

ORIGINAL RESEARCH ARTICLE

“A STUDY ASSESSING EFFICACY OF ALOE VERA AS AN ADJUVANT TO CONVENTIONAL THERAPY IN PATIENTS OF TYPE 2 DIABETES MELLITUS WITH HYPERLIPIDAEMIA”.

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Abstract:

Diabetes mellitus has been described as the most common endocrine disorder that impairs glucose homeostasis resulting in severe complications. Lipid abnormalities are commonly associated with diabetes. Currently, there is renewed interest in the plant based medicines. One such herbal drug, *Aloe vera* used for different clinical purposes claimed for its effect on blood glucose levels and lipid profile.

Total of 240 newly diagnosed type 2 diabetes mellitus with hyperlipidaemia patients were allocated to group A and B. Group A received a combination of Metformin + Glimiperide with rosuvastatin and Aloe vera as add on therapy, while group B received combination of Metformin + Glimiperide with rosuvastatin.

While assessing the results and comparing the overall degree of glycaemia control between group A & B, A significant ($p < 0.001$) difference with lower mean fasting (93.16 ± 2.54) and mean PP blood glucose (138.69 ± 3.45) were observed in group A and a significant ($P < 0.0001$) difference was also noted in the mean lipid profile recorded before starting the treatment when compared with the mean lipid profile after starting the treatment in patients who were treated with treatment regimen A.

The study concluded that the subjects who were treated with drugs of group A has comparatively produced better clinical outcome in terms of glycaemia control and effect on increased lipids.

Keywords: Diabetes mellitus, Hyperlipidaemia, Aloe vera.

Introduction:

Diabetes is a chronic metabolic disorder that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces and characterized by hyperglycaemia, glycosuria, hyperlipidemia, negative nitrogen balance and sometimes ketonaemia.¹

The most common lipid abnormalities include hyper-triglyceridemia, cholesterol and reduced high-density lipoprotein (HDL) levels because there is a strong relationship between all forms of vascular disease in patients with type 2 diabetes and hyperlipidemia.²

According to National Commission on Macroeconomics and Health (NCMH), a government of India undertaking, there would be around 62 million patients with CAD by 2015 in India.³

Inspite of the advent of various treatment strategies available for the treatment of diabetes mellitus and hyperlipidaemia, are not free from complications like hypoglycaemia, GIT related etc. There has always been a constant search for newer, cheaper, and safer natural supplements which can effectively normalize the metabolic derangement underlying the onset of clinical diabetes and hyperlipidemia is essential.

One such herbal drug *Aloe Vera* which is a part of many herbal medicine preparations used for different clinical purposes and has a long history of popular and traditional use.⁴

Previous studies showed significantly greater improvements in blood sugar levels among those who given aloe vera over the 2 weeks treatment period.⁵

The antidiabetic effects of Aloe vera are thought to be due to the presence of mannans anthraquinones and lectins.⁶

There is a paucity of the literature to explore these possibilities of use of Aloe vera in large population of diabetes in India and globally.

The present study aimed to assess the efficacy of *Aloe Vera* as an add on therapy with conventional antidiabetic regimens in terms of glycaemia control and effect on hyperlipidaemia in type 2 diabetics with hyperlipidemia.

Material and Methods:

This was a prospective, open label, randomized study conducted in the Out-Patient Department of General Medicine in association with Department of Pharmacology, at tertiary care hospital, in Jaipur, on type 2 diabetes mellitus with hyperlipidemic subjects. A total of 240 subjects fulfilling inclusion and exclusion criteria were enrolled in the study after obtaining informed consent. Ethical clearance for the study was obtained.

Inclusion Criteria:

1. Newly diagnosed Type 2 Diabetes Mellitus subjects with hyperlipidaemia receiving Glimepiride 1 mg, Metformin 500 mg and Rosuvastatin 5 mg per day.
2. Subjects of either sex of age group 18-70 years.
3. Willing to participate in the study and undergo all study related procedures.
4. Subjects able to give a written informed consent.

