

The Effect of Combined Exercise Course and Aloe-Vera Supplementation on Renal Function and Lipid Profile in Type 2 Diabetes Mellitus Patients: A Randomized Clinical Trial

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Abstract

Objective: Renal failure is a complication of diabetes. It can be the risk factor of cardiovascular disease. This study aimed to evaluate the effect of exercise course and Aloe-Vera supplementation on renal function and lipid profile in type 2 diabetes mellitus (T2DM) patients.

Materials and Methods: This is a clinical trial double blind with pre-test and post hoc test analyses with a control group. The studied population included a group of T2DM diagnosed patients among whom 24 men (40-60years) were selected voluntarily and purposefully and were classified into three groups by balanced block randomization method, exercise(E), exercise + supplement (E+S), and control (C), (n=8/group). Combined exercise was planned in two 12-minute repetitive sets with 70% 1RM. Then the participants ran for two 10- minute sets with 70-75% maximum heart rate intensity on treadmill. E+S participants consumed 500 mg/day Aloe Vera for 6 weeks. Obtained data by SPSS-19 software were analyzed using co-variance analysis method with Bonferroni post hoc test (P -value<0/05).

Results: Results showed that E and E+S significantly improved GFR (P -value=0.011) and E with or without Aloe-Vera consumption decreased creatinine levels (P -value=0.042) and increased HDL levels (P -value<0.001). The results demonstrated that LDL and TG levels showed no significant difference in reaction to the combined exercise and supplementation.

Conclusion: Combined exercise along with Aloe-Vera supplementation has had significant effect on improving renal factors and lipid profile of T2DM diagnosed patients.

Keywords: Combined exercise, Type 2 diabetes, High density lipoprotein, Low density lipoprotein, Creatinine

Introduction

Diabetes is one of the most important all over the world. By the year 2050, the number of affected people by diabetes will have increased to 300 million (1). The lipid profile, cardiovascular function, renal system, nervous system and etc. are

affected by diabetes and increase the mortality (2). Type 2 diabetes (T2DM) includes heterogenic group of metabolic diseases, the main characteristics are chronic hyperglycemia, disorders in carbohydrate, lipid, and protein metabolism induced by defected in the secretion or function of insulin (3). About 5% of newly diagnosed T2DM have shown renal diseases induced by diabetes. Nearly 30-40 % will have suffered renal failure in 10 years (4). As patients with T2DM are at risk of diseases like coronary heart diseases, peripheral artery disease (PVD), and capillary disease, controlling blood sugar and blood lipid are two most important issues.

Regular exercise and increased physical activity can prevent metabolic syndromes and overcome many side effects like obesity and increasing dangerous factors like total cholesterol, triglyceride (TG), increasing low density lipoprotein (LDL-C) and decreasing high density lipoprotein (HDL-C). These factors which are identified as lipid profile indices will be considered important forecasting factors for diabetes affected people especially those suffering T2DM. On the effects of physical activities on renal function and lipid profile of T2DM affected patients, numerous studies have been done. Aerobics training improves total cholesterol and HDL significantly while it does not affect TG and LDL levels in people with diabetes. Resistance exercise improves HDL significantly but it does not change other variables of lipid protein (5). In a study on the effects of 8 weeks aerobic high intensity exercise in water on blood lipid levels of T2DM patients, it was reported that aerobic high intensity exercise in water improves blood lipid indices in T2DM patients significantly (6). Metabolic disorders have been shown to affect kidney disease, and the relative risk of chronic kidney damage increases with increasing metabolic abnormalities (7,8).

Studies on Aloe-Vera demonstrated that it affects physiological functions such as improving the control of blood glucose and

cholesterol (9), Effectiveness to improve the lipid profile and liver and kidney function (10). The study of diabetes diagnosed rats has shown that Aloe-Vera extract can decrease plasma levels of LDL, VLDL, and TG while it increases HDL (11). However, Saka et al. showed that oral consumption of Aloe-Vera is associated with impaired kidney function (12). According to the findings on the Aloe-Vera effects on diabetes diagnosed patients and the role of doing exercise in controlling renal function and lipid profile of people with diabetes (4,13), the specifications of favorable activities to maximize effective feedback and to reduce possible side effects are not completely approved. Considering the potential dangers of diabetes, its expensive costs, and its treatment and also development of inactiveness in societies, it will be advantageous to do studies, to present some procedures like changing and correcting lifestyles, and using herbal medicine to treat it. Therefore, the aim of this study was evaluation effect of a combined exercise course and the consumption of Aloe-Vera supplement on the renal function and lipid profile of diagnosed patients with T2DM.

