Original Article

Effects of Aloe Vera & Rosiglitazone on Diabetics

To Measure the Synergistic Effects of Aloe Vera and Rosiglitazone on Blood Glucose, Insulin and Insulin Resistance in Stretozotocin Induced Diabetic Rats

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ABSTRACT

Objective: To measure the synergistic effects of Aloe vera and Rosiglitazone on blood glucose, insulin and insulin insensitivity in non-insulin dependent diabetes mellitus.
Study Design: Randomized control trail study
Place and Duration of Study: This study was conducted at Army Medical College, Rawalpindi in the Physiology Department from January 2009 to September, 2010 in alliance with National Institute of Health (NIH) Islamabad
Materials and Methods: Thirty healthy rats were made diabetic according to Srinivasan model. After confirming type 2 diabetes in them they were randomly segregated into two equal groups. The groups named diabetic were injected with normal saline and other combined group were given 150mg/kg body weight of Aloe vera extract and 2.5mg/kg body weight of rosiglitazone diabetic group. It was half their effective dose as their effective dose was calculated through pilot study.
Results: Plasma glucose, insulin, and TG/HDL ratio were significantly reduced ($p<0.0000001$) in combined group then diabetic control group
Conclusion: The significant result was obtained in combined group in lowering plasma glucose, insulin and insulin resistance though half their effective doses were used. It will also help in reducing side effects associated with use of rosiglitazone.
Key Words: Aloe vera, rosiglitazone, T2DM, insulin

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INTRODUCTION

World is facing the epidemic of Type 2 diabetes mellitus especially in developing countries.[1] A large number of population in Pakistan is affected by diabetes mellitus and it is estimated that if increased by same rate, by the year 2030, it will touch the figures of 13.9 million.[2] Diabetes is a. chronic disease associated with number of complications. Changing life style is the first option for treating diabetes whereas appropriate medication is required if one fails to achieve the acceptable glycemic control by conservative means[3]. However these medications in their long term use are associated with list of complication. The use of herbs and other form treatments is becoming popular[4]. Herbal medicines are used in both types of diabetes[5]

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Aloe vera is a short stemmed succulent herb with fleshy leaves which consist of gel, latex and outer green rind. The Aloe vera and diabetes link can probably first be traced to Arabian Peninsula[6].A study based on the use of traditional phytotherapy conclude this formula is very old and 100% effective[7]. However no study was available to use Aloe vera whole leaf extract with rosiglitazone for synergistic action.
Rosiglitazone is from thiazolidiones group.. Though the drug is very effective in reducing triglycerides however is associated with cardiac problems in long term[8]
The present study was designed to use of Aloe vera and rosiglitazone in half there effective doses as anti diabetic and this may help in reducing complication associated with rosiglitazone.

MATERIALS AND METHODS

Aloe vera plant, approximately three to four years old, was purchased from a commercial nursery at Lahore. By department of plant sciences, Quaid-e-Azam University Islamabad, plant identification was done. Accession number 46624 and voucher specimen number 157 was obtained. The whole leaf was processed to make Aloe vera juice according to published procedure with slight modification.[9]

We purchased thirty healthy Sprague Dawley rats, which were 90 days old, from National Institute of Health (NIH), Islamabad. They were kept at animal house of NIH throughout treatment period. Each rats weigh about 220±50 grams approximately. For preparation of High fat diet (HFD) large amount of animal fat and casein were added to normal pallet diet to prepare high fat diet.[10]

All healthy rats were made diabetic type 2 by feeding them animal fats for 3 weeks and then an intra-peritoneal injection of 35mg/kg body weight of streptozotocin.[10] To confirm diabetes and insulin resistance cut off value of glucose and TG :HDL ratio was greater then11.11mmol/l and 1.8 respectively.[11]

After confirmation of T2DM, thirty Sprague Dawley rats were indiscriminately segregated into two groups. For next 21 days both groups were given different treatments. Normal saline 0.01 centiliter was injected in Diabetic control group and combined group were given 50% of their effective dose combinely, that is, Aloe vera extract (150mg/kg body weight) with intra gastric tubing and rosiglitazone (2.5mg/kg body weight) I/P (three weeks of treatment). For analysis intra cardiac sampling was done.Samples were analysed at Army Medical College, Rawalpindi, Pakistan in its research center (CREAM).Glucose was measured by Trinder'smethod[12]An enzymatic colorimetric method GPO-PAP (Glycerol phosphate oxidase) was used for serum triglycerides estimation.[13]The HDL were measured by Hiroshi method and inslin resistance was measured by taking the proportion between TG and HDL.[14]Estimation of **I**nsulin is a solid phase two-site enzyme immunoassay.