Exclusion Criteria:

1. Subjects suffering from Type-1 Diabetes.
2. Pregnant and lactating women.
3. Subjects on chronic corticosteroid or any other drug precipitating Diabetes Mellitus.
4. Subjects suffering from some infection at the time of enrolment into the study.
5. Clinically relevant hepatic disease or impaired renal function.
6. Subjects having history of diabetic ketoacidosis.
7. Any mental condition rendering the subject unable to give informed consent.
8. Any other condition that in the opinion of the investigator does not justify the patient's participation in the study.

STUDY DESIGN:

On screening each patient was subjected to the detailed medical history, demography and physical examination. Routine investigations of fasting and post prandial blood glucose, HbA1C and lipid profile analysis were done for confirmation. After reconfirming all the inclusion and exclusion criteria and the subjects turned out to be diabetic and hyperlipidemic, he/she was enrolled in to the study. After being educated about diet, importance of anti-diabetic and anti-hyperlipidemic therapy with special emphasis on need to adhere to treatment, the patients were subjected to randomization by odd even system and allocated in to treatment groups A and B receiving regimens as illustrated-

Group A: Aloe Vera 600 mg + Glimepiride 1 mg, Metformin 500 mg and Rosuvastatin 5 mg per day

Group B: Glimepiride 1 mg, Metformin 500 mg and Rosuvastatin 5 mg per day

Lifestyle modifications were also advised to both groups.

In both groups, all the drugs were given orally, however Group A in addition to anti-diabetics and lipid lowering agent, *Aloe vera* was given as add on therapy.

Follow up visits, visit 2, visit 3 and visit 4 were performed at 28 day (\pm 3 days), 54 day (\pm 3 days) and 84 day (\pm 3 days). At each visit complete physical examination was carried out, including fasting and post prandial blood glucose. HbA1C and lipid profile were examined only at the time of screening visit and visit 4.

Study Drug: Brand of Aloe vera from Morpheme aloe vera, capsule 300 mg were used for the study purpose.

Dose Selection of study drug: Subjects received 300 mg dry inner gel capsule of Aloe vera twice daily.^{7,8}

Sample Size calculation: The patient sample size for this study was calculated as per the incidence of Type 2 Diabetes mellitus in the projected area and the power of study is more than 80%. The incidence of Type 2 Diabetes mellitus in the projected area was 8.6 %.⁹

Statistical Analysis: The results are expressed as mean ± SEM. The chi-square test was employed for analysis of the complications and Analysis of variance (ANOVA) one way classification for rest of the data. Statistical analysis was done by Statistical Package for the Social Sciences (SPSS) version 10.0 statistical software. A probability value of less than 0.05 (p<0.05) was considered to be statistically significant and probability value less than 0.001 (p<0.001) was taken as highly significant.

Results:

A total of 240 type 2 diabetes mellitus subjects with hyperlipidaemia were recruited and randomly allocated to two treatment group vij. A and B. 17 subjects, 8 from group A and 9 from group B could not complete the study hence a total no. of 227 subjects have completed the study. The subjects in both the groups were assessed for glycaemia control and effect on lipid profile.

