Diabecon (D-400) in the Treatment of Diabetes Mellitus

Seshaih V,
Department of Medicine, Apollo Hospitals, Madras, India.
Sundaram A,
Moses A,
Department of Medicine, Prof. Ambedkar Institute of Diabetes,
Kilpauk Medical College Hospital, Madras, India,
Balaji V, Ramkumar,
Department of Medicine, Apollo Hospitals, Madras, India.

ABSTRACT
Efficacy and safety of Diabecon (D-400) was assessed in thirty NIDDM patients (15 freshly diagnosed diabetic patients and 15 diabetic patients already on a very high dose of OHA). Findings of the present study revealed a significant reduction in fasting and postprandial blood sugar levels as well as in glycosylated haemoglobin levels (p<0.1), in both the groups. However, no significant change was observed in plasma insulin and blood lipid levels after Diabecon (D-400) treatment. Withdrawal of the drug was not required in any patient and no side-effects were observed. Diabecon (D-400) did not affect hepatic, renal and haematological functions in any patient during or after months of treatment. All the patients reported a sense of well-being. Diabecon (D-400) can be used alone or in combination with other OHA’s in the treatment of non-insulin dependent diabetes mellitus.

Key Words: NIDDM, Herbal, Diabecon (D-400)

INTRODUCTION
Diabetes mellitus is a chronic disease affecting millions of people all over the world. In patients with NIDDM the risk for the development of macrovascular disease is greatly increased. During the treatment of diabetes mellitus, it is important to control hyperglycaemia as well as correct the risk factors involved. Some studies have suggested that insulin resistance is the underlying defect in NIDDM which eventually causes a relative and finally, an absolute deficiency in insulin secretion. Other studies have shown that the primary defect in NIDDM is a decrease in insulin secretion that ultimately leads to insulin resistance. From the therapeutic point of view almost all the patients who are hyperglycaemic have some deficiency in insulin secretion.

The relationship between metabolic control and development of long-term complication of diabetes mellitus remains one of the most contentious issues in medicine. Major advances in general medical care, and especially in cardiac care, have now made it possible for older patients with type II diabetes to live longer. Although frequency of retinopathy and nephropathy is relatively lower in type II than in type I diabetes, the ten-fold greater prevalence of type II diabetes makes it a major contributor to visual loss and renal failure. The prevalence of dyslipidaemia is more common in NIDDM as compared to IDDM patients.

Atherosclerosis accounts for 80% of all diabetic mortality and diabetes is the most common cause of heart disease in young people.
Various antidiabetic drugs are available worldwide for the treatment of diabetes mellitus. But the difficulty in global metabolic control and prevention of vascular complications continues to persist. In this context indigenous drugs may be expected to be of value.

Diabetes mellitus (madhumeha) was known to ancient Indian physicians 3000 years ago. An elaborate description of its clinical features and its effective management has been discussed in Ayurvedic tests. Diabecon (D-400) is a herbal formulation containing Eugenia jambolana, Pterocarpus marsupium, Gymnema sylvestre, Momordica charantia and Ocimum sanctum etc.

Eugenia jambolana, the fruit, powdered seeds and aqueous extract of seeds have all been shown to lower the level of blood sugar. The powdered seeds decrease the urine sugar and allays polydipsia, a common manifestation of diabetes.

Pterocarpus marsupium, an aqueous infusion of the wood is said to be of use in diabetes. Tests on mice and rabbits with alcohol and aqueous extracts have shown hypoglycaemic action by hindering the absorption of glucose in the intestine. It has been claimed that this extract causes pancreatic beta-cell regeneration by the flavonoid fraction (epicatechin). In a study on alloxan-induced diabetic rats, it was shown to decrease blood sugar levels, improve insulin levels and increase synthesis of proinsulin. In another study, epicatechin isolated from the bark of P. marsupium has been shown to protect animals against the diabetogenic effect of alloxan. It has also been shown to have a hypocholesterolaemic effect.

Gymnema sylvestre, its leaves have been used as a remedy for diabetes. They caused hypoglycaemia in experimental animals when administered orally or by injection. This effect is due to indirect stimulation of insulin secretion by pancreas. The leaf extracts contain gymnemic acid which is said to inhibit the adrenohypophyseal stress response and the hyperglycaemic response to adrenalin and growth hormone. It has also been shown to have a regenerative effect on beta-cells.

Momordica charantia, the fruits, leaves and roots have long been used in India as a remedy for diabetes mellitus. The fruits and seeds yield a polypeptide considered to be similar to bovine insulin, which has been shown to have a hypoglycaemic effect in all types of diabetes. It also promotes peripheral utilisation of glucose and potentiates the action of tolbutamide.

