish whether it is possible to implement routine exercise programmes for patients with renal failure during hemodialysis, in order to improve solute levels and oedema.

MATERIALS AND METHODS

Participants

Participants for this study were recruited from two Medi-Clinic Hospital Renal Units (namely, Newcastle Private Hospital Renal Unit and Bloemfontein Medi-Clinic Renal Units, South Africa) where they had been on maintenance hemodialysis for at least 3 months. All patients who participated in the study were on a three times a week dialysis programme. Thirty-four patients with ESKD who were on hemodialysis were included. Seventeen patients were in the intervention group (aged between 25 and 60) and seventeen in the control group (aged between 18 and 60). Random allocation was utilised to assign the patients to their respective groups, with patients taking a letter (A or B) out of an envelope. A total of twenty patients were recruited from Bloemfontein (ten in group A and ten in group B) and fourteen from Newcastle (seven in group A and seven in group B).

Patients in the intervention group did not exercise for the first three months of the study in order to establish a baseline period. Thereafter, exercising began from the fourth to the ninth month of the study period. Patients in the intervention group pedalled on an exercise cushion for fifteen minutes every hour to achieve a total of sixty minutes of exercise over a four-hour dialysis session. The study protocol was approved by the University Ethics Board and written informed consent was obtained from each participant. Patients suffering from diabetes, symptomatic ischaemic heart disease, orthopaedic or musculoskeletal problems interfering with exercise training were excluded. On completion of the study, the patients recruited, continued on a chronic dialysis programme as was recommended by the nephrologist.

Study design

This was a quasi-experimental investigation, as patients participating in the research knew whether they were in the intervention group or in the control group. Patients in Group A, who were in the intervention group, pedalled on an exercise cushion for fifteen minutes every hour to achieve a total of sixty minutes of exercise over the four-hour dialysis sessions. Those in Group B (control group) were not required to exercise during the hemodialysis sessions. This was one of the limitations of this project. However, both groups were dialysed by the associate renal units with the assistance of nurses and technologists wherever necessary. All patients were treated the same in terms of drawing blood and motivating them to maintain a good QoL with regards to exercise, diet, joining social groups and attending psychological counselling if necessary.