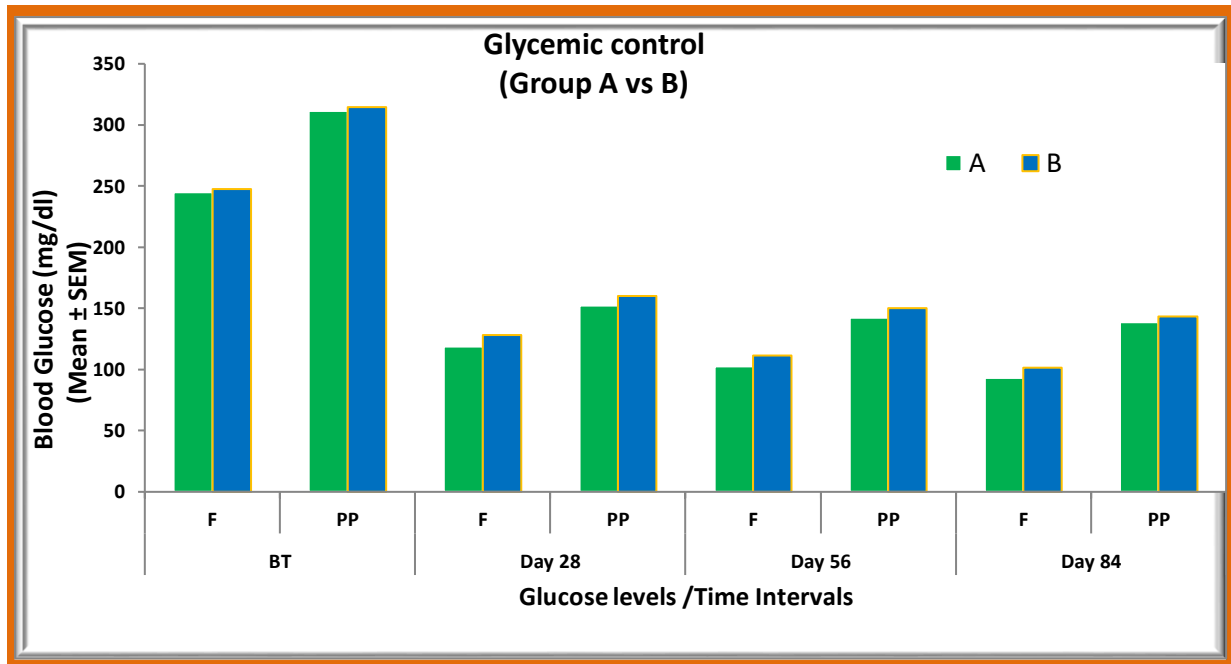
Table 1: Characteristics of the subjects

Parameter		Group A	Group B
No. of subjects (n =)		120	120
Mean Age (years)		46.86 ± 8.31	47.73 ± 7.98
Sex	Male (n=)	81 (67.5 %)	76 (63.33 %)
	Female (n=)	39 (32.5 %)	44 (36.66 %)

Table 2: Comparison of glycaemia control achieved by group A Vs group B.

Group	Blood Glucose (Mean ± SEM)								HbA1c (Mean ± SEM)	
	Before Treatment		After Treatment						Before	After
	F	PP	Day 28		Day 56		Day 84			
			F	PP	F	PP	F	PP		
A	245.06 ± 4.76	311.63 ± 4.41	118.67 ± 2.11	152.47 ± 2.16	102.66 ± 2.42	142.33 ± 2.96	93.16 ± 2.54	138.69 ± 3.45	8.37 ± 0.03	6.24 ± 0.05
B	247.41 ± 4.40	314.50 ± 4.24	127.98 ± 1.91	159.97 ± 1.79	111.37 ± 2.34	150.09 ± 2.78	101.49 ± 2.69	143.37 ± 3.57	8.35 ± 0.02	6.92 ± 0.05

Fig. 1: Comparison of glycaemia control achieved by group A Vs group B.



While comparing the mean fasting and post prandial (PP) blood glucose obtained before starting the treatment, with glycaemia control achieved after the treatment, a statistically significant ($P < 0.001$) difference was observed in both the treatment regimens.