Ocimum sanctum, the ethanolic extract has been shown to have a hypoglycaemic, anti-bacterial and anti-stress adaptogenic activity. In a study, oral administration of alcoholic extract of its leaves was shown to markedly reduce the blood sugar level in normal and streptozotocin-induced diabetic rats. Further, it was shown to potentiate the action of exogenous insulin in normal rats.

It has been found effective in lowering the blood sugar level in NIDDM patients. In many experimental and clinical trials it has significantly reduced cholesterol and triglyceride levels.

With the above information, a clinical trial was conducted to evaluate the efficacy of Diabecon (D-400) in controlling blood sugar, glycosylated haemoglobin and lipid profile, in NIDDM patients.

**PATIENTS AND METHODS**

The study was conducted on thirty NIDDM patients. Fifteen were freshly diagnosed diabetics and the rest were diabetic patients already on sulphonylurea. The freshly diagnosed patients were put on diet and exercise for a period of 3 months and only those showing persistent hyperglycaemia at the end of the period were included in this trial. Patients of either sex and over 30 years of age who were not grossly obese (weight not more than 20% of the average) were also recruited in this study, after informed consent. Those with severe cardiovascular disorders, pregnancy, hypertension and
obvious noncompliance were excluded from this study. The freshly diagnosed diabetes group has 7 males with mean age (in years) of 44 ±8.39 and 8 females with mean age (in years) of 41 ± 4.04. In the adjuvant group there were 6 males with mean age (in years) 5.05 ± 6.4 and 9 females with mean age 54.1 ± 7.67. Detailed history and clinical examination was done and blood was collected for baseline assessment of biochemical parameters. Patients were advised to take Diabecon (D-400) in the dose of 2 tablets thrice a day for 6 months and their fasting and postprandial blood sugar levels were noted every 15 days. Plasma lipid profile, glycosylated haemoglobin and insulin were assessed initially, after 3 and 6 months. At each fortnightly follow-up, patients were interrogated and examined for side-effects. Results were analysed at the end of 6 months. Statistical analysis was done by using MANOVA and paired ‘t’ test.

RESULTS

In freshly diagnosed diabetics, there was a significant reduction in fasting and postprandial blood sugar levels ($p<0.001$). Although the fasting insulin level showed increase after Diabecon (D-400) treatment, it could not reach to the level of statistical significance. There was significant reduction in glycosylated haemoglobin level ($p<0.001$). Paired ‘t’ testing revealed a significant fall in HbA$_{1c}$ level between 0 and 90 days ($p<0.002$) and between days 90 and 180 ($p<0.001$) (Table 1).

<table>
<thead>
<tr>
<th>Fasting blood sugar (mg/dl)</th>
<th>Postprandial blood sugar (mg/dl)</th>
<th>Fasting insulin (IU/L)</th>
<th>Postprandial insulin (IU/L)</th>
<th>Glycosylated haemoglobin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>186.67 ± 3.68</td>
<td>279.13 ± 9.92</td>
<td>18.70 ± 1.98</td>
<td>23.08 ± 6.44</td>
</tr>
<tr>
<td>Final</td>
<td>109.50 ± 5.40*</td>
<td>176.00 ± 9.40*</td>
<td>28.23 ± 9.15</td>
<td>43.75 ± 7.59</td>
</tr>
</tbody>
</table>

* $p<0.001$ as compared to respectively initial values.

Table 1: Effect of Diabecon (D-400) on fasting/postprandial blood sugar, insulin and glycosylated haemoglobin levels in freshly diagnosed diabetic patients (n=15)

In patients where Diabecon (D-400) was used as an adjuvant, a significant fall in both fasting and postprandial blood sugar level was observed ($p<0.001$). The descriptive Statistics for changes in the glycosylated haemoglobin levels revealed a significant decrease ($p<0.001$). Paired ‘t’ testing revealed a significant decrease in HbA$_{1c}$ level between days 0 and 90 ($p<0.002$) and between days 90 and 180 as well ($p<0.001$) (Table 2).

<table>
<thead>
<tr>
<th>Fasting blood sugar (mg/dl)</th>
<th>Postprandial blood sugar (mg/dl)</th>
<th>Glycosylated haemoglobin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>185.00 ± 7.28</td>
<td>8.61 ± 0.26</td>
</tr>
<tr>
<td>Final</td>
<td>106.47 ± 3.52*</td>
<td>7.41 ± 0.13*</td>
</tr>
</tbody>
</table>

* $p<0.001$ as compared to respective initial values.

