Is pseudocholinesterase activity related to markers of triacylglycerol synthesis in Type II diabetes mellitus?

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ABSTRACT

Hypertriglyceridaemia is a risk factor for cardiovascular disease in patients suffering from Type II diabetes mellitus, and is due to enhanced synthesis and/or impaired clearance of triacylglycerol-rich lipoproteins. In the present study we investigated whether pseudocholinesterase (PChE) activity could serve as a marker for the rate of triacylglycerol synthesis in these patients. Patients were stratified according to their apolipoprotein E (apoE) phenotype, i.e. E3E2, E3E3 or E3E4. In study I, the relationship between PChE activity and serum triacylglycerols was investigated in 224 insulin-treated patients with Type II diabetes. In study II, which had a cross-over design, PChE activity was measured in 45 dyslipidaemic, insulin-treated patients with Type II diabetes that were treated with bezafibrate or pravastatin. In study I, PChE activity was correlated positively with serum triacylglycerol concentrations, but did not differ significantly between apoE phenotypes. The strongest relationship was found in the E3E4 group ($r = 0.50; P = 0.001$), the phenotype for which hypertriglyceridaemia is expected to be the result of increased triacylglycerol synthesis. In a stepwise multiple regression analysis, serum triacylglycerol concentrations were found to be the strongest predictor of PChE activity in the E3E4 group. In study II, PChE activity decreased as a result of bezafibrate treatment in all three apoE groups. The decrease in PChE activity with bezafibrate treatment paralleled the decrease in serum triacylglycerol concentrations in the apoE subgroups. Pravastatin treatment did not significantly affect PChE activity. Thus the present study suggests an association between PChE activity and the rate of triacylglycerol synthesis. Measurement of PChE activity may therefore be a useful tool in the choice of drug for treatment of hypertriglyceridaemia in patients with Type II diabetes.

INTRODUCTION

Pseudocholinesterase (PChE; EC 3.1.1.8; also known as butyrylcholinesterase or serum cholinesterase) is an enzyme that is synthesized in the liver and is present in plasma, and to a lesser extent in adipose tissue, small intestine and smooth muscle cells [1]. The physiological function of PChE is unknown, but high serum activities have been observed in patients with obesity [2] and hyperlipoproteinaemia [3–5]. In such patients, PChE activity decreases as a result of treatment with bezafibrate, a fibrinolytic drug used for the treatment of hyperlipoproteinaemia [6]. The present study investigated whether PChE activity could serve as a marker for the rate of triacylglycerol synthesis in Type II diabetes mellitus patients. Patients were stratified according to their apolipoprotein E (apoE) phenotype, i.e. E3E2, E3E3 or E3E4. In study I, the relationship between PChE activity and serum triacylglycerols was investigated in 224 insulin-treated patients with Type II diabetes. In study II, which had a cross-over design, PChE activity was measured in 45 dyslipidaemic, insulin-treated patients with Type II diabetes that were treated with bezafibrate or pravastatin. In study I, PChE activity was correlated positively with serum triacylglycerol concentrations, but did not differ significantly between apoE phenotypes. The strongest relationship was found in the E3E4 group ($r = 0.50; P = 0.001$), the phenotype for which hypertriglyceridaemia is expected to be the result of increased triacylglycerol synthesis. In a stepwise multiple regression analysis, serum triacylglycerol concentrations were found to be the strongest predictor of PChE activity in the E3E4 group. In study II, PChE activity decreased as a result of bezafibrate treatment in all three apoE groups. The decrease in PChE activity with bezafibrate treatment paralleled the decrease in serum triacylglycerol concentrations in the apoE subgroups. Pravastatin treatment did not significantly affect PChE activity. Thus the present study suggests an association between PChE activity and the rate of triacylglycerol synthesis. Measurement of PChE activity may therefore be a useful tool in the choice of drug for treatment of hypertriglyceridaemia in patients with Type II diabetes.
activity is correlated strongly and positively with the concentration of very-low-density lipoprotein (VLDL), VLDL being the major carrier of triacylglycerols (TGs) in the serum. Furthermore, serum PChE activity was positively correlated with low-density lipoprotein (LDL) concentration, and inversely correlated with high-density lipoprotein (HDL) concentration [5,6]. In animal experiments, the induction of diabetes caused a rise in both PChE activity and serum TG concentrations, while treatment with insulin resulted in normalization of these changes. Administration of a specific inhibitor of PChE after induction of diabetes in these animals also reversed hypertriglyceridaemia [7]. In a study of patients with Type I or Type II diabetes, PChE activity was correlated positively with TG concentrations and inversely with insulin sensitivity [8]. These observations suggest a relationship between PChE activity and TG metabolism. However, a metabolic basis for such a relationship is lacking so far, and the rationale for the connection between PChE activity and TG synthesis is unclear.