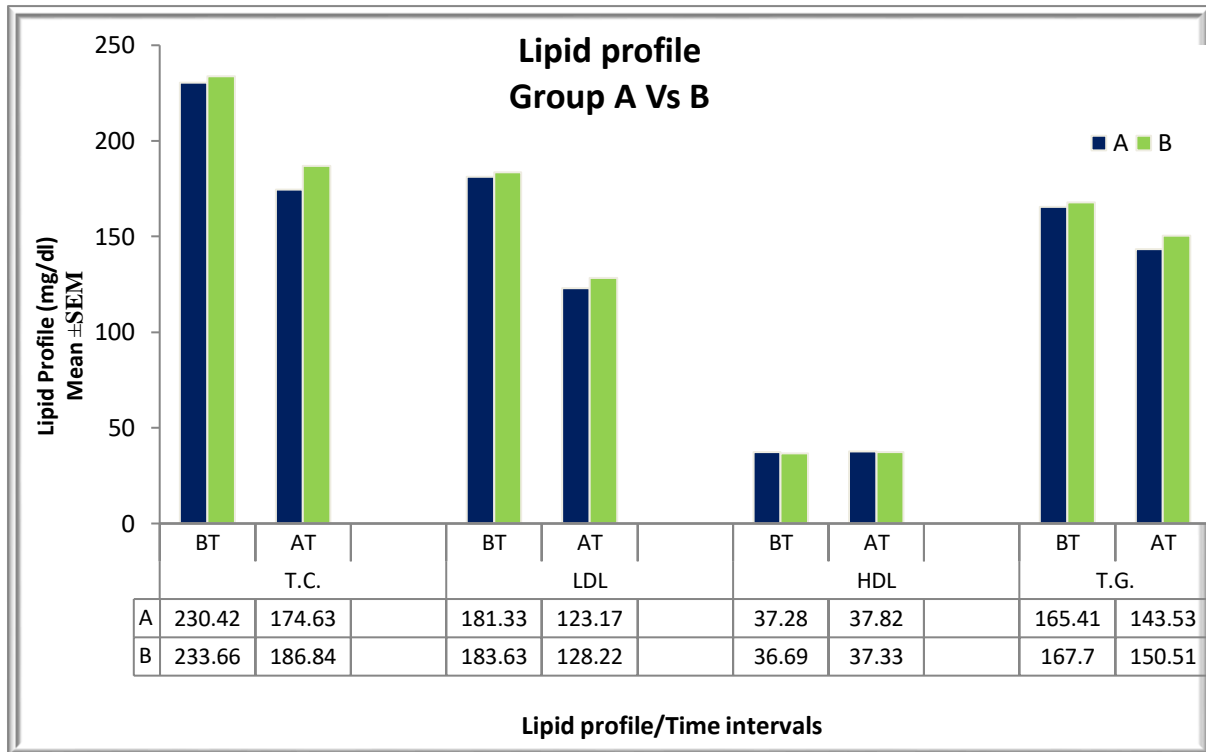
While comparing the mean HbA1c recorded before treatment with mean HbA1c after treatment, a significant ($P < 0.0001$) difference was observed in both the treatment regimens. Comparatively a lower mean HbA1c value after starting the treatment with group A was observed.

A statistically significant difference ($P < 0.0001$) was observed in mean fasting and PP blood glucose levels obtained before starting the treatment when compared with the mean fasting blood glucose values recorded at different intervals of time after starting the treatment in group B.

Table 3: Comparison of Lipid profile achieved by group A Vs group B

G R O U P	Mean Lipids ± SEM							
	Before Treatment				After Treatment			
	T. Chol.	LDL	HDL	Triglyce.	T. Chol.	LDL	HDL	Triglyce
A	230.42 ± 1.88	181.33 ± 1.23	37.28 ± 0.34	165.41 ± 1.23	174.63 ± 4.85	123.17 ± 0.71	37.82 ± 1.04	143.53 ± 3.91
B	233.66 ± 2.38	183.63 ± 0.61	36.69 ± 0.32	167.7 ± 1.29	186.84 ± 5.09	128.22 ± 0.62	37.33 ± 1.06	150.51 ± 4.15

Fig. 2: Comparison of Lipid profile achieved by group A Vs group B



While comparing the mean total cholesterol obtained before starting the treatment in both the treatment regimens a significant ($P < 0.0001$) difference exist in addition a statistically significant ($P < 0.0001$) difference was observed in mean LDL, mean HDL and mean triglycerides after treatment in both the groups.

Interestingly a significant ($P < 0.0001$) difference in mean lipid values *vij*. Total cholesterol, mean LDL and mean triglycerides was observed between group A and group B. After treatment though the mean lipid levels were comparatively lower with group A. However this difference was statistically insignificant.

Discussion:

Diabetes mellitus and hyperlipidaemia is still a disease which needs to be injured by use of current antidiabetic and antihyperlipidaemic regimens, as no complete cure till date is available for the treatment of both disorders.

