SERUM LIPIDS, LIPOPROTEINS AND URIC ACID IN TYPE II DIABETES MELLITUS ON SULPHONYLUREA AND INSULIN MEDICATIONS

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(Received: 24 April 2005)

ABSTRACT

One hundred and forty-five, non-insulin-dependent-diabetes Mellitus (NIDDM), without ischemic heart disease, one hundred and twenty-three, NIDDM, with ischemic heart disease patients and eighty-seven healthy subjects were selected in this study. NIDDM patients (group II) showed a highly significant increase in total LDL, VLDL cholesterol, triglycerides and uric acid with low levels of HDL-c compared to NIDDM (group I) and healthy subjects (group I). Except for uric acid and HDL-c, all parameters of NIDDM group showed high concentrations compared to healthy subjects. The NIDDM group without ischemic heart disease showed a significantly increase for triglycerides (TG) and VLDL-c but no significant increase was noticed for uric acid (UA) on oral medication of hypoglycemic agent (sulphonylurea) compared to the medication of insulin.

The NIDDM patients with ischemic heart disease showed a higher results for total cholesterol (TC), LDL-c, VLDL-c, TG and a lower result for HDL-c upon medication of oral hypoglycemic agent (sulphonylurea) compared to medication on insulin.

INTRODUCTION

There were lipid abnormalities in diabetes, the most common lipid abnormalities in diabetes is raised TG levels due to excess of V-LDL-c concentration (Pickup and Wiffen 1994). HDL-c levels are reduced in NIDDM, in proportion to increased TG and VLDL-c, and thus associated with increased risk of premature isomic heart disease and increased mortality and morbidity in patients with coronary heart disease (Mamall and Bousses 1995). Kennedy et al. (1979) found that HDL-c concentrations were shown to be lower in NIDDM than in those with insulin dependent-diabetes (IDDM) and control.

Commencement of therapy with either insulin or oral sulfonilureas leads to a reduction in VLDL-c levels and an increase in HDL-c, despite the weight gain that often accompanies the initiation of therapy in NIDDM patients (Rabin et al. 1503 and Abate and Brunelli 1990).

The actual mechanisms by which HDL-c levels are determined are not known, but a current hypothesis is that HDL-c reflects the rate of catabolism of TG and VLDL-c (Tall et al. 1979). On entering plasma, chyominoles and VLDL-c become a substrate for the endothelial bound...
enzyme, lipoprotein lipase, this enzyme, which requires insulin for its synthesis and hydrolysis triglycerides from the core of the lipoproteins. As the particles are successively cleaved lipoproteins and lipids on its surface are believed to form nascent HDL particle. Thus, situation in which chromomicrosomes of VLDL flux is impaired would lead to low levels of nascent HDL. Laakso et al. (1986) showed an association between low levels of HDL-c and coronary heart disease (CHD) in both NIDDM and IDDM.

The aim of this work is to throw some light on the effect of diabetes mellitus type II and ischemic heart disease on serum lipids, lipoproteins and uric acid.

MATERIALS AND METHODS

Subjects
The subjects were divided into three groups: Group-I: controls, eighty-seven subjects (45 males and 42 females) with mean age 57.1 ± 9.89 years were selected randomly. They were non-smokers, non-alcoholics, no family history of coronary heart disease (CHD), not obese and not diabetics or hypertension. Group-II: one hundred and forty-five adults (65 males and 79 females), non-insulin dependent, diabetes Mellitus (NIDDM group) with mean ages 58 ± 10.46 years were selected randomly at the diabetic clinic during their routine visits from Gene-Ehsain Polyclinic. Patients were not on medication except for the antidiabetic therapy oral hypoglycemic agent (sulphonylurea) or insulin. Group-III: diabetic patients; one hundred and twenty-three adults (45 males and 78 females) with mean ages 59.32 ± 8.93 years who were apparently suffering from ischemic heart disease as judged from their medical history were selected at randomly from Gene-Ehsain Polyclinic, 7th October Hospital, and El-Jenatheria Hospital, Benghazi, Libya, during the period from 1st May 2002 to 1st March 2003. All patients received antidiabetic therapy and didn`t take lipid lowering medication.

