SOME CARDIOVASCULAR RISK FACTORS IN TYPE II DIABETIC PATIENTS WITH MICROALBUMINURIA

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ABSTRACT

Serum uric acid, fibrinogen, lipid profile, fasting blood glucose, body weight and duration of the diabetic state were assessed in both groups. The results showed that there was a direct and significant relationship between the duration of diabetes and the occurrence of microalbuminuria (P < 0.03).

Although there was no statistical significance between the body weight, blood pressure and microalbuminuria there was significant higher total cholesterol (P < 0.04), LDL Cholesterol (P < 0.03), atherogenic index (P < 0.07) and triglyceride levels (p < 0.05) revealing the dangerous effect of microalbuminuria on the cardiovascular system.

Serum HDL cholesterol, uric acid, fibrinogen and fasting blood glucose levels on the other hand were similar in both groups.

INTRODUCTION

Although it has been known for many years that the mortality rate among patients with non insulin dependent diabetes mellitus is increased, it is not easy to predict early death, even from a statistical point of view in any specific group of patients.

In addition to age, and to a certain extent the duration of diabetes, a slightly increased urinary albumin excretion rate (Microalbuminuria) is probably the most important predictor of early mortality in these patients, as it appears to be more important than the classical risk factors e.g. hypertension, unfavourable lipid profile and poor metabolic control (Mogensen 1990).

The major causes of death among non-insulin dependent diabetic patients with microalbuminuria are myocardial infarction and cardiac insufficiency (Schmitz et al., 1990).

To determine whether non insulin dependent diabetic patients with microalbuminuria have increased cardiovascular risk...
factors, we studied the duration of diabetes, blood pressure, serum lipid profile, fibrinogen, urine acid and fasting blood glucose levels in non insulin dependent diabetic patients with and without microalbuminuria.

**PATIENTS AND METHODS**

The study was carried on two groups of patients with non insulin dependent diabetes mellitus.

The first group included 14 patients with microalbuminuria (8 males & 6 females), their ages ranged between 36 and 70 yrs with a mean age of 52.5 ± 11.4.

The second group also comprised 14 patients but without microalbuminuria (8 males and 6 females), their ages ranged between 35 and 68 yrs with a mean age of 54.7 ± 8.3.

All cases were randomly chosen from the diabetes clinic, Interna Medicine Department, Faculty of Medicine, Cairo University.

All cases were treated by diet and / or oral hypoglycaemic drugs. None of them receiving medications or consuming alcohol or had any other factors that may alter the lipid, uric acid or fibrinogen levels.

For all cases the following was done :

* Blood pressure measurements.
* Estimation of the body weight.
* Detection of Microalbuminuria using the Beckman immunochemistry system and the ~Micro - albumin reagent (Sternberg, 1977).

* Fasting blood glucose estimation using Astra-4, employing a Beckman oxygen electrode (Albert, 1973).

* Lipid profile estimation:

  Serum cholesterol was carried out by quantitative enzymatic calorimetric technique using Hitachi 704 (Alain et al., 1974). Serum Triglycerides was carried out by enzymatic calorimetric test with lipid clearing factors using Hitachi 704 (Varley 1980).

  Serum HDL - cholesterol was carried out by enzymatic calorimetric test using Hitachi 704 (Frieldworld 1972).

  Serum LDL - Cholesterol was evaluated using Friedldworld Formula (Tietz 1987) by the following equation :

  \[
  \text{LDL (mg / dl)} = \text{Total cholesterol} - (\text{HDL} + \text{Triglyceride} / 5).
  \]

* Estimation of fibrinogen level was performed by chronometric determination of fibrinogen according to the Clauses method (Caen et al., 1975).

* Estimation of serum uric acid by enzymatic calorimetric test using Hitachi 407.

**RESULTS**

The results are presented in table (1).

