THE EFFECTS OF DIET AND HYPOGLYCEMIC AGENTS ON FASTING BLOOD SUGAR AND GLYCOXYLATED HAEMOGLOBIN CONCENTRATIONS IN TYPE TWO DIABETIC PATIENTS IN MOSUL POPULATION

Isam Hamo Mahmood & Wail Moneer Mohammed Sadiq

ABSTRACT

The study was conducted on 210 patients of both sexes suffering from Type 2 Diabetes Mellitus to investigate the effects of diet or hypoglycemic agents therapy on fasting blood sugar (FBS) and glycosylated haemoglobin (HbA1c). Seventy-two of the patients treated by diet only and 138 by hypoglycemic agents. Another 95 adult individuals taken from the same population who were apparently healthy and not suffering from diabetes mellitus were used as controls. A statistical higher values of FBS (178.13±70.84 mg/dl for diet and 219.08±73.02 mg/dl for hypoglycemic group) and HbA1c (8.35±2.07% for diet and 9.57±1.83 % for hypoglycemic group) were found among the diabetic patients in comparison with the control group (FBS=99.73±9.04 mg/dl, HbA1c=5.64±0.71%). Comparison between FBS and HbA1c of the diet and those of the hypoglycemic groups showed a highly significant differences (P<0.0001 for both). A strong correlation was found between FBS and HbA1c of the patients treated with diet or hypoglycemic agents (r=0.85 and 0.78, respectively, P<0.0001). The study concluded that, diabetes mellitus is a progressive disease which is difficult to control even by continuous use of diet or hypoglycemic therapy, and measurement of HbA1c can be used to assess the glycemic state and to confirms FBS measurements.

INTRODUCTION

Diabetes mellitus is one of the most widely distributed metabolic disorders and occurs in almost all populations of the world at a variable prevalence[1]. Of relevance are the findings that both environmental and genetic factors are implicated as possible modulators of the prevalence of diabetes mellitus[2]. The disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both[3,4]. It can be classified into 2 main types: type 1 diabetes mellitus which accounts for 5% to 10% of diabetes[5] and type 2 diabetes mellitus which accounts for 90% to 95% of all patients with diabetes[6]. It has been confirmed that there is a strong positive association between the duration of obesity and an impaired glucose tolerance test and diabetes[11]. A study in Saudi Arabia showed that 85% of patients with type 2 diabetes were overweight at the time of initial diagnosis[7]. Obesity probably acts as a diabeticogenic factor (through increasing resistance to the action of insulin) in those genetically predispose to develop type 2 diabetes, insulin resistance lead to higher level of insulin, which increases the appetite so people eat more and put on weight[8]. The diagnosis of symptomatic diabetes is not difficult. The symptoms of increased thirst, polyuria, polyphagia, and weight loss coupled with an elevation of the plasma glucose level are virtually pathognomonic. When diabetes is suspected in an asymptomatic patient, the primary diagnostic test is measurement of fasting plasma glucose concentration. If the value is not elevated, an oral glucose tolerance test can be done[9]. Glycosylated haemoglobin (HbA1c) concentration is an indicator of average blood glucose concentration over three months and has been suggested as a diagnostic or screening tool for diabetes[10]. The measurement of HbA1c in at risk individuals enhances the ability to diagnose diabetes in early stage[11]. A single fasting blood glucose measurement is an indication of the patients immediate past condition (hours), but may not represent the true status of blood glucose regulation. An accurate index of the mean blood glucose concentration may be established by the measurement of HbA1c every two to three months[12]. Normally HbA1c represents up to 4% of the total HbA in man. In hyperglycemic states, the synthesis of HbA1c increases and mean concentration raises approximately two fold. Since the glycosylation is irreversible, the rise in HbA1c persists for the life of the red cell[13].

This study was carried out to evaluate patients with type 2 diabetes mellitus who are taking diet or hypoglycemic therapy in Mosul by measurement of fasting blood sugar (FBS) level confirmed by HbA1c level and to compare the results of this study with those of other studies.
PATIENTS AND METHODS
The study was conducted on 210 patients of both sexes suffering from Type 2 Diabetes Mellitus over a period of 11 months (from 1 July 2001 to 31 May 2002) in Al-Wafaa Diabetic Clinic in Mosul. Ethical approval was obtained from the regional ethics committee in Ninevah Health Administration. The patients are chronic diabetic patients of both sexes who visit the diabetic clinic regularly. Seventy two patients were taking diet therapy; an appropriate diet for diabetes mellitus is constructed from the exchange system provided by the American diabetes System which contains restricted amounts of carbohydrates, fats and proteins[14] and one hundred thirty eight taking oral hypoglycemic drugs. Ninety five adult males and females collected from the same population who were apparently healthy and not suffering from Diabetes Mellitus were used as control.

