JR.A.S. Vol. XXIV, No. 3-4, (2003) pp.62-70

CLINICAL TRIAL OF AN AYURVEDIC COMPOUND IN PRAMEHA WITH SPECIAL REFERENCE TO NIDDM

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Diabetes is a major problem in our society which is increasing day by day and Indian people are higher in incidence, have been observed by different epidemiological studies. This disease not only increasing but also creates multi organ dysfunction and longstanding illness. So different chemicals have already been introduced as a antidiabetic drugs. Because of the side effect of these drugs and diabetes is an longstanding metabolic diseases more and more approach have been given towards the alternative medicine.. In Ayurveda number of Pramehaghna drugs are described. Some of these drugs have also medaghna properties. So attempt have been done by this study to evaluate the hypoglycaemic effect of these drugs. Jambu, Jarul, Khadir and Bhumiamla powder given as trial drugs in 50 patient. Out of these 43 patient have completed their follow up and shows very much encouraging result, specially obese diabetic patient comes to normal glucose level even after 45 days of treatment.

INTRODUCTION

Diabetes mellitus is a world wide problem. The incidence of this disease is increasing day by day due to the change in dietary habit, socioeconomical status and sedentary life style. Importance also increasing not only due to the increasing in the prevalence of this disease from 4% in 1995 to 4.2% by 2000 and suspect around 2025, it will be moves upto 5.4% of the total world wide population but also lack of suitable long effective drugs which will not develop resistance in future. In India the incidence is so much increasing that around 2025 highest percentage (6%) of diabetic patient will be in India.

Diabetes mellitus is a metabolic disorder of multiple aetiology characterized by hyperglycaemia with disturbance of carbohydrate, fat and protein metabolism from defect in insulin secretion, insulin action or both. The effect of diabetes mellitus includes reversible and irreversible damage of multi system and organ i.e. retinopathy, nephropathy, coronary heart disease, sexual impotency, peripheral vascular disease, cataract etc. Type 1 diabetes is dependent on insulin therapy but Type 2 diabetes which causes predominantly due to the insulin resistance. Some other endocrinal cause, genetic cause, chemical induce diabetes are

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included as other specific type and carbohydrate intolerance which develop and diagnose during pregnancy is termed as Gestational diabetes mellitus (GDM).

These four classification is the newer classification of diabetes. Diagnosis of diabetes done when FBS will be.more than 126 mg/dl and PPBS $\geq$ 200mg/dl and casual blood sugar (at any time of the day) $\geq$ 200mg/dl. Blood sugar which are less than the diabetic range and more than the expected level is termed in case of FBS as imparied fasting glucose (> 110 - <126 mg/dl) and in case of PPBS as impaired glucose tolerance (> 140mg - < 200mg). These patient can controlled by strict diet and behavioral restriction. Cut off the normal blood sugar (FBS - 110mg/dl, PPBS 140mgfdl) range is only to control the longstanding complication because evident shows that if a patient remains in a IFG, IGT can developed retinopathy within 7 years.

Ayurveda the ancient life sciencc mentioned the full fledged description of disease prameha synonomus to diabetes mellitus. Prameha consists of two words, pra and meha. Pra means excessive in quantity and frequency and meha means passing of urine. So Prameha 'means passing of urine profusely both in quantity and frequency. Starting from the Aetiology to the Management point of view most of the ancient description are very much scientific. So that more approach are giving towards the management of diabetes with the alternative approach.

So many pramehaghna drugs have been mentioned in Ayurveda. So our approach have been given with the drugs Khadir, Bhumiamla. Jambu and Jarul. Most of them describes as Pramehaghna and medaghna. So approach have been made to reduce the blood sugar by increasing the insulin sensitivity to the tissue with the help of weight reduction along with to assess the insulinotropic action of these drugs. These drugs have been studied by different authors and shows the hypoglycemic effect.