Analysis of data was done on SPSS version 16.0. Values were analyzed by taking their mean and standard deviation. Two sample T- Test was used for analysis of data. The "p value" <0.05 was considered statistically significant.

RESULTS

After treating the groups for 21 days the plasma glucose in diabetic control group was 18.15 ± 1.70mmol/l which drop to4.41±0.52mmol/l (76%) in combined group. The evaluation showed a significant reduction (p<0.0000001) in combined group as compared to the diabetic group. In diabetic control group the ratio between triglycerides and HDL was 5.4±0.40 which reduced to 1.3 ± 0.22 in combined group There was a statistical difference (p<0.0000) between the means of two groups .The means TG in diabetic control group was2.70 ± 0.14which drop to 0.82 ± 0.14 mmol/l and the mean HDL levels in diabetic group was 0.50 ± 0.08mmol/l which raised to 0.60± 0.07

When statistically analyzed by sample T test the difference between two groups was significant as (p<0.0000001) for TG and (0.0005) for HDL (table 1).

Table 1: Plasma glucose, insulin and TG: HDL ratio in between groups by using two Sample T-Test

Variables	Diabetic control group	Combined group	t.test	p value
Plasma glucose (mmol/l)	18.15 ± 1.70	4.41 ± 0.52	29.9338	<0.0000001
Triglyceride (mmol/l)	2.70 ± 0.14	0.82 ± 0.14	36.7757	<0.0000001
HDL (mmol/l)	0.50 ± 0.08	0.60 ± 0.07	-3.912	0.0005
TG:HDL ratio	5.4 ± 0.40	1.3 ± 0.22	23.755	<0.0000
Insulin (µU/ml)	18.30 ± 2.2	11.03± 0.71	12.1799	<0.0000001

Table No.2: Percent reduction in blood glucose, insulin and TG: HDL ratio in treated group in comparison to the diabetics

Group	Blood Glucose mmol/l	TG/HDL ratio	Insulin	TG	HDL
Control	18.15	2.70	18.30	2.70	0.50
Combined	76% ↓	76% ↓	74% ↓	70% ↓	20% ↑

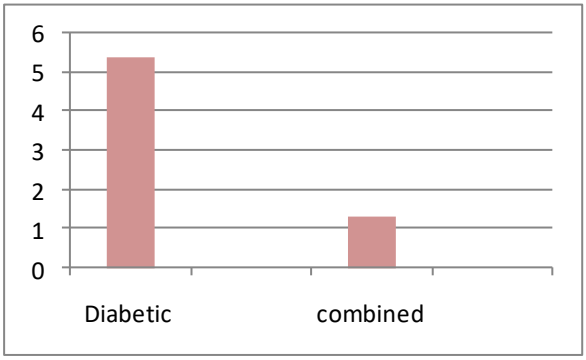

Figure No.1: Comparison between TG: HDL ratio in combined and diabetic groups

Similarly the level of insulin was 18.30 ±2.2 µIU/ml in diabetic group which dropped in combined group upto11.03± 0.71µU/ml. The evaluation between the two group assessed by sample T test showed a statistically significant (p<0.0000001) difference in diabetic and combined group.

DISCUSSION

The usage of Sprague Dawley rats as experimental model for testing antidiabetic drugs is very appropriate as it resemble humans in sequence of diabetes mellitus. our study Sprague Dawley rats were used as experimental animal model resemblance with human metabolic characteristics of diabetes mellitus.[15]

By giving animal fats for two weeks followed by a single dose of 35mg/kg streptozotocin causes hyperglycemia (18.85± 1.70mmol/l), in rats. In the study by Srinivasan plasma glucose levels increased

upto 23 mmol/l after the induction of T2DM which are comparable with our results.

We used the proportion between triglycerides and high density lipoprotein as indicator for insulin resistance which was above 1.8. However in other study hyper-insulinemia was taken as indicator for insulin resistance[10].

At the end of our study all the variables in the diabetic control group have progressively increased to manifest severe hyperglycemia (18.15 ± 1.70mmol/l) hyper-insulinemia and insulin resistance which could be the manifestation of the course of the disease with intake of high fat diet and advancing age. These findings were also observed in previous studies..[10,15,16]

In the present study combined group supplementation has considerably reduced($p<0.0000001$) plasma glucose levels despite that half of their effective dose was used, in comparison to diabetic group. The finding of another study supported our results).[17].They used treated Aloe vera gel for eight weeks which reduced the fasting plasma glucose level significantly ($p<0.01$. The reduction in terms of percentage was 52% and dose dependent in diabetic mice in comparison to the untreated diabetic mice. Despite longer duration of treatment (8 weeks) with Aloe vera in their study the results of our study on plasma glucose level was much better as resulted in 76 % reduction which could be due to synergistic effects of Aloe vera and rsiglitazone rather using it Aloe vera alone

Ghannam et al., used aloes (latex) in five T2DM patient and alloxon induced.[18]Our study results showed far better reduction in fasting plasma glucose level. This could be due to the fact that we used whole leaf of Aloe vera instead of only the latex part.

This beneficial result of whole leaf may be attributed to its high fiber content. It delays the absorption of glucose in the small intestine.[19]

In combined group the insulin resistance was greatly reduced that is by 76%. The effect of combined therapy on glucose and lipid may play its role in reducing insulin resistance. In another study the reduction in insulin resistance was attributed to antioxidants present in Aloe vera.[20]. In another study in which Aloe vera was used in lower dose but for longer period of time than our study showed a statistically significantly results. However our study results were much better than Kim's study. The difference (150mg/kg) in dose Aloe vera used in our study can be one of the reason[17]

Like other studies insulin level in our study was raised in diabetic control group.

In study conducted, on fructose fed insulin resistant type 2 diabetic rats. The obtained data showed that serum insulin level in Aloe vera group significantly decreased ($p<0.05$) by 49% than in diabetic group. They contributed this outcome of Aloe vera extract on activation of insulin receptor in membrane of skeletal muscles and fat cells to increased glucose upake[21]. However in our study 74 % decrease was observed in insulin level after three weeks of treatment with combined extract. This can attributed to the alteration in type of trial model used in both studies as well as the synergistic effects

Rosiglitazone has been used for the treatment of type 2 DM since 1991.It works by binding to peroxisome proliferators activated receptor (PPAR- gamma) and reduces insulin resistance. [22]We achieved 76% and 74%reduction in glucose and insulin levels respectively with 20% rise in HDL level in combined group at end of our study. Our results are comparable with studies on rosiglitazone as antidiabetic

In one of the study in which rosiglitazone was given for 3 weeks in dose of 3mg/kg. This caused an obvious reduction in plasma glucose TG and insulin. But increase in body weight of rats was observed in this study.[23] A different animal model and mode of giving drug may be responsible for variance in results. In our study it was I/P while in Elena's study it was administered orally.

The positive results of combination therapy on glucose, insulin and insulin resistance in type 2 diabetics specially when half the effective dose of Rosiglitazone was used. This will also help in minimizing the side effects associated with this drug reported through various studies.[23,24]

The results of this study are much better than our previous study in which Aloe vera whole leaf extract was used alone to determine its effects on plasma glucose, insulin and insulin resistance[25]

Our study had disclosed boosting results to develop new approach for treatment of T2DM particularly for developing countries. Keeping the financial status of public in mind the use of natural herb with synthetic drug may help to reduce monetary load. Using half the effective dose will reduce the side effects associated with oral hypoglycemic drugs.

The result of our study demands for a study on human T2DM patients by using it with rosiglitazone half the effective dose of rosiglitazone to explore a new combination of treatment.

CONCLUSION

The significant result was obtained in combined group in lowering plasma glucose, insulin and insulin resistance though half their effective doses were used.It will also help in reducing side effects associated with use of rosiglitazone.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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