



Research Article

Effects of Aloe Vera Supplements on Blood Glucose Level and Lipid Profile Markers in Type 2 Diabetic Patients – A Randomized Clinical Trial

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ABSTRACT

Background: One of the most studied methods to adjust the blood glucose level and dyslipidemia in diabetic patients is administrating of herbal supplements. This double blinded randomized clinical trial (RCT) study we are aimed to study the effect of Aloe vera supplements on blood glucose level and lipid profile of diabetes mellitus type 2 patients. **Methods:** 44 patients (25 male and 19 female) fulfilling inclusion criteria, were divided into two groups of intervention and placebo randomly. The patients in intervention group received 1000 mg of Aloe vera supplements and the patients of placebo group received placebo, daily for two months beside the main treatment for diabetes mellitus. Before and after the intervention blood samples were taken from all the patients; and were measured for blood glucose level and lipid profile. The data were analyzed using independent T-test method. This RCT study was submitted in IRCT center by submitted code of IRCT201307269626N3. **Results:** The results revealed that the levels of the fasting blood sugar (FBS), HbA1c, Total Cholesterol, Triglyceride, high density lipoprotein (HDL), low density lipoprotein (LDL) were not significantly different between the pre-intervention and post intervention blood samples in both intervention and placebo group. Also there was not any significant difference in blood glucose level and lipid profile comparing intervention and placebo groups. **Conclusion:** In this study, we can conclude that Aloe vera supplement beside the main treatment for diabetes mellitus has no significant effect in blood glucose level and lipid profile in diabetes mellitus type 2 patients.

Introduction

Diabetes mellitus (DM) is one of the most prevalent metabolic diseases worldwide; in which, there is a reduction in production of insulin or the ability of the body cells to use the produced insulin in the body; so the blood glucose level increases and resulting in diabetes symptoms such as polydipsia and polyuria.¹ Worldwide prevalence of DM was 285 million people in 2010 while it was 382 million people in 2013; and it is estimated that it will be doubled by 2030.²⁻⁵ As it is mentioned, in DM type 2, in which body cells cannot use the produced insulin, although the blood glucose level is high but cells cannot use it as energy source; instead they use lipids to produce energy resulting in dyslipidemia in DM type 2 patients. In these patients high blood glucose level is define as high fasting blood sugar and high HbA1c and dyslipidemia is defined as high total cholesterol (T-Chol), Triglyceride (Tg), low density lipoprotein (LDL) and low high density lipoprotein (HDL) of blood.⁶ In the study of Rajiv

Singla et al these changes in the blood glucose level and lipid profile was also shown.⁷ Many studies have demonstrated that changes in blood glucose level and lipid profile is the main pathophysiology of type 2 DM complications; they have proven that by adjusting blood glucose level and dyslipidemia in type 2 DM patients we can prevent and even treat micro vascular and macro vascular complications of type 2 diabetes.⁸⁻¹²

Nowadays there is big tendency to use herbal remedies as treatment for diseases especially metabolic ones.^{13,14} In a systematic review done by LEE T and Dugoua JJ, it is revealed that using herbal supplements is effective in treating and also preventing diabetes mellitus type 2.¹⁵ Aloe vera is one of species of genus Aloe which is classified as belonging to Aloe barbadensis Miller.¹⁶ It is used traditionally for treating hypertension, constipation, worm infection, skin diseases and in some countries as a treatment for diabetes.¹⁷⁻¹⁹ Aloe vera is one of the herbs which many studies have been

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conducted to evaluate the effects of this herb on diabetes mellitus and blood glucose level.²⁰ Many studies have shown that Aloe vera extract can decrease blood glucose level;²¹⁻²⁴ for example in a study done by Tanaka M et al on diabetic and non diabetic mice, it is demonstrated that Aloe vera extract can reduce blood glucose level.²⁵ As many studies revealed positive effect of Aloe vera extract on blood glucose level and lipid profile markers in diabetic patients, many other studies have shown that administrating Aloe vera in diabetic patients reduces the micro vascular and macro vascular complications of this metabolic disease such as healing diabetic wound, eliminating diabetic nephropathy and retinopathy, decreasing the risk of cardiovascular complications etc.²⁶⁻³²

As there is a controversy in effect of Aloe vera extract on diabetes mellitus disease and its effect on blood glucose level in DM patients and also most of the studies in this regard have been conducted on animal samples, in this study we are aimed to evaluate the effect of Aloe vera supplements on blood glucose level and lipid profile of patients with type 2 DM.

