Evaluation of efficacy of a herbomineral formulation in combination with oral hypoglycaemic agents (OHA's) in the management of type 2 diabetes Indian patients

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INTRODUCTION

Diabetes is now pandemic with a worldwide incidence of 5% in the general population. It has been estimated that probably 100 million of the world's population, by the end of year 2000 would reach the diabetic mark. This is only the tip of the iceberg; the situation seems to be more grievous.

Studies in the Indian subcontinent have shown that if all the glycaemic population is clubbed, about 20% of the Indian population have abnormalities of glucose metabolism.

Type 2 diabetes mellitus (Non Insulin Dependent Diabetes Mellitus or NIDDM) is the commonest form of diabetes and constitutes nearly 90% of the diabetic population in any country. In India, the prevalence of type 2 diabetes was considered to be low till 1970. However, the prevalence in several parts of India has shown an increasing trend in the past 15 years.

Efforts are being made to control diabetes, which owing to its various complications, results in morbidity and mortality. Various pharmacological approaches can be used to improve glucose homeostasis via different modes of action, besides diet and lifestyle modification.

New drugs are needed because diet, weight reduction, exercise, and life-style modification, (assuming these are religiously followed) are not enough to achieve the desired glycaemic control in more than about 10% of type 2 diabetes patients. Besides, the available drugs have shortcomings. For e.g. secondary failure is a problem with all sulphonylureas. In the United Kingdom Prospective Diabetes Study (UKPDS), the secondary failure rate on sulphonylureas was 28% at the end of 3 years, and 53% at the end of 5 years.

Furthermore, achieving a tight control of blood glucose with sulphonylureas is beset with the problems of weight gain and reactive hypoglycemia in the early phase and secondary failure in the late phase.

One can combine biguanides with sulphonylureas, but in tolerable doses they may not be able to achieve tight glycaemic control. One has also to consider the possibility of lactic acidosis, especially in elderly patients with impaired renal function.

A number of herbs have been long known to possess antidiabetic properties in both experimental animals and humans. Significant among these are *Gymnema sylvestre, Pterocarpus marsupium, Engenia jambolana and Swertia chiraita,* which are the main ingredients of the antidiabetic herbal formulation and has shown to have blood glucose lowering activity in type 2 diabetes mellitus[1].

With even the World Health Organization (WHO) acknowledging the contribution of ethno-medicine in tackling several diseases, physicians too are having a second look at alternative therapies all over the world.

In this emerging scenario, the following study was undertaken to evaluate the efficacy and safety of this herbomineral formulation as an effective third Oral Hypoglycaemic Agent (OHA) that can be added to sulphonylurea and metformin to postpone insulin therapy.

MATERIALS AND METHODS

Thirty-five type 2 diabetes patients of either sex, who were not grossly obese (body weight not more than 20% of average), were included in this open trial. These patients were on the maximum tolerated dose of OHAs and were on the verge of being shifted to insulin therapy. Freshly detected diabetics, Insulin dependent diabetes mellitus patients, gestational diabetics, and patients with severe cardiovascular disorders were excluded from this trial.

After explaining the treatment schedule, a written informed consent was obtained from the patients who were enrolled in the trial. A detailed history, a thorough clinical examination along with anthropometric measurements, and a battery of investigations, prior to commencing the treatment was done. Patients were instructed to follow a standard meal pattern, avoiding simple sugars. All patients were put on a herbomineral formulation (HYPONIDD) in the dose of two tablets twice daily half an hour before meals. Each patient was asked to followup every two weeks where they would be re-examined for improvement/deterioration of condition and adverse effect of treatment, if any. Laboratory investigations were repeated as and when necessary.

RESULTS

Thirty-five patients were recruited for the study comprising twenty-one men and fourteen women in the age group of 32 to 78 years. The mean age was 55 ± 9.62 and the mean weight was 63.36 ± 0.27 kgs. (Table 1).

