J.R.A.S. Vol. XVI. No. 1-2 , (1995) pp.1-14

AN EFFECTIVE AYURVEDIC HYPOGLYCEMIC FORMULATION

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Received on 16.12.91

*In 80 **Non- Insuline** Dependent Diabetes Mellitus (NIDDM) cases, an Ayurvedic formulation code named Ayush-82 and Shudha Shilajitu were oraely administered for a period of 24 weeks. Fasting and post prandial blood sugar were estimated at 6th weekly intervals. There was statistically significant reduction in both fasting and post prandial blood suger in both males and females. On physician's rating, there was "good response" in 74% of the cases.*

Introduction

In Ayurveda 20 types of *Prameha* have been described. There is one school of thought (Tripathi S.N.-1972) that *Prameha* possesses abundant similarly with diabetes mellitus and may be treated as its synonym and all the 20 sub-types finally leading to *Madhumeha*. There is another school of thought which recognises 20 types of *Prameha* as 20 different urinary disorders; for example *Udhakameha* as diabetes insipidus, *Sandra- meha* as chyluria, *Sukla-meha* as spermethorhoea, *Rakta/Manjistha- meha* as Haematurea, *Madhumeha* as diabetes mellitus, *Iksumeha* as glycosuria etc.

The word *Prameha* is derived from the root (*Dhatup*) *'Mih'* meaning to void or pass urine (Monier Williams (1979) with reference to the disease in human body it is to mean "passing urine". Qualified by the prefix 'Pra' it means

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passing of urine in excess quantity. In Ayurvedic classics the disease is characterised by excessive urination (*Prabhutamutrata*) and turbidity (*Avila mutrata*).

On the basis of etiology Susruta has classified *Prameha* into two types (i) *Heriditary* (*Kulaja- Sahaja*) (ii) Acquired (*Apaathyaja*). For the sake of effective treatment, Caraka has classified patients of diabetes mellitus into two groups namely i) Obese (*Atisthaulya*) and (ii) Asthenic (*Krisa*)

Obese patients are improved by dieting and by use of elimination therapy while special care need to be taken in maintaining the nutrition of asthenic patients. The prognosis of treatment is good in obese patients and bad in asthenic patients.

All the 20 types of *Pramehas* on the basis of pathogensis belong to three broad group *Vatika, Paittika* and *Kaphaja*. If one goes through carefully the elaborate description of the *Tridosya* types, the Vatika type resembles very well to the true insulin deficiency associated with β cells of islets of langerhans degeneration, whereas the *Kaphaja* and *Paittika* types resemble the malfunctioning of pitutary and adrenals. (Tripathy S.N. -1972)

Diabetes mellitus (DM) has been mentioned since time immemorial and claims have been made by Indians, Egyptians, Greek and Chinese. It was described in Ist Century A.D. by Aretaeus who described the diseases as "melting down flesh limbs in Urine" and named the disease "Diabetes", the Greek word for "Syphon" because of the polyurea and polydypsia that characterise the disease. Thomas Wills in 1679 wrote that those suffering from this disease pass more urine than they drink water and the urine is wonderfully sweet as if imbibed with sugar and honey.(J. Steinke-1971) In 1815, the famous French Chemist Chevreul discovered that the sugar is Glucose. In 1810 Claude Bernard described the conversion of liver glycogen to blood glucose. In 1889, Minkowski and Mering showed that complete pancreatectomy in dogs produced a condition corresponding to servere DM. In 1921, Banting and Best isolated insulin from pancreatic extract, which is a landmark. Another development is the invention of oral anti-diabetics by Franke and Fuch in 1955.

A large number of classifications of DM patients have also been suggested from time to time. The recent classification of Juvenile and Maturity onset DM has been replaced by the present W.H.O. classification (1980)

1) Insulin dependent DM (IDDM) and

2) Non- Insulin dependent DM (NIDDM)

The initial euphoria of the advent of insulin was slowly fading as more and more metabolic studies revealed that in many NIDDM cases the blood insulin level is normal to high (Daniel. W. Foster-1987) and it was antagonised by other hormones or quickly destroyed by

insulinase; hence the present classification of insulin dependent and non-insulin dependent types emerged. Of the total diabetic clinic population from South India only 0.8 to 28 (Mohan R.-1988) are reported to be insulin dependent. The rest are controlled by diet and exercise alone or along with some oral hypoglycemic agents. The oral hypoglycemics that have been introduced into clinical use for the past 35 years falls under two broad groups the sulphonylureas and biguanides. In view of the serious side effects of these drugs (which are discussed later in the article) attention is being increasingly shown on herbal oral anti-hypoglycemic drugs.

A number of reviews on herbs which have been proved to possess anti-hypoglycemic properties are available. (Satyawathy G.V. -1984, Patnaik G.K. -1986)

Line of treatment

According to Caraka there are two types of patients of *Prameha*, one is obese and strong while the other is thin and weak. Promotive treatment should be given to the thin patients and evacualtion in case of patients having abundance of *Dosa* and *Bala* (Strength).

CHIKITSĀ SUTRĀ

Sthūla Prameha	*Kriśa Prameha*
Samśodhana	Brmhana
Snehana	Santarpaṇa
Vamana	Saṁśamana
Virecana	Maṁtra
Santarpana	kaṣāya
	Yavacūrṇa
	Leha
	Laghu Āhāro

Methods and Materials

350 provisionally diagnosed diabetes mellitus cases attending the OPD of Central Research Institute for Ayurveda, Punjabi Bagh, New Delhi were considered for inclusion in the trial. The following criteria were rigidly adopted to include a case into the trial.

1. Age- 40 years and above.
2. Sex- Both sexes
3. Hyperglycemic status- Patients having fasting blood sugar of 120 mg/dl and above and Post prandial (2 hour Blood sugar of 180 mg/dl. and above.
4. Glycosuric status- Patients having fasting urine sugar one and above and post prandial urine sugar two and above.
5. Patients complaining of polyurea, polydypsia and tiredness.
6. Known diabetic cases of less than three years duration. The cases having the following signs and symptoms were exluded from the trial.

1. Age Below 40 years and above 70 years.
2. Failing vision.
3. On clinical examination with presenting symptoms of neuropathy retronopathy and nephropathy.
4. Infection of the skin, lungs or urinary track.
5. Insulin dependent Ketonurics.
6. Irregularity in the consumption of the trial drugs as evaluated by "sachet drug quantum"
7. Aggravation of clinical symptoms with the concomitant raise in blood sugar level beyond 350 mg./dl for post prandial blood sugar.
8. Known diabetic cases of more than three years duration.

On adopting the rigid criteria of inculsion and exclusion, 80 cases of both sexes were included into the trial. A detiled clinical history and medical examination of each patient was carefully recorded.

The routine clinical examinations, pathological and biochemical investigations were carried out. The clinical examination of pathological and biochemical investigations were repeated at intervals of six weeks for four times (inclusive of initial one) during the course of study. G.T.T. with 75 gm. glucose load was done only once for diagnosis and parametric investigations for assessment viz., fasting and post prandial blood sugar were repeated at stipulated intervals.

Estimation of Parameteric Investigations

After overnight fasting the blood sample was collected from antecubital vein in flouride and oxalate mixture. Second sample was collected 90 minutes after a standardised 1200 cal. cabohydrate rich hospital diet, uniformly for all the trial cases. The blood glucose was estimated by Folin- Wu- Method.

Clinical Assessment

1. Statistical Criteria

The mean difference and the standard error of fasting and post prandial blood sugar before and after treatment was calculated and statistically analysed using student-t-test and level of significance.

2. Physicians Rating

a) The control of diabetes was considered good if fasting and 90 minutes post prandial glucose values were less than or equal to 120 mg./dl. and 160 mg./dl. respectively.

b) The control was considered fair if one of the values was elevated.

c) Poor if both values were elevated despite slight reduction.

