Effect of Diabecon (D-400), an Ayurvedic Herbal Formulation on Plasma Insulin and C-Peptide Levels in NIDDM Patients

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INTRODUCTION
The goal for treatment of diabetes is to prevent its acute manifestations and long-term microvascular and macrovascular complications. NIDDM is one of the most common disorders in developed and developing countries. Reaven has reported that abnormalities of beta cell function and secretion exist in patients with NIDDM. O’Rahilly et al. observed that the inherited component of familial Type II diabetes may be the impaired insulin secreting response of the beta cells. While fasting serum insulin may be in the normal range, glucose-induced insulin release is reduced, leaving below-normal insulin levels in the postprandial state. Oral hypoglycaemic drugs play an important role in the treatment of Type II diabetes mellitus but none have been found effective in maintaining euglycaemia. In about one-quarter of patients with an initially good response, the drugs later lose their effectiveness.

Adverse effects of oral hypoglycaemic agents occur in roughly 3% of patients. Hypoglycaemia is one of the most important and often fatal adverse effect of sulphonylureas. Often, particularly in elderly patients, hypoglycaemia is recurrent, prolonged, and its onset can be extremely delayed. Even though there is an awareness of prolonged and recurrent hypoglycaemia, there is little awareness of its delayed onset, following sulphonylurea therapy. There is a misconception that chlorpropamide alone, among the presently available sulphonylureas, is responsible for prolonged and recurrent hypoglycaemia and other sulphonylureas are safe. Glibenclamide, one of the most commonly used drugs in diabetes, is eliminated slowly in NIDDM patients and its biological half-life is much longer than what is traditionally quoted in the literature. Accumulation of glibenclamide in pancreatic islets and its persistent effect on beta cell membrane are the factors responsible for prolonged/delayed hypoglycaemia following glibenclamide therapy.

Ancient Indian medicine mentions various plants and mineral formulations in the treatment of diabetes mellitus. There are different combinations of these plants and minerals which can be given orally and for prolonged periods without side-effects.

Diabecon (D-400) an Ayurvedic herbomineral formulation containing Gymnema sylvestre, Momordica charantia, Eugenia jambolana, Pterocarpus marsupium and Yasad bhasm as its main ingredients, has been found to be safe and effective in lowering blood glucose levels in experimental trials. It has also been reported to reduce blood sugar and triglyceride levels in several multicentric clinical trials.

On the basis of these observations, an open clinical trial was conducted to evaluate the effect of Diabecon (D-400) on plasma insulin, C-peptide and glycated haemoglobin levels in poorly controlled Type 2 (NIDDM) diabetes mellitus patients.
MATERIAL AND METHODS
Twenty diabetic patients comprising 13 males and 8 females were enlisted in this trial after informed consent. They were enlisted at various times and had been on conventional oral hypoglycaemics by the time the present study was initiated. The study was conducted in the Department of Endocrinology, SSKM Hospital, Calcutta, between September 1994 and February 1995. The patients ages ranged from 22-65 years and the duration of diabetes varied from 2-8 years. The blood sugar maintenance was poor inspite of oral hypoglycaemic drugs.

Venous blood samples were drawn under fasting conditions from the patients for the estimation of blood glucose, glycated haemoglobin, plasma insulin and C-peptide. The patients were then put on Diabecon (D-400), in the dose of 2 tablets thrice daily along with existing oral hypoglycaemic drugs. The dosage was adjusted to prevent hypoglycaemic episodes. The patients were advised to come every 15 days for 6 months. Plasma insulin and C-peptide were estimated after 2 weeks of treatment with Diabecon (D-400). Both fasting and postprandial blood glucose estimation were done every 15 days. Glycated haemoglobin was assessed initially and after 6 months.

Statistical analysis was done by using paired ‘t’ test and Pearson’s product moment correlation coefficient to assess the strength of relationship between pairs of valuables. All tests were two tailed.

