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Clinical Evaluation of *Palingu abraga parpam* in The Management of Diabetes Mellitus (Niddm)

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ABSTRACT
Diabetes mellitus is one of the metabolic disorders prevalent worldwide and causes increase in the blood glucose level due to insufficient insulin secretion. Due to this peripheral utilization of glucose is reduced, which in turn disturbs the basic metabolism. Diabetes mellitus is categorized into Type I or Insulin dependent diabetes mellitus (IDDM) and Type II or Non-Insulin dependent diabetes mellitus (NIDDM). Complete destruction of islets of Langerhan's leads to sole dependence of insulin for the metabolic requirements in Type I diabetic patients, whereas relative insufficiency of insulin in Type II DM can be managed by oral hypoglycemic drugs. Palingu Abraga Parpam is one of the herbo-mineral based Siddha anti diabetic formulation for Type II non insulin dependent diabetes mellitus. So the present research work was carried out to validate the anti diabetic activity of Palingu Abraga Parpam clinically on patients with Type II diabetes mellitus. Open clinical trial was conducted in 75 diabetic patients for the period of six months. Fasting and post prandial serum blood glucose level and HbA1c were estimated before the enrollment of the study, during the trial period and after the completion of the study. At the end of the study period all these parameters were statistically analyzed. The clinical studies revealed that Palingu Abraga Parpam was highly significant in NIDDM (Blood sugar level varies from 180 to 300 mg / dl). The blood sugar level was controlled effectively within 4 weeks, when compared to its initial blood sugar level. Whereas HbA1c was decreased to its normal reference range within 3 months. During the study period there was no side effects identified and which confirms the traditional use of Palingu Abraga Parpam (PAP) for the treatment of Type II diabetes mellitus.
KEY WORDS: Anti diabetic activity, diabetes mellitus, FBGL, HbA1c, insulin, Palingu Abraga Parpam (PAP), PPBGL, Type II NIDDM.

INTRODUCTION

Diabetes is one of the ancient diseases. The history of diabetes is stated that in the Ebers papyrus (1500 BC) [1]. Polyuria and honey urine was noted as early as 400 BC by the Indian Physician *Susrutha* and he has described this disease as '*Madhumeham*' which means the honey in the urine [2]. Type II Diabetes mellitus is a metabolic disorder due to deficiency of insulin leads to hypoglycaemia which is characterized by polyuria, polyphagia, and polydipsia. Diabetes mellitus is one of the metabolic endocrine disorder that affects more than 200 million people worldwide and 300 million will have the disease diabetes mellitus by 2025 [3-5]. If it is not controlled by medicine it will affect most of the internal organs and produce short term and long term complications like nephropathy, neuropathy, retinopathy etc. [6] Though numerous anti diabetic drugs available in day today practice either have a source directly or indirectly from the nature. According the ethnobotanical information report, nearly 800 plants used to treat the diabetes mellitus and said to possess anti diabetic property [7]. In the past decade, research has been focused on scientific evaluation of traditional drugs of herbal and mineral origin were screening of more effective and safe hypoglycemic agents has continued to be an important area of present day research[8]. In developing countries 80 % of population is using traditional medicine in primary medical problems [9]. In the present study, an attempt has been made to investigate the anti-diabetic activity of *Palingu Abraga Parpam* (PAP) in Type II NIDDM patients clinically. *Palingu Abraga Parpam* is a herbo-mineral formulation and this is well known for its anti diabetic activity in the traditional Siddha system of medicine from time immortal for their various therapeutic properties especially hypoglycemic activity [10].

MATERIALS AND METHODS

The Open clinical trial was conducted at Arignar Anna Government Hospital of Indian Medicine, Chennai from January 2012 to June 2012. The protocol of this clinical study was approved by the Institutional Ethical Committee and conducted according to the guidelines of the Declaration of Helsinki [11]. A written informed consent in both English and Tamil was obtained before the enrollment of the patients. Total number of 75 cases of either sex irrespective of socio economic status was selected for this clinical trial from OPD and IPD in the department of medicine. The patients registered in the study showed the baseline characteristics of age ranging from 35 years of age to 65 years. They were all under the medical care on direct supervision by the author.