Materials and Methods

In this double blinded, randomized clinical trial study we were aimed to evaluate the effect of supplement therapy of Aloe vera extract on blood glucose level and lipid profile markers in type 2 diabetic patients. In this study 44 patients with at least 6 month of diagnosed type 2 diabetes who had all the inclusion criteria were randomly selected from all outpatient diabetic patients who were referring endocrine clinic of Imam Reza Hospital, Tabriz, Iran in first half of 2014. Inclusion criteria were having at least 6 months of diagnosed type 2 diabetes, having the age of 30 to 65 years old, taking only blood glucose-lowering drugs, not using insulin. The patients, who were taking antioxidant agents in previous three months, having renal or hepatic failure, having hepatic disorders and having thyroid diseases, were excluded from the study.

The 44 patients, who were enrolled in the study, were randomly allocated to intervention and placebo group based on random block procedure produced by Random Allocation Software (RAS). A computer-generated random sequence was kept in a remote secure location and administered by an independent third party who was not involved with the clinical conduct of study until all study data were collected and verified. Patients and those involved in enrolling participants, administering interventions and assessing outcomes were blind to group assignments. Both groups were matched in base line characteristics including age, weight, body mass index, duration of diagnosed diabetes and kind of glucose lowering agents.

In the beginning of study, after 12 hours of overnight fasting, 5ml venous blood sample was taken from all patients before administrating the intervention; and the

serum samples of all patients were analyzed for blood glucose markers including FBS and HbA1c and blood lipid profile markers including T-Chol, Tg, HDL and LDL. These data were measured and recorded by independent blind third party. Then the patients in intervention group received a tablet of 1000 mg of Aloe vera extract daily for 2 months and the patients in placebo group received a tablet of 1000 mg of placebo which were the same as Aloe vera tablets in size, color, shape and smell each day for 2 months. After two months of administrating intervention, 5ml venous blood sample was taken from all patients and analyzed for blood glucose level and lipid profile markers. These data were also measured and recorded by independent blind third party. Figure one shows the study flow diagram (Fig. 1). Patients were advised to follow their nutrition diet as routine diet for diabetic patients.

Laboratory tests

Serum samples of all patients were analyzed for blood glucose level markers including fasting blood sugar, which was measured using enzymatic colorimetric method and Monobind kit respectively and HbA1c, which was measured with Nycocard READER II. Also serum samples were analyzed for lipid profile markers including T-Chol, Tg, HDL and LDL; T-Chol, Tg and HDL were measured using enzymatic colorimetric method and Monobind kits respectively, and LDL was measured using formula of $LDL = Total\ cholesterol - (TG/5 + HDL)$.

Ethical considerations

This parallel design randomized clinical trial was approved by the Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran; and also it is submitted in IRCT center by the randomized clinical trial number of IRCT201307269626N3 (available at: <http://www.who.int/trialsearch>). At the beginning of the study after explaining all steps of the study for patients a written consent was obtained from all participants; and they were assured that their information will be kept totally secret. All of them were free to leave the study whenever they want.

Statistical Analysis

All data were measured and recorded by an independent blind third party, and they were analyzed using software of SPSS20. The result of descriptive variables including blood glucose markers level and blood lipid profile markers level in each group before and after intervention, were presented as mean \pm standard deviation (SD). Independent compared t-test was used for comparing the differences of quantitative variables between pre intervention variables and post intervention variables in each group. Also Independent compared t-test was used for comparing the differences of quantitative variables between two groups. P value less than 0.05 was considered statistically significant.