Drug

The drug coded as Ayush-82 consists of shade dried, pounded and sieved (100

mesh). Powders of the following four plants

1. Amra Bija (seed of *Mangifera indica* Linn): 1 part
2. Jambu Bija (seed of *Syzygium cumini* (L.) skeels): 1 part
3. Karvellaka Bija (seed of *Momordica charantia* Linn): 1 part
4. Gudmar (leaves of *Gymnema pylvestre* R.Br.): 1/2 part.
5. With *Shudh Silajita* (Mineral) Pitch/ Rock exudate of fossiled Herbo-mineral materials purified in decoction of three myrobalans viz. *Terminalia bellirica*, *Terminalia chebula* and *Emblica officinalis*.

Effectiveness of the drugs

Sl. No.	Name of the Drug	Guna Karma	Pharmacology
1.	Jambu (*Syzygium cumini* (Linn.) skeels.)	Pitta, Kapha Hara, Vata- Kara, Stambhana Mutrasangrahaniya Deepana Roopana	*Significant (308) hypoglycemic effect in fasting rabbits.
2.	Karvellaka (*Momordica charantia* Linn.)	Rasa Tikta, Leghu Pitta-Kaphaghana Krimighna & Madhumeha Man upyogi.	*Charantin was more potent than tolbutamide in hypoglycemic activity.
3.	Amra Bija (Mango Kernel) (*Mangifera* indica Linn)	laghu, Rukha Rasa Kasaya	Hypoglycemic activity
4.	Gudmar leaves (Gymnema sylvestre R.Br.)		++ leaves regulate blood sugar in alloxan diabetic rabbits.
5.	Shudha Silajita		Hypoglycemic activity

* " Pharmacological studies on certain Medicinal Plants and compound formulations used in Ayurveda & Siddha" (Under Publication-CCRAS) ++ E.R.B. Shammugasundaram et. al. Jour. Ethnopharmacol. 7, 205 (1983)

Dose

Ayush -82: 5 gm. three times a day.

Shudh Shilajit: 500 mg. two times a day.

All the 5 drugs have been mentioned in classical Ayurvedic literature as potent anti-diabetic drugs (P.V. Sharma-1981). There has been a number of clinical and experimental studies on the efficacy of each individual and or combination of these 5 drugs as potent oral Hypoglycemic anti-diabetic drugs (Mukherjee. B-1957). These studies has prompted the Council to formulate Ayush-82+ Shilajita.

Diet

All the patients were given a diet chart for 1200 calories and were advised to rigidly follow the same.

Withdrawal of Modern Drug

Most of the patients except 4 or 5 were found to be taking modern oral Hypoglycaemics. Over a period of 15 days from the initiation of the Ayurvedic drugs, the modern drugs were gradually withdrawn and the day when it was totally withdrawn was taken as "zero" day for the trial.

Interrelated Complications

Diabetes mellitus, obesity and Hypertension are interrelated complications, the presence of one or more makes the prognosis of vascular accidents, cardiocereloral 'bad'. The cases were further devided into

(a) obese: based on Broca's index. (B.1)

Height in cm-100 ideal weight in kg.

$$\text{B.I.} = \frac{\text{Actual wt. (in kg.) X 100}}{\text{Ideal wt. (in kg.)}}$$

If B.I.> 1208 the case is considered as obese.

b) Hypertensive

At four intervals of examination for 3 consecutive days at each examination, at all positions, if the diastolic pressure exceed 90 mm. Hg. and systolic 160 mm/ Hg. the case is termed as hypertensive.