**Analysis of results :**

1. **Duration of the Diabetic state :**

   In patients with microalbuminuria (group 1) the duration ranged between 0.83 and 22 yrs with a mean duration of 8.5 ±
Statistical analysis of results in NIDDM patients with microalbuminuria (Group I) & without microalbuminuria (Group II):

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of diabetes (years)</td>
<td>8.5 ± 6.7</td>
<td>4.5 ± 4.1</td>
<td>&lt; 0.03</td>
</tr>
<tr>
<td>Fasting Bl. glucose (mg/dl)</td>
<td>201.7 ± 79.4</td>
<td>204.8 ± 74.7</td>
<td>&lt; 0.3</td>
</tr>
<tr>
<td>Bl. pressure (mm/Hg) systolic</td>
<td>147.9 ± 23.3</td>
<td>147.1 ± 18.6</td>
<td>= 0.5</td>
</tr>
<tr>
<td>Diastolic</td>
<td>94.3 ± 11.4</td>
<td>89.3 ± 13.8</td>
<td>= 0.4</td>
</tr>
<tr>
<td>S. fibrinogen (mg/dl)</td>
<td>389.8 ± 114.2</td>
<td>359.4 ± 104.6</td>
<td>= 0.4</td>
</tr>
<tr>
<td>S. Uric acid (mg/dl)</td>
<td>4.4 ± 0.97</td>
<td>4.2 ± 0.9</td>
<td>= 0.15</td>
</tr>
<tr>
<td>S. Total Cholesterol (mg/dl)</td>
<td>215.4 ± 32.6</td>
<td>190.3 ± 40.3</td>
<td>&lt; 0.04</td>
</tr>
<tr>
<td>S. Triglycerides (mg/dl)</td>
<td>242.4 ± 134.4</td>
<td>177.4 ± 58</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>HDL - Cholesterol (mg/dl)</td>
<td>47.1 ± 7.3</td>
<td>48.7 ± 7.2</td>
<td>&lt; 0.3</td>
</tr>
<tr>
<td>LDL - Cholesterol (mg/dl)</td>
<td>118.6 ± 30.9</td>
<td>99.4 ± 19.2</td>
<td>&lt; 0.03</td>
</tr>
<tr>
<td>Atherogenic Index</td>
<td>4.48 ± 0.4</td>
<td>3.93 ± 0.5</td>
<td>&lt; 0.02</td>
</tr>
</tbody>
</table>
6.7 yrs, while in patients without microalbuminuria (group II) it ranged between 0.5 and 13 yrs with a mean duration of 4.5 ± 4.1 year.

The duration of the diabetic state in group I was significantly higher than in group II (P < 0.03).

2- Body weight:
There was no statistically significant difference in the body weight between the two groups as the mean weight in patients with microalbuminuria (group I) was 81.4 ± 11.2 kg, while in patients without microalbuminuria (group II) it was 80.4 ± 14.1 kg (p = 0.4).

3- Blood Pressure:
There was no statistically significant difference in either diastolic or systolic pressure between the two groups, as the mean systolic and diastolic blood pressures in patients with microalbuminuria (group I) were 147.9 ± 23.3 & 94.3 ± 11.4 respectively, while in patients without microalbuminuria (group II) were 147.1 ± 18.6 & 84.3 ± 13.9 respectively. (p = 0.5 & p = 0.4 respectively).

4- Fasting blood glucose:
In patients with microalbuminuria (group I) their mean fasting blood glucose level was 201.7 ± 79.4 mg / dl, while in patients without microalbuminuria (group II) it was 204.8 ± 74.7 mg / dl, and this difference was statistically not significant (p = 0.4).

5- Serum uric acid:
In patients with microalbuminuria (group I) their mean serum uric acid was 4.5 ± 0.97 mg / dl, while in patients without microalbuminuria (group II) it was 4.2 ± 0.98 mg / dl, and this difference was statistically not significant (p = 0.15).

6- Serum fibrinogen:
In patients with microalbuminuria (group I) their mean serum fibrinogen was 380.8 ± 114.2 mg / dl, while in patients without microalbuminuria (group II) it was 359.4 ± 104.6 mg / dl, and this difference was statistically not significant (p = 0.4).