Elevated serum TG and VLDL-TG concentrations are often observed in patients with Type II diabetes mellitus, as a result of enhanced VLDL synthesis and/or impaired removal of TG-rich lipoproteins [9]. Apolipoprotein E (apoE) plays an important role in the clearance of TG-rich lipoproteins, by acting as a ligand for the apoB/E and apoE receptors [10]. The receptor-binding capacity differs with respect to the circulating apoE isoform. The affinity of the apoE2 isoform for binding to the apoB/E and apoE receptors is about 1% of that of isoforms apoE3 and apoE4 [11], resulting in impaired clearance of apoE2-containing lipoprotein remnants [12]. Thus it is very likely that hypertriglyceridaemia in patients with Type II diabetes with the apoE2 phenotype is caused, in part, by defective clearance of VLDL remnants. In contrast with apoE2, apoE4 binds more avidly to the apoE receptor [13]. Therefore hypertriglyceridaemia in patients with Type II diabetes with the apoE4 phenotype is assumed to be caused mainly by increased VLDL-TG synthesis. We are not aware of studies with patients with Type II diabetes in which the turnover of VLDL-TG has been measured in relation to their apoE phenotype. In light of the above, it could be speculated that serum PChE activity in patients with Type II diabetes with the apoE2 phenotype differs from that in those with the apoE4 phenotype.

Two classes of lipid-lowering agents with different mechanisms of action are currently in use in the treatment of hypertriglyceridaemia in patients with Type II diabetes [14]. Fibric acid derivatives induce TG lowering by increasing fatty acid oxidation in the liver and decreasing the hepatic secretion of TG-rich lipoproteins. Fibric acid derivatives also stimulate lipoprotein lipase activity, which promotes the catabolism of TG-rich lipoprotein particles [15]. Statins (3-hydroxymethylglutaryl-CoA reductase inhibitors) lower TG concentrations by raising the activity of apoB/E receptors [16], which enhances the removal of TG-rich remnant particles [17].

In the present study we tested our hypothesis that PChE activity is related to the rate of TG synthesis in patients with Type II diabetes. In a cross-sectional study, the association between serum PChE activity and serum lipid variables was determined for the different apoE phenotypes. In the second part of the study, the effects of treatment with bezafibrate or pravastatin on PChE activity and TG concentrations were investigated.

**MATERIALS AND METHODS**

**Subjects**

Insulin-treated patients with Type II diabetes were recruited from those consecutively attending the outpatient clinic of the Amstelveen Hospital. The diagnosis of Type II diabetes mellitus was based on the 1985 World Health Organisation criteria [18]. Patients treated with oral blood glucose-lowering agents were excluded from the study because of possible effects of these drugs on plasma lipids. Patients with glycated haemoglobin (HbA1c) levels of >10% were excluded, to avoid the influence of hyperglycaemia on serum lipid concentrations. Other exclusion criteria were primary hyperlipidaemia, secondary hyperlipidaemia due to hypothyroidism (three patients with a stable dose of thyroxine and normal levels of thyroid-stimulating hormone were included) or nephrotic syndrome, alcohol or drug use influencing carbohydrate and lipid metabolism, the use of immunosuppressive drugs, hepatitis or endocrine diseases, pancreatitis, porphyria and malignancy. The chronic use of diuretics, β-blocking agents and hormone replacement therapy was allowed, provided that no need for discontinuing treatment or changing the dose during the study was foreseen.

**Study design**

In study I, apoE phenotype was determined in 231 patients; PChE activity and lipid variables were investigated in 224 of these subjects (see the Results section). PChE activity and lipid variables were determined as the mean of two measurements taken within 1 year (with an interval of at least 3 months).