Materials and Methods

This study is a clinical trial double blinded with pre-test and post hoc test analyses with a control group. It generally studies the effect of a combined exercise course and the consumption of Aloe-Vera supplement on the renal function and lipid profile of diagnosed patients with T2DM. The studied population included a group of T2DM diagnosed patients in Zahedan who were evaluated according to the obtained information of diabetes community of Zahedan. Additional inclusion criteria were no heart disease, asthma, no history of limb fractures, no insulin use and no complications of diabetes, including diabetic foot ulcers and exclusion criteria were do not follow the recommendations of researchers and do not attend training regularly or do not take regular supplements. To do so, after declaring a call, based on the experimental

nature of the study and to honor moral and ethical principles, samples were selected purposefully. After informing about the study process, supplement consumption method, and exercise protocol, 24 participants were selected. The participants completed written consent, personal information, and the health condition forms. Then they were classified into three groups (two experimental and one control group) by balanced block randomization method. They were placed into exercise+ Aloe-Vera supplement (E+S) group, exercise (E) group and control (C) group (n=8/group). The members of each group were homogenized considering their age, blood pressure, and weight. At the beginning of intervention in pretest step, the control and experiment group's participants were asked to get ready for sampling after 10 hours of fasting in Novin laboratory of Zahedan. After about 15 minutes of rest, 5 cc of blood was taken from the right arm vein of each subject. Then the participants started either doing combined exercise course (6 weeks) or Aloe-Vera capsule consumption. 48 hours after lasting exercise session, sample gathering was repeated same as the pretest.

Blood samples were gathered in special tubes. After clotting, they were rapidly centrifuged (2000 round in a minute for 10 minutes). Resulted serum was placed in distinct tubes in -80^{OC} until analysis. Measurement of TG concentration index (mg/dl) was performed based on enzyme method using Pars Azmoon technical kit and auto analyzer (RA1000). Cholesterol concentration index (mg/dl) was measured according to Pars Azmoon technical kit and auto analyzer (RA1000). To measure HDL-C concentration index (mg/dl), dual capacity anion and cation sediment method was applied. In order to estimate LDL-C concentration level (mg/dl), Friedewald formula was applied. Plasma creatinine level was estimated using photometric test kit made by Pars Azmoon company with mg/dl sensitivity and 2/3 change coefficient and GFR was calculated by the equation Modification of Diet in Renal Diseases (MDRD) (8):

$$eGFR = 186 \times (\text{Creatinine}/88.4)^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$$

Combined exercise consisted resistance exercise and aerobics. As the participants did not do regular exercise, 1RM formula was applied to determine maximum repetition percent (strength) (14). Combined exercise consisted of 2 sets of 12 specific and repetitive resistance exercise with 70 % 1RM concentrated mostly on big muscles. Resistance exercised included foot press, knee bending, bench press, and arm pit with wire puller. Resting intervals was set for 2 minutes. Then, the participants ran for two ten- minute sets with 70-75 % maximum heart rate intensity on treadmill. A Polar heart rate monitor was used to control the desired heart rate. It is noteworthy that the combined course of exercise performed for 6 weeks –three times a week for 50-60 minutes in the afternoons. Participants performed static stretching movements before and after each session. Doing exercise was repeated and the moved weights in each session were recorded (15). Same as the exercise procedure, supplements were consumed during 6 weeks, 500 mg Aloe-Vera capsules made by Supernatural Company in Canada were consumed by the members of E+S (16). They were consumed every day. The participants were asked to avoid using any antioxidants, multivitamins, and changing their daily diets and their consumed supplement dose. At the end of each week, capsules for the upcoming week were given to the participants.

Statistical analysis

One-way ANOVA test was used to evaluate the homogeneity of the basic levels of research variables and analysis of covariance was used to determine the difference between the groups and Bonferroni post hoc test was used to determine the location of the difference between the groups. Significance level was considered $P\text{-value} \leq 0.05$.

Ethical considerations

The trial was registered at the Iranian registry

of clinical trials (<http://www.irct.ir>) with the IRCT ID: IRCT20180923041097N2

This study was approved in ethic committee of medical science university of Zahedan (IR.ZAUMS.REC.1397.512).

Results

The individual characteristics of the subjects in the pre-test stage are presented in table 1. Table 2 provides information on changes in levels of HDL, LDL, TG, GFR and creatinine in the pre-test and post-test stages.