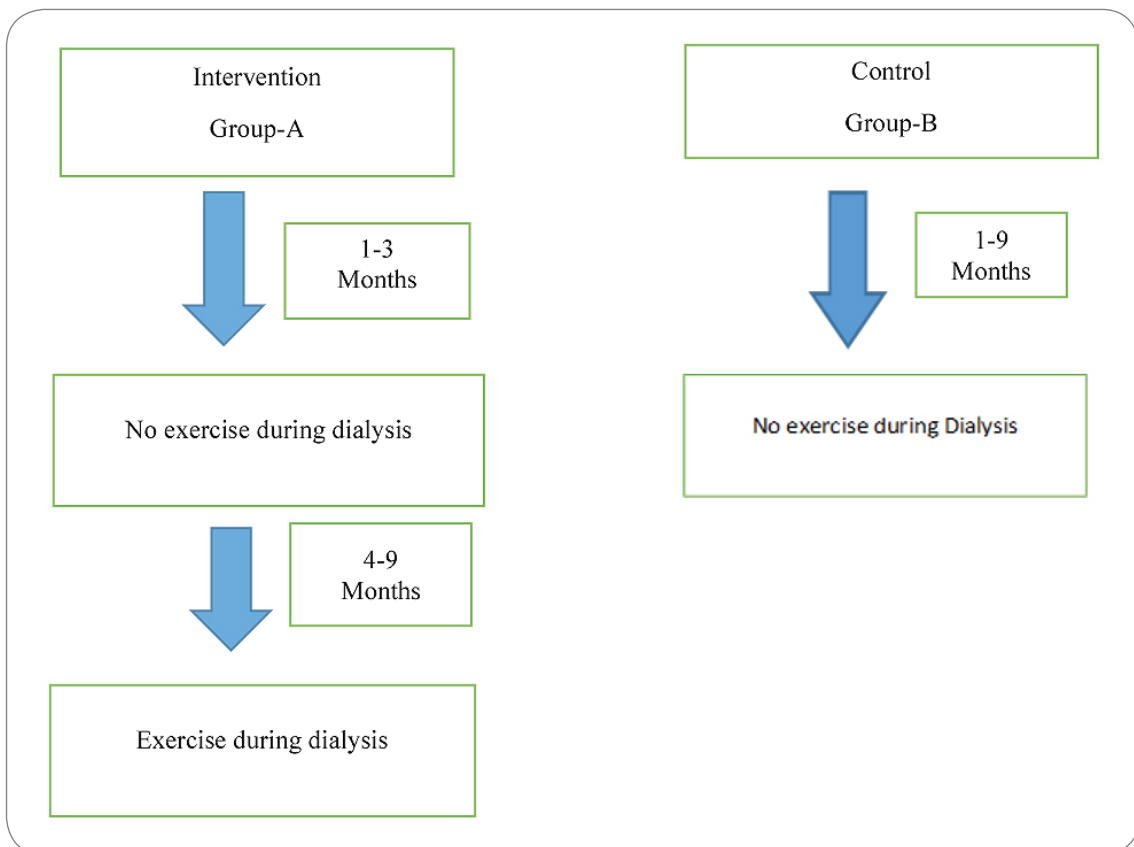


Figure 1. Overview of time frame of airogym exercise training during study period

Intervention

The duration of intervention was nine months. During the first three months, patients in the intervention group did not exercise on the exercise cushion in order to establish a baseline. Thereafter, from the fourth month until the ninth month patients in the intervention group pedalled on the exercise cushion during hemodialysis (Figure 1). All patients exercised at a slow steady state in order to target their heart rate at 100 beats per minute and then slowed down gradually to recovery. A total of sixty minutes of exercise was performed over the four hours when on hemodialysis.

Blood Sample Collection:

Pre and post hemodialysis blood samples were drawn from each patient monthly, over a nine month period, using a slow flow pump technique that prevents sample dilution with recirculating blood and minimizes the confounding effects of urea rebound. After blood samples were taken they were sent immediately to the pathology laboratory for measurements of urea, creatinine and potassium.

Measurement of Oedema:

Oedema of the lower limbs was measured in centimetres around the ankles (right and left) before and after dialysis as described by Mora *et al.*^[21] with slight modifications. These modifications confirmed whether exercising during hemodialysis caused a further reduction in oedema apart from the efficiency of the hemodialysis treatment.

Biochemical analysis:

Urea, creatinine and potassium levels were quantitatively measured using standard laboratory techniques.

Urea estimation:

Blood urea nitrogen (BUN) was estimated using the urease method on the the Abbot Architech C800 analyser (Abbott Laboratories, Abbott Park, Illinois, U.S.A) as described by Sampson and Baird,^[22] with modifications.

Briefly, 1mL of urea nitrogen (BUN) was added to tubes labelled: "standard", "control", "patient" (pre hemodialysis and post hemodialysis) and all tubes were then pre-incubated at 37°C for at least 5 min. 10µL of sample was then added and mixed thoroughly. After exactly 30 sec the absorbance was recorded at 340nm (A_1). At exactly 60 sec after reading (A_1), the reading and recording of absorbance (A_2) was noted. The initial rate of decrease in absorption at 340nm is proportional to the urea concentration in the sample.

Creatinine estimation:

The Abbot Architech C800 analyser was used to measure the creatinine levels in the blood using the Kinetic Jaffe Method.^[23]

Briefly, the serum samples were mixed with alkaline picrate to form the creatinine picrate complex and the rate of change in absorbance was measured. The creatinine picrate complex is directly proportional to the concentration of creatinine in each of the samples.

Potassium estimation:

The Ion Selective Electrode method was used to quantitate the potassium levels (<http://www.nico2000.net/analytical/potassium.htm>). An electric potential is developed across the

membranes between the reference and measuring electrodes in accordance with the Nernst equation. The voltage is then compared to a previously determined calibrated voltage and converted into ion concentration.^[24]

Urea Kt/V:

The dialysis efficiency was determined according to Dialysis Outcomes Quality Initiative (DOQI) guidelines of The National Kidney Foundation^[25] using the following formulae:

$$KtV = - \ln (R - 0.03) + (4 - 3.5 \times R) \times UFAW$$

$$R = \text{post/pre plasma urea nitrogen ratio}$$

$$UF = \text{ultrafiltrate volume (litres) removed}$$

$$W = \text{post dialysis weight (kg)}$$

Statistical Analysis

All analyses were carried out by using the statistical package SPSS 9.0 for Windows (SPSS, Chicago). The paired student t-test was used to determine levels of significance. The level of significance was defined as $p < 0.05$. Figures were then displayed using the function "boxplot" using MATLAB R2009 software. On each box, a central line is the sample median indicating central tendency or location. A box denotes variability around the central tendency (the edges of the box are the 25th and 75th percentiles). Whiskers around the box describe the range of variability; and observations beyond the whisker length are marked as outliers, equivalent to 1.5 times the interquartile range away from the top or bottom of the box.^[26] The one-way analysis of variance (ANOVA) is used to determine whether there are any significant differences between the means of control or intervention groups.