7- Serum total cholesterol:
In patients with microalbuminuria (group I) their serum total cholesterol ranged between 174 and 272 mg/dl with a mean value of 215.4 ± 32.6, while in patients without microalbuminuria (group II) it ranged between 128 and 288 mg / dl with a mean value of 190.3 ± 40.3.

Serum total cholesterol was significantly higher in group I than in group II (p < 0.04).

8- Serum triglycerides:
In patients with microalbuminuria (group I) their serum triglycerides ranged between 111 and 589 mg / dl with a mean value of 242.4 ± 134.4, while in patients without microalbuminuria (group II) it ranged between 102 and 279 mg / dl with a mean value of 177.4 ± 58.04.

Serum triglycerides was significantly higher in group I than in group II (p < 0.05).

9- Serum HDL Cholesterol:
In patients with microalbuminuria (group I) their mean serum HDL cholesterol was 47.1 ± 7.32 mg / dl, while in patients without microalbuminuria (group II) it was 48.7 ± 7.18 mg / dl, and this difference was statistically not significant (p < 0.28).
10 - Serum LDL Cholesterol:

In patients with microalbuminuria (group I) their serum LDL cholesterol ranged between 62 and 154 mg/dl with a mean value of 118.6 ± 30.9, while in patients without microalbuminuria (group II) it ranged between 70 and 123 mg/dl with a mean value of 99.4 ± 19.2.

Serum LDL cholesterol was significantly higher in group I than in group II (P < 0.03).

11 - Atherogenic Index:

In patients with microalbuminuria (group I) their atherogenic index ranged between 4 and 5.2 with a mean value of 4.5 ± 0.4, while in patients without microalbuminuria (group II) it ranged between 2.7 and 4.8 with a mean value of 3.9 ± 0.5.

The atherogenic index was significantly higher in group I than in group II (P < 0.02).

DISCUSSION

Unlike the relatively diabetes-specific problems of retinopathy and nephropathy, macrovascular disease in patients with diabetes resembles that in non diabetic individuals namely ischemic heart disease, peripheral vascular disease and cerebrovascular disease, although with much increased frequency.

Whether measured by cause-specific death rates, clinical mortality or quantitative estimates of ischemia, macrovascular complications occur approximately twice as frequently in men with diabetes as in non diabetic men and in women the difference is even greater and particularly at younger ages (Keen, 1988).

Mortality studies showed that patients with diabetes die at a younger ages from cardiovascular disease, mainly insulin dependent type I disease than non diabetic individuals (Connell & Louden, 1983).

The classical risk factors for cardiovascular disease include hypertension, obesity and hyperlipoproteinaemia. In addition to these, there is also others of major importance they include hypertriglyceridaemia and rheological factors (Hoffmeister, 1992).

The concept of risk factors in the development of atherosclerosis has been greatly extended by the inclusion of haemorheological factors mainly fibrinogen, as it must be considered as an independent atherogenic factor which is probably just as important as cholesterol (Leschke, 1992).

Although it has been known for many years that the mortality rate among non-insulin dependent diabetic patients is increased, it is not easy to predict early death even from a statistical point of view, in any specific group of patients, one significant break through in this regard was the discovery that any early increase in urinary albumin excretion rate was closely associated with subsequent increased mortality (Mogensen, 1990).

Matlock & Morrish (1992) concluded from their study on the predictive power of microalbuminuria in non insulin dependent diabetic patients, that it is a significant risk marker for mortality and its presence should be regarded as an index of increased
cardiovascular permeability and a signal for vigorous efforts at correction of known risk factors.

In this work we studied some of the cardiovascular risk factors in non-insulin dependent diabetics with and without microalbuminuria, and the results showed that there were a significant higher serum triglycerides, total cholesterol, LDL cholesterol and the atherogenic index which is the ratio of total serum cholesterol to LDL cholesterol, in the group of patients with microalbuminuria than those without microalbuminuria. There was higher serum uric acid, fibrinogen & both systolic and diastolic blood pressure in the group of patients with microalbuminuria than those without microalbuminuria. Although they were statistically not significant.