Six weeks combined exercise and Aloe-Vera supplementation had no significant effect on LDL (P -value= 0.136), TG (P -value= 0.690) in T2DM diagnosed patients but it demonstrated a significant effect on HDL (P -value= 0.001). In addition, obtained results approved the significant effects of 6 weeks Aloe-Vera supplementation along with combined exercise course on creatinine and GFR in T2DM affected people. Bonferroni post hoc test results confirmed the significant difference in creatinine indices in E group compared with the C group (P -value= 0.039),

while there was no significant difference in E group, E+S group and C group (P -value= 0.393). In GFR, E+S group and C group (P -value= 0.018) and E+S and E group (P -value= 0.041) there was a significant difference while E group and C group showed no significant difference (P -value= 1.000).

Discussion

Research results have shown that 6 weeks Aloe-Vera supplementation along with combine exercise has had no significant effect on LDL and TG levels. They are inconsistent with the obtained results by Hosseini et al. (2020) who in a study on diabetic rats in an experimental study used 100 mg kg⁻¹ of Aloe-Vera gel with swimming training daily. Their results showed the significant reduction of LDL and TG after six weeks Aloe-Vera consumption with swimming training (13). Inconsistency of the so-called study results with this study may be related to dosage and type of supplement used. present study, a constant amount of Aloe-Vera capsule was used for all subjects.

Table 1. The baseline characteristics in the studied groups

Variable	Group	Mean (±SD)	P-value
Age (Year)	Exercise	45.12 (±8.11)	0.505
	Exercise+Supplementation	11.96 (±51.25)	
	Control	47.25 (±10.95)	
Height (Cm)	Exercise	1.65 (±0.32)	0.402
	Exercise+Supplementation	1.68 (±0.41)	
	Control	1.63 (±0.42)	
Weight (Kg)	Exercise	74.25 (±2.12)	0.322
	Exercise+Supplementation	73.41 (±2.17)	
	Control	75.42 (±1.13)	
BMI (Kg/m ²)	Exercise	27.29 (±0.45)	0.112
	Exercise+Supplementation	26.3 (±0.12)	
	Control	28.46 (±1.02)	
HDL (mg/dl)	Exercise	46.62 (±7.36)	0.14
	Exercise+Supplementation	45.37 (±4.53)	
	Control	50.62 (±1.40)	
LDL (mg/dl)	Exercise	114.88 (±5.30)	0.152
	Exercise+Supplementation	111.62 (±12.01)	
	Control	119.38 (±1.06)	
TG (mg/dl)	Exercise	188.63 (±10.21)	0.08
	Exercise+Supplementation	175.38 (±10.21)	
	Control	135.25 (±9.61)	
Creatinine (mg/dl)	Exercise	1.18 (±0.13)	0.15
	Exercise+Supplementation	1.27 (±0.27)	
	Control	1.18 (±0.02)	
GFR (cc/min)	Exercise	70.83 (±10.84)	0.15
	Exercise+Supplementation	70.69 (±18.26)	
	Control	70.38 (±4.57)	

The results of one-way ANOVA to compare age, height, weight, BMI, HDL, LDL, TG, Creatinine and GFR in pretest

Table 2. HDL, LDL, TG, GFR and Creatinine levels in the study groups

Variable	Group	Mean (\pm SD)	P-value (posttest)
HDL (mg/dl)	Exercise	44.87 (\pm 4.85)	< 0.001*
	Exercise+Supplementation	42.00 (\pm 4.24)	
	Control	50.37 (\pm 1.40)	
L (mg/dl)	Exercise	90.87 (\pm 17.77)	0.136
	Exercise+Supplementation	99.50 (\pm 7.54)	
	Control	117.88 (\pm 2.23)	
TG (mg/dl)	Exercise	90.87 (\pm 17.77)	0.690
	Exercise+Supplementation	173.88 (\pm 13.01)	
	Control	142.88 (\pm 7.08)	
Creatinine (mg/dl)	Exercise	1.05 (\pm 0.11)	0.042*
	Exercise+Supplementation	1.13 (\pm 0.14)	
	Control	1.18 (\pm 0.02)	
GFR (cc/min)	Exercise	80.66 (\pm 12.00)	0.011*
	Exercise+Supplementation	72.01 (\pm 13.56)	
	Control	70.87 (\pm 5.64)	

The results of covariance to compare HDL, LDL, TG, Creatinin and GFR in post-test (*P-value \leq 0.05)

As the studied samples are diagnosed men with T2DM, to confirm the obtained results, it will be announced that Aloe-Vera is able to activate existing enzymes in pancreas and help to balance and regulate blood glucose in the patients affected by hypoglycemia and diabetes. The results clarify that Aloe-Vera supplement + exercise could not lesson LDL. Maybe, it is the chronic condition of high blood glucose and increasing process of blood lipid in its extreme level in patients with T2DM that has made its reduction process lower and justifies treatment with blood lipid reducing medicine instead of supplement treatment. It is clear that existing materials in Aloe-Vera gel extract especially phytostrol sources, through the obstruction of developing the lipid and the reduction of atherosclerosis development, cause the reduction of lipid in blood. Although combined exercise along with 500 mg Aloe-Vera capsule has not been effective on HDL levels, it has been effective on LDL levels. It seems Aloe-Vera supplement had been affected by other mechanisms like consumed diet during the day. As the diabetes diagnosed people's diet is generally based on hydro carbohydrate reduction (17).