The mean fasting blood sugar was 197.22 ± 37.25 mg% at baseline. There was a reduction of 10.53% of the mean blood sugar at the end of 60 days of treatment. By the end of three months of treatment, there was a reduction of 26.2%, i.e. to a level of 145.63 ± 29.81mg%. (Table 2 and Figure 1).

A statistically significant decrease in the post-prandial blood sugar level was observed from the 45th

Table 1 Demographical characteristics

Parameters	
Mean age in years	55.6 ± 9.62
Mean Weight in Kgs	63.36 ± 0.27
Mean Height in cm	160.79 ± 7.14
M:F Proportion	61.0 : 39.0

Table 2 Changes in fasting blood sugar after therapy

Duration in Days	Mean Blood Sugar (± SD) (mg/dL)
D0	197.22 ± 37.25
D15	180.11 ± 38.03
D30	183.17 ± 30.59
D45	180.35 ± 36.80
D60	* 176.46 ± 36.78
D70	* 179.56 ± 39.57
D90	* 145.12 ± 29.81
(By Student 't' test)	* P < 0.05 Significant

Figure 1 Changes in fasting blood sugar after the therapy

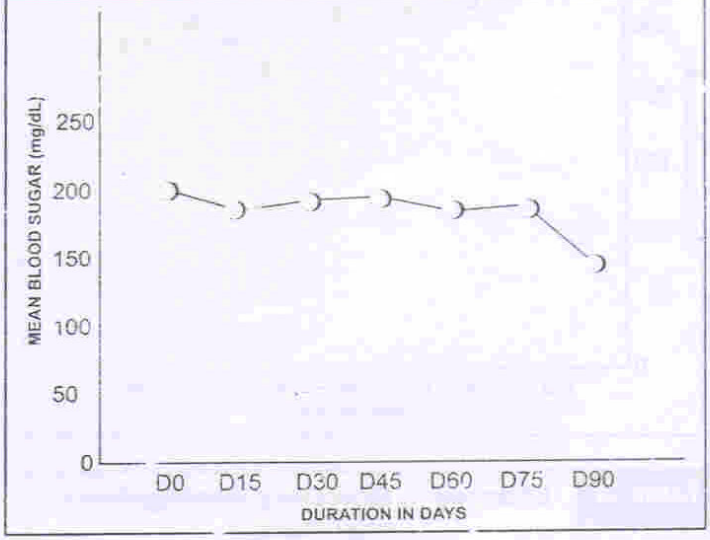

Table 3 Changes in blood sugar levels (PP) after therapy

Duration in Days	Mean Blood Sugar (± SD) (mg/dL)
D0	277.28 ± 45.06
D15	265.98 ± 37.77
D30	264.22 ± 45.92
D45	* 265.06 ± 44.82
D60	* 229.94 ± 38.95
D70	* 256.18 ± 34.07
D90	* 240.63 ± 58.26
(By Student 't' test)	* P < 0.05 Significant

Table 4 Changes in HbA1c after therapy

Duration in Days	Mean HbA1c % (± SD)
D0	9.08 ± 1.40
D30	8.92 ± 0.86
D60	8.72 ± 1.52
D90	* 8.14 ± 1.10
(By Student 't' test)	* P < 0.05 Significant

