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Original Research Paper

Ayurveda

CLINICAL STUDY TO EVALUATE THE EFFICACY OF POLY-HERBAL COMPOUND *(NEEM, GUDUCHI AND DEVDARU)* IN THE MANAGEMENT OF LONG STANDING CASES (> 5 YEARS) OF TYPE2 DIABETES MELLITUS

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ABSTRACT Response to the treatment of Type2 Diabetes Mellitus is seen to be better in newly diagnosed cases than long standing cases. Especially in the patients who are suffering from more than 5 to 10 years, it is seen that, response to any hypoglycemic treatment is less. Keeping this view in mind, 48 numbers of patients have been selected randomly of the age group 35-70 years and suffering from Type2 Diabetes mellitus for more than 5 years and under modern hypoglycemic treatment but have HbA1c more than 7%; which means their hypoglycemic drugs have failed to reduce the HbA1c level below the target value of treatment. In this study, the patients have been given the poly-herbal compound of Neem (Azadirachta indica), Guduchi (Tinospora cordifolia) and Devdaru (Cedrus deodara), (at 1:1:1 w/w ration) in the form of tablets (500mg each) at a dose of 3g/day before meal for 90 days. FBS, PPBS and HbA1C were tested and recorded before treatment and FBS and PPBS were reviewed at 15 days interval and HbA1C has been reviewed at the end of 90 days. It was found that the drug showed statistically signifiβcant results from 30 days onwards in case of FBS and 45 days onwards in case of PPBS. At 90 days there was statistically significant reduction in HbA1c as well.

KEYWORDS : Devdaru, Guduchi, Neem, Type2 Diabetes mellitus

INTRODUCTION

Now a days Ayurveda is gaining popularity in the field of Non-communicable diseases, as long term treatment for any incurable disease with modern medications sometimes leads to serious adverse effects and various deficiencies. In Ayurveda, There is a condition called Madhumeha which can be co-related with Type2 Diabetes Mellitus by the similarity in the clinical features and complications. Madhumeha has been explained as the last condition of the 20 types of Prameha and it is mentioned that it arises as a sequel of all the other Pramehas [1]. From Ayurvedic Point of view, it has been also enlisted in 8 incurable diseases and it is the most complicated condition among the metabolic diseases [2].It is an established fact that with time the number of functioning β cells reduces to substantial extend the patients of Type2 Diabetes Mellitus in. This develops complete absence of first phase insulin secretion and the second phase insulin release is substantially reduced. For these reasons, most of the long standing patients are needed to be converted to insulin therapy which is not convenient for few patients. Hence, in this study an attempt has been made to find an alternative means to control hyperglycemia by using Herbal compounds mentioned in Ayurvedic Classics along with conventional Anti-Hyperglycemic treatment.

MATERIAL AND METHOD

AIM AND OBJECTIVE

The Aim of the present study is to evaluate the Efficacy of poly-herbal Compound (Neem, Guduchi and Devdaru) in the management of Long standing cases (> 5years) of type-2 Diabetes Mellitus.

Selection Of Patients:

48 numbers of already diagnosed cases between age group 35- 70 were selected from the OPD and IPD of Dept. of Kayachikitsa, Govt. Ayurvedic College and Hospital, Guwahati; according to the inclusion and exclusion criteria of the study. All the patients were suffering from Type 2 Diabetes Mellitus for more than 5 years and were on oral Anti-Hyperglycemic drugs (Allopathic) but HbA1c was more than 7% i.e. the drugs they were taking were failing to reduce the average Blood sugar below the target of treatment.

Inclusion Criteria

1. Male and female subjects between the ages of 35 and 70 years.
2. Subjects must have Body Mass Index (BMI) < 36 kg/m^2.
3. Newly diagnosed case of Madhumeha (Type-2 DM).
4. Subjects with Stable glycemic control (7%≤ HbA1c≤ 9%).
5. Patients on oral Anti- hyperglycemic (Allopathic) drugs.