Blood samples were obtained from the patients and control individuals after 12 hours of fasting. The samples were used for the estimation of blood glucose and HbA1c blood levels. Measurement of serum glucose concentration was done by enzymatic method established by Lott and Turner[15] which is available as a kit made by Biomaghreb company. The measurement of HbA1c in human blood is done by using the Variant HbA1c Program utilizing the principles of ion exchange HPLC for the automatic and accurate separation of HbA1c[16]. Statistical analysis was done by using unpaired student Z-test to compare the results for various parameters among control group, diabetic patients using diet only and diabetic patients using hypoglycemic agents. Linear regression analysis was performed for finding the relationship between the dependent and independent variables. All values quoted as the mean ± SD. Differences between observations were considered not significant at P>0.05[17].

RESULTS
(Table-1) shows, the characteristics and biochemical findings of the control subjects.

(Table-2) shows, the patient’s characteristics and biochemical findings of the diabetic patients treated by diet only. High values of FBS and HbA1c were found in 55 and 50 patients, respectively

(Table-3) shows, patient’s characteristics and biochemical findings of the diabetic patients treated with hypoglycemic agents. High values of FBS and HbA1c were found in 128 and 129 patients, respectively.

**Table 1. Characteristics and biochemical findings of the control group.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No.</th>
<th>Range</th>
<th>Mean ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (Age, years)</td>
<td>48</td>
<td>37-65</td>
<td>49.1±7.36</td>
</tr>
<tr>
<td>Female (Age, years)</td>
<td>47</td>
<td>29-60</td>
<td>46.4±7.11</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>95</td>
<td>24.5-31.0</td>
<td>27.9±1.49</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>95</td>
<td>72.0-123.0</td>
<td>99.7±9.04</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>95</td>
<td>4.1-7.3</td>
<td>5.6±0.71</td>
</tr>
</tbody>
</table>

**Table 2. Patients characteristics and biochemical findings of the diet group.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No.</th>
<th>Range</th>
<th>Mean ± s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (Age, years)</td>
<td>37</td>
<td>33-63</td>
<td>49.2±6.85</td>
</tr>
<tr>
<td>Female (Age, years)</td>
<td>35</td>
<td>29-58</td>
<td>46.9±6.56</td>
</tr>
<tr>
<td>Duration of treatment (years)</td>
<td>72</td>
<td>0.5-3</td>
<td>1.4±0.61</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>72</td>
<td>25.3-38.0</td>
<td>30.6±2.16</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>72</td>
<td>89-480</td>
<td>178.1±70.84</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>72</td>
<td>5.5-12.5</td>
<td>8.35±2.07</td>
</tr>
</tbody>
</table>

**Table 3. Patient's characteristics and biochemical findings of the hypoglycemic drugs group.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No.</th>
<th>Range</th>
<th>Mean ± s.d.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (Age, years)</td>
<td>46</td>
<td>32-70 y</td>
<td>48.9±7.12</td>
</tr>
<tr>
<td>Female (Age, years)</td>
<td>92</td>
<td>30-65 y</td>
<td>46.2±6.34</td>
</tr>
<tr>
<td>Duration of treatment years)</td>
<td>138</td>
<td>0.5-24</td>
<td>4.3±4.11</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>138</td>
<td>23.0-42.1</td>
<td>31.2±3.42</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>138</td>
<td>90-410</td>
<td>219.0±73.02</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>138</td>
<td>5.5-15.0</td>
<td>9.5±1.83</td>
</tr>
</tbody>
</table>
Diabetic Patients Treated by Hypoglycemic Agents:

Types of hypoglycemic agents:

- 89 patients taking glibenclamide (Doses 5mg to 15 mg daily).
- 38 patients taking metformin (Doses 500 mg to 1500 mg daily).
- 11 patients taking glibenclamide and metformin.

Statistical comparison between FBS and HbA1c of the diet group or hypoglycemic group with those of the control group showed a highly significant differences for both groups (P<0.0001).

Statistical comparison between FBS and HbA1c of the diet and hypoglycemic groups showed a highly significant differences (P<0.0001).

A strong correlation was found between FBS and HbA1c of the patients treated with diet or patients treated with hypoglycemic agents (r=0.85 and 0.78, respectively, P<0.0001)

The number of obese individuals (BMI ≥30 kg/meter²) found among the 3 groups were appeared in (Table-4). The numbers of obese individuals were higher in the diabetic patients compared with the control group.

Table 4. Obese individuals in the diabetic patients and control group (Number, %).