RESULTS

Pre and post hemodialysis serum urea levels

The effect of airogym exercise during pre and post hemodialysis on serum urea levels in the intervention and control groups over a nine month period are tabulated in Table 1. Throughout the intervention period (6 months) the serum urea mean values and SD were 29.1 ± 8.0 mmol/L at the start (April) and 29.5 ± 10.3 mmol/L at the end (September). These values indicate that there were no significant changes in the serum urea levels at baseline in the control group ($p = 0.89$).

During the intervention period in post hemodialysis, the serum urea levels remained constant. Although there was a slight rise in the serum urea mean value in March, it was not significant over the overall baseline period. After six months, there was a significant reduction in the mean serum urea levels by 30% i.e. between April and September.

Pre and post hemodialysis serum creatinine levels

The intervention group, during pre hemodialysis at baseline from April to June (Table 2) showed a significant decrease in serum creatinine levels ($p = 0.007$) suggesting that exercise during hemodialysis had an effect on pre hemodialysis creatinine levels. From July to September the creatinine mean values and SD showed no significance in creatinine clearance levels ($p = 0.9$). Furthermore, no significant changes were observed in creatinine clearance levels in the control group over the study period ($p = 0.63$).

Table 1. Pre and post hemodialysis mean serum urea values ± SD (mmol/L) in the intervention and control groups over nine months

BASELINE				INTERVENTION					
Month	January	February	March	April	May	June	July	August	September
<i>Pre hemodialysis</i>									
Control	31.2±9.5	31±8.2	30.7±10.3	30.4±9.3	30.9±8.1	32.6±6.9	31.6±8.1	30.8±9.3	34.4±9.6
Intervention	29.9±8.2	31.0±8.4	31.4±8.1	29.1±8.0	29.6±7.3	30.4±8.5	29.9±7.7	30.9±8.5	29.5±10.3
<i>Post hemodialysis</i>									
Control	7.9±2.0	8.3±1.5	7.9±2.1	8.1±2.0	7.7±1.9	8.2±0.8	8.0±1.8	8.1±2.1	8.9±2.0
Intervention	8.3±2.6	8.3±2.5	8.6±2.7	7.1±2.1	6.7±2.0	6.3±1.6	6.0±2.0	5.7±2.1	5.0±1.9

Data represent mean ± SD

Table 2. Pre and post hemodialysis creatinine mean values ± SD (µmol/L) in the intervention and control groups over nine months

BASELINE				INTERVENTION					
Month	January	February	March	April	May	June	July	August	September
<i>Pre hemodialysis</i>									
Control	961±312	870±388	921±293	956±337	945±325	948±294	993±338	966±302	895±381
Intervention	1162±357	1109±312	1053±272	914±201	859±194	787±227	798±179	793±175	796±175
<i>Post hemodialysis</i>									
Control	428±142	398±144	409±154	433±152	386±136	422±155	453±195	419±125	397±165
Intervention	627±218	560±148	521±133	452±122	418±123	369±108	342±94	341±91	340±92

Significant reductions in the mean creatinine levels were observed at baseline during post hemodialysis in the intervention group ($p = 0.001$). There were no significant changes in creatinine level mean values at baseline in the control group ($p = 0.01$). From April to September the creatinine level mean values in the control group varied marginally, but was of no statistical significance ($p = 0.9$).

Effect of exercise during hemodialysis on urea Kt/V

The mean serum urea Kt/V in the intervention group at baseline

remained constant (Table 3). The serum urea Kt/V level and SD were 1.2 ± 0.14 in January, 1.2 ± 0.13 in February, and 1.2 ± 0.14 in March respectively; indicating no change. Therefore overall, there were no significant changes in Kt/V at baseline. In April, after the first month of exercising the mean serum urea Kt/V value increased to 1.3. In June there was another increase in mean serum urea Kt/V value to 1.4. Thereafter the serum urea Kt/V values maintained a constant level until September. The serum urea Kt/V mean values increased from 1.2 at baseline to 1.4 in September after six months of exercising. This was a