Material and Method:

Selection of Cases:

Considering the aim of study 50 patient with diabetes were selected from OPD and IPD of S.S. Hospital, Kayachikitsa Department, IMS, BHU, Varanasi who have fulfill the inclusion criteria. Out of 50 patient 43 patient have been completed the follow up :

Inclusion Criteria:

* Patient having classical symptoms of diabetes without marked weight loss.
* Increased FBS $\geq$ 126 mg/dl, more than two occasion in different day.
* Increase PPBS $\geq$ 200mgldl.
* Patients having the B.M.I. above the healthy range are preferable.
* Patient having B.M.I. normal and subnormal level to assess response in both obese and non obese.

Exclusion Criteria:

* Patient having the FBS > 250 mg / dl and PPBS > 350 mgldl.
* Severe complicated patient.

* Patient who are insulin dependent.
* Excessive emaciated patient.

Grouping of the Patient :

All diagnosed and registered patient divided into two groups and following therapies was given -

Group A - Trial drugs only

Group B - Trial drugs + Ongoing sulphonyl urea groups of drugs whatever he was taking but blood sugar does not fall to the base line.

Preparation and Dose of Trial Drugs

Trial compound preparation consists Bhumamla Panchanga, jambu beej, jarul leafs one part each of them along with Khadir sar (heart wood extract of Khadir) half part and make them fine powder form, given 10 gm daily divided into three doses.

Powder was given in empty stomach with fresh water, 30 minutes before meal.

Parameters for assessment of the drugs response

Subjective Assessment - In each follow up all patient were assessed for the subjective improvement of the symptoms polyuria, polydipsia, polyphagia, weakness, and cramps on walking by means of scale of grading.

Objective Parameters

Under the objective parameters laboratorical and other findings have been adopted as follows:

* FBS and PPBS done in each follow up to the 3 occasion (15 days interval and completed 45 days).
* Routine urine examination in each follow up
* Lipid profile before and after treatment in some selected cases,
* Regular check up of BMI in terms of Body weight.

OBSERVATION AND RESULTS

Therapeutic responses on Symptomatic Profile

The response of therapeutic trial in group A patient statistically highly significant result were found in the symptoms of Polyuria ($t = 3.19$, $p. < 0.01$) Polydipsia ($t = 2.95$, $P < 0.01$), weakness ($t = 4.98$, $p. < 0.001$) Cramps on walking ($t = 2.44$, $P < 0.05$).

Group B patient also shows statistically highly significant result in polyuria ($t = 4.5$, $P < 0.001$), Polydipsia ($t = 3.79$, $p. < 0.01$), weakness ($t = 6.71$, $P < 0.001$), cramps on walking ($t = 5.5$, $P < 0.001$).

Both these groups not response to polyphagia ($p < 0.05$)

After taking this medicine patient feels more comfortable even those patients who were unable to do any type of physical works they were also regain their working power and feel enthusium after completion of treatment. As Polyuria decreases, so patient does not awake at night for urination and goes for sound sleep, so at day time they feel comfortable.

Effect of treatment on Fasting and Post Prandial Blood Sugar

Effect of treatment on FBS group A shows highly significant result after completion of the treatment ($t = 4.011$, $P < 0.001$), similarly group B patient also shows highly significant result ($t = 6.87$, $P < 0.001$).

In case of PPBS both groups shows highly significant result (group A - $t=3.88$, $P<0.001$, Group B - $t= 9.21$, $p< 0.001$)

Group B shows more t value in both FBS and PPBS and PPBS response more than FBS.

Effect of Treatment on Body Mass Index (B.M.I.)

Both the groups reduced body weight statistically highly significantly after completion of the treatment (Group A : t - 11, $P < 0.0$ 1), Group B : $t = 7.57$, $P <0.001$).

Effect of Treatment of B.M.I. of Different Level

Response of drugs who have above the level of 30 kg/m2 of B.M.I. shows that group A patient statistically highly significant value both in FBS and PPBS (FBS - $t = 5.55$, $p < 0.001$), PPBS ($t = 4.73$, $P < 0.01$). In Group B patient also shows highly significant result in both FBS & PPBS (FBS - $t = 3.76$, $p< 0.01$). (PPBS - $t = 14.67$. $P< 0.001$).

Group B patients blood sugar falls almost to the normal range in comparison to the group A patient.