Thus non-insulin dependent diabetic patients with microalbuminuria in our study have atherogenic lipid pattern than those without microalbuminuria, and the relationship of these lipid pattern to the occurrence of premature coronary heart disease was previously documented (Schaefer 1990). This might explain the results of other respective studies demonstrating that microalbuminuria is a predictor of early mortality especially from cardiovascular causes in non-insulin dependent diabetes.

Our results agree with those of Kodama et al., (1991) who made a case control study on blood pressure, platelet aggregability, serum lipid profile, fibrinogen and uric acid levels in 21 Japanese non-insulin dependent patients with microalbuminuria and 21 individually pair matched non-insulin dependent diabetic patients with normal urinary albumin excretion in order to determine whether microalbuminuric patients have increased cardiovascular risk factors, and the results showed significantly higher systolic blood pressure, serum fibrinogen and atherogenic lipid profile in microalbuminuric patients, and he suggested that some of the coronary risk factors may already increased in non-insulin dependent diabetic patients with microalbuminuria which may contribute to an increased of cardiovascular disease in these patients.

Also our results agree with those of Zambou et al., (1993) who studied whether lipoprotein abnormalities in non-insulin dependent diabetes with microalbuminuria could account for accelerated atherosclerosis in these patients, and he found that these patients had high serum triglycerides, Low HDL-cholesterol and small LDL particles, and concluded that this atherogenic lipoprotein profile might at least partially explain the association between microalbuminurie and cardiovascular disease in type II diabetes.

So microalbuminuria in non-insulin dependent diabetes should be therefore a signal for vigorous effort at correction of other risk factors for coronary heart disease. Indeed the st. Vincent declaration action programme recommends that all non-insulin dependent diabetic patients be screened for microalbuminuria at least once a year from the time of diagnosis until the age of 70, emphasizing that risk factors should be corrected in micro and macro albuminuric patients (Kranz et al., 1992).
REFERENCES


بعض موافقة الخطر على الجهاز الدوائي في المرضى المصابين بالزائفة الميكروسكوبية البولية من مرضى السكر الغير معتمدين على الأنسولين

لم تسلم لنا حتى الآن أي تفاعلات مع الأنسولين، مع العلم أن الأنسولين يعتبر أداة مثالية لمنع تأثير الكولسترول الكلي، الكولسترول الكلي، الفيبرينوجين، الدهون، الكولسترول في البروتينات الدوائية والكبدية.

كانت دراسة على 14 مريض مصاب بالسکر الغير معتمد على الأنسولين، و16 مريض مصاب بالسکر الغير معتمد على الأنسولين. ونلاحظ أن مرضى السکر الغير معتمد على الأنسولين يعانون من الازلال الميكروسكوبية البولية، (المجموعة الأولى)، و16 مريض مصاب بالسکر الغير معتمد على الأنسولين. حيث تمت دراسة مستوي كل من حمض البولي، الفيبرينوجين، الكولسترول الكلي، الكولسترول في البروتينات الدوائية والكبدية.

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وقد أظهرت النتائج أن هناك علاقة ذات دلالة إحصائية بين مستوى الكوليسترول الكلي، الكوليسترول في البروتينات الدوائية والكبدية، والكوليسترول الكلي حيث أنها كانت أعلى في المجموعة الأولى من خلال مجلس الأطباء. كما أن هناك أيضاً علاقة ذات دلالة إحصائية بين مدة الإصابة بالسکر وجود الازلال الميكروسكوبية البولية.

وعلى الفمك لم توجد علاقة ذات دلالة إحصائية بين المجموعتين بالنسبة لمدى حمض البولي، الفيبرينوجين، الكوليسترول في البروتينات الدوائية والكبدية، والكوليسترول الكلي، الكوليسترول في البروتينات الدوائية والكبدية، والكوليسترول الكلي، الكوليسترول في البروتينات الدوائية والكبدية.

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وتنافز هذه الدراسة تشير إلى أهمية الاستكشاف المبكر والعلاج للزائفة الميكروسكوبية البولية لمرضى السکر ونظامهم، ولديهم تأثيرات سلبية على صحتهم.