Table 3. Serum urea Kt/V in intervention and control groups

BASELINE				INTERVENTION					
Month	January	February	March	April	May	June	July	August	September
Control	1.2± 0.16	1.2± 0.16	1.3± 0.13	1.2± 0.13	1.3± 0.13	1.3± 0.12	1.3± 0.13	1.2± 0.13	1.3± 0.13
Intervention	1.2 ± 0.14	1.2+ 0.13	1.2± 0.14	1.3± 0.13	1.3± 0.12	1.4± 0.10	1.4± 0.11	1.4± 0.12	1.4± 0.12

Table 4. Pre and post hemodialysis potassium (mmol/L) levels in the intervention and control groups

BASELINE				INTERVENTION					
Month	January	February	March	April	May	June	July	August	September
<i>Pre hemodialysis</i>									
Control	5.2±0.8	4.9±0.7	5.1±1.0	5.0±0.7	5.1±0.6	4.9±0.6	5.0±0.7	4.8±0.4	4.6±0.4
Intervention	5.5±1.0	5.0±0.9	5.1±1.1	5.3±1.0	4.9±1.0	4.8±0.9	5.0±1.0	5.0±0.9	5.0±0.7
<i>Post hemodialysis</i>									
Control	3.8±0.3	3.6±0.3	3.7±0.5	3.8±0.3	3.5±0.4	3.6±0.2	3.7±0.4	3.6±0.1	3.5±0.2
Intervention	4.2±0.7	3.8±0.4	3.9±0.7	4.0±0.6	3.6±0.8	3.7±0.6	3.9±0.6	3.8±0.4	3.7±0.5

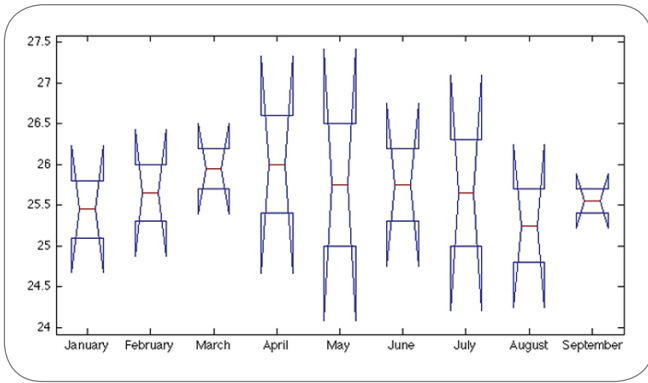


Figure 2a. Mean right ankle circumference (cm) in the pre hemodialysis group categorised by months

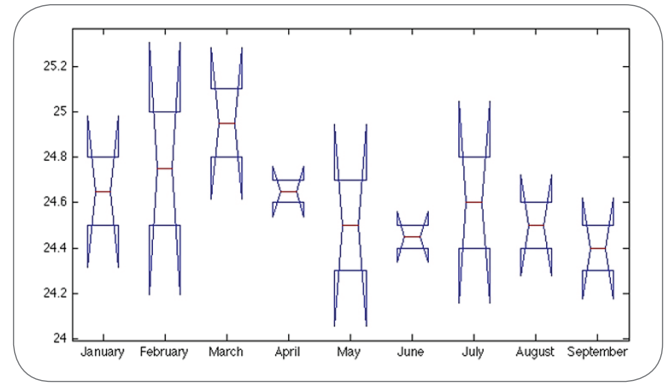


Figure 2b. Mean right ankle circumference (cm) in the post hemodialysis group categorised by months

17% increase in serum urea Kt/V after six months of exercising. The serum urea Kt/V in the control group at baseline remained constant.

Pre and post hemodialysis on serum potassium levels

Pre and post hemodialysis serum potassium levels are shown in Table 4. During pre hemodialysis, the potassium levels at baseline in the control and intervention group (April to September) remained constant ($p = 0.09$). On the other hand, potassium mean values from April to July ($p = 0.9$) and August to September ($p = 0.4$) respectively, displaying significant differences between the two groups. Whereas during the post hemodialysis, potassium mean values in the intervention group at baseline, showed no significant differences with $p = 0.013$.