The results also have shown that TG levels in T2DM patients had no significant change following 6 weeks of combined exercise along with the Aloe-Vera supplement consumption. In this research, consumed dose of Aloe-Vera

supplement could not influence TG levels and being affected by diabetes will be one of the important reasons influencing its effectiveness. As insulin resistance in these people may induce it. In addition, it will be noted that the duration of exercise and its lower intensity have made no significant change in TG levels. Combined exercise could not reduce serum levels of TG in blood whether through burning or secretion (4,18).

On the other hand, the results proved that 6 weeks combined exercise + Aloe-Vera supplement consumption invoked significant increase of HDL which was consistent with findings in Etemadi Borojeni et al (2014) (5). Obtained results in our study are consistent with findings in Negall et al. (2013) study whose findings confirmed the significant increase of HDL after a course of a combine schedule (19). Our findings are compatible with those found in Mohammad Rahimi et al. (2013) who studied the effects of aerobics on HDL levels, which demonstrated that aerobics did not change HDL levels significantly (20). Among the most important causes of incompatibility of results, different exercise protocols and exercise intensity would be mentioned. To explain obtained results of our present study, it will be pointed that Aloe-Vera extract can approach the distribution of blood fatty acids to a normal range through controlling lipid metabolism in liver. In fact, Aloe-Vera extract invokes the production of

incompatible compounds of fatty acids which can remove free radicals from blood and control lipid metabolism in body (4). It is found that β -Sitosterol, compositrol, and Estigmasterol are similar to Phytosterols. Existing β -Sitosterol chain in some plants like Aloe-Vera causes significant increase of HDL levels through lipid absorption mechanisms (21). In addition, exercise activates Lecitin-cholesterol acyltransferase (LCAT) and nourishes HDL particles. Other possible explanations for the HDL increase are the augmentation of HDL production in liver due to the LPL enzyme activity and the reduction of liver lipase following the physical activity (22).

Six weeks combined exercise along with Aloe-Vera supplement consumption has imposed significant effects on creatinine and GFR and decreased them significantly. These findings are compatible with Siavoshi et al. (2014) study (23). Samavati Sharif et al. (2015) reported the same findings as our study. Their results showed the significant decrease of creatinine levels in plasma (24). Bjornasted et al. (2015) reported same findings as our present study (25). One of the most important polysaccharide in Aloe-Vera is Acemannan which is like Glucomannan. It is proved that Glucomannan reduces Nitrogen, urea, urea acid, and creatinine levels and leads to the reduction of enzyme activity of Xanthine Oxidase (XOD) and Adenosine Deaminase (ADA) in diabetes diagnosed patients (26). As Aloe-Vera extract has an extremely strong antioxidant activity by the reduction of lipid per oxidation and active oxygen specie (27-29), probably by the same mechanism in the present study has reduced the serum creatinine in diabetic patients. To clarify finding, it will be noteworthy that physical activities cause marvelous change in renal hemodynamic and

protein secretion. Extreme physical activities reduce plasma flow in kidneys. The reduction of plasma flow leads to the reduction of GFR. After a long activity, these changes starts affecting GFR and urea absorption and consequently functional systems are affected (30). On the other hands, it is shown that exercise changes renal blood hemodynamic, permeability of glomerular base membrane, electrical load of membrane and blood activity. In addition, hormone and enzyme changes induced by physical activities make changes in GFR (31). One of the major limitation of the present study was that the participants were given 500 mg Aloe-Vera daily which were not adjusted by their body weight.

Conclusions

The present study showed that in T2DM, the effect of combined exercise on improving GFR increases with Aloe-Vera supplementation. Also, combined exercise with or without Aloe-Vera supplementation increases HDL and decreases creatinine.

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The results showed that Aloe-Vera had a significant adjuvant effect only on GFR to combined exercise and did not have a significant adjuvant effect on combined exercise to other research indices.

Conflict of Interest

No potential conflict of interest relevant to this study was reported.

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