Selection Criteria

Patients selected for this study were based on inclusion criteria and exclusion criteria. Inclusion criteria for the patients with confirmed diagnosis of type 2 diabetes, patients of either sex between the age of 35-65 years, patients with FBGL ≥ 140 mg/dl and PPBGL ≥ 240 mg/dl[12-13] were included. American Diabetes Association Standards of Medical Care in Diabetes recently added the HbA1c ≥ 48 mmol/mol (≥6.5%) as another criterion for the diagnosis of diabetes [14]. Hence, HbA1c ≥ 7 criteria was also included in the present study. Patients more than 65 years and less than 35 years, inter current treatment for major or other chronic health conditions like gastro intestinal disturbances, liver disorders, cardiac involvements, hypertension, kidney disorders and endocrine disorder other than diabetes mellitus, Type I DM, AIDS, STD, pregnancy, lactation, habits of alcohol intake and smoking were identified and excluded from the study.

Proper history taking and clinical assessment were done including the estimation of fasting blood glucose level (FBGL), Post Prandial Blood Glucose Level (PPBGL) and HbA1c at the time of enrollment, during the visits and at the end of the study. Statistical comparison of the initial and final readings were analyzed and recorded.

Study Design

All the patients enrolled in the present study were divided into three groups.

Group I (n=25) : Diabetic standard group. In this group all the diabetic patients were treated with standard oral hypoglycemic drugs which were prescribed by the primary physicians.

Group II (n=25) : In this group all the diabetic patients were treated with PAP 100 mg twice a day with hot water.

Group III (n=25) : In this group all the diabetic patients were treated with PAP 100 mg twice a day with hot water and oral hypoglycemic drugs of their own .

Formulation of the trial drug

The mineral formulation of *Palingu Abraga Parpam* described in *Anuboga Vaithiya Navaneetham Part-2* [10]

Ingredients of the drug

According to Siddha classical text, the ingredients of *Palingu Abraga Parpam* (PAP) are *Mica (White Abragam), common oyster shell, Potassium nitrate (Vediyuppu)* and the plant *Eclipta alba (Karisalai).* The raw materials were collected from country drug shop at Chennai and the plant *Eclipta alba* (*Karisalai*) was collected in and around Chennai. The entire raw materials and plant were identified and authenticated by the *Gunapadam* (Pharmacology) experts and by the botanist of Government Siddha Medical College, Chennai. The vouchers specimens of each sample of the raw materials and plant were kept in the department for future reference. Each raw material were cleaned and purified separately as per the Siddha text. For the purification of mica, the following "*Suddhi*" (Purification process) was adopted. The *Eclipta alba (Karisalai)* cleaned well with water and grind to get juice. 70 gm of mica rake was taken and immersed with 700 gm *Eclipta alba (Karisalai)* juice which was kept under the shade for drying. After complete drying, mica was taken for further process. A small pit having a measurement of 2 x 2 x 2 feet was made and the mica was placed in the pit between the 100 cow dung cakes (*Varatties*) and fired. The next day the mica was taken and allowed for cooling which was placed in a glass jar. This is the purification method of mica (*white Abragam).* Then crucible was taken and filled partially with *unhydroxylated common oyster shell* and *potassium nitrate (Vediyuppu)* respectively. Then the purified mica (*white Abragam)* was kept above the two layers in the center. The same process of filling with *unhydroxylated common oyster shell* and potassium *nitrate* respectively were applied once again

above the mica (*white Abragam)*. Then the crucible was sealed with seven layers of mud cloth (*Seelai man*) and allowed for drying. After drying the crucible kept in another 5 x 5 x 5 feet pit for "*Pudam*" (calcinations process) with 1000 cow dung cakes and ignited. After 24 hours, the crucible was taken out and allowed for cooling. Then the drug was taken away from the crucible and powdered well. Good manufacturing practice was followed during the preparation. Then the prepared drug was kept in an air tight container and labeled as PAP.

Dosage and Advise: The drug PAP was given to the patients at the dose of 100 mg twice a day with hot water. All the patients were advised to avoid direct sugar, underground root vegetables and advised to take plenty of leafy and fiber vegetables.