In study II, after a dietary lead-in period of at least 8 weeks, 45 dyslipidaemic patients (total cholesterol ≥5.0 mmol/l but <8.0 mmol/l; TG ≥1.8 mmol/l but <5.0 mmol/l) with Type II diabetes (nine with the E3E2 phenotype, 24 with the E3E3 phenotype and 12 with the E3E4 phenotype) were treated with either 40 mg of pravastatin or 400 mg of bezafibrate for 12 weeks. After a wash-out period of 10 weeks, patients 'crossed over' to the second treatment period with the other drug (pravastatin or bezafibrate) for 12 weeks. During the
Pseudocholinesterase in hyperlipidaemic Type II diabetes mellitus

Table 1 Characteristics of the 224 patients with Type II diabetes investigated in study I

Values are means ± S.D. Statistically significant differences (P < 0.05) between groups are indicated by: *E3E3 compared with E3E2; †E3E4 compared with E3E2. Reference ranges are as follows: fasting plasma glucose, 3.5–6.0 mmol/l; HbA1c, 3.5–6.5%; γ-Gt, 5–30 units/l.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>E3E2</th>
<th>E3E3</th>
<th>E3E4</th>
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<tbody>
<tr>
<td>n</td>
<td>34</td>
<td>146</td>
<td>44</td>
</tr>
<tr>
<td>Men (%)</td>
<td>13 (40.6%)</td>
<td>57 (46.3%)</td>
<td>25 (65.7)†</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.1±9.4</td>
<td>67.0±10.6</td>
<td>65.4±10.3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.4±7.9</td>
<td>28.4±5.0</td>
<td>28.2±4.7</td>
</tr>
<tr>
<td>Fasting plasma glucose (mmol/l)</td>
<td>9.6±2.4</td>
<td>9.6±2.5</td>
<td>9.0±2.6</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.8±2.2</td>
<td>8.2±1.1</td>
<td>7.9±1.2</td>
</tr>
<tr>
<td>Insulin dose (units/kg)</td>
<td>0.68±0.29</td>
<td>0.67±0.26</td>
<td>0.61±0.26</td>
</tr>
<tr>
<td>γ-Gt (units/l)</td>
<td>19.9±5.2</td>
<td>26.0±21.2</td>
<td>24.9±19.4</td>
</tr>
</tbody>
</table>

Laboratory evaluation

Blood samples were taken following an overnight fast of 12 h. PChE activity was measured using butyrylthiocholine iodide as substrate [20]. Cholesterol and TG were measured by standard enzymic methods (Boehringer Mannheim) on an Hitachi 911 analyser. The precision and accuracy of the cholesterol measurements were within the limits set by the NCEP Lipid Standardization Panel [20a]. The laboratory followed the certification protocol of the Department of Clinical Chemistry, University Hospital Dijkzigt, Rotterdam, The Netherlands.

In study I (227 patients), LDL cholesterol was calculated using the Friedewald formula [21], and HDL cholesterol concentrations were measured using a homogeneous enzymic assay (Boehringer Mannheim) on an Hitachi 911 analyser. This enzymic assay uses poly-(ethylene glycol)-modified enzymes and sulphated α-cyclodextrin and dextran sulphate [22]. In study II, LDL cholesterol concentrations were measured using β-quantification ultracentrifugation for removal of VLDL, and precipitation of LDL by MnCl. LDL cholesterol was measured using the CDC reference method [22].

ApoE phenotype was determined as described by Havekes et al. [23], by means of isoelectric focusing of a lipid-protein-enriched serum fraction on a polyacrylamide gel containing Ampholine (pH range 5–7). After electrophoresis, the serum protein fractions were transferred by electroblotting to a nitrocellulose membrane. This membrane was incubated with a goat anti-apoE specific antiserum and then with horseradish peroxidase-labelled rabbit anti-(goat IgG) antiserum. The apoE pattern develops after incubation with 4-chloro-1-naphthol as substrate, and was interpreted visually.

γ-Glutamyl transpeptidase (γ-Gt) and glucose were determined using standard techniques. HbA1c was measured using the Bio-Rad Diamat HPLC procedure.

Statistical analysis

Comparisons of patient characteristics between apoE groups were made using Student’s t-test. Continuous variables were compared using Student’s t-test. Correlation coefficients were calculated using the least-squares technique with Pearson’s correlation coefficient. Stepwise multiple linear regression analysis was used to estimate the effect of several variables on PChE activity. All tests were two tailed, and the P value was preset at <0.05 for statistically significant differences and correlations.