Exclusion Criteria

i) Subjects having history or presence of clinically significant cardiovascular, respiratory, hepatic, renal, gastrointestinal, neurological or infectious disorders which are capable to constitute a risk factor for the medication under study.
ii) Patients already diagnosed with Type-1 Diabetes Mellitus.
iii) Secondary diabetic (Cushing's syndrome, Acromegaly) glucocorticoid induced DM etc.
v) Evidence of significant active hematological disease and/or cumulative blood donation of 1 unit (500 mL) or more in the last 3 months.
vi) Positive hepatitis B (hepatitis B surface antigen) and/or hepatitis C (hepatitis C Antibody) serology or positive HIV serology.
vii) Malignancy, tuberculosis, Sepsis etc.
x) Pregnant woman.

Preparation Of Trial Drug:

Raw material of Neem (*Azadirachta indica), Guduchi (Tinospora cordifolia) & Devdaru (Cedrus deodara)* were bought from Bhramhanath Pharma pvt. Ltd. Ahmednagar, Maharastha and each ingredient was tested for its authenticity at the Drug Testing Laboratory, Govt. Ayurvedic College and Hospital.

The water extracts were mixed properly at a ratio of 1:1:1 and to that Gum Acacia was added at 10% (w/w) as a binding agent for tablet preparation.

Then 500 mg Tablets were obtained and packaging was done following the rules and regulations of Good Manufacturing Practice (GMP) at Girijananda Chowdhury Institute of Pharmaceutical Science (GIPS), Azara ,Guwahati-14, Assam, India.

COMPOSITION OF THE PREPARED TABLETS

Each tablet is of 500 mg (variation ± 5mg)

Neem	*Azadirachta indica A. Juss*	30% w/w
Guduchi	*Tinospora cordifolia(Willd)*	30 %w/w
Devdaru	*Cedrus deodara (Roxb.) Loud*	30% w/w
Gum Acacia	Binding Agent	10% w/w

Dose

1g (2 tablets) thrice daily before meal i.e. 3 g per day.

***Clinical Study*:**

Each patient was given the trial drug at a dose of 2 tablets thrice daily (3g/day) before meal for 90 days along with their Allopathic Anti-Hyperglycemic drug which they were taking for a long duration. FBS and PPBS were reviewed at 15 day interval and HbA1c was reviewed at the end of 90 days. Review of physical signs and symptoms and general condition of the patient was also done at an interval of 15 days.

Statistical Analysis:

The obtained information was analyzed statistically using Microsoft Excel @ 2010 edition ® Microsoft. Co. Pvt. Ltd. And in terms of mean score (x), Standard Deviation (S.D.), Population Variance (P. Var). 'Z' test was carried out at the level of 0.02, 0.05, 0.01, 0.001 of P levels. The results were interpreted as -

P<0.05, <0.02, <0.01 Significant.

P<0.001 highly significant.

P>0.05 Insignificant improvement.

OBSERVATIONS AND RESULTS

Assessment Of FBS (Fasting Blood Sugar)

Table 1: Changes In FBS Along With Statistical Analysis.

Parameter	BT	FU1	FU2	FU3	FU4	FU5	FU6
Mean	174.31	168.54	165.31	161.44	157.49	152.31	143.62
SD	16.03	15.88	14.42	14.17	14.25	14.70	14.80
P.Var	251.79	246.99	203.75	196.66	198.95	211.83	214.6
Z value		1.79	2.92	4.21	5.49	7.07	9.83
P value		> 0.05	<0.01	<0.001	<0.001	<0.001	<0.001

The mean FBS was reduced from 174.31 mg/dl to 143.62g/dl in 90 days. The reduction of FBS was significant from second follow-up onwards and highly significant from 3rd follow-up onwards.

Assessment Of PPBS (Post-Prandial Blood Sugar)

Table 2: Changes In PPBS Along With Statistical Analysis

Parameter	BT 2h PG	FU1	FU2	FU3	FU4	FU5	FU6
Mean	283.35	278.22	272.68	265.41	260	245.87	230.29
SD	40.16	39.06	36.88	33.66	33.53	30.86	30.45
P.Var	1597.4	1493.9	1332.25	1109.4	1101.2	932.65	907.95
Z value		0.64	1.36	2.39	3.12	5.18	7.37
P value		>0.05	>0.05	<0.02	<0.01	<0.001	<0.001

The mean PPBS were reduced from 283.25 mg/dl to 230.29 mg/dl. The reduction of PPBS was significant from 3rd follow-up onwards and highly significant from 5rd follow-up onwards.