Table 2: Effect of Diabecon (D-400) as an adjuvant on glycosylated haemoglobin and fasting/postprandial blood sugar levels (n=15)

Diabecon (D-400) therapy did not influence serum cholesterol, triglyceride and LDL and HDL levels (Table 3).

<table>
<thead>
<tr>
<th>Cholesterol (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
<th>HDL (mg/dl)</th>
<th>LDL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>190.53 ± 9.72</td>
<td>181.20 ± 19.02</td>
<td>46.26 ± 2.03</td>
</tr>
<tr>
<td>Final</td>
<td>176.27 ± 6.62</td>
<td>172.60 ± 18.84</td>
<td>48.86 ± 1.81</td>
</tr>
</tbody>
</table>

After Diabecon (D-400) treatment, hepatic, renal or haemopoietic functions remained unaltered (Table 4). Also, there was no change in the Body Mass Index (BMI) or in the systolic and diastolic blood pressure after Diabecon (D-400) therapy (Table 5).
<table>
<thead>
<tr>
<th></th>
<th>SGPT (IU/L)</th>
<th>Alkaline Phosphatase (IU/L)</th>
<th>Serum bilirubin (mg/dl)</th>
<th>Blood urea nitrogen (mg/dl)</th>
<th>Serum creatinine (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>23.06 ± 4.48</td>
<td>147.60 ± 8.99</td>
<td>0.65 ± 0.03</td>
<td>22.13 ± 0.99</td>
<td>0.79 ± 0.04</td>
</tr>
<tr>
<td>Final</td>
<td>20.26 ± 2.28</td>
<td>148.93 ± 6.07</td>
<td>0.68 ± 0.03</td>
<td>23.93 ± 1.52</td>
<td>0.75 ± 0.02</td>
</tr>
</tbody>
</table>

Table 4: Effect of Diabecon (D-400) on hepatic and renal functions in NIDDM patients (n=30)

<table>
<thead>
<tr>
<th></th>
<th>Body Mass Index</th>
<th>Systolic BP (mm of Hg)</th>
<th>Diastolic BP (mm of Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>22.73 ± 0.63</td>
<td>127.33 ± 3.00</td>
<td>78.00 ± 2.23</td>
</tr>
<tr>
<td>Final</td>
<td>22.20 ± 0.16</td>
<td>127.33 ± 2.06</td>
<td>77.33 ± 2.48</td>
</tr>
</tbody>
</table>

Table 5: Effect of Diabecon (D-400) BMI, systolic and diastolic blood pressure in NIDDM patients (n=30)

All patients reported a sense of well being. No side-effects were observed in any one of the patients throughout the study period.

**DISCUSSION**

Prevention of microvascular and macrovascular complication is one of the major goals of diabetes management. Increased non-enzymatic glycosylation of proteins and enhanced poly pathway activity resulting from sub-optimal plasma glucose control appears to play an important role in the pathogenesis of long-term effects. The standard therapeutic approaches have been disappointing in this regard. Sulphonylurea therapy is associated with high primary and secondary failure rates, and many patients with NIDDM eventually require insulin. However, insulin therapy promotes weight gain and increase insulin resistance.

Diabecon (D-400) has been found to be effective in lowering blood sugar levels in NIDDM patients\textsuperscript{12-13}.

In the present study, Diabecon significantly reduced both fasting and postprandial blood sugar levels, when used alone in freshly detected diabetics. In patients with NIDDM insufficiently controlled by maximal sulphonylurea therapy, administration of Diabecon (D-400) brought about better glycaemic control thereby delaying the need for initiation of insulin therapy.

In conditions of sustained hyperglycaemia such as diabetes mellitus, the proportion of haemoglobin that is glycosylated is increased substantially. This glycosylation is the result of post translation modification of haemoglobin A molecules. The amount of glycosylated haemoglobin in a patient, reflects the glycaemic control during the previous 6-8 weeks.

In the present study, Diabecon (D-400) significantly reduced glycosylated haemoglobin level in both the groups, which is an indication of its overall glycaemic control.

Although an increase in fasting plasma insulin level was observed in freshly diagnosed diabetics, it could not reach the level of statistical significance because of large standard error. Reductions were observed in blood lipid levels in both the groups but, they were not found statistically significant.

It can thus be concluded that Diabecon (D-400) represents a useful first line therapy in patients with NIDDM insufficiently managed with diet alone, and as an adjuvant in those insufficiently managed with other antidiabetic agents.
REFERENCES