RESULTS

Study I

Because of the small numbers of subjects with the E2E2 and E4E4 phenotypes (one and two patients respectively), and the differential effects on plasma lipid concentrations of the E2E4 phenotype (four patients), PChE activity and lipid analyses were performed in 224 subjects with the three common phenotypes: E3E2, E3E3 and E3E4. Patient characteristics according to apoE phenotype are provided in Table 1. The E3E4 group contained dietary lead-in and wash-out periods, patients received placebo matching pravastatin or bezafibrate. Patients were instructed by a dietician to adhere to a low-fat (30% of energy; max. 10% saturated fat), low-cholesterol (max. 300 mg/day) diet [19], with appropriate energy intake to maintain a stable body weight during the study. Dietary compliance was checked by the dietician by means of a 24 h recall method at each visit during the study. Patients were asked not to make important changes in lifestyle during the study. Patient compliance to treatment was monitored by counting tablets at each visit. All patients gave informed consent, and approval was obtained from the local ethical committee. The study was conducted in accordance with the declaration of Helsinki.
Table 2  PChE activity and serum lipid concentrations in 224 patients with Type II diabetes with different apoE phenotypes

Values are means ± S.D. Statistically significant differences (P < 0.05) in lipid variables and PChE activity between groups are indicated by: *E3E2 compared with E3E3; †E3E3 compared with E3E4; ‡E3E4 compared with E3E2. Reference ranges for PChE: women, 2000–6700 units/ml; men, 2300–7400 units/ml.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>E3E2 (n = 34)</th>
<th>E3E3 (n = 146)</th>
<th>E3E4 (n = 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PChE (units/l)</td>
<td>6371 ± 1867</td>
<td>6752 ± 1478</td>
<td>6646 ± 1477</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>5.58 ± 1.40</td>
<td>5.85 ± 1.00‡</td>
<td>6.34 ± 1.09‡</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>3.24 ± 0.82*</td>
<td>3.73 ± 0.87†</td>
<td>4.17 ± 0.89‡</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.30 ± 0.46</td>
<td>1.33 ± 0.40</td>
<td>1.36 ± 0.49</td>
</tr>
<tr>
<td>TGs (mmol/l)</td>
<td>2.19 ± 0.79</td>
<td>1.79 ± 1.08</td>
<td>1.87 ± 1.35</td>
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</table>

PChE activity did not differ between apoE phenotype groups (Table 2), or between men and women. Total cholesterol concentrations were higher in the E3E4 group compared with the E3E2 and E3E3 groups. LDL cholesterol concentrations were highest in the E3E4 group and lowest in the E3E2 group. HDL cholesterol and TG concentrations did not differ significantly between apoE groups, although TG concentrations tended to be higher in the E3E2 group (Table 2). PChE activity was correlated positively with serum TG concentrations in the whole patient population (r = 0.84, P < 0.0001) and in the E3E3 (r = 0.34, P = 0.0001) and E3E4 (r = 0.50, P = 0.0014) groups. The strongest relationship was found in the E3E4 phenotype group (Figure 1). PChE activity was correlated inversely with HDL cholesterol concentrations in the E3E3 group (r = -0.19, P = 0.03) and in the E3E4 group (r = -0.52, P = 0.0009), but not in the E3E2 group. No significant correlations were found between PChE activity and age, gender, fasting glucose or γGt concentration. Stepwise multiple regression analysis with PChE activity as the dependent variable and serum TG, fasting glucose and HbA1c concentrations as independent variables showed that serum TG concentrations were the strongest predictor of PChE activity in the E3E3 and E3E4 groups. HbA1c was also an independent predictor of PChE activity in these groups. In the E3E2 group, no such relationship of either variable with PChE activity was established.