Figure 2 Changes in blood sugar levels (PP) after therapy

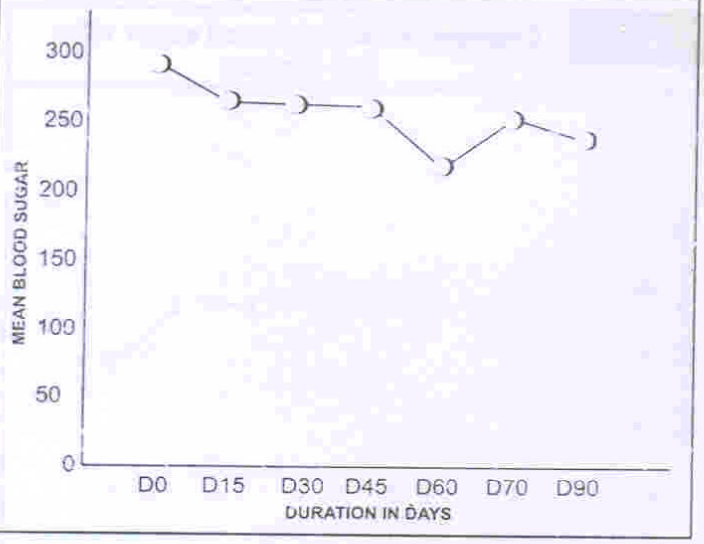

Table 5 Changes in laboratory investigations after therapy

Parameters	Mean Levels (± SD)	
	Basal	End of Treatment
S. Fructosamine	537.09 ± 248.83	472.44 ± 89.05
S. Cholesterol	182.23 ± 28.19	164.94 ± 35.18
S. Triglyceride	176.82 ± 31.15	163.94 ± 38.93
HDL	40.88 ± 4.29	42.87 ± 5.38
LDL	115.43 ± 33.82	115.0 ± 44.89
BUN	16.24 ± 4.24	13.74 ± 3.97
S. Creatinine	1.02 ± 0.27	0.90 ± 0.11
(By Student 't' test)	P > 0.05 Not Significant	

day of treatment i.e. 8.1% from the baseline value of 277.28 ± 48.06 mg%. By the end of three months of therapy the blood sugar level had reduced to 240.63 ± 58.26 mg% i.e. a 13.22% reduction (Table 3 and Figure 2). The glycosylated haemoglobin levels fell from 9.08 % at baseline to 8.14% at the end of three months i.e. a decrease of 10.4% (Table 4 and Figure 3).

Above data (Table 5) shows that all laboratory investigations like S. cholesterol, triglyceride, HDL, LDL and BUN did not show any significant change.

Figure 3 Changes in HbA1c after therapy

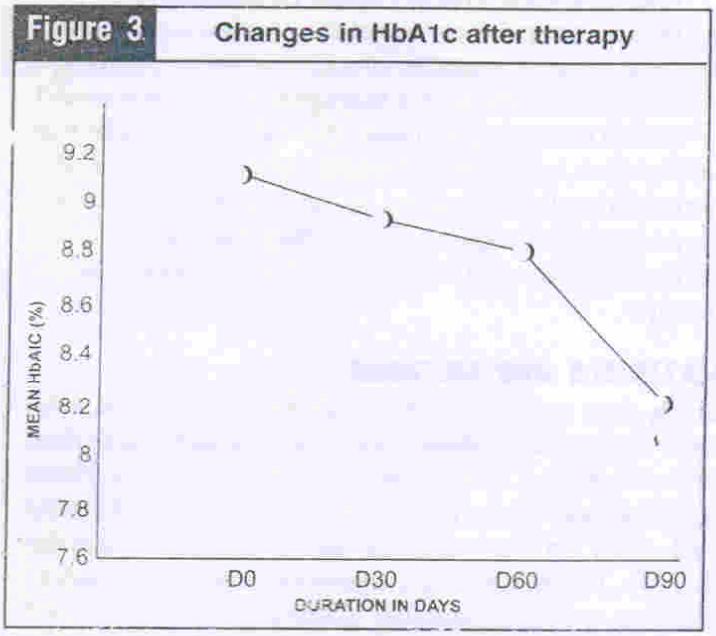

Table 6 Changes in anthropometric measurements

Parameters	Mean Levels (± SD)	
	Basal	At Day-90
Weight (kg)	63.36 ± 10.27	61.89 ± 9.88
Height (cms)	160.79 ± 7.14	160.79 ± 7.14
BMI	24.42 ± 7.12	23.89 ± 6.17
W/H Ratio	0.387 ± 0.61	0.374 ± 0.58
(By Student 't' test)	P > 0.05 Not Significant	

But S. fructosamine had a reduction of 12.1% after the treatment, which was not significant. Above data (Table 6) shows that after treatment anthropometric measurements like weight, height, BMI and W/H ratio did not show any significant change.