More than 400 plants species having hypoglycaemic and hypolipidemic activity have been available in the literature; Herbal medicines are often used as therapeutic remedies in combination with allopathic drugs. Usually ayurvedic drugs are being used due to their minimum toxicity and low cost. However, searching for new anti-diabetic drugs from natural plant sources is still attractive because they contain substances which have alternative and safe effect on diabetes mellitus and hyperlipidaemia.

Many traditional medicines have been evaluated for their role in controlling diabetes mellitus from time to time and one such traditional medicinal herbal preparation of *Aloe vera* is claimed for its effect on blood glucose levels and lipid levels.^{6, 10, 11}

While comparing the overall degree of glycaemia achieved in subjects who were treated with a combination of Metformin + Glimiperide and Aloe vera and the subjects who were treated with combination Metformin + Glimiperide, a comparatively lower mean fasting (93.16 ± 2.54) and mean PP blood glucose (138.69 ± 3.45) were observed with combination Metformin + Glimiperide and Aloe vera. (Table-2, Fig.-1). These results are in support of a study stating that the *Aloe vera* produced a significant decrease in blood glucose levels significantly ($p=0.041$) in type 2 diabetes mellitus patients.¹²

Present study result showed agreement which reported that diabetic mice group treated by AV extract at the dose of 300 and 500 mg/kg body weight, orally. It significantly ($p<0.05$) reduced the blood glucose and normalized biochemical parameters compared with alloxan induced diabetic group. The results suggested that the extract of aloe vera leaves possess protective effect against alloxan induced diabetic mice.¹³

These differences in degree of glycaemia could possibly be due to Aloe vera's detoxifying properties. As an adjuvant and nutritional supplement, Aloe vera has high fiber content and the polysaccharides and glycoproteins in it are believed to help the body to use glucose effectively and remove excess from the blood.¹⁴

The results of the present study also similar with previous study on pre diabetic subjects, results showed the 300 and 500 mg Aloe vera capsules decrease significantly fasting blood glucose levels in four weeks ($p=0.006$ and $p= 0.001$) and eight weeks ($p=0.002$ and $p<0.001$) and suggested the use of Aloe vera extract in pre diabetic patients can significantly regulate levels of fasting blood glucose levels and could be an interesting supplement strategy to alleviate impaired serum glucose levels.¹⁵

Furthermore the lower HbA1c (6.24 ± 0.05) values were also noted in patients who received Aloe vera as add on therapy. (Table- 2, Fig.-1)

These results are supported by the results of a study mentioning that a significant mean 6.6 (1.1) $p=0.036$ reduction in HbA1C reported with the use of Aloe vera in type 2 diabetics.¹⁶ Huseini HF et. al. also indicate that the Aloe vera lowered the HbA1C level significantly ($p=0.023$).¹²

This study also evaluated the effect of both the treatment regimens on lipid profile of the patients.

A significant ($P < 0.0001$) difference was noted in the mean lipid profile recorded before starting the treatment when compared with the mean lipid profile after the treatment in patients who were treated with treatment regimen A. (Table 3, Fig. 2). The result of present study also agreed with the previous study that showed highly significant ($p<0.1$) reduction in cholesterol and triglyceride levels by consumption of oral Aloe vera.¹⁴

Nasiff et. al. studied the effect of oral aloe vera extract on lipid metabolism in patients with hyperlipidaemia and when lipid profile measured a significant reduction were noted in all the lipid parameters so this data also support the present study results¹⁷ but disagree with the earlier reports showing no effect of Aloe vera on the cholesterol levels.^{18,19}

Aloe vera's effects on lipid markers may be explained by its ability to suppress adipogenic gene expression.¹⁰ It has also been hypothesized that normalization of the plasma lipid status by *Aloe vera* is mediated by the control of lipid metabolism, specifically increased

clearance and decreased production of the major transporters of endogenously synthesized cholesterol and triglycerides.²⁰

Conclusion:

This study suggests the rationale for using Aloe vera as add on therapy for diabetes mellitus and as add on therapy has comparatively produced better clinical outcome in terms of glycaemia control and lipid lowering action.

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