Result

1. The socio-economic status of the patients under study is given in table No.1.
2. Fasting and post-prandial blood sugar values in all the cases and under the sub-heading obese, hypertensive etc. are given in Table Nos. II to VI)
3. Physicians rating is given in table No. VII
4. Reduction in fasting and Post-prandial blood sugar values, both in males and females, at six week intervals are graphically illustrated in Figs. No.1 and 2.
5. **Statistical Assessment**

The fasting and post prandial blood

sugar values of all cases were statistically analysed inclusive of student 't' test and levels of significance. It can be seen. from the table II and III that the reduction in blood sugar in both fasting and post prandial between the initial and final levels (before and after treatment respectively) in both sexes is statistically highly significant. (PO<001).

6. Physician's Rating

It can be seen from table VII that 74% are responding from fair to good for the treatment, as per Physician's rating.

7. Interrelated Complications

It can be seen from table IV and V in obese/non-obese, hypertensives/normal i.e. in all sub-classifications, there is substantial reduction in both fasting and post-prandial blood sugar after treatment. However, these results were not statistically analysed.

Discussion

Only two groups of oral hypoglycemic agents (OHA) viz., sulphonyl ureas, biguanides have been widely put to clinical use for the past 75 years or so (since 1926), inspite of the fact that hundreds of compounds synthesised in the laboratories have been tested in experimental animals for their hypoglycemic action and were found to be toxic and could not be cleared for clinical use. Even between the two groups put to clinical use, many drugs have been withdrawn over the past 3 decades. The first biguanide synthalyn had to be withdrawn because of its severe hepatotoxic effect. Alarming reports of frequently fatal lactic acidosis in diabetics on phenforimin (biguanide) therapy were reported (Tripathy B.B. -1984) from several western countries, Austrilia and Newzeland. A ban on its use had been imposed in "USA and FRG". The much more dreaded complication of lactic acidosis with the biguanides, is associated with a mortality of 50% even in the best of hands and in hospitals with the most sophisticated equipments. Biguanides are strictly prohibited in cases suffering from measureable hepatic, renal or circulatory decompensation.

The case of sulphonyl ureas is also not very encouraging. Life threataening reactions like the Stwens Johnson Syndrome (Sadikot. B.M. -1989) has been reported in the occasional patients using sulphonyl ureas. Carbutamide introduced in 1955 had to be withdrawn because of severe side effect and toxic effects. Tolbutamide, chloropropamide have been shown in the UGDP (Klimt. et. al.- 1970) studies that there is increased rate of cardiac deaths due to the use of these drugs. Patients who get hypoglycemic reaction with the use of chloropropamide have a tendency to go into repeated attack of hypoglycemia over the next 4-5 days after the initial episode; such patients often need to be put on continuous drips of glucose for 4-5 days before all tracks of Chloropropamide can be washed out from the body, such severe hypoglycemic reactions should be considered as a life threatening emergency. Alcoholic

Table -I

Socio-economic status (Classification on age, sex and income basis)

Sl.No.	Age group (in years)	Sex	Low income	Middle income	High income	Total	
1.	40-49	Male	2	9	5	16	= 30
		Female	2	12	NIL	14	
2.	50-59	Male	1	13	3	17	= 38
		Female	1	18	2	21	
3.	60 & above	Male	Nil	8	1	9	= 12
		Female	1	1	1	3	
	Total		7	61	12	80 = 80	

Note: Middle income group constitutes 76%

Table No. II

Showing blood sugar values before and after treatment

Blood Sugar	Sex	Before treatment	After treatment	
	Mean + S.D.	First	Second	Third
		Means + S.D.	Means + S.D.	Means + S.D.
Fasting	Male (42) 195 ± 48	110 ± 1	139 + 40	131 + 64
	Female (38) 191 ± 48	155 ± 67	142 + 48	141 + 64
Post Prandial	Male (42) 288 ± 74	213 + 70	205 + 83	204 + 89
	Female (38) 279 ± 105	229 + 106	219 + 103	201 + 83

Table No. -III

Showing result of treatment

Blood sugar	Sex	Mean difference + S.E.	Student-t	Level of significance
Fasting	Male (42)	60 +6	9.75** P	< 0.001
	Female (38)	67 +10	6.58** P	< 0.001
Post prandial	Male (42)	93 + 10	9.04** P	< 0.001
	Female (38)	99 +14	6.93** P	< 0.001

** Statistically highly significant
( ) Figures within parentheses are number of cases.

Table No. -IV

Table showing number of patients according to obesity and hypertension

	Hypertensive	Non-Hypertensive	Total
Obese	3	9	12
Non-obese	26	42	68
Total	29	51	80

Note:- Non-obese/non- hypertensive constitute the bulk.