There was no significant change in weight or other laboratory parameters such as the haemogram and kidney function tests. None of the patients noticed any adverse reactions including hypoglycaemia during the study. All patients reported a sense of well being during the trial.

DISCUSSION

In the present study, significant glycaemic control was achieved after the herbomineral formulation in patients who showed glycaemic levels uncontroiled even by maximum permissible dosage of OHAs, without any adverse event or significant weight gain.

The reduction of glycosylated haemoglobin by 10.4% indicates an overall glycaemic control. According to the UKPDS, even a 10% reduction in the glycosylated haemoglobin level will help in reduction of long-term

complications by around 30%. Thus, the herbomineral formulation would be of benefit in preventing the long-term complications as well.

The herbomineral formulation (HYPONIDD) is a comprehensive formulation enriched with time-tested ingredients of superior efficacy and high safety used in the treatment of diabetes mellitus.

It contains 12 harmoniously blended ingredients, the prominent among them being Vijaysar *(Pterocarpus marsupium)*, Gurmar *(Gymnema sylvestre)*, Jambu beej *(Syzigium cumini)*, Amla *(Emblica officinalis)*, Haldi *(Curcuma longa)*, Neem *(Melia azadirachta)* and Shilajit. All these agents have proven antidiabetic action.

It is claimed to act by normalizing the blood glucose levels, stimulating the production of insulin and minimizing its peripheral destruction. It produces benefits of efficacy similar to other oral hypoglycaemic agents without the risk of side effects and contraindications.[1]

The following are some of the active ingredients, which have been shown to confer beneficial effects in diabetes.

Pterocarpus marsupium (Vijaysar)

The active antidiabetic principle has been found to be epicatechin. It has been claimed that its extract causes pancreatic beta-cell regeneration by the flavanoid fraction (epicatechin)[2]

Vijaysar has been found useful in the treatment of newly-diagnosed or untreated type 2 DM patients[3]

Syzigium cumini (Jambu beej)

The seed powder of *Syzigium cumini* has been used in diabetes as it reduces the sugar in urine and ameliorates the unquenchable thirst. It may also promote the endogenous release of insulin[4,5]

Gymnema sylvestre (Gurmar)

It has been shown to neutralize the excess sugar. Recent pharmacological and clinical studies have shown that *Gymnema sylvestre* acts on the taste buds in the oral cavity as well as in the intestine. It contains "Gymnemic acid" and its atomic arrangement is similar to that of glucose molecules. Gymnemic acid molecules fill the receptor locations on the taste buds, thereby, preventing activation of the taste buds by sugar molecules present in the food; thus curbing the sugar craving. Similarly, Gymnemic acid molecules fill the receptor locations in the absorptive external layers of the intestine, thereby preventing the sugar molecules absorption in the intestine, which results in low blood sugar level. Studies have shown that in vitro and in vivo *Gymnema sylvestre* releases insulin probably by causing regeneration of pancreatic beta cells.[6-10]

In addition to possessing antidiabetic effect, Haldi, Amla (a rich source of vitamin C) and Shilajit, possess free radical scavenging properties. As free radicals have now been implicated in the pathogenesis of diabetes mellitus, the desired antioxidant action can be useful in treating a diabetic patient.

Vijaysar possess additional rejuvenative properties, which can be beneficial in treating an undesired complication like impotence, which about 40-50% of men with long-standing diabetes present with.

Thus, HYPONIDD is a comprehensive formulation, which may be beneficial in treating not only the cause and symptoms of diabetes but also ameliorating associated problems, thereby improving the quality of life in the diabetic.

CONCLUSION

Thus, it can be concluded that the herbomineral formulation (HYPONIDD) represents a safe and effective third OHA that can be added in patients inadequately controlled by sulphonylurea and metformin, to postpone insulin therapy.

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