The patients were diagnosed as myocardial infarction and angina pectoris, at the time of blood sampling. None of patients had acute myocardial infarction within 3 months.

Sampling
Five ml of various blood samples were collected after fasting overnight at least 10 hr. The samples were kept for 30 minutes at room temperature, then serum was separated by centrifugation at 4,000 r.p.m. for 15 minutes. The serum stored at about - 18°C until analysis.
Methods

Triglycerides were determined by means of kits obtained from Bicron Company, Germany according to the method of Fassati and Principe (1982). Total cholesterol was determined according to Richmond (1973). HDL-c was determined according to Lopas et al. (1977). LDL-c was determined according to the method of Levy (1981) and uric acid was determined according to Piaggi and Barthelmai (1982). VLDL-c was calculated from the following equation according to Bugrim et al. (2005).

\[
VLDL-c = \frac{[Total\ Cholesterol]}{[LDL-c + HDL-c]} \text{mg/dL}
\]

Statistical Analysis

The recorded data in this study were subjected to statistical analysis according to Schaum's (1992).

RESULTS

Serum lipids, lipoproteins and uric acid of healthy subjects (control-group I), NIDDM group without ischemic heart disease (group II) and NIDDM patients suffering from ischemic heart disease (group III) (Table 1). The mean levels of serum total-c, triglycerides and VLDL-c in all NIDDM group in spite of with or without ischemic heart disease were significantly higher than in healthy group, while a significant decrease in HDL-c were observed. The difference in uric acid was not significant in NIDDM and healthy groups.

The mean levels serum total-cholesterol, triglycerides and uric acid in NIDDM patients were significantly increase than that observed in NIDDM and healthy groups, while a significant decrease in HDL-c were found.

Data in Table 2 represent the serum cholesterol, TG, HDL, LDL, VLDL and uric acid in NIDDM (group II) without ischemic heart disease, oral hypoglycemic agent (sulphonylureas) and insulin treated. The mean serum levels of triglycerides, VLDL-c and uric acid in NIDDM group on medication of oral hypoglycemic agent (sulphonylureas) were higher than that observed in NIDDM group on medication of insulin. The difference in mean serum levels of total-c and LDL-c were not significant.
### Table 1. Serum lipids, lipoproteins and uric acid concentration in healthy group, NIDDM group and NIDDM patient.

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>CHOL</th>
<th>TG</th>
<th>HDL</th>
<th>LDL</th>
<th>VLDL</th>
<th>UA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy group</td>
<td>67</td>
<td>163.7± 33.40</td>
<td>120.35± 35.55</td>
<td>40.60± 0.11</td>
<td>54.92± 25.68</td>
<td>54.45± 6.92</td>
<td>0.32± 0.06</td>
</tr>
<tr>
<td>NIDDM group</td>
<td>145</td>
<td>184.95± 30.10</td>
<td>198.35± 95.40</td>
<td>30.70± 0.01</td>
<td>111.88± 27.47</td>
<td>30.00± 16.99</td>
<td>0.33± 0.60</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.003</td>
<td>0.006</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td>0.36</td>
</tr>
<tr>
<td>NIDDM Patients</td>
<td>123</td>
<td>215.5± 48.6</td>
<td>235.1± 156.3</td>
<td>32.5± 6.28</td>
<td>130.2± 40.76</td>
<td>46.66± 30.66</td>
<td>6.13± 1.39</td>
</tr>
<tr>
<td>P¹</td>
<td></td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
</tr>
<tr>
<td>P²</td>
<td></td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
<td>&gt; 0.001</td>
</tr>
</tbody>
</table>

n: number of patients

P: p values of NIDDM group vs. control

P¹: p values of NIDDM group vs. NIDDM patients

P²: p values of NIDDM patients vs. control

### Table 2. Serum lipids, lipoproteins and uric acid in NIDDM group oral hypoglycemic agent (sulphonylurea) and insulin treated as mean ± SD.

<table>
<thead>
<tr>
<th>NIDDM Groups</th>
<th>CHOL</th>
<th>TG</th>
<th>HDL</th>
<th>LDL</th>
<th>VLDL</th>
<th>UA</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Long Treated</td>
<td>194.3± 26.59</td>
<td>245.0± 38.63</td>
<td>118.5± 9.03</td>
<td>27.8± 21.37</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>(B) Insulin Treated</td>
<td>193.1± 27.12</td>
<td>37.4± 113.97</td>
<td>33.8± 13.72</td>
<td>0.77± 0.92</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>0.46</td>
<td>6.39</td>
<td>2.20</td>
<td>2.22</td>
<td>9.05</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Data in Table 3 show the serum total cholesterol, TG, HDL, LDL, VLDL and uric acid in NIDDM patients with ischemic heart diseases oral hypoglycemic agent (sulphonylurea) and insulin treated.
Table 3: Serum levels, lipoproteins and uric acid in NIDDM patients with ischemic heart disease oral hypoglycemic agent (sulphonylurea) and insulin treated as lipid mean ± SD.

<table>
<thead>
<tr>
<th>NIDDM Patients</th>
<th>CHDL</th>
<th>TG</th>
<th>HDL</th>
<th>LDL</th>
<th>VLDL</th>
<th>UA</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Oral treated</td>
<td>213.74 ± 46.03</td>
<td>272.58 ± 177.36</td>
<td>31.87 ± 6.50</td>
<td>145.71 ± 42.00</td>
<td>51.48 ± 31.56</td>
<td>6.10 ± 1.27</td>
</tr>
<tr>
<td>(B) Insulin treated</td>
<td>267.26 ± 47.72</td>
<td>261.41 ± 102.63</td>
<td>33.16 ± 5.85</td>
<td>135.6 ± 38.52</td>
<td>48.3 ± 29.36</td>
<td>6.10 ± 1.90</td>
</tr>
</tbody>
</table>

The mean serum levels of triglycerides and VLDL-c in NIDDM patients on medication of oral hypoglycemic agent were significantly higher than that observed in NIDDM patients on medication of insulin. While the difference in means levels of total, LDL and HDL cholesterol and uric acid were not significant.

**DISCUSSION**

The high plasma triglycerides and low HDL values in NIDDM is consistent with reported decrease lipoprotein lipase activity and with impaired catabolism of TG-rich lipoprotein in type II diabetics (Nikifor 1981 and Brunzell et al. 1979). As lipoprotein lipase required insulin for its synthesis and hydrolysis of TG from the core of the lipoproteins, type II diabetes whose hyperglycemia dose not respond to a diabetic diet and oral medication can be treated with insulin (Rosenzweig 1994). Also, the major effect of the sulphonylureas oral hypoglycemic compound is the lowering of the blood sugar level by stimulation of production or release of insulin from the beta-cells of the pancreas (Harrod 1994).

This study showed that a significant difference in serum levels TG and VLDL-c between NIDDM group and NIDDM patients on medication of oral hypoglycemic agent (sulphonylurea) and medication of insulin. But there was no difference between total cholesterol and LDL-c values in the two groups. The increased level of TG and VLDL-c in oral hypoglycemic agent is consistent with hypothesis which was suggested that the level of TG and VLDL-c are related to impairment in TG rich
lipoprotein catabolism. The only other attribute postulated to explain HDL-cholesterol differences in diabetics, sulphonylurea therapy, did not contribute to HDL-cholesterol differences in diabetics in this population (Nikita 1981 and Brunzell et al. 1979). In contrast to previous reports of lower levels of HDL-cholesterol in sulphonylurea treated diabetics (Kennedy et al. 1978 and Stanton 1978), in this study there was no significant difference in HDL-cholesterol levels in patients on sulphonylurea hypoglycemic agents vs. those on insulin treatment alone. These findings are in consistent with study by Hopkins (1983). Furthermore, a statistical significant incidence of hyperuricaemia in group of diabetic patient with GH-2 has been evident in our study. Also, we found the difference in uric acid levels in diabetic with oral hypoglycemic agent were significantly higher than that of diabetics on medication of insulin. These differences for the two treatment diabetics with GH-2 was not detected.

REFERENCES

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تأثير مرض السكري من النوع II على الأنتروجين والكويلنكورن وحافز النوريد
في مرضى الفيلق

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دكتور جمعية ك. د. ا. م..، 36، 2005.