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Research Article

ANTIHYPERGLYCEMIC ACTIVITY OF HEARTWOOD POWDER OF *Pterocarpus marsupium* (VIJAYASAR) AS ADD ON THERAPY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

The aim of study was to compare the blood glucose lowering effect of *Pterocarpus marsupium* (vijayasar) as add on therapy with oral hypoglycemic drugs in patients with type 2 diabetes mellitus, and to determine adverse effects if any. The study was carried out at tertiary care hospital of Gajra Raja Medical College, Gwalior (M.P.). The study was initiated in September 2009 and intake was stopped in September 2010. A total of 56 old uncontrolled hyperglycemic (type 2 diabetes mellitus) patients already taking oral hypoglycemic drugs were enrolled on the basis of inclusion and exclusion criteria. The duration of treatment with vijayasar as add on therapy was 12 weeks with 4 weekly clinical attendances for review and collection of drug. It was prospective, open, non-randomized, interventional, efficacy and safety type of study, the dosage of vijayasar being 2 to 4 gm/day. At the end of treatment (12 weeks) with vijayasar as add on therapy mean fasting blood glucose, postprandial blood glucose and glycosylated haemoglobin were compared with baseline using student's paired t – test. Calculated P – value for all parameter is <0.05 i.e. it is highly significant. It is concluded that vijayasar is an effective blood glucose lowering Indian traditional plant agent, its glycemic effect being comparable as add on therapy in patients with type 2 diabetes mellitus and free from any side effects.

Key words: Complementary and Alternative Medicine, Diabetes Mellitus, *Pterocarpus marsupium*

INTRODUCTION

The prevalence of diabetes mellitus is rapidly increasing all over the world and it has become a global public health crisis [1]. According to International Diabetes Federation, 387 million people worldwide have diabetes and it is projected to reach 592 million by 2035 [2]. Diabetes mellitus increases with aging. In 2010, the prevalence of diabetes mellitus in the United States was estimated to be 0.2% in individuals aged <20 years and 11.3% in individuals aged >20 years. In individuals aged >65 years, the prevalence of diabetes mellitus was 26.9%. Diabetes is a major cause of mortality, but several studies indicated that diabetes is likely unreported as a cause of death. In the United States, diabetes was listed as the seventh leading cause of death in 2007; a recent estimate suggested that diabetes was the fifth leading cause of death worldwide and was

responsible for almost 4 million deaths in 2010 [3]. A number of medicinal plants, traditionally used for over 1000 years named rasayana are present in herbal preparations of Indian traditional health care systems [4]. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as "Botanical Garden of the World" [5]. In Indian systems of medicine most practitioners formulate and dispense their own recipes. More than one-third of Canadians are using complementary and alternative medicine (CAM) therapies, often without consulting or even informing their family physicians. It is important for family physicians to ask patients about their CAM use and provide evidence-based information about the safety and efficacy of commonly used CAM therapies [6].

Pterocarpus marsupium (vijayasar) has a long history of use in India as a treatment for diabetes. It is also known as Indian kino tree or Malabar kino tree. The bark contains l-epicatechin. The heartwood yields liquiritigenin, isoliquiritigenin, alkaloid (0.017%) and resin (0.9%) [7]. Ethyl acetate extract of powdered dried heartwood of *Pterocarpus marsupium* revealed the presence of following constituents: (-) epicatechin (a flavonoid), pterosupin (a dihydrochalcone), marsupin (a benzofuranone), pterostilbene, liquiritigenin (a stilbene), isoliquiritigenin, (2S)-7-hydroxyflavanone, 7, 4'-dihydroxyflavone, p-hydroxybenzaldehyde, (2R) - 3 - (phydroxyphenyl) - lactic acid and pm-33 [8]. Pterostilbene, a constituent derived from wood of this plant caused hypoglycemia in dogs [9, 10] showed that the hypoglycemic activity of this extract is because of presence of tannates in the extract. Flavonoid (epicatechin) fraction from *Pterocarpus marsupium* has been shown to cause pancreatic beta cell regeneration [11]. Other mechanism of *Pterocarpus marsupium* may be increase release of insulin from β-cells [12], prevent insulin resistance [13] and hindering the absorption of glucose from intestine [14].

OBJECTIVES:

To evaluate the efficacy, safety and tolerability of *Pterocarpus marsupium* (vijayasar) heartwood powder as add on therapy in patients with type 2 diabetes mellitus.

MATERIALS AND METHODS

The study was conducted in J. A. hospital, Gwalior (M.P.) India, after approval of protocol by Institutional Ethical Committee of G. R. Medical College, Gwalior (M.P.) India (Ethical clearance No. 383/Bio/MC Gwalior, Date: 18/08/2009). The study was prospective, open, non-randomized, interventional, efficacy and safety type of study. The study was conducted from September 2009 to September 2010.

Patient Selection

Patients were enrolled from department of Medicine OPD on the basis of inclusion and exclusion criteria.

Inclusion Criteria

1. Patients willing to give written informed consent and ready to come regularly for follow up.
2. Patients with type 2 diabetes mellitus taking <50% of maximum dose of oral hypoglycemic drugs for last 3 months but with uncontrolled blood glucose level.
3. Patients of >30 years of either gender.
4. Fasting blood glucose (FBG) >126 mg/dl.

5. Postprandial blood glucose (PBG) >180 mg/dl
6. Glycosylated haemoglobin (HbA_{1c}) $\geq$7%.

Exclusion Criteria

1. Type 2 Diabetes Mellitus patients taking insulin.
2. Type 1 Diabetes Mellitus patients.
3. Patients age of <30 years.
4. Fasting blood Glucose >230 mg/dl.
5. Body Mass Index (BMI) <19 kg/m^2
6. Patients with complications like retinopathy, nephropathy, diabetic foot and coronary artery disease (CAD).
7. Patients with severe liver and/or kidney disease.
8. Pregnant and lactating women.

MATERIAL

Wood of *Pterocarpus marsupium* was collected from ayurvedic herb store at Gwalior (Madhya Pradesh) and identified by research officer (Botany) and confirmed by test. It was to be made in fine powder form by grinding and provided to patients without encapsulation in air tight container with a capacity of 1 gm spoon.

Study Design

The study was prospective, open and non-randomized. The duration of drug treatment was 12 weeks, with 4 weekly clinical attendances for assessment and drug collection. The recommended dietary schedule was advocated to avoid dietary aberration. The patients were instructed to avoid the use of other drugs for any ailment without consulting the treating physician. If patient developed any major ailment that required institution of new treatment modalities, he/she was to be withdrawn from the trial.

The patients were enrolled after considering selection criteria. Free and written informed consent was obtained from each patient before entering the study. Patients were advised primary investigations (fasting and postprandial plasma glucose), secondary investigation (HbA_{1c}) and some other investigations whichever are required at the start of study. During the study, patients were advised to stick to their previous drug regimen (Metformin 500 mg + Glimepiride 1 mg daily or Metformin 500 mg + Glimepiride 1 mg + Pioglitazone 15 mg daily) prescribed by the physician. Vijayasar wood powder (starting dose 2 gm/day in divided doses) was added as add on therapy and advice to take with previous drug regimen 30 minutes before meal. At each 4 weekly follow up visit primary measurements (fasting and postprandial blood glucose) were estimated and any adverse event(s) if encountered was thoroughly evaluated by concerned physician and separately reported. Patients who tolerated vijayasar powder with oral hypoglycaemic drugs and have controlled blood glucose were continued on same dose till the end of study. Dose of vijayasar was increased from 2-4 gm/day (in divided doses) in unresponsive patients. After completion of 12 weeks therapy, each patient was advised for fasting blood glucose, postprandial blood glucose and glycosylated haemoglobin (HbA_{1c}). Total 56 patients were recruited for the study. Out of these, 4 patients dropped out from the study due to unknown region.

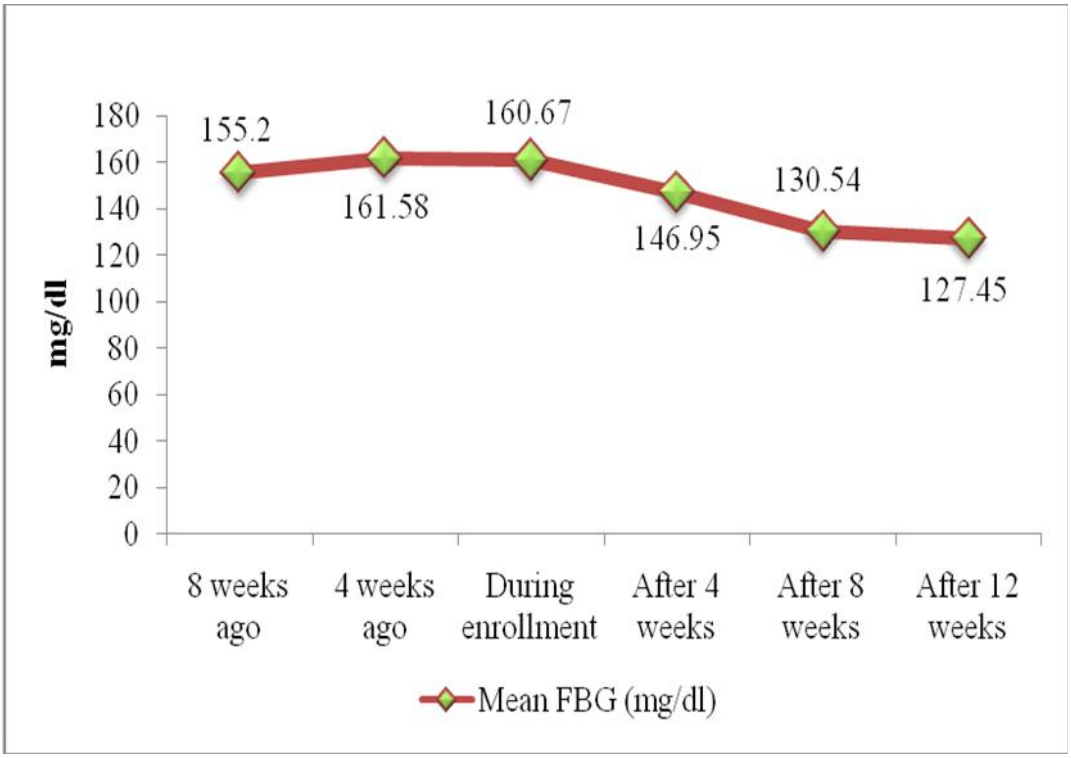
STATISTICAL ANALYSIS

The data of 52 patients was recorded in the structured proforma. Student's paired t – test was used to compare the mean of initial (baseline) 3 values of fasting and postprandial blood glucose (before the start of study) with the mean of 3 values of fasting and postprandial blood glucose (after the start of study) and also to compare the value of HbA_{1c}. Mean and standard deviation were obtained and data are expressed as mean ± SD. P – value was calculated using epicalc statistical software. P – value <0.05 was taken as statistically significant value.

RESULTS

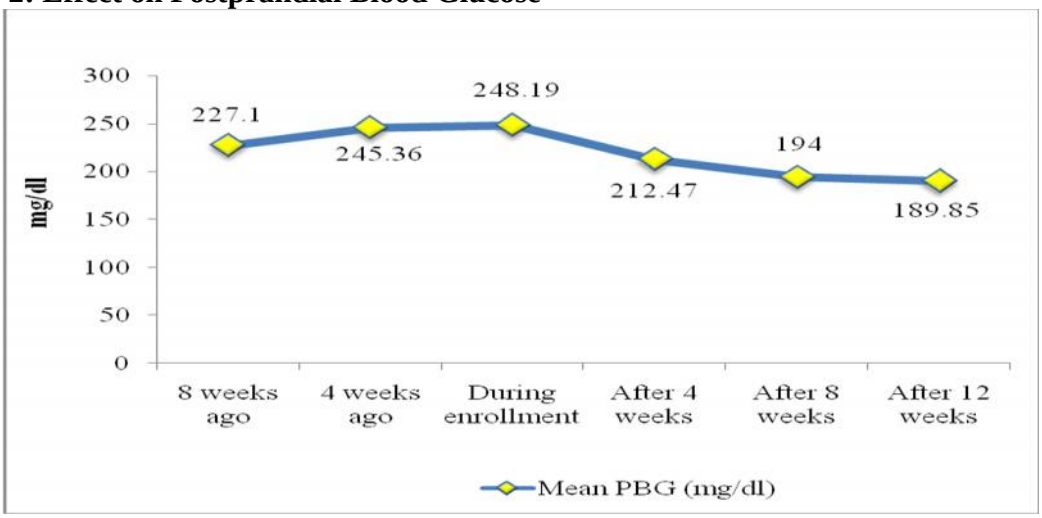
52 patients (25 male and 27 female) reached to end of trial. Previous drug regimen of 34 patients was Metformin 500 mg + Glimepiride 1 mg daily and of 18 patients Metformin 500 mg + Glimepiride 1 mg + Pioglitazone 15 mg daily. 3 patients maintained on 2 gm/day, 28 patients on 3 gm/day and 21 patients on 4 gm/day of vijayasar wood powder.

Figure 1: Effect on Fasting Blood Glucose



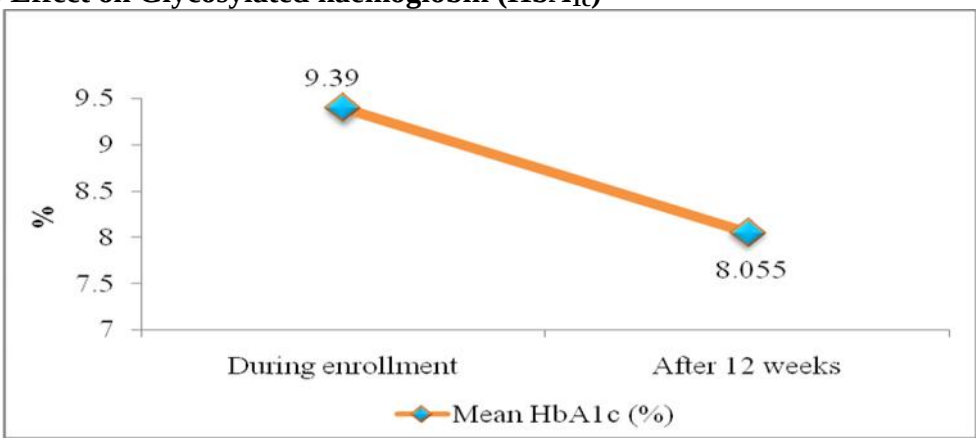
Data are expressed as mean ± SD. Baseline mean fasting blood glucose of type 2 diabetic patients was found to be 159.15 ± 30.38 mg/dl and at the end of treatment with vijayasar as add on therapy 134.7 ± 30.31 mg/dl. Mean fasting blood glucose at baseline and mean fasting blood glucose at the end of treatment with vijayasar as add on therapy was compared using student's t – test and calculated P – value is 0.000081(P<0.05) i.e. it is highly significant.

Figure 2: Effect on Postprandial Blood Glucose



Baseline mean postprandial blood glucose of type 2 diabetic patients was found to be 240.22 ± 65.77 mg/dl and at the end of treatment with vijayasar as add on therapy 198.53 ± 39.66 mg/dl. Mean postprandial blood glucose at baseline and mean postprandial blood glucose at the end of treatment with vijayasar as add on therapy was compared using student's t – test and calculated P – value is 0.000164(P<0.05) i.e. it is highly significant.

Figure 3: Effect on Glycosylated haemoglobin (HbA_{1c})



Baseline mean HbA_{1c} of type 2 diabetic patients was found to be 9.39 ± 1.68 % and at the end of treatment with vijayasar as add on therapy 8.05 ± 1.19 %. Mean HbA_{1c} at baseline and mean HbA_{1c} at the end of treatment with vijayasar as add on therapy was compared using student's t – test and calculated P – value is 0.0000009 (P<0.05) i.e. it is highly significant.

Adverse Drug Event

Out of 52 patients, 01 patient report with loss of appetite on 1st follow up visit but not on subsequent visit and 01 patient with weakness that was last for 7-10 days. Hypoglycemia was not reported in any case.

DISCUSSION

This prospective, open and non-randomized trial has ascertained the blood glucose lowering effect of vijayasar as add on therapy in patients with uncontrolled type 2 diabetes mellitus. Mean FBG, PBG and HbA_{1c} at baseline and mean FBG, PBG and HbA_{1c} at the end of treatment with vijayasar as add on therapy with conventional oral hypoglycaemic drugs was compared and calculated P – value (<0.05) is highly significant for all these parameter. The safety aspect of vijayasar was also established with the dosage up to 4 gm per day. There was no episode of hypoglycemia occur in any patient. *Pterocarpus marsupium* is important herbal drug of various pharmacological properties and it requires further exploitation.

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