Study II: effects of treatment with pravastatin or bezafibrate on PChE activity and lipid variables

Baseline patient characteristics of the 45 dyslipidaemic patients with Type II diabetes that participated in study II did not differ from those of the whole group of patients.
Table 3  Changes in PChE activity and serum TG concentrations following treatment with pravastatin and bezafibrate in 45 dyslipidaemic patients with Type II diabetes

Drugs were administered for 12 weeks. Values are means ± S.D. Statistically significant differences (P < 0.05) are indicated as follows: *pravastatin treatment compared with baseline; †bezafibrate treatment compared with baseline; ‡between drug treatments. Reference ranges for PChE: women, 2000–6700 units/ml; men, 2300–7400 units/ml.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Pravastatin</th>
<th>Bezafibrate</th>
<th>Baseline</th>
<th>Pravastatin</th>
<th>Bezafibrate</th>
<th>Baseline</th>
<th>Pravastatin</th>
<th>Bezafibrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PChE (units/l)</td>
<td>7543 ± 1726</td>
<td>−131 ± 197</td>
<td>−546 ± 413</td>
<td>7461 ± 899</td>
<td>−134 ± 459</td>
<td>−348 ± 498</td>
<td>7190 ± 852</td>
<td>174 ± 541</td>
<td>−241 ± 498</td>
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<tr>
<td>Total TG (mmol/l)</td>
<td>3.22 ± 0.93</td>
<td>−0.73 ± 0.96</td>
<td>−1.37 ± 0.97</td>
<td>2.79 ± 1.25</td>
<td>−0.41 ± 0.81</td>
<td>−1.10 ± 0.60</td>
<td>3.10 ± 1.65</td>
<td>−0.60 ± 0.96</td>
<td>−0.93 ± 0.75</td>
</tr>
<tr>
<td>VLDL-TG (mmol/l)</td>
<td>2.71 ± 0.92</td>
<td>−0.65 ± 0.91</td>
<td>−1.30 ± 0.90</td>
<td>2.27 ± 1.17</td>
<td>0.28 ± 0.77</td>
<td>−1.03 ± 0.57</td>
<td>2.54 ± 1.57</td>
<td>0.50 ± 0.84</td>
<td>−0.83 ± 0.70</td>
</tr>
<tr>
<td>LDL-TG (mmol/l)</td>
<td>0.31 ± 0.08</td>
<td>−0.09 ± 0.10</td>
<td>−0.04 ± 0.08</td>
<td>0.31 ± 0.10</td>
<td>0.08 ± 0.08</td>
<td>0.05 ± 0.13</td>
<td>0.37 ± 0.13</td>
<td>0.08 ± 0.08</td>
<td>0.00 ± 0.11</td>
</tr>
<tr>
<td>HDL-TG (mmol/l)</td>
<td>0.19 ± 0.03</td>
<td>0.01 ± 0.07</td>
<td>−0.03 ± 0.04</td>
<td>0.19 ± 0.06</td>
<td>0.02 ± 0.05</td>
<td>−0.05 ± 0.05</td>
<td>0.18 ± 0.05</td>
<td>−0.02 ± 0.04</td>
<td>−0.05 ± 0.05</td>
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</table>

In study I, PChE activity and lipid variables at baseline and after treatment with either pravastatin or bezafibrate are provided in Table 3. PChE activity at baseline did not differ between the apoE groups. For comparison of baseline lipid concentrations between apoE subgroups, baseline values of both treatment periods were summarized. Baseline concentrations of total TG, VLDL-TG, HDL-TG and HDL cholesterol did not differ between the apoE groups.

Pravastatin treatment did not significantly influence PChE activity in any of the three apoE phenotype groups. However, bezafibrate treatment lowered PChE activity significantly in the E3E2 group (7.2%; P = 0.0057) and in the E3E3 group (4.7%; P = 0.00276), but not in the E3E4 group.

Baseline lipid concentrations were similar at the start of each treatment period. Bezafibrate decreased total serum TG concentrations more effectively than did pravastatin in the total group of 45 patients, and also lowered total TG, VLDL-TG and HDL-TG concentrations more effectively in the E3E3 group. LDL-TG in the E3E3 group was lowered more effectively by pravastatin than by bezafibrate treatment.

Control parameters

Glycaemic control was monitored on the basis of fasting glucose concentration and HbA1c level. Pravastatin treatment induced a small but significant increase in HbA1c concentration in the E3/E3 group (6.2%; P < 0.05) and the E3/E4 group (4.5%; P < 0.001), while bezafibrate treatment induced significant decreases in fasting glucose (20.6%; P < 0.001) and HbA1c (4.6%; P < 0.05) in the E3/E3 group (all compared with baseline). Body mass index did not change significantly during either treatment period in any apoE group. During the study, the amount of insulin used and the %Gt concentration did not change. No serious adverse events were reported in either treatment period, and none of the patients discontinued the study. Compliance with trial medication was > 90%.