In case of BMI > 25 kg/m^2 and < 30 kg/m^2 patient also shows highly significant result in both group (Group A = FBS - $t = 7.23$, $P < 0.001$, PPBS - $t = 2.98$, $P <0.05$), (Group B = FBS - $t.= 9.90$, $P < 0.01$, PPBS - $t = 8.64$, $P < 0.001$). But mean difference before and after treatment in both the groups shows that group B reduced more sugar than group. A and response in PPBS is more than FBS.

But when B.M.I. level was less than 25 Kg/m^2 patient shows statistically insignificant result in group A both in FBS ($t = 0.55$, $t> 0.05$), and PPBS ($t = 0.38$, $P > 0.05$). But group B shows highly significant result in FBS ($t = 4.17$, $P < 0.01$) and insignificant result in PPBS ($t = 2.64$, $p < 0.05$).

Effect of Treatment at Different Level of Blood Sugar

It have been observed in our study that our trial drugs reduced blood sugar more rapidly whenever it will be in high range and reduced steadily when it will be in lower range. Both the groups response in the same manner but group B response more than the group A.

Effect of treatment on Lipid Profile

Only 15 patient have been done lipid profile before and after completion of the treatment (group A =8, Group B = 7). Group A shows statisticilily highly signiticant result to reduced cholesterol ($t = 5.82$, $P < 0.001$) and significant result in group B ($t = 3.31$, $p.= <0.05$).

Similarly Triglycerides also falls statistically highly significantly in Group A ($t = 4.35$, $P = <0.01$) and significantly in group B ($t = 2.76$, $P = <0.05$).

Serum HDL level increased highly significantly in both group. A ($t = 4.04$. $p = <0.01$) and group B ($t = 4.03$. $P = <0.01$).

It is important to know that serum HDL level is good for health and cholesterol and Triglycerides are alarming for the health when increased from the normal range.

DISCUSSION

In the demographic profile maximum number of patient was between 51-60 years of age (44.19%), male (55.81%) are more than female. Type 2 diabetes mostly occurs in the later life due to the faulty dietary and low physical active life. Maximum number of patient was middle socioeconomical status (58.14%), urban people (60.47%), illiterate (34.89%) vegetarian (41.86%), low physically active (62.80%), smokers (46.51%).These all factors precipitate diabetes directly have been proved previously and our study also support this view. Most of the patient have shown positive family history (64.44%) strongly indicate the possibility of genetic involvement in this disease.

Symptomatic relief is directly proportional to the metabolic improvement. So in our study statistical significancy have been observed in most of the symptoms i.e. polyuria, polydipsia, weakness, cramps on walking, but polyphagia does not shows significant result. It may be because of stressful conditions of the diabetic patient because it is an longstanding disease. In objective parameters FBS and PPBS falls statistically highly signiticantly and respond of drugs was more in PPBS than FBS. Fasting blood Sugar in the serum has been maintailned by Hepatic Glycogenolysis and neoglucogenesis, is necessary and post prandial blood sugar depends on Peripheral glucose utilization by the tissue and secretion of insulin in response to diet and drugs. So more effect on PPBS directly indicate peripheral glucose utilizing and insulin secretary effect of the trial drugs, or both phenomenon may involves. Response of drugs was more when blood sugar level remains in high and falls less when remains in lower level, this view directly indicate normoglycaemic effect or no any unwanted abrupt hypoglycaemic effect. Trial drugs reduced BMI in terms of body weight and in obese patient blood sugar falls to the base line comparing to the over weight and normal weight patient, directly indicate peripheral glucose utilization by clearing the receptors blocks of the tissue and increase receptors population at the tissue level. Cholesterol, Triglyseride reduction capacity and increasing HDL level indicate that the trial drugs note only reduced fats from the body but it also clears from the body.

At last it have been observed that group B patients responese more than the group A in all respects. It may be due to combined effect to trial drugs along with insulinotropic drugs (sulphonyl urea).

CONCLUSION

From the whole discussion of the study we come to conclusion that our drugs act via the following pathway.

1. Decreases body weight in both group.
2. Decreases PPBS more than FBS
3. High level sugars response more than low level.
4. High BMI patient response more than others.
5. Clears cholesterol, TG and increase HDL level
6. Response more in group B than group A.

