Original Article

Effects of Telmisartan Compared with Eprosartan on Blood Pressure Control, Glucose Metabolism and Lipid Profile in Hypertensive, Type 2 Diabetic Patients: a Randomized, Double-Blind, Placebo-Controlled 12-Month Study

Giuseppe DEROSA, Pietro D. RAGONESI*, Amedeo MUGELLINI, Leonardina CICCARELLI, and Roberto FOGARI

We evaluated the antihypertensive activity, glucose homeostasis and plasma lipid profile in patients with mild hypertension and type 2 diabetes mellitus treated by diet and exercise, and not in receipt of oral hypoglycemics, following 12-month treatment with either telmisartan or eprosartan. In this double-blind, placebo-controlled trial, 119 patients with mild essential hypertension (diastolic blood pressure [DBP] 91–104 mmHg) and type 2 diabetes were divided into three groups and randomized to receive once-daily telmisartan 40 mg, eprosartan 600 mg, or placebo for 12 months. At enrollment, patients were advised on diet (1,400–1,600 kcal/day) and exercise (physical aerobics on a bicycle for at least 30 min on 4 days each week). Compared with baseline, a significant reduction (p < 0.01) in seated trough systolic blood pressure (SBP) was detected after 12-month treatment with either telmisartan or eprosartan. Seated trough DBP was also reduced by telmisartan (p < 0.01) and eprosartan (p < 0.05); the antihypertensive effect of telmisartan was significantly superior (p < 0.05). No change in body mass index or glucose metabolism was observed with either active treatment, or with placebo. Telmisartan, but not eprosartan, significantly improved plasma total cholesterol (p < 0.01), low-density lipoprotein cholesterol (p < 0.01) and triglycerides (p < 0.05) compared with eprosartan. In conclusion, 12-month telmisartan treatment produced a significantly greater reduction in DBP than eprosartan and significantly improved plasma lipids. The improvement could be due to varying pharmacokinetic/pharmacodynamic properties of telmisartan compared with eprosartan, even if it is not clear about the relationship between angiotensin-II receptor blockade and 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibition. (Hypertens Res 2004; 27: 457–464)

Key Words: type 2 diabetes mellitus, telmisartan, eprosartan, lipid profile, glucose metabolism

Introduction

The incidence of hypertension in the diabetic population is 1.5–3 times higher than in non-diabetic age-matched individuals (1). In addition, the risk of any cardiovascular event or stroke is almost doubled when the hypertensive patient has diabetes mellitus (2). The lowering of blood pressure markedly decreases the rate of cardiovascular events and renal deterioration in these patients (3).

Diabetic patients exhibit a number of characteristic changes in plasma lipoproteins, including elevated triglyc-
erides (TG) and reduced high-density lipoprotein cholesterol (HDL-C) levels, with total cholesterol (TC) commonly remaining at or close to the normal range (4). Several classes of antihypertensive drugs can alter lipid metabolism (5).

Two classes of antihypertensive agents—angiotensin-converting enzyme (ACE) inhibitors and angiotensin-II receptor blockers (ARBs)—target the renin–angiotensin–aldosterone system (RAAS) and control the action of angiotensin II, which is responsible for elevated blood pressure and pathogenesis in the cardiovascular system (6). Metabolic abnormalities that are frequently associated with hypertension, such as insulin resistance and lipid profile impairment, can be improved by ACE inhibitors (7). In addition, ACE inhibitors have been shown to have no adverse effects on glycemia or lipid profile (8, 9) and may have special protective properties against vascular and renal toxic effects of metabolic abnormalities (10).

Compared with ACE inhibitors, the ARBs offer more complete blockade of the RAAS (11), specifically inhibiting the actions of angiotensin II at the level of the angiotensin-II type 1 (AT1) receptor. The ARBs are well tolerated and do not appear to cause cough, a side-effect relatively frequently observed in patients treated with ACE inhibitors (12). Many patients find this dry, persistent cough unacceptable; thus, the superior tolerability profile of the ARBs may translate into improved compliance compared with ACE inhibitors. There are, however, few clinical data on the action of ARBs on metabolic parameters (13–17).

Telmisartan is an ARB that is highly selective for the AT1 receptor (18). Unique pharmacological features of telmisartan include a long duration of action, as a result of a long terminal elimination half-life of about 24 h (18). At the recommended once-daily doses of 40 and 80 mg, telmisartan has demonstrated good antihypertensive efficacy in double-blind, randomized, placebo-controlled clinical trials in both men and women with mild-to-moderate hypertension (18).

Eprosartan is the first non-biphenyl, non-tetrazole ARB to be used clinically (19). Unlike telmisartan, which has a high volume of distribution of about 500 l (18), that of eprosartan is less than 131 (20). Also, the terminal elimination half-life of eprosartan following oral administration is only 5–7 h (20), and it has a short duration of action (21). Unlike other ARBs, eprosartan appears to inhibit prejunctural and postsynaptic AT1 (22), but the clinical implications are unknown. In clinical trials, at the recommended dose of 600 mg once daily, eprosartan has been shown to be as effective an antihypertensive as enalapril or losartan (19); there has, however, been no direct comparison of the antihypertensive efficacy of eprosartan with that of telmisartan. Furthermore, there are no data directly comparing ARBs in hypertensive patients with diabetes mellitus.

In this double-blind, placebo-controlled study, we evaluated glucose homeostasis and plasma lipid profile in patients with mild hypertension and type 2 diabetes mellitus controlled by diet and exercise alone after 12-month treatment with either telmisartan or eprosartan.

Methods

Patients

Patients with type 2 diabetes, according to the American Diabetes Association criteria (23), were eligible for inclusion. All patients were required to have been diagnosed as being diabetic for at least 2 years. During this time, diabetes had been treated exclusively by diet and exercise in accordance with the American Association of Clinical Endocrinologists for intensive diabetes self-management guidelines (24); oral hyperglycemics had not been prescribed. In addition, all patients had to display mild essential hypertension according to the World Health Organization—International Society of Hypertension criteria (i.e., diastolic blood pressure [DBP] 90–99 mmHg) on repeated measurements (25). Patients with secondary hypertension, malignant hypertension, unstable angina, myocardial infarction within the preceding 6 months, liver dysfunction or renal impairment, or contraindications for or already receiving ARBs or ACE inhibitors were excluded. Eligible patients were fully informed of the aim of the study, and their written informed consent was obtained.

Study Design

This 12-month, randomized, double-blind, placebo-controlled trial was performed in accordance with the principles of the Declaration of Helsinki and was approved by the local Ethics Committee. It was conducted in the Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy.

At the time of enrollment, there was reinforcement of the importance of diet (1,400–1,600 kcal/day: 54% carbohydrates, 24% proteins, 22% lipids [6% saturated], 108 mg cholesterol and 35 g fiber) and patients were instructed to maintain the same diet throughout the study. Alcohol consumption was not permitted during the study, and patients were not allowed to take any other drugs, including oral hyperglycaemics or hypocholestermic agents, or vitamin and/or mineