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Effects physical activity on creatinine, and metabolic syndrome in females with transplanted kidney

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Abstract

Introduction: Chronic kidney disease is a significant general disease, which affects a large number of people around the world. Chronic kidney disease is identified by blood test for

creatinine, the blood levels of creatinine rises. The one main causes of chronic kidney disease is diabetes. The aim of this study was to determine the effects of physical activity on creatinine and metabolic syndrome (Mets) in females with transplanted kidney.

Material & Methods: 20 females with transplanted kidney 24.3 ± 2.5 years participated. Subjects were divided into two equal groups. Prior and after study both groups underwent a blood test to check creatinine, Insulin Resistance and metabolic syndrome. The experimental group conducted 8 weeks of submaximal activities and 3 sessions each week. To analyze the data independent and dependent t-test were used. To validate if the data distribution is normal, Kolmogorov-Smirnov test was utilized.

Results: The results show experimental group had decreased their total cholesterol (TC) (0.026), triglyceride (TG) (0.002), fasting blood Sugar (FBS) (0.026), creatinine (C) (0.043), glomerular filtration rate (GFR) (0.02), insulin resistance (IR) (0.044) and increase of high density lipoprotein (HDL) (0.003), Also there were no changes of waist circumference (WC) (0.896) SBP (0.602) and DBP (0.0781) in both groups.

Conclusions: According to the results we can express eight weeks of Physical activity has a Decreasing significant effect on C and Mets. So it can be concluded that physical activity is useful for female with KT.

Key words: Creatinine, Metabolic syndrome, Physical Activity, Transplanted kidney, Females

1. Introduction

Chronic kidney disease is a significant general disease, which affects a large number of people around the world. Patients suffering from this disease are exposed to an advanced form of kidney disease that results in dialysis and kidney transplantation (KT) (1). Kidney dysfunction

increases the risk of death and cardiovascular disease, reduced muscle mass, attenuated muscle strength and power, diabetes and an apparent decreased tolerance to exercise (2-4). In order to estimate the health status of kidney, it is possible to estimate the glomerular filtration rate (GFR) by serum creatinine. The amount of creatinine in blood is not the best way to check kidney health, that's because the level of creatinine in blood is affected by age, race, gender, and weight. The best way to know if kidneys are working properly is by looking at GFR (5). Creatinine is a chemical waste product in the blood that passes through the kidneys to be filtered and eliminated in urine. Most women with normal kidney function have between 0.5 to 1.1 mg/dL of creatinine (6).

Studies show that individuals with a kidney transplant, who take part in regular physical activity can benefit from improved physical fitness and higher health-related quality of life in comparison with individuals who do not engage in physical activity (7,8). Exercise training appears to have an important role in protecting against chronic diseases such as renal disease, diabetes mellitus, stroke, blood pressure and heart failure (9,10). Baxman et al. (2008) studied body composition and activities effect on urinary creatinine. They concluded that Serum and urinary creatinine correlated significantly with body weight, but the level of correlation with lean mass was even greater (11). Researches show that kidney damage probability rises with the increase of metabolic disorders and Mets is very common among recipient of transplant kidney (12-14). Mets is the name for a group of risk factors that raises one's risk for heart disease and other health problems, such as diabetes, stroke and kidney disorder. Also Mets is a disorder of energy utilization and storage, diagnosed by a co-occurrence of three out of five of the following medical conditions, waist circumference (WC) (central obesity), elevated blood pressure and elevated fasting plasma glucose, high serum triglycerides, and low high-density lipoprotein cholesterol (HDL-C) levels (15). Evidences show that participation in regular, moderate-intensity physical activity may be a preventive intervention of the Mets and that activity of greater intensity may provide even greater benefit (16,17).

LDL and total cholesterol also decreased significantly in training, while HDL level increased (saman10). Bruce et al (2004) launched a survey on the sensitivity level of insulin in type 2 diabetic patients. The results of

their survey demonstrated that training causes a drop in HbA1 c level from 7.9 % to 7% and the fasting plasma, blood glucose dropped from 8.3m mol to 7.9 m mol, although this change was not significant. Plasma insulin level was also decreased significantly and some factors such as total cholesterol, HDL and LDL did not show any changes (18). According to the fact that the recent evidences prove that Mets is related with high risk of exposure to Chronic kidney disease (CKDs,) and because of the rise in recent decades of CKD incidence and its Associated with cardiovascular risks and damage thus the growing epidemic of obesity and old societies, Mets and CKD are considered as health problem globally25. Furthermore, there are few, if any, randomized control trials that have been published examining the effects of exercise on changes in GFR and Mets in females diagnosed with kidney transplantation (KT) especially in Iran, the purpose of this study was to investigate the effect of physical activity on changes in GFR creatinine and Mets components as risk factors of kidney.

2. Materials and Methods

Subjects

Twenty inactive females voluntarily with average age of 24.3 $\pm$ 2.5 years with TK from Association of Specific Patients and Organ Transplant of Shiraz Iran participated in the study. Subjects with TK complications that prohibited participation in exercise and smokers were excluded from the study. Subjects were not engaged in any systematic exercise programs at least 6 months before the study. They take anti- immunity medications of Mycophenolic acid (1500 mg per day) and Cyclosporine (100mg per day). Written informed consent was obtained from each subject prior to participation. The subjects were informed of the protocol and the possible risks and difficulties of the study. Subjects were divided into two similar groups' experimental and control based on their BMI. The study was approved by the ethics Committee of Islamic Azad University, Marvdasht branch.

GFR and Metabolic syndrome measurement

Blood samples were obtained in the morning after 8-12 hours fasting a day prior to the start of the study and again 8 weeks after at the end of the study under the same conditions. The serum creatinine level was measured by photometric method without deletion of protein by Jaffe method, then using the formula MDRD, the GFR value was.

$$GFR=186\times [\text{Serum Creatinin}]-1.154\times \text{age (year)}- 0.203\times(0.742)$$

The definition of Mets was based on the presence of three or more components out of five defined criteria for metabolic syndrome by the amended National Cholesterol Education Program's Adult Treatment Panel III (ATP-III) (19). The ATP-III criteria include:

*: waist circumference $>$ 88 cm (women)

*: SBP $>$ 130 mmHg, DBP $>$ 85 mmHg, or use of antihypertensive medications

*: fasting plasma glucose $>$ 110 mg/dl or use of diabetes medications

*: fasting triglycerides $>$ 150 mg/dl or lipid medications and

*: HDL cholesterol $<$50 mg/dl (women).

Serum triglyceride levels was measured by enzymatic kits (Mann Chemical Company) using an auto analyzer. HDL-C was measured by an Auto analyzer using commercial kits (Pars Azema Company, Teheran, Iran). Serum fasting blood sugar levels was measured by Selectra-E auto analyzer using an enzymatic kit (Mann Chemical Company). Insulin was measured using American insulin kit manufactured by Cobas CO and by Electrolytic luminescence method using the Hitachi Elecy 2010 device. Glucose was assayed by glucose oxidase using enzymatic kit (Iran's Pars Azema CO) and by Auto Analyzer device RA1000 model. Insulin resistance (IR) index was calculated using the following formula and using fasting glucose and insulin values.

HOMA IR =[Fasting insulin (μU/ml)×Fasting glucose (m.mol/ l)]÷22.5

Anthropometric and Blood Pressure Measurements

All anthropometrical measurements were done with the subjects wearing light underwear and without shoes. Body weight was measured to the nearest 0.5 kg; using digital scale (made in Germany). Height was measured to the nearest 0.5 cm against a wall mounted tape. Body mass index was calculated by dividing the weight in Kilograms by height in meters squared and according to World Health Organization. Central obesity was measured in centimeters at the midpoint between the iliac crest and the rib cage using a non- stretchable tape without compression of the skin and defined on the basis of waist circumference (WC). Blood pressure was measured on the right arm after resting for 10 min in the supine position, using the standard mercury sphygmomanometer pre and post study (20).

Protocol of study

The experimental group involved in eight weeks of exercise, 3 sessions a week with 55-70 percent of maximum heart beat rate. The exercise program of each session included 10 minutes of warm-up, 30 minutes running, and at the end of each session, cool down for 10 minutes was done. 55-60% of maximum heart beat rate, for the first two weeks, 60-65% for the next 3 weeks, and 65-70% for the last three weeks. The experimental group did not involve in any other exercise aside from the program. Control group underwent the same testing battery but did not participate in any exercise training during eight weeks of study. The protocol was designed by researchers.

Statistical analysis methods

In this randomized clinical trial study data were analyzed using descriptive statistics (mean and standard deviation). To analyze the data of GFR and the factors affecting the metabolic syndrome including: TC, TG, BP, blood glucose and HDL in groups, independent-samples t test was used and paired-samples t test was used to assess their changes before and after the test (intergroup comparison). To validate if the data distribution is normal, Kolmogorov-Smirnov test was utilized. Statistical

significance was set at ($P<0.05$). Data were analyzed using SPSS version 20.

3. Results

There were no significant differences between groups for any of the variables at baseline. Independent-samples t test showed that GFR changes were significantly different in the training and control groups (0.02) in addition the results of paired-samples t test shows experimental group had decreased their TC (0.026), TG (0.002), FBS (0.026), creatinine excreted in the urine (0.043), GFR (0.01) IR (0.044), HDL (0.003), Also there were no changes of WC (0.896), SBP (0.066) and DBP (0.0781) in both groups (table 1).

Table1. Pre and post test of anthropometric and biochemical factors of the subjects (mean ± SD)

Group	Control		Experimental	
Variables	Pre	Post	Pre	Post
Age (y)	23.9 ± 2.6	-	24.4 ± 2.5	-
Height (cm)	162 ± 2.4	-	161 ± 4.2	-
Weight (Kg)	59.5 ± 4.04	58.9 ± 4.6	57.9 ± 1.8	56.5 ± 3.6
BMI (Kg/m^2)	23.8 ± 1.2	23.7 ± 3.6	23.6 ± 2.1	22.1 ± 1.8
WC (cm)	89 ± 0.07	90 ± 0.07	89 ± 0.05	89 ± 0.03
TG (mg/dl)	144 ± 5.4	151.2 ± 5.9	145.2 ± 7.2	138.8 ± 6.9*
TC (mg/dl)	281 ± 15.5	293.1 ± 20.1	276.5 ± 20.1	258.4 ±19.5
HDL (mg/dl)	39 ± 2.1	41 ± 2.6	39 ± 2	44 ± 4.27*
FBS (mg/dl)	105 ± 9.4	107 ± 8.8	106 ± 7.03	100 ± 6.07*
IR	3.9 ± 0.52	4.9 ± 1.32	4.1 ± 1.5	2.8 ± 1.05*
GFR (ml/min)	129 ± 5.2	135.024 ± 6.2	130.2 ± 1.3	119.4 ± 5.5*
Creatinine excreted in the urine(mg/24h)	1157.2 ± 321.2	1011.3 ± 301.2	1112.9 ± 412.3	1399.2 ± 331.4*
SBP (mmHg)	134 ± 7	132 ± 7	131 ± 7	130.5 ± 5
DBP (mmHg)	81 ± 3	82 ± 5	79 ± 3	77 ± 4

* Significant differences between control and experimental groups ($P<0.05$)

4. Discussion

The aim of this study was to investigate the effect of aerobic exercise on C, GFR and Mets in patients with KT as risk factors of CKD. The study showed the effect of reducing physical activity on TC, TG, FBS, creatinine excreted in the urine, GFR, IR and increasing of HDL, Also there were no changes of WC, SBP and DBP in both groups. The main finding of this study involving individuals with transplanted kidney is that Physical activity can provide benefits for individuals with TK and reduces the risk of GFR and Mets. Our study showed that GFR increased and creatinine excreted in the urine and some factors of Mets decreased. In this regard, Bijag et al. (2013) showed that the glomerular filtration rate increases after exercise (21). Rafati et al. (2011) also stated that aerobic activity leads to an increase in the amount of glomerular purification, and in the prevention of chronic renal disease in the early stages or postponement has been effective (22). In another study, Straznicky et al. (2011) showed that exercise can reduce creatinine levels and increase glomerular purification levels (23). Pechter et al. (2003) reported that a 12-week low-intensity aquatic exercise program in 26 patients with mild to moderate chronic kidney disease resulted in decreased blood pressure, decreased proteinuria, and a slight improvement in GFR (24). A possible mechanism for the effect of aerobic exercises on blood pressure reduction is through its effect on reducing body weight, which is justified by the performance and structure changes in vascular system, Renin angiotensin system modifications and sympathetic nervous system reduction38. Also it seems water immersion improves renal function, probably due to an improvement in renal hemodynamics associated with decreases in vasopressor and increases in vasodepressor hormones (25,26). Serin et al. (2009) studied creatinine serum level after submaximal exercises. The results showed there was no change before and after the exercise period and the researchers stated that 8 weeks of aerobic training does not have an effect on creatinine and kidney performance (27). Baxman et al. (2008) studied body configuration and activities effect on urinary creatinine. They reported that creatinine is not affected by physical activity which is not in line with our study (28).

The difference between results of the studies could be for the difference between the intensity and duration of exercise, sex, KT or other renal disorder and also a different training environment (land or water). Also our analyzed shows that aerobic training is associated with lower risk of Mets among females with KT. A number of studies have showed correlations between Mets and CKD (29). Chen et al (2004) found that having metabolic syndrome results in a 2-fold higher chance of developing CKD compared with the general population (30). Furthermore physical activity improves Mets significantly. Lakka et al. (2007) and Shenoy et al. (2009) reported the same results (31,32), but the studies of Bruce et al. (2004), Eriksson et al. (2002) and Vincnt et al. (2006) are not agree with results of present study (33-35). One of the reasons could be the use of drugs like anti immune system for organ transplantation, such as cyclosporine, as most studies state that cyclosporine has side effects such as increase TC and TG levels (29). Another common issue after transplantation is the increase in blood pressure. High blood pressure results in nephron sclerosis, through dependent on or independent mechanism. In patients suffering from high blood pressure and urinary protein excretion, GFR declines which means that even a slight increase in blood pressure can expose these patients to kidney damage (36).

Blood sugar showed decreases in experimental group which is conceivable, because following physical activity, muscle contractions , like insulin, transfer a great deal of glucose into muscle cells (37). It is also expected that physical activity will result in an increase in the level of GLUT4, improving insulin function in glucose metabolism (38).

Nevertheless the duration and intensity of the trainings, the primary level of subjects' readiness, the individual differences and the basal level of blood sugar are all among reasons for inconsistencies.

Several of the early studies observed significant improvements in glucose tolerance (39) which is in same direction as present study. It is may be exercise promotes weight loss, that reverses the insulin resistance which is the characteristic of obesity (40). Mohebi et al. (2006) reported that TG and LDL levels decrease after a period of exercise (41), on the other hand Sigal et al. (2007) reported that they failed to find such effect after

physical activity (42). Also there is relationship between physical activity and body mass index (BMI), hip-waist ratio, and WC (43,44). Reduction in fat mass is helpful in increasing adiponectin levels and improving cytokine profiles which are associated with the Mets (45,46). Exercise-induced increases in plasma IL-6 correlate with the muscle mass involved in exercise activity and also with the mode, duration, and, especially, the intensity of exercise (47).

It is worth highlighting that regular physical activity is critically important for prevention of the Mets and its components and also healthy kidney in both early life and later life.

5. Conclusion

Eight weeks of aerobic exercise has a significant effect on Creatinine on females with KT, and Mets components. Thus, according to the fact that the Mets components increase after the transplant and can have negative effects on kidney performance in long-term, therefore, according to the results of the study can say aerobic exercise effect on these components. It seems that creatinine excreted in the urine is also affected by aerobic activity; however there should be more studies with various exercise types, duration and intensity in order to present proper solutions for patients, as well as increasing the knowledge.

Conflict of interests: No conflict of interests amongst authors.

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