Effect of exercise during hemodialysis on Oedema

In this study, oedema of the right ankle and the left ankle were studied separately:

A. Pre and post hemodialysis right ankle circumference in the intervention and control groups

In the intervention and control groups (Figure 2a) baseline values of the pre hemodialysis right ankle circumference remained constant showing no significant changes ($p = 0.9$). From April to September the mean ankle circumference remained constant with the values in April and September, 25.4 cm. Similarly, post hemodialysis mean right ankle circumference at baseline remained constant with no significant changes ($p = 0.9$) (Figure 2b). There was a significant reduction in the right ankle

circumference in the intervention group at the start of exercising in April and reduced to four months and increased in the last three months of the study period. Nevertheless, increase in the ankle circumference in the last three months showed no significant improvement in oedema ($p = 0.6$).

B. Pre and post hemodialysis left ankle circumference in the intervention and control groups

The mean circumference of the left ankle in the control and intervention group over the study period in the control group, pre hemodialysis is shown in (Figure 3a). Ankle circumference at baseline remained constant ($p = 0.9$), no significance. Likewise, the intervention group (April to September) displayed no significance ($p = 0.9$) during post hemodialysis (Figure 3b). The control group from April to September also displayed consistent values of no significance ($p = 0.002$).

DISCUSSION

Pre and post hemodialysis serum urea levels in the intervention and control groups at baseline presented no major changes. In the intervention group, pre urea levels exhibited no significance but during post hemodialysis urea levels from April to September indicated a significant reduction by 30% ($p < 0.001$). These findings strongly suggest that exercise during hemodialysis reduced serum urea levels by 30%. There were no major changes in the serum urea levels of the control and intervention groups during pre hemodialysis. Post hemodialysis serum urea levels in the intervention group at baseline compared to pre hemodi-

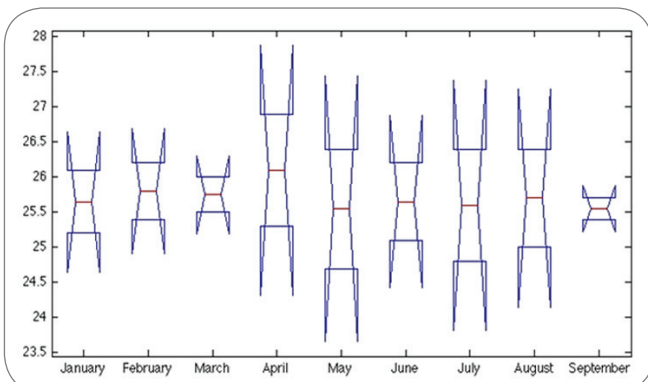


Figure 3a. Mean left ankle circumference (cm) in the pre hemodialysis group categorised by months

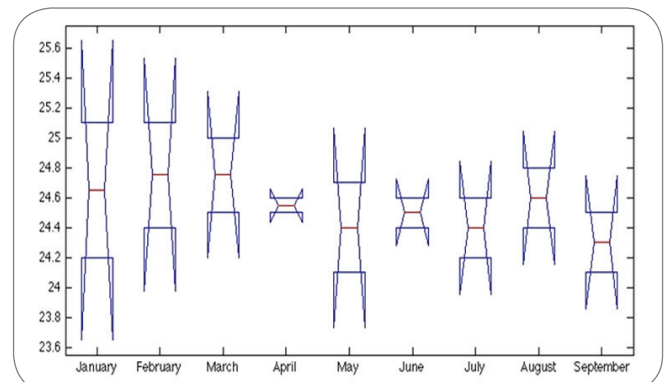


Figure 3b. Mean left ankle circumference (cm) in the post hemodialysis group categorised by months

alysis serum urea levels displayed major differences. However, both remained constant all throughout the nine month period. These findings are in agreement with Ronco *et al.*^[27,28] Increased serum urea removal is dependent upon rapid blood flow^[29] and additional exercise during conventional dialysis reduces urea rebound, increases creatinine removal and, importantly, increases phosphate removal. It also contributes to the general well-being of the dialysis patient.

In the intervention group the creatinine levels during pre hemodialysis at baseline showed a significant reduction of 9% ($p = 0.007$). April to June the creatinine levels were significantly reduced by 14% during pre hemodialysis ($p < 0.001$) and maintained consistency from July to September with no further reduction. Furthermore, post hemodialysis creatinine levels at baseline showed a significant reduction of 17% ($p = 0.01$). In this study, the intervention group showed a greater reduction in creatinine levels at baseline than the control group. The possible reason for this larger reduction in creatinine levels in pre hemodialysis and at baseline could be due to the fact that patients were aware that this research project could improve their QoL and possibly their blood results. This motivated them to exercise on their non-dialysis days, follow their renal diet more strictly and be more compliant with administering their medication promptly. These findings are in agreement with previous studies^[29,30] where creatinine removal was significantly increased by exercise, during hemodialysis. These results demonstrate that intense exercise training on non-dialysis days is the most effective way of training. Exercise during HD is also effective and preferable.