Assessment Of HbA1c

Table 3: Changes In HbA1c Along With Statistical Analysis

Parameter	BT	AT
Mean	8.02	7.30
SD	0.19	0.17
P.Var	0.1878	0.1695
Z value		8.33
P value		<0.001

The mean HbA1c reduced from 8.02% to 7.30% in 90 days. This reduction was statistically highly significant but the final value is more than 7% which is more than the target value of hypo-glycemic treatment.

DISCUSSION AND CONCLUSION

Diabetes is one of the most complicated multi-system diseases which require continuous medical care with multifactorial risk-reduction strategies. With time the capacity of insulin production by pancreas of the patients reduces gradually and eventually the first phase insulin secretion abolishes with marked reduction in second phase insulin secretion. With increase in insulin resistance and uncontrolled gluconeogenesis at liver, overt hyperglycemia takes place which conventional oral anti-hyperglycemic drugs finds hard to control over time. In this study, we have tried to finds out a complimentary herbal preparation which may be used concomitantly along with the conventional treatment so that better glycemic control can be achieved at the expense of less adverse effects. For this we have selected Neem (*Azadirachta indica), Guduchi(Tinospora cordifolia) & Devdaru (Cedrus deodara)* not only because of their mention in Ayurvedic Literature but also because there is strong evidence from the modern experimental research as well. The findings are very promising and some researchers have also tried to explain the mode of action of the plants as well. Some references are as follows.

1. Azadirachta indica (Neem) constitutes 30% (W/W) of each tablet which acts in hyper glycaemia via either through significant blockage of the inhibitory effect of serotonin on insulin secretion mediated by glucose or peripheral utilization of glucose and glycogenolic effect due to epinephrine action blockage.[3]

2. Tinospora cordifolia (Guduchi) also constitutes 30%(W/W) of each tablet and it effects hyperglycemia through mitigating oxidative stress, promoting insulin secretion and also by inhibiting gluconeogenesis and glycogenolysis.[4]

3. Lastly *Cedrus deodara (Devdaru)* (30%W/W) might be affecting hyperglycemia via enhancing islet regeneration in the pancreas and restoration of normal cellular size of the islet with hyperplasia. And it acts in a dose cum duration dependent manner. [5].

The findings of this clinical study have been discussed in the following headings.

a) In case of FBS, the Mean FBS was reduced from 174.31 mg/dl to 143.62 mg/dl in 90 days and the reduction rate was uniform i.e. there was a gradual decline in the FBS from the second follow-up i.e. 30 days and on each review since 2nd follow up the reduction was statistically significant.(Table 1).

b) In case of PPBS, The mean PPBS were reduced from 283.35 mg/dl to 230.29 mg/dl. In 90 days. But it was observed that there was no statistically significant reduction in the first 15 days and 30 days but from 45 days onward there was a uniform reduction rate in the PPBS value. Hence, it can be concluded that the onset of action of the trial drug on PPBS was a little slower than that of FBS but the final results were statistically highly. (Table 2).

c) In case of HbA1c, the mean was reduced from 8.02% to 7.30% in 90 days and the reduction is statistically highly significant. But the final results after 90 days were not below 7% which is the target value of any anti-hyperglycemic treatment. May be in due course of treatment, the HbA1c will attain such a value.(Table 3)

Hence, from the findings of this clinical study, it can be concluded that the *Poly-Herbal compound of Neem (Azadirachta indica), Guduchi (Tinospora cordifolia) & Devdaru (Cedrus deodara) is effective in controlling the blood sugar in type2 Diabetes Mellitus*. Though the onset of action was found to be a little slower than conventional medications but in the long run, considering the factor of adverse effect and toxicity the proposed compound is much safer for use for a long duration for patients and has additional benefits as well.

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