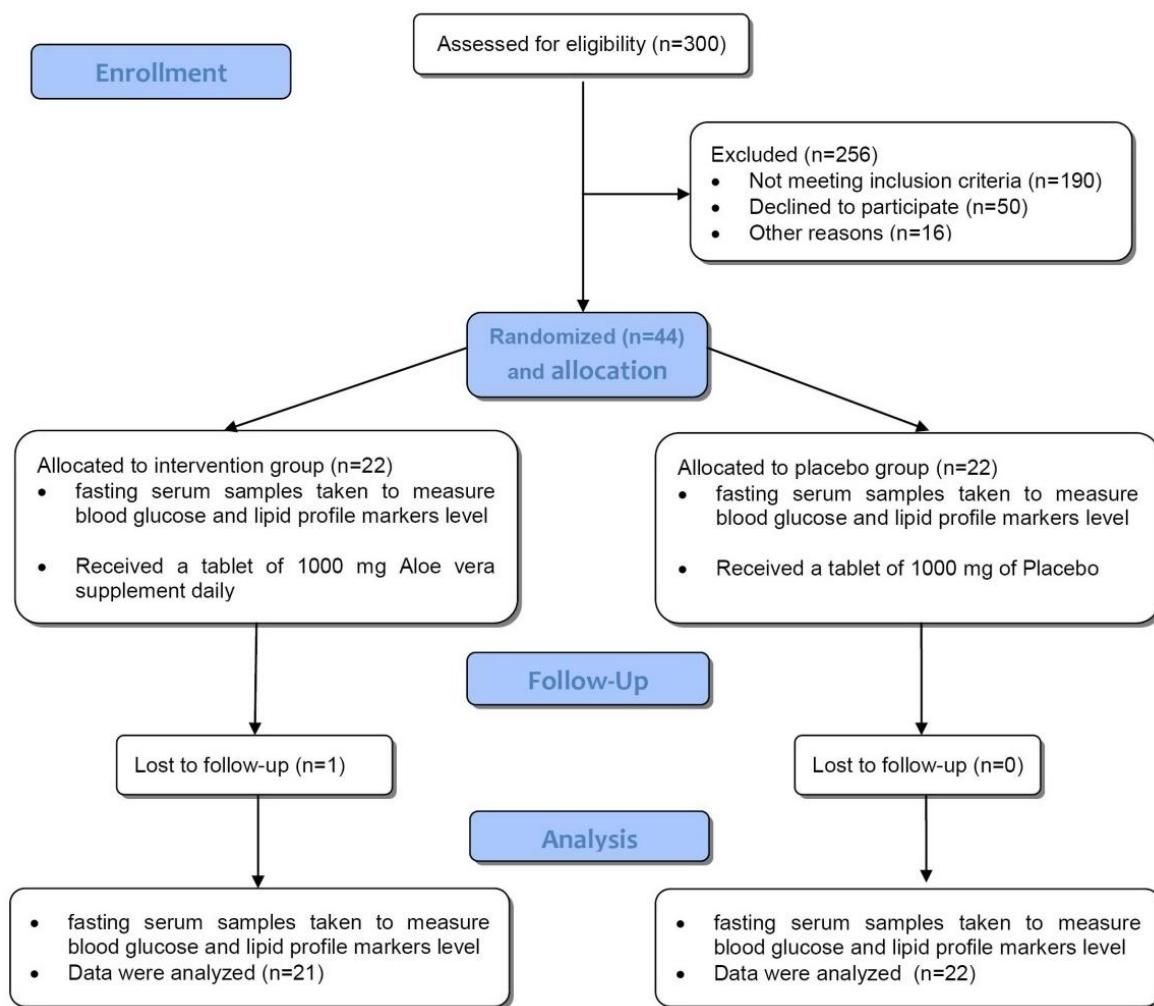


Figure 1. Study diagram shows the summary of the study.

Results

This study was conducted to evaluate the effect of administrating 1000 mg of Aloe vera extract on blood glucose and lipid profile markers in type 2 diabetic patients. In this study 44 diabetic patients, 25 male patients (56.8%) and 19 female patients (43.2%), were enrolled; all the patients participated in the study until the end of study except one of them in intervention group who was excluded due to not taking the intervention. The intervention group was consisted of 12 male patients (54.5%) and 10 female patients (45.5%) and the placebo group was consisted of 13 male (59.1%) and 9 female patients (40.9%). The mean age of all participants was 52.61 ± 10.575 ; which was 51.09 ± 10.734 in intervention group and 54.14 ± 10.435 in placebo group.

Blood glucose level markers

Mean FBS of all patients before administrating intervention was 175.41 ± 38.59 mg/dl and after administrating intervention was 170.53 ± 47.37 mg/dl. In intervention group, there was no significant

difference between the mean FBS before intervention and after 2 months of administrating 1000 mg of Aloe vera extract supplement (P value > 0.05). In the placebo group also there was no significant difference between pre and post intervention samples (P value > 0.05). Also there was not any meaningful difference between changes in the FBS level before and after intervention in intervention group compared to placebo group.

The result showed that, considering HbA1c in both groups, there was not any significant differences between pre intervention samples and post intervention samples in each of the groups separately (p Value > 0.05). Also changes in the level of HbA1c before and after intervention in intervention group was not statistically meaningful compared to placebo group. Considering all patients, mean level of HbA1c before intervention was $8.59 \pm 1.32\%$ and after taking two months of intervention was $8.55 \pm 1.47\%$.

Lipid profile markers

The analysis of data revealed that there were no

statistically meaningful changes in pre and post intervention serum samples of each group considering lipid profile markers. It means that, there was not any significant change in the level of none of lipid profile markers before and after intervention in both intervention and placebo group (p Value>0.05). Also changes in the level of blood lipid profile markers (T-

Chol, Tg, HDL, LDL) before and after intervention in intervention group was not statistically meaningful compared to placebo group.

Table 1 demonstrates the mean level of blood glucose and lipid profile markers before and after intervention in both groups of intervention and placebo and also all patients (Table 1).

Table 1. Mean level of blood glucose and lipid profile markers before and after intervention in case group, control group and all patients.

	Pre intervention	Post intervention	Pre intervention	Post intervention	Pre intervention	Post intervention
FBS	181.05 ± 42.83	184.90 ± 51.04	169.77 ± 33.89	161.36 ± 31.35	175.41 ± 38.59	170.53 ± 47.37
HbA1c	8.53 ± 1.34%	8.63 ± 1.61%	8.65 ± 1.32%	8.47 ± 1.36%	8.59 ± 1.32%	8.55 ± 1.47%
T-Chol	185.91 ± 60.63	180.29 ± 50.04	165.18 ± 36.17	163.23 ± 37.86	171.00 ± 43.21	171.56 ± 44.54
Tg	183.68 ± 94.39	218.90 ± 161.04	141.18 ± 70.36	170.55 ± 82.90	162.43 ± 85.03	193.95 ± 128.125
HDL	48.14 ± 11.12	47.43 ± 11.03	51.59 ± 9.39	49.95 ± 9.30	49.86 ± 10.32	48.72 ± 10.14
LDL	91.94 ± 39.13	89.16 ± 29.45	85.35 ± 28.02	79.57 ± 25.12	88.65 ± 33.80	84.04 ± 27.35

FBS: Fasting Blood Sugar, T-Chol: Total Cholesterol, Tg: Triglyceride, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein.

Discussion

Diabetes mellitus is one of the most prevalent metabolic diseases which its prevalence is increasing very fast. In type 2 DM the cells of body cannot use the produced insulin so the blood glucose level will increase and the cells will use lipids as the energy source instead; which will result in dyslipidemia in patients of type 2 Dm (1-5). Studies have shown that high blood glucose level as high FBS and high HbA1c and dyslipidemia as high T-Chol, Tg and LDL and low HDL are the main pathogenesis for micro and macro vascular complication of DB type 2;³²⁻³⁴ as it is revealed in the meta-analysis study by Sarwar N et al, high blood glucose level is linked with cardiovascular complications of DM.³⁵

Nowadays there is big tendency to use herbal remedies to treat disease especially metabolic diseases such as diabetes mellitus.^{13,14} Aloe vera is one of the most studied herbs to evaluate its effects on diabetes.¹⁶ In this randomized double blinded clinical trial study we were aimed to evaluate the effect of 1000 mg of Aloe vera extract as supplement therapy blood glucose level and blood lipid profile on 44 type 2 diabetic patients. The results of our study showed that there was no significant difference on blood glucose level markers including FBS and HbA1s and blood lipid profile markers including T-Chol, Tg, LDL and HDL between pre intervention and post intervention samples in both intervention and placebo group. In other words the result of our study showed that Aloe vera supplement therapy has no significant effect on blood glucose level and lipid profile markers of type 2 diabetic patients. Our study also showed that the changes in the level of blood glucose and lipid profile markers before and after intervention in intervention group has no meaningful difference compared to placebo group.

Many studies have conducted to evaluate the effect of Aloe vera extract on blood glucose level and lipid profile markers on diabetic cases. In a study done in

India by Rajasekaran S et al, was to evaluate the effect of oral administration of 300 mg/kg bodyweight of Aloe vera extract for 21 days in diabetic rats; the results showed that supplement of this herb can have positive effect in decreasing LDL, VLDL and Tg and increasing HDL. In this study also it is shown that using Aloe vera extract can decrease hepatic transaminases.³⁶ Comparing the result of this study to ours, we can assume that the dosage of administrating Aloe vera extract and whether the study is being conducted on human samples or animals can affect the results of study.

Bunyaphatsara N et al in another study demonstrated that administrating Aloe vera supplements beside glibenclamide will lower blood glucose level and blood triglyceride level in diabetic patients; while administrating glibenclamide won't have the same effect if it is used solely.³⁷

Unlike the result of our study which showed that Aloe vera supplement therapy has no meaningful effect on blood glucose level and blood lipid profile, the result of Dr Huseini et al clinical trial study on 30 type 2 diabetic patients of 40 to 60 years old, demonstrated that administrating of a 300 mg capsule of Aloe vera gel every 12 hours a day for 2 months can result in lowering FBS, HbA1c, total cholesterol and LDL in intervention group. However, results of Dr Huseini et al study did not show any positive effect of Aloe vera gel capsule on other blood lipid profile markers (Tg and HDL).³⁸ The explanation for the differences between Dr Huseini study and ours may be due to the inclusion and exclusion criteria of the studies; in our study patients with any HbA1c could enter the study and there were not any exclusion criteria for patients with higher levels of HbA1c in our study. The other reason for this may be the type of Aloe vera extract supplements which are used in the studies, in our study the supplements were used as tables however in Dr Huseini study it is used as capsule or gel type.

Although the mentioned studies suggest that administrating Aloe vera as a herbal supplement in diabetic patients can result in decreasing blood glucose level and adjusting blood lipid profile markers, in a systematic review of 10 studies regarding clinical effects of Aloe vera on diabetic patients, done by B K Vogler and E Ernst, it is concluded that even though most of studies declare the effectiveness of Aloe vera on diabetic patients, but there is not sufficient result regarding positive clinical effectiveness of Aloe vera on diabetic patients.³⁹

There are factor which can influence the study. The dosage of the Aloe vera supplement, duration of the study, the shape of the supplement of Aloe vera which is used in the study (for example tablet, capsule, syrup etc), sample size etc. Some limitation can be noticed in our study, one of the important limitations in our study was the inclusion criteria; in this study all the patients with any amount of HbA1c or having diabetes mellitus for any years before the study could enter the study, and there was not any exclusion criteria for the patients with upper levels of HbA1c or for the patients having diabetes mellitus for a long years ago. These limitations may be the reason for contrast of the results of our study compared to the previous done studies which declare that Aloe vera supplements can have positive effect in adjusting the level of blood sugar and lipid profile markers. It could be explained this way that herbal therapy as using Aloe vera supplements for treating diabetes, can only be effective in new onset disease or in the patients with appropriate control of their theses.

Conclusion

The results of our study showed that administrating 1000 mg of Aloe vera extract tablets daily for 2 months as supplements beside pharmacologic treatment of diabetes, has no meaningful and significant effects on FBS, HbA1c, T-Chol, Tg, HDL and LDL in type 2 diabetic patients. Also the results revealed that the differences in the level of blood glucose and lipid profile markers pre and post intervention has no meaningful differences in two group (intervention and placebo) compared to each other. Considering the result of previous studies in this regard and our study, we recommend that in order to evaluate the effect of Aloe vera extract on progression, treatment and preventing of type 2 diabetes, further studies need to be conducted on large samples of human cases with various dosage ranges of Aloe vera supplements. Also there is a necessity of doing further studies to assess the effectiveness of Aloe vera gel in treating and preventing diabetes complications.

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Conflict of Interest

The authors report no conflicts of interest.

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