RESULTS
Table 1 presents the general data on age, sex and body mass index. There was no significant change in body mass index after 6 month of treatment with Diabecon (D-400) treatment.

| Table 1: Characteristics of non-insulin-dependent diabetes patient of Diabecon (D-400) treatment (n=20) |
|----------------|----------|------------|--------|-------|
| Age (Yrs)     | Sex      | BMI Initial | Final  |
|               | Male     | Female     |        |       |
| 45 ± 21.6     | 13       | 07         | 22.3 ± 1.2 | 21.2 ± 1.1 |

Diabecon (D-400) treatment had reduced the blood and urine sugar levels significantly (Table 2). In eight out of twenty patients the oral hypoglycaemic drugs were stopped, in the dose of hypoglycaemics was reduced and in six patients no change in the dose was required. All the patients were able to maintain the glucose homeostasis with Diabecon (D-400). The patients reported a sense of well being and less exhaustion.

| Table 2: Shows the effect of Diabecon (D-400) on fasting and postprandial blood sugar and urine sugar levels (Tabular data represent Mean ± SD) |
|----------------|------------------------------|----------------|----------|
| Parameter       | Pre-treatment                | Post-treatment  |
| Fasting blood sugar (n=20) | 170.95 ± 50.04              | 102.40 ± 44.76* |
| Postprandial blood sugar (n=20) | 272.15 ± 85.27              | 158.35 ± 81.65* |
| Urine sugar (n=20) | 2.88 ± 1.22                  | 0.88 ± 1.41*    |
*P<0.001 as compared to initial values

| Table 3: Effect of Diabecon (D-400) serum insulin (µg/ml) C-peptide (µg/ml) levels in non-insulin dependent diabetes patients (n=18) |
|----------------|----------|--------|-------|
| Parameters     | Initial  | Final  |
| Serum insulin (µg/ml) | 12.34 ± 3.7 | 16.07 ± 3.6* |
| C-Peptide (µg/ml) | 1.6 ± 0.5  | 2.16 ± 0.58* |
*P<0.001 as compared to initial values
There were 17 patients in whom HbA$_{1c}$ was analysed. The mean ± standard deviation (m ± S.D.) of HbA$_{1c}$ value was reduced from 11.54 ± 1.84 (before Diabecon (D-400) treatment) to 7.94 ± 2.02 (after Diabecon (D-400) treatment). The difference between the initial and the final HbA$_{1c}$ values was 3.61 ± 2.29.

This difference was statistically significant ($p<0.001$). Diabecon (D-400) produced a 31.31\% reduction in HbA$_{1c}$ values (Fig.1).

![Fig. 1: Effect of Diabecon (D-400) glycated haemoglobin levels in NIDDM patients (n=18)](image)

**DISCUSSION**

The salient features of the present clinical observations are that oral administration of Diabecon (D-400) to the existing hypoglycaemic therapy has lowered the fasting and postprandial blood sugar significantly. There was significant decrease in glycated haemoglobin levels measured at the end of the trial. Improper glycaemic control results in the development and progression of diabetic microangiopathy in humans and West has observed that good control of diabetes has a retarding effect on the development of such complications. Poor blood sugar control results in diabetic microangiopathy with the accumulation of glycated proteins producing a thickening of basement membrane in the kidney. Kennedy et al. have observed that measurement of HbA$_{1c}$ reflects blood glucose equilibrium state of the 6 to 8 weeks prior to sampling. Significant reduction of HbA$_{1c}$ in the present study confirms that blood glucose control is improved by the herbal therapy. It is possible that with significant decrease in HbA$_{1c}$ levels, the onset of secondary complications may be delayed by Diabecon (D-400).

Insulin lowers plasma glucose levels both by stimulating glucose uptake into the muscle and by inhibiting hepatic glycogen breakdown. Catecholamines cause hyperglycaemias by stimulating hepatic glycogenolysis and inhibit insulin stimulated glucose utilisation in muscles. Diabecon (D-400) has been found to inhibit catecholamine induced hyperglycaemia and significantly improved liver glycogen store and also has been found to increase incorporation of C$^{14}$ glucose in liver slices in alloxan-induced diabetes in rats.

Gymnema Sylvestre, one of the improvement ingredients of Diabecon (D-400), has been proved to be effective in diabetes by increasing beta cell function possibly by repair/regeneration of the beta cells. Momordica charantia seeds another important ingredients of Diabecon (D-400), was found to contain molecules with insulin like bioactivity.

In the present study there was significant increase in plasma insulin and C-peptide levels within 2 weeks of treatment with Diabecon (D-400).
It can thus be concluded that Diabecon (D-400) had reduced the blood sugar levels by improving the plasma insulin levels, increasing peripheral utilisation of glucose, improving liver glycogen store and also by its intrinsic antidiabetic action.

These lend evidence to the use of Diabecon (D-400) as an antidiabetic drug which might also help in reducing the long-term complications of diabetes.

REFERENCES
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