A study to identify the hypoglycemic activity of Cyamopsis tetragonoloba (Guar)

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Abstract:

Diabetes mellitus is a one of the disastrous chronic disorder in the endocrine system which is major cause of mortality globally.Many disorders develop including hyperinsulinemia, hypertension, hyperlipidemia and atherosclerosis associated with diabetes mellitus.Semi-hydrolyzed guar gum possesses hypoglycemic potential. A total of 50 subjects fulfilling inclusion and exclusion criteria as listed below were enrolled to identify the antidiabetic potential of guar gum as an add on therapy.significant difference between first and last screening visit of fasting blood sugar level and post prandial blood sugar level in both control (P= 0.00) and treatment groups(P=0.00) and also a significant difference between first and last screening visit of HbA1C (glycatedhaemoglobin) in both control (P=0.00) and treatment groups (P= 0.00).

Subjects who were treated with combination of Metformin + Glimiperide + Rosuvastatin and Guar powder as add on therapy comparatively better clinical outcome in terms of glycaemia control, lipid lowering action. This study also suggests the rationale for using guar as add on therapy for diabetes mellitus.

Key Words: Diabetes Mellitus, Cyamopsis tetragonoloba (Guar)

Introduction

Diabetes mellitus is a one of the disastrous chronic disorder in the endocrine system which is major cause of mortality globally (Chen et al., 2011)[1]. Its symptoms are insufficiency in insulin secretion and/ or insulin action related with chronic hyperglycemia and imbalance of carbohydrate, lipid and protein metabolism (El-Alfy et al., 2005)[2]. Therefore, many disorders develop including hyperinsulinemia, hypertension, hyperlipidemia and atherosclerosis (Lai et al., 2004)[3]. Different types of oral hypoglycemic agents such as biguanides and sulphonyl urea are available along with insulin for the treatment of diabetes mellitus but they have some toxicity against living cells (Chang et al., 2013)[4]. Therefore, there is an urgent requirement to explore for the drugs of a natural origin with fewer side effects. Flavonoids, possess significant biological activity are abundant in plants. They have been recommended against the development of diabetes as well as a mitigation effect of diabetes consequences (Gupta et al., 2009)[5].

Semi-hydrolyzed guar gum possesses hypoglycemic potential by decrease in post prandial blood glucose and glucose fascination from lumen of small intestine (Toru et al., 2009)[6]. The efficiency of granulated guar gum was reported in diseased persons with powerful hypercholesterolemia for 34 weeks. So it has been proved that guar gum can be used as a powerful drug for extensive duration treatment of hypercholesterolemia (Jaakko et al., 1988)[7].

Grizard et al., 2001 investigated the power of continuing utilization of cellulose, dietary fiber and guar gum upon metabolic strictures in both diabetic and controlled adult Chinese hamster and they reported that guar gum utilization provides to best long duration management in diabetic and non-insulin dependent adult Chinese hamsters. They observed reduction in corticosterone and insulin levels when guar gum and low molecular weight pectin's were subjected to rats for 3 weeks[8].

Material and methods

This was a prospective, open label, randomized study was conducted in a tertiary care hospital, Jaipur, on subjects of type 2 diabetes mellitus. A total of 50 subjects fulfilling inclusion and exclusion criteria as listed below 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 receiving Glimepiride 1 mg, Metformin 500 mg and Rosuvastatin 5 mg per day.
2. Subjects of either sex of age group18-70 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 in to 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 analysis were done for confirmation.

After reconfirming all the inclusion and exclusion criteria and the subjects turned out to be diabetic, he/she was enrolled in to the study. After being educated about diet, importance of anti-diabetic and 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 (Treatment) and B (Control) receiving regimens as illustrated:

Group A (Treatment): 4gm whole pods fine powder of M83 variety of Guar+Glimepiride 1 mg, Metformin 500 mg and Rosuvastatin 5 mg per day.

Group B (Control): Glimepiride 1mg, 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, Plant extract was given as add on therapy.

Follow up visit, visit 4 was performed at 84 days (± 3 days) as per the study flow chart. At each visit complete physical examination was carried out, including fasting and post prandial blood glucose. HbA1C were examined at the time of screening visit and visit 4.

In addition, Blood glucose was measured at any time if a subject experiences symptom of hypoglycaemia or if requested by treating physician. Apart from glycaemia the complications attributable to the treatment regimens were also recorded in both the group to assess the safety of the regime.

A case report form was used for collecting the data required for the study.

Estimation of blood glucose

The blood glucose estimation was done by glucose oxidase test in the central laboratory of the study site by using auto-analyzer. HbA1C estimation was done by using Nycocard or Afinion HbA1C test method at the central laboratory of the study site. A blood sample of 10µl for estimation of blood glucose was done within half an hour after the sample collection.

Study Drug: Whole pod fine powder of M83 variety Guar was used for the study purpose.

Dose Selection of study drug: Subjects received 4gm pod powder of M83 variety of Guar.

Statistical Analysis

The results obtained for Hypoglycemic activity in human beings were statistically evaluated through repeated measures analysis. The statistical analysis was conducted on PASW SPSS 18.0 trial version and MINITAB 15.0 trial version software.

Results

A total of fifty type 2 diabetes mellitus subjects were enrolled and randomly allocated to two group vij. A (Treatment) and B (Control). The subjects in both the groups were assessed for glycaemia control. The studies include various patients which were visited from beginning to 84 days.

Table1: Characteristics of the subjects

Parameter		Group A	Group B
No. of subjects (n)		25	25
Mean Age (years)		47.64±1.73	46.12±1.25
Sex	Female (n)	9	10
	Male (n)	16	15

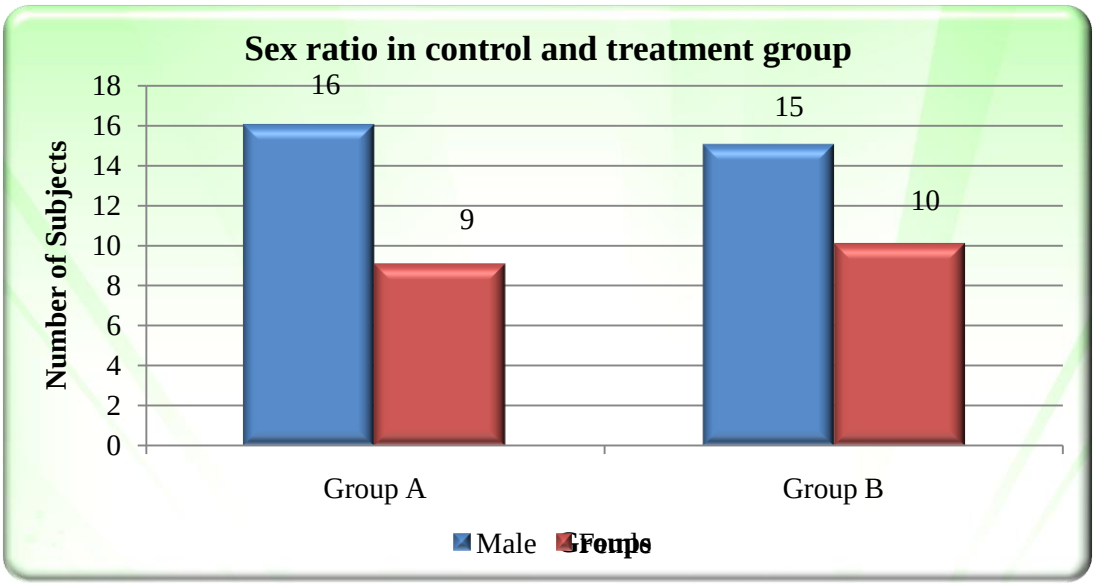

Figure 1: Sex ratio in control and treatment group

Firstly, I have applied a Normality test on data to check the Normality of data. Then t–test was performed to Normal data and MWU test applied to non- Normal data in both control and treatment groups. Then repeated measure analysis test was performed to compare all variables of both groups in following aspect:

Comparison of all variables of both control and treatment groups on the basis of first and last screening visit.

Table 2: Comparison of blood sugar between first and last screening visit

Comparison -time wise											
Pairs	Blood sugar	Control					Treatment				
		Mean	N	SD	Std. Error Mean	P value	Mean	N	SD	Std. Error Mean	P value
Pair 1	Fasting blood	232.40	25	38.113	7.623	0.000	259.92	25	56.030	11.206	0.000

	sugar Screening visit										
	Fasting blood sugar last visit	110.12	25	8.368	1.674		98.40	25	10.595	2.119	
Pair 2	Post prandial blood sugar Screening visit	316.64	25	35.754	7.151	0.000	334.68	25	53.919	10.784	0.000
	Post prandial blood sugar last visit	154.04	25	5.160	1.032		143.72	25	5.366	1.073	

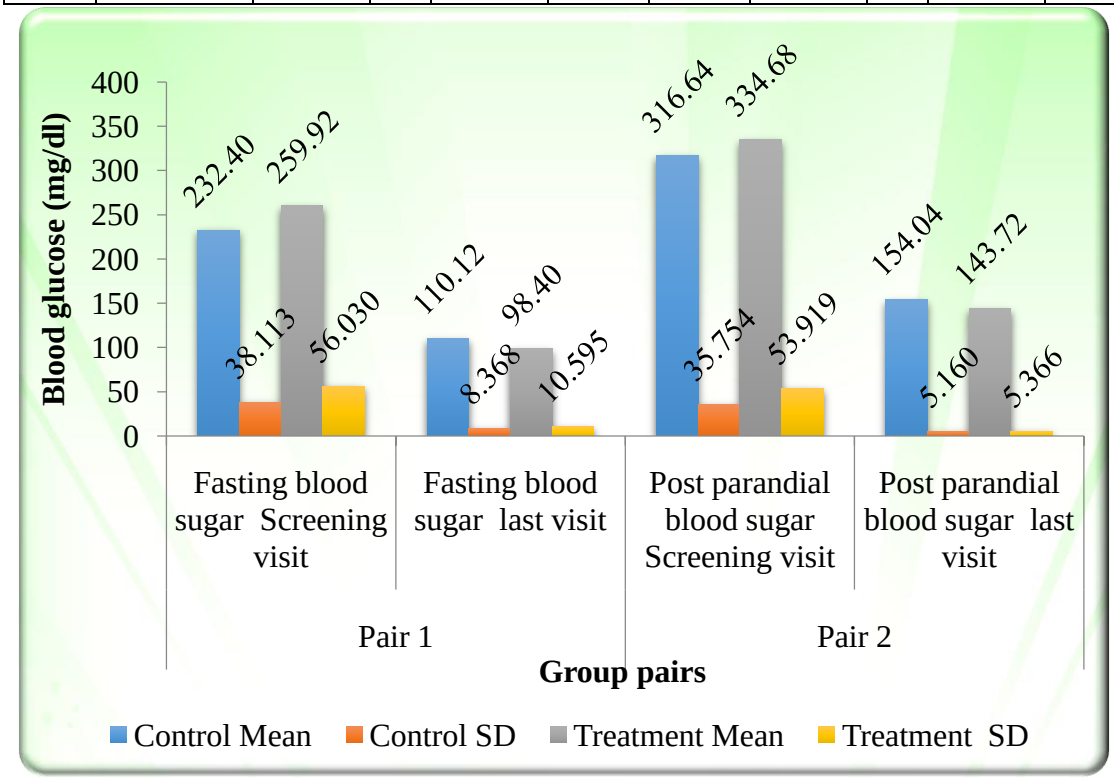

Figure 2: Comparison of blood pressure between first and last screening visits

In this table pair 1 and pair 2 indicates that there is a significant difference between first and last screening visit of fasting blood sugar level and post prandial blood sugar level in both control (P= 0.00) and treatment groups(P=0.00).

Now we compare HbA1C of both groups on the basis of their first and last screening visit.

Table 3: Comparison of HbA1C between first and last screening visit

Comparison -time wise											
Pairs	**HbA1C**	**Control**					**Treatment**				
		Mean	N	SD	Std. Error Mean	P value	Mean	N	SD	Std. Error Mean	P value
Pair 1	**HbA1C Screening visit**	8.47	25	0.219	0.044	0.000	8.40	25	0.305	0.061	0.000
	HbA1C last visit	6.91	25	0.385	0.077		6.26	25	0.187	0.037	

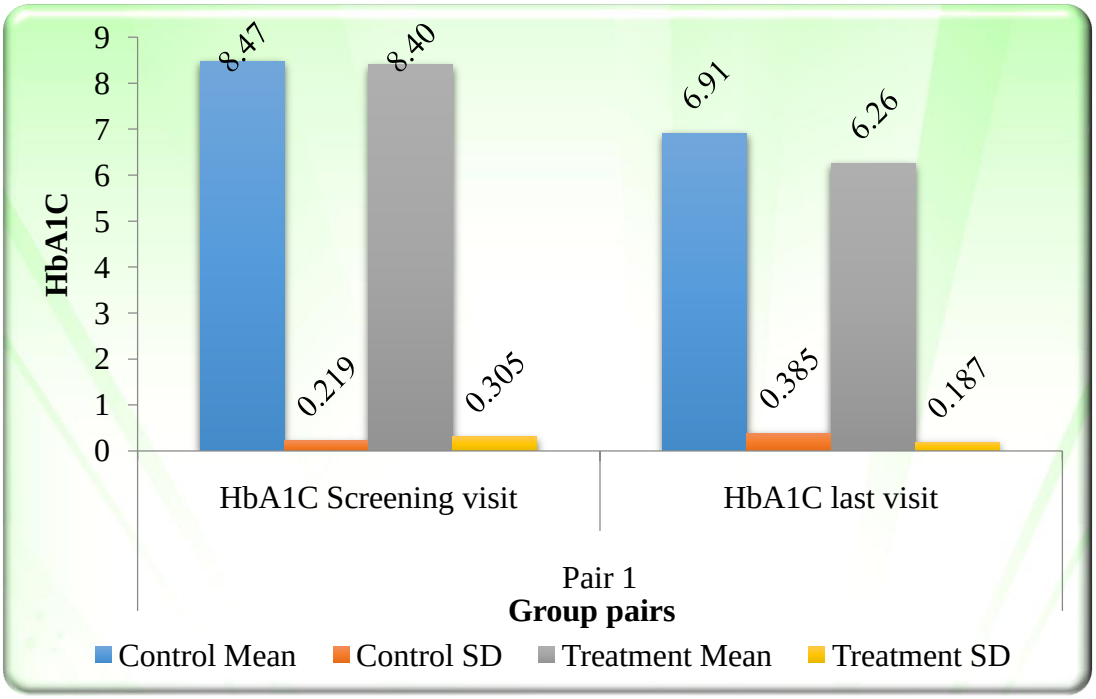

Figure 3: Comparison of HbA1C between first and last screening visits

In this table pair 1 indicates that there is a significant difference between first and last screening visit of HbA1C (glycatedhaemoglobin) in both control (P=0.00) and treatment groups (P= 0.00).

Discussion

Current scenario indicates the prevalence of diabetes among adults in India is 12.33% (Dasaapa et al, 2015)[9]. The treatment for DM consists of the intake of either insulin or other

hypoglycaemic agents in concurrence with recommendations for dietary control and physical exercise. However, these hypoglycaemic agents can results in hostile effects such as, renal toxicity, gastrointestinal disorders and hepatotoxicity (Caprio and Fonseca, 2014)[10]. These short comings of chemical drugs thus created alternative therapies, including herbal formulations. Secondary metabolites have become increasingly crucial in primary health care. In fact, the WHO reported that 82% of the population living in the developing countries depends on herbal medicine for their primary health care. Medicinal plants have gained due to their less side effects, for the presence of secondary metabolites, which may have numerous biological activities against numerous disorders, including infertility (Peiris, Dhanushka and Jayatilleka, 2015)[11], cancer and various infectious diseases (Fodouop et al., 2015)[12]. Many therapeutic ventures are carried out to identify new drugs for the treatment of these diseases. Therefore, most of these plants have largely been used in conventional medicinal systems since many decades to treat DM.

Mukhtar et al (2004)[13] reported effect of aqueous extract of Cyamopsistetragonoloba Linn.beans on blood glucose level in normal and alloxan-induced diabetic rats. They reported that at in half an hour after glucose intake, the blood glucose concentration increased rapidly from the fasting value and then attained nearly the same value at the end of the study i e, at 90 min. Administration of gliclazide (25 mg/kg body weight) prior to glucose loading, induced time dependent and statistically significant hypoglycemic effect.

Saeed et al (2012)[14] reported antihyperglycemic and antihyperlipidemic effects of guar gum on streptozotocin-induced diabetes in male rats. They reported that in spite of the fact that diabetes elevated blood lipids in all rats after 14 days, the guar gum diet significantly decreased the serum concentration of cholesterol, triacylglicerols and LDL-C and atherogenic index. The most significant result in this study was the reduction of blood glucose in diabetic rats treated with the guar gum diet after 28 days versus non- and glibenclamide-treated rats. The gum promoted a general improvement in the condition of the diabetic rats in body weight and food intake in comparison with non-treated rats. In the present research total seventy-two type 2 diabetes mellitus subjects with hyperlipidaemia were divided into two groups viz. A (Treatment) and B (control). But fifty subjects have completed the study. Then all the variables of both control and treatment groups were compared on the basis of three aspects.

We compared all the variables of both groups on the basis of their first and last screening visit. It was estimated that guar powder with medication in treatment group can more effectively decrease the level of fasting as well as post prandial blood sugar level in comparison to control group from first to last screening visit. For glycosylated heamoglobin it was observed that guar powder with medication in treatment group can more effectively decrease the level of HbA1C in comparison to control group from first to last screening visit.

Conclusion

Bio efficacy of experimental plant was tested for its hypoglycemic activity in human beings. The results of this study reveal that subjects who were treated with combination of Metformin + Glimiperide + Rosuvastatin and Guar powder as add on therapy comparatively better clinical

outcome in terms of glycaemia control, lipid lowering action. This study also suggests the rationale for using guar as add on therapy for diabetes mellitus.

Since, the time and financial constraints were the major limitations of the study, more short and long term studies in this direction are warranted to explore and validate the differences in clinical outcomes in larger number of diabetic patients.

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