Table No.-V

Table showing mean blood sugar values (mg./dl.) of obese and non- obese patients.

	Fasting mg/dl.		Post prandial mg./dl.	
	B.T.	A.T.	B.T.	A.T.
Obese (12)	172	109	274	149
Non -obese (68)	191	138	284	200

B.T.- Before Treatment
A.T.- After Treatment
Number of cases are given within parentheses.

Table No.- VI

Table showing: mean blood sugar values (mg./dl.) of hypertensive and non-hypertensive patients:

	Fasting mg./dl.		Post prandial mg./dl.	
	B.T.	A.T.	B.T.	A.T.
Hypertensive (29)	184	124	270	207
Non -Hypertensive(51)	198	129	281	189

B.T. : Before treatment
A.T.: After treatment
Number of cases are given within parentheses.

Table No. -VII

Physician's rating

Good	Fair	Poor
61.04%	12.99%	25.97%

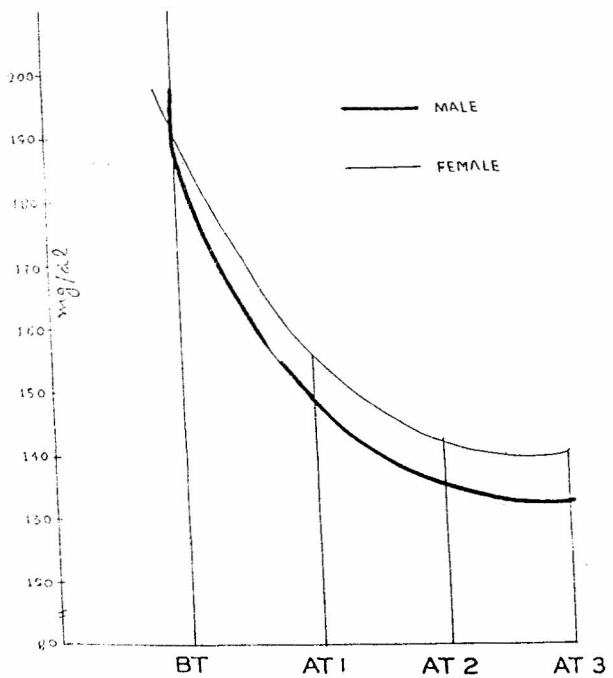

Fig 1. Hypoglycemic effect of Ayush- 82 (Blood sugar fasting)

diabetics develope a complication known as chloropropamide -Alcohol flusing (CPAF) syndrome resulting in breathlessness, severe chest pain, headache, vomiting and the B.P. goes alarmingly low. Association of chloropropamide with jaundice is well known. chloropropamide, tolbutamide, glibenclamide glipizide (all sulfonlyl ureas)are associated with "inapprorpiate" secretion of antidiuretic hormone resulting in low serum sodium levels which if not identified in time and corrected may lead to complications in high blood pressure/ diabetic patients on diuretics only a couple of sulphanyl ureas invented after 1969 are in use.