In this study potassium levels were significantly reduced by 8% from April to September in both the intervention and control groups, during pre and post hemodialysis ($p = 0.2$). However, the potassium in the intervention group was reduced by 12% from January and in the control group by 8% from January to September during post hemodialysis. Thus, there was a 4% greater difference in the reduction of potassium in the intervention group than the control group. This is in agreement with a previous study which proved that exercise during hemodialysis increases the efficiency of the dialysis treatment in ESKD patients^[31] probably by increasing muscle strength^[32] and reducing the rebound of solutes due to increased perfusion of the skeletal muscles.^[33]

The Kt/V urea values at baseline in the intervention group showed no significance ($p = 0.2$), and the Kt/V values were 1.2 from January to March. From April to September the Kt/V urea increased by 8% ($p = 0.5$) and 17% from January to September ($p < 0.001$). Furthermore, the intervention group showed an overall 9% increase in Kt/V urea compared to the control group between January and September. Similar findings were reported by Sun *et al.*,^[34] where Kt/V urea levels were significantly higher in the intervention group than those of the control group. Gianakki *et al.*^[35] using a prolonged intra-dialytic exercise programme during optimal HD observed that particularly the Kt/V, urea reduction ratio, and the creatinine reduction ratio significantly improved by 20%, 11%, and 26%, respectively, while potassium plasma levels were also reduced by 77.5%

($p < 0.05$). Unusually, exercise during dialysis improved dialysate urea removal, but not serum urea clearance.^[36] Alterations in the modality and the timing of exercise during dialysis may be required to acquire an increase in serum urea clearance.

The change between the pre and post ankle circumference of the right ankle at baseline displayed no significant changes in the intervention group ($p = 0.3$). However, there was a major reduction in the right ankle circumference in the intervention group at the start of exercising in April and increased in the last three months of the study period. This increase in the ankle circumference in the last three months had no improvement in oedema ($p = 0.6$). The possible reason for the change in right ankle size in the intervention group between April and June (45%) could be because patients were interested in being part of an investigation which could reduce the discomfort of ankle oedema and were motivated to do further exercising on their non-dialysis days and complying strictly with their fluid restriction, diet and medication. The present data are in agreement with Sakkas *et al.*^[37] who reported a significant increase in muscle morphology in dialysis patients after six months of aerobic exercise training in ESKD patients.

The variation between the pre and post ankle circumference of the left ankle at baseline showed no significant changes in the intervention group ($p = 0.9$). In the intervention group the variation in size of the left ankle from March to August showed a 60% decrease compared to baseline ($p = 0.002$). From August to September the difference in the ankle size between pre and post hemodialysis increased by 25% compared to baseline. The possible reason for the increase in left ankle size in the last month of hemodialysis could be because patients in the intervention group were not as enthusiastic as they were during the previous months. This may be because they were feeling well and stronger from their previous months of exercising and did not feel that it was necessary to put in the same extra effort on their non-dialysis days. Skeletal muscle atrophy in HD patients contributes to their poor exercise tolerance.^[38] The application of an exercise training programme improves muscle atrophy markedly, and therefore warranted beneficial effects in overall work performance.

CONCLUSION

The results of this study demonstrate that airogym exercise training on solute removal and oedema during hemodialysis, is most probably due to the acute increase in blood flow and consequently increased perfusion of skeletal muscles. This study also showed a significant reduction in the solute levels and oedema in ESKD patients. Furthermore, there was a significant improvement in oedema of 45% in the right ankle for the first three months of exercise and thereafter there was an increase in ankle size in the last three months, which was a 13% reduction in oedema overall as compared to that of the baseline. The reason for the increase in ankle size in both ankles in the last three months is inconclusive and future investigation is recommended.

In conclusion, exercise training during hemodialysis is likely to prove to be an economic, safe and efficacious method of

increasing the wellbeing and QoL of dialysis patients. However, future research is necessary. For example, this research's main focus would be on the length and size of the study group. This would identify other beneficial effects of exercise intervention on solute removal and oedema. It would further identify the possible reasons for the urea Kt/V and creatinine levels remaining constant in the last three to four months of this study and also the possible causes for the increase in the change in ankle size in the last three months of the study period.

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DECLARATION OF INTEREST

The authors declare no conflict of interest.

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