<table>
<thead>
<tr>
<th>Group</th>
<th>Individual</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>12 (12.7 %)</td>
<td>7 (7.4 %)</td>
<td>5 (5.3 %)</td>
</tr>
<tr>
<td>Diet</td>
<td>50 (69.4 %)</td>
<td>24 (33.3 %)</td>
<td>26 (36.1 %)</td>
</tr>
<tr>
<td>Hypoglycemic</td>
<td>93 (67.4 %)</td>
<td>23 (16.7 %)</td>
<td>70 (50.9 %)</td>
</tr>
</tbody>
</table>

DISCUSSION

Two groups of diabetic patients participated in the current study. Patients of the first group were treated with diet alone and patients of the second group treated with hypoglycemic agents. Diet is the cornerstone of treatment of diabetes mellitus, the aims of diet are to correct obesity and reduce hyperglycemia, and ultimately the threat of chronic diabetic complications[18]. Unfortunately between 40% and 60% of newly diagnosed Type 2 Diabetes Mellitus patients do not respond adequately

After 3 months of diet alone and many who are initially successful then later fail[10].

In the present study, about 76% of the patients on diet alone possess high FBS. Those uncontrolled cases of diabetes may be explained on the light of the above statements where failure to diet treatment attained and also because most of the patients were still overweight and obese which augment the insulin resistant state of the diabetic patients. In the UK Prospective Diabetes Study only 23% of patients allocated to diet alone attained fasting plasma glucose levels below 140.4 mg/dl[20].

About 92% of the diabetic patients on hypoglycemic agents in the present study possess FBS level above 126 mg/dl. This higher figure compared with the diet group may be due to the long period of the disease in such patients compared with the diet group. Warren-Boulton et al[21] reported that as the physiologic abnormalities of type 2 diabetes progress gradually over time, both diet and drug therapies tend to initially succeed and then slowly lose efficacy.

In a study done by United Kingdom Prospective Diabetes Study Group[22] to assess the relative efficacy of diet, glibenclamide or metformin in patients with newly diagnosed Type 2 Diabetes Mellitus, found that all therapies had similar lowering efficacy, although most patients remained hyperglycemic. The median FBS at 3 years treated by diet alone 172 mg/dl, glibenclamide 153 mg/dl and metformin 138.6 mg/dl.

Type 2 Diabetes Mellitus patients starting sulphonylureas after failure of diet show an average fall in fasting blood glucose of about 3 mmol/L[18]. At best 60-70% of such patients might achieve good glycemic targets; those with fasting glucose over 270 mg / dl and severe obesity rarely succeed[23]. The initial failures will be joined by a steady trickle (about 10% per year) of those who responded at first[18]. The causes of failure include non-compliance, weight gain, declining beta cell function and infection[24].

In the present study the mean BMI and prevalence of obesity (defined as BMI ≥30 kg/meter square) were high in the population samples in Mosul (69.4% in the diabetic patients treated by diet only and 67.4% in the
diabetic patients treated by hypoglycemic agents in both male and female). The prevalence of obesity and the mean BMI were higher than reported in surveys of population samples in Bahraini population (mean BMI 28±4.7) and the prevalence of obesity was 37% in women and 22% in men[25]. The prevalence of obesity and overweight in diabetic Saudis[26] were 20% and 37% in males respectively and 39% and 29% in females respectively. BMI reported in British Columbia, Canada[27] were 28.1±5.7 kg / meter square in men and 28.9±5.7 kg / meter square in women.

In the present study, high values of HbA1c were found in 50 patients (54.35%) on diet alone compared to 55 patients (59.78) with high FBS and 129 patients (93.48%) with high HbA1c in hypoglycemic agents group compared to 128 patients (92.75%) with high FBS. A strong correlation was found between FBS and HbA1c of patients with diet (r=0.85, P<0.0001) and those with hypoglycemic agent (r=0.78, P<0.0001). This means that HbA1c is an alternative indicator for hyperglycemia in diabetic patients and measuring HbA1c can confirm FBS.

McCane et al, (28) reported that the determination of glycated haemoglobin or fasting plasma glucose concentrations may be acceptable alternative to measuring glucose concentrators 2 hours after challenge with 75 g glucose for the diagnosis of diabetes. This may explain the strong correlation between HbA1c and FBS reported in the present study i.e. measurement of HbA1c alone may represent the glycemic states of our patients.

In conclusion, diabetes mellitus is a progressive disease which is difficult to control even by continuous use of diet and hypoglycemic drug therapy. A strong correlation exists between HbA1c and FBS, which indicates that HbA1c can be used to assess the glycemic state of the diabetic patients and to confirm FBS measurements.

REFERENCES

19. UK Prospective Study of Therapies of Maturity-Onset Diabetes. Effects of diet, sulphonylurea, insulin or biguanide therapy on fasting plasma glucose and body weight over one year. Diabetologia 1983; 26: 404-411.