Discussion

In the present study we found a positive association between PChE activity and serum TG concentrations in insulin-treated patients with Type II diabetes. To prevent the influence of various glucose-lowering therapies on lipid concentrations, we included patients with Type II diabetes treated with insulin and by diet only. Hypertriglyceridaemia in these patients is caused by increased synthesis and/or defective clearance of TG-rich lipoproteins.

Plasma apoE plays a key role in the receptor-mediated uptake of remnant lipoproteins by the liver, and thus in the regulation of plasma lipoprotein concentrations [24]. ApoE may also play a role in facilitating the hepatic secretion of VLDL-TG [25,26]. For example, in non-diabetic normolipidaemic subjects with the E2E2 and E4E4 phenotypes, the rate of VLDL synthesis was found to be reduced compared with that in subjects with the E3E3 phenotype [27]. In our study, we used apoE phenotyping to identify diabetic patients with normal (E3E3), enhanced (E3E4) and impaired (E3E2) removal of remnant lipoprotein particles by the liver. In diabetic subjects with the E3E2 isoform, impaired removal of TG-rich remnant particles may contribute to the development of hypertriglyceridaemia [28]. In subjects with
the E3E4 isoform, hypertriglyceridaemia is probably caused mainly by increased VLDL-TG synthesis.

In study I, a cross-sectional investigation in 224 subjects with Type II diabetes, PChE activity and serum TG concentrations did not differ significantly between the three apoE groups studied. Group mean PChE activity tended to be lower in the E2E3 than in the E3E4 group, in spite of a higher mean serum TG concentration in the former (Table 2). Although not conclusive due to the lack of statistical significance, the difference in PChE activity between the E2E3 and E3E4 phenotypes is in agreement with our expectation. In other words, low PChE activity might be associated with low TG synthesis, whereas high activities of PChE might be associated with high rates of VLDL-TG synthesis. We found a positive correlation between PChE activity and serum TG concentration (Figure 1). The strongest relationship between PChE activity and serum TG concentration was observed in the E3E4 group. Stepwise multiple regression analysis showed that serum TG concentrations were the strongest predictor for PChE activity in the E3E3 and E3E4 groups, but not in the E3E2 group. Thus, in our patients with Type II diabetes with the E3E4 phenotype, in which hypertriglyceridaemia is expected to be the result of increased VLDL-TG synthesis, we found a significant correlation between PChE activity and serum TG concentrations. PChE activity was correlated inversely with HDL cholesterol concentrations in the E3E3 and E3E4 groups, but not in the E3E2 group.

In study II, 45 dyslipidaemic, insulin-treated patients with Type II diabetes were treated separately with pravastatin and bezafibrate in a cross-over design. PChE activity was lowered by bezafibrate treatment in all three apoE isoform groups. Bezafibrate effectively decreased total TG, VLDL-TG and HDL-TG concentrations, with the effect on serum total TG concentration being greatest in the E3E2 group and least in the E3E4 group. The effect of bezafibrate in lowering PChE activity paralleled the decreases in serum TG concentration in the three apoE groups, being greatest in the E2E3 group and least in the E3E4 group. Pravastatin treatment decreased serum total TG concentrations less effectively than did bezafibrate, but lowered the LDL-TG concentration more effectively in all apoE phenotype groups. The effect of pravastatin in lowering LDL-TG can be attributed to up-regulation of apoB/E receptor activity, resulting in enhanced clearance of LDL. Pravastatin treatment did not affect PChE activity, confirming an earlier report [29], and induced a moderate increase in HbA1c levels, while bezafibrate treatment induced decreases in both fasting glucose and HbA1c. These changes could not be attributed to changes in body weight or insulin dose.

The present study, on insulin-treated patients with Type II diabetes, extends previous observations showing a positive association between PChE activity and serum TG concentration. By dividing our patients into different apoE isoform groups, and by subjecting them to TG-lowering drug treatments, we have attempted to test our hypothesis that PChE activity is related to TG synthesis, even though we did not measure TG synthesis directly. The data obtained are in line with and extend previous observations suggesting that PChE activity and TG synthesis are associated. Measurement of PChE activity may be a useful tool in the choice of drug for the treatment of hypertriglyceridaemia in patients with Type II diabetes.

REFERENCES


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