Laboratory Investigations

All the patients enrolled in the study were subjected to the following laboratory investigations which include the biochemical analysis of initial FBGL, PPBGL and HbA1c. Blood samples were obtained from each patient prior to, during and after administration of *Palingu Abraga Parpam* (PAP). About 3 cc of blood was obtained from each patient through vene-puncture by using disposable sterile syringes for FBGL, PPBGL and HbA1c which were investigated in nearby laboratories and at the hospital of confinement.

Statistical Analysis

The above data of pre and post treatment were analyzed statistically by Student's Paired t - test. P value ≤0.001 was considered statistically highly significant and P value ≤0.0001 was considered as extremely significant which were shown in Table No. 3.

RESULTS AND DISCUSSION

The six months period of open labeled clinical study was performed to evaluate the efficacy of PAP in patients with Type II NIDDM. A total number of 75 patients were participated in the present study, in which 40 were men and 35 were women with in the age range of 35 – 65 years (Table No.1). Out of 75 patients, 65 patients were treated as out-patients and 10 patients who were very sick and were hospitalized. During the trial period no drop outs were recorded. The baseline clinical features of the enrolled subjects were summarized in Table No.2. After baseline evaluation, these patients were divided into three groups. Standard group (Group I) was treated with modern oral hypoglycaemic drugs prescribed by the primary physician. Second group (Group II) was treated with PAP 100 mg twice a day with hot water and third group (Group III) was treated with PAP 100 mg twice a day with hot water combined with their own oral hypoglycaemic drugs. The signs and symptoms such as polyuria, polyphagia, polydipsia, general weakness and body pain of all groups were noted separately and recorded at initial visit, each weekly visit and at the end of the study. After 4 weeks of trial period, there was a gradual improvement in the clinical features were observed in all the three groups. However, the signs and symptoms were more markedly observed in the group III. The result of the clinical features and improvement status were summarized in Table No.2.

FBGL, PPBGL and HbA1c level of all the three groups were regularly monitored and recorded from the initial period to end of the study period with weekly interval and the statistical analysis between pre test and post test was summarized in Table No.3. The initial FBGL value (Mean ± SD) of group I, II and III were 164.44±5.24, 165.56±3.65 and 167.04±3.92 respectively. After three months of treatment FBGL value (Mean ± SD) were 104.72±3.40, 117.32±4.36 and 100.04±2.26 respectively (Fig.No.1). The initial PPBGL (Mean ± SD) of group I, II and III were 255.72±4.55, 256.48±3.45, and 260.96±4.46 respectively. After completion of the trial the PPBGL (Mean ± SD) were 157.48±3.47, 176.76±3.27 and 150.20±2.73 which was shown in Fig No.2. The initial level of HbA1c of groups I, II and III were 8.17±0.25, 7.99±0.14 and 8.02±0.19 and after treatment the level of HbA1C were 6.59±0.18, 7.10±0.15 and 6.35±0.12 respectively which was shown in Fig No.3.

Significant decrease in FBGL, PPBGL and HbA1c were observed in all the three groups and maintained better control of their blood sugar levels during the follow up period. Fall in blood sugar level in group II was found to be highly significant and nearer to the standard drug group which confirmed the hypoglycaemic effect of PAP. The patients of group III receiving PAP and standard hypoglyceamic drug showed extremely significant reduction in FBGL, PPBGL and HbA1c value when compared with group I and II and gradually reached to normal level at the end of one

month and maintained during the follow-ups without notable fluctuations which was confirmed the synergistic effect of the combination of trial drug PAP and modern standard drug. During the study period no side effect was observed.

In this clinical study the diabetic patients were participated actively in the management of sugar level along with life style modifications and they were developed their confidence level successfully. HbA1c is an important marker for better glycaemic control therapy. In this present study HbA1c levels in Group I, II and III decreased within the reference range confirmed the hypoglycemic effect of standard drug and the trial drug PAP. Mica (*Abragam)* was used traditionally in the management of Type II diabetes mellitus patients in Siddha system of medicine and the anti diabetic activity of *Abragam* was scientifically confirmed by preclinical research works [15]. The result of this clinical study also provides the successful proof of the traditional practice and preclinical research work of PAP.