There is an international search for alternative oral hypoglycemics which are effective but having least toxicity especially for NIDDM cases. As is the case all over the world, in our country also the insulin dependent diabetics constitute only 2% of the total diabetic population leaving approx. 98% NIDDM cases. One of the sources being looked for is natural products such as herbal and relatively

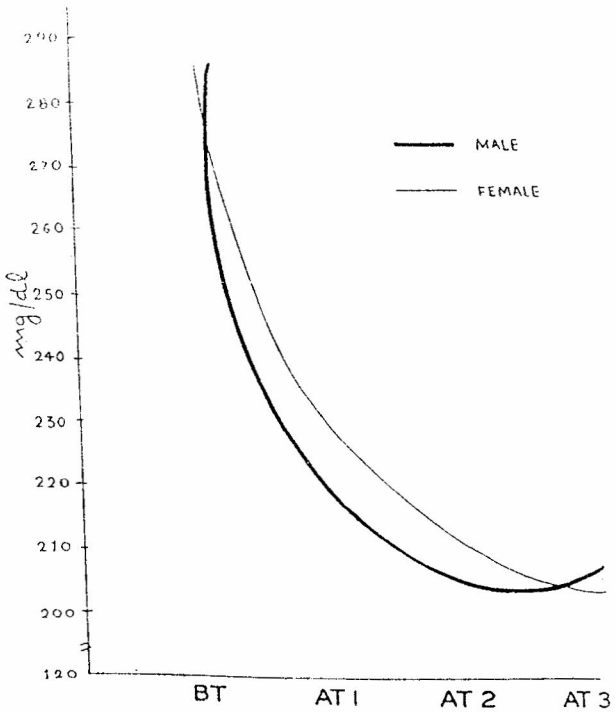

Fig 2. Hypoglycemic effect of Ayush- 82 (Blood sugar P.P.)

safer mineral sources. A number of plants and their extracts have been experimentally tried on a number of animals rendered diabetic such as rats, rabbits, guineapigs, mongrel dogs and rhesus monkey etc. A review on hypoglycemic properties of 150 herbs and their isolates has been recently reported (Handa.S.S. et. al.-1989). In most of the cases the hyperglycemia was induced using adrenaline: but both the models though very useful to study the mechanism of these hypoglycemics, do not exactly resemble the clinical diabetes. In this controlled clinical study, the authors have shown in a fairly large sample size, the test formulation viz., "Ayush-82+ Shilajita" brings down a statistically highly significant reduction in fasting and post-prandial blood sugar in both sexes of non-insulin dependent diabetes mellitus cases.

Conclusion

In a controlled clinical trial on 80 cases of non-insulin dependent deabetes mellitus (NIDDM) an Ayurvedic formulation code named as "Ayush-82 + Shilajita" brings down statistically highly significant reduction in both fasting and post-prandial blood sugar in both sexes. On physician's rating also 74% fair to good response to treatment has been found.

Acknowledgement

The authors are thankful to Vd. M.P.S. Arya, Assistant Director Incharge, Central Research Institute for Ayurveda, New Delhi and Dr. K.D. Sharma, Research Officer (Ay.), C.C.R.A.S., New Delhi for their keen interest in the work.

The authors are also thankful to the Central Council for Research in Ayurveda and Siddha for financial assistance. They wish to thank Sh. Suresh Shanbhogue for Statistical analysis of the results and the Bio-chemistry and Pathology laboratory staff of Central Research Institute for Ayurveda, New Delhi for Lab. investigation.

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हिन्दी सारांश

वी० एन० पाण्डेय, एस० एस० राजागोपालन एवं डी० पी० चौधरी

कतिपय इन्सुलीन पर अनाश्रित मधुमेह के 80 आतुरो पर आयुष- 82 नामक आयुर्वेदीय योग के साथ-साथ शुद्ध शिलाजीत के सेवन द्वारा (दोंनो ही लिंगो के) प्राक भोजन तथा भोजन के पश्चात् के रक्त शर्करा परिणाम में महत्वपूर्ण अधोगामी परिवर्तन पाया गया, जिसे कि सांख्यिकीय कसौटी द्वारा भी प्रतिपादित किया जा चुका है। चिकित्सकीय परिणामों की प्रातिशतिक अंशाश निर्धारण के आधार पर लाभ व पूर्ण लाभ 74 प्रतिशत पाया गया।