So at last we can say that the trial drug have the capacity to reduce the bloodsugar by means of increased insulin sensitivity to the tissue, insulin like effect and may have minor insulino tropic effect.

ACKNOWLEDGEMENTS

The author is very much thankful to the Director, Institute of Medical Sciences, Banaras Hindu University, Varanasi for providing necessary facility to carry out the research work. We are also thankful to Dean, Faculty of, Ayurveda, IMS, BHU, Medical Superintendent & Deputy Medical Superintendent, S.S. Hospital, B.H.U., Varanasi.

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Scale of Diabetic Symptoms

Symptoms	Score	Grade	Grading Criteria of Symptoms
	0	Absent	Normal Frequency 1-4 times in day, 0-2 times at night
Polyuria	1	Mild	Frequency 5-7 times in day, 3-5 times at night
	2	Moderate	Frequency 8-10 times in day, 6-8 times at night
	3	Severe	Frequency > 10 times in day, >8 times at night
	0	Absent	Normal 1.5 - 3 lt / day
Polydipsia	1	Mild	Increased but can controlled (3-4 lt/day)
	2	Moderate	Increased frequency without control (4-5 lt/day)
	3.	Severe	Very much increased (more than 5 lt/day)
Symptoms	**Score**	**Grade**	**Grading Criteria of Symptoms**
	0	Normal	Normal meal
Polyphagia	1	Mild increased	Meal 2 light breakfast 2-3 / day
	2	Moderate increased	Main meal 2 but light breakfast 3-5/day
	3	Excessive increased	Main meal 2 or 3 light breakfast 3-5 / day

Scale of Diabetic Symptoms

Symptoms	Score	Grade	Grading Criteria of Symptoms
Weakness	0	Absent	Absent of weakness
	1	Mild	With feeling of weakness
	2	Moderate	Routine activity distrurbed with feeling of weakness
	3.	Severe	Severe weakness leads to bed ridden
Cramps on Wlaking	0	Absent	No Cramps
	1	Mild	Cramps after walking 14 km
	2	Moderate	Cramps after walking 1/2 km
	3	Severe	Inability to walk even upto 1/2 km

Grading of Urinary Sugar

Urine Sugar	Grading
Nil	0
+	1
++	2
+++	3

प्रमेह में एक आयुर्वेदिक औषधि योग का चिकित्सकीय परीक्षण विशेषकर एन०आई०डी०डी०एम० के सन्दर्भ में

सारांश

मधुमेह हमारे समाज की एक व्यापक समस्या है, जो दिन प्रतिदिन बढ़ती जा रही है विभिन्न सर्वेक्षणों से पता चला है कि भारतीय लोग इससे सर्वाधिक प्रभावित हो रहे हैं, सिर्फ इस बीमारी से पीड़ितों की संख्या वृद्धि ही नहीं हो रही है, अपितु इसके द्वारा शरीर के अनेक महत्त्वपूर्ण अंगो का कार्य प्रभावित हो रहा है तथा साथ ही साथ दीर्घकालिक बीमारी भी उत्पन्न हो रही है। इसलिए डायबीटिज के इलाज के लिए पहले से ही बहुत सारी मधुमेहनाशक रसायनिक औषधियाँ वर्णित की गयी है।

रसायनिक औषधियों के दुष्प्रभाव एवं मधुमेह की चिरकालिता को देखते हुए वैकल्पित औषधि की ओर अधिक ध्यान दिया गया है।

आयुर्वेद में प्रमेहनाशक अनेकों औषधियों का वर्णन है, जिनमें से कुछ औषधियाँ मेदोनाशक गुणकर्म भी रखती है।

अतः इन औषधि द्रव्यों के बढ़ी रक्त शर्करा स्तर को कम करने के प्रभाव के मूल्यांकन का प्रयास किया गया है। परीक्षण औषधि के रूप में जम्बू, जारूल, खदिर एवं भूमि आँवला के चूर्ण का प्रयोग 50 रोगियों पर किया गया है। जिसमें से विशेषकर स्थूल प्रमेही **(Obese diabetics)** का रक्त शर्करा स्तर **45** दिनों में सामान्त स्तर पर आ गया।