Table No.1 Showing Age and Sex distribution

Category	35 - 43 yrs	44-51 yrs	52-59 yrs	60 – 65 yrs
Type 2 DM (n= 75)	Male: **12** Female: **10**	Male: **14** Female: **16**	Male: **10** Female: **6**	Male: **04** Female: **03**

Table No.2 Showing the signs and symptoms of Type 2 DM patients and showing the clinical improvement at the end of the study

Clinical features	Group I (n=25)			Group II (n=25)			Group III (n=25)		
	BT	AT	% of Imp	BT	AT	% of Imp	BT	AT	% of Imp
Polyuria	25	24	96	25	21	84	25	25	100
Polydipsia	25	23	92	25	20	80	25	25	100
Polyphagia	24	22	92	24	19	90	24	24	100
General weakness	25	23	92	25	20	80	25	24	96
Itching	08	06	75	09	05	56	10	10	100
Body pain	16	13	82	15	11	73	18	17	94

BT - Before Treatment, AT - After Treatment, % of Imp - Percentage of improvement

Table No. 3: Showing the efficacy of *Palingu Abraga Parpam* on FBGL, PPBGL and HbA1c in treated patients

Group (n = 25)	Fasting glucose (mg/dl)		Post Prandial (mg/dl)		HbA1C (mg %)	
	BT	AT	BT	AT	BT	AT
Standard drug	164.44±5,24	104.72±3.40***	255.72±4.55	157.48±3.47***	8.17±0.25	6.59±0.18*
PAP 100 mg	165.56±3.62	117.32±4.36**	256.48±3.45	176.76±3.27**	7.99±0.14	7.10±0.15*
Standard drug + PAP 100mg	167.04±3.92	100.04±2.26***	260.96±4.46	150.20±2.73***	8.02±0.19	6.35±0.12**

Fig No.1. Showing FBGL

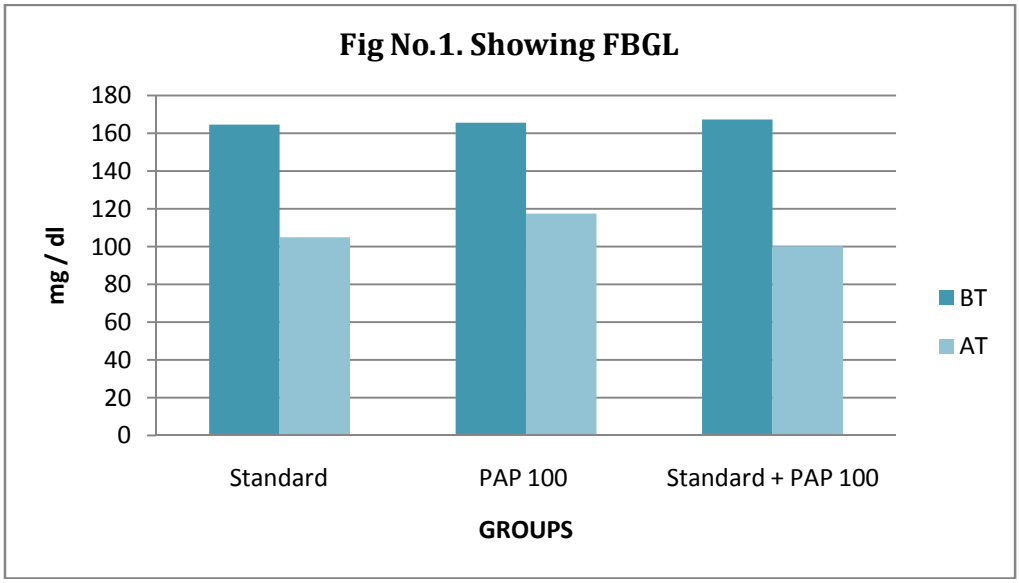


Fig No. 2. Showing PPBGL

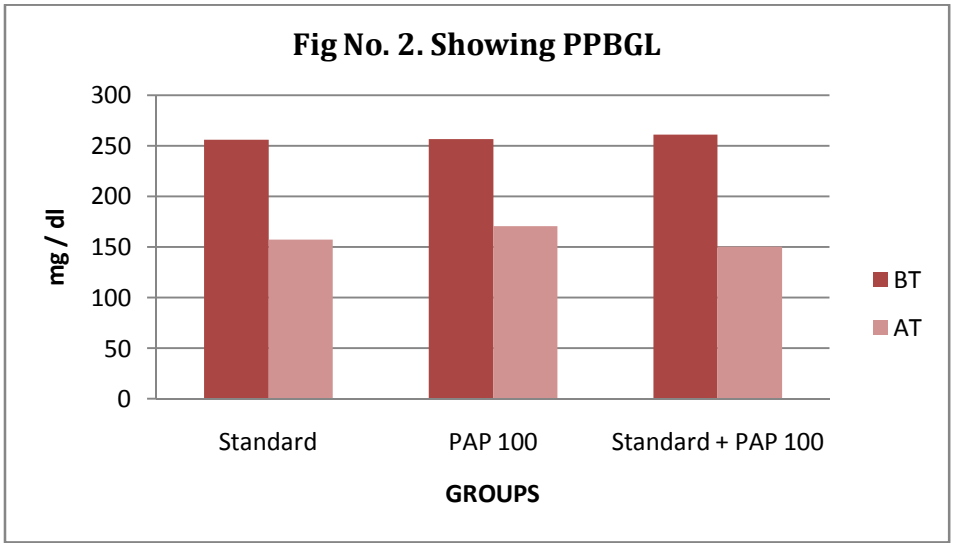
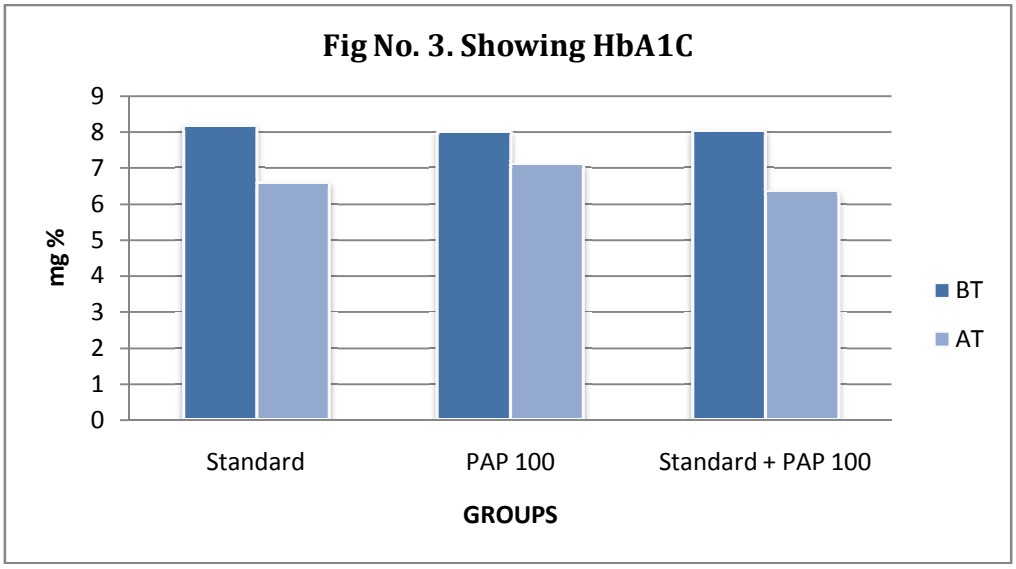


Fig No. 3. Showing HbA1C



CONCLUSION

From this above study the test drug PAP is highly significant in Type II NIDDM patients which are confirmed by the statistical analysis. All the patients were gradually improved their signs and symptoms and reduction of FBGL, PPBGL and HbA1C values over the period of three months. The trial drug PAP lowers the fasting blood glucose level, post prandial blood glucose level and provide the reference range of HbA1C level. No untoward or side effects were noted during the study period. The clinical study revealed that the herbo-mineral drug PAP was well tolerated in dose of 100 mg twice a day with hot water and was effective in type II diabetes mellitus as indicated by reduction in blood sugar levels after 4 weeks. The hypoglycaemic effect of PAP may be due to the increase in the utilization of peripheral metabolism of glucose or by increased insulin secretion from beta cells of pancreas [16]. From this study we concluded that the trial drug PAP may be administered as alternative drug for diabetic treatment or combined with standard oral hypoglycaemic drug for uncontrolled diabetes mellitus and maintain the blood glucose level with in the normal range which favors the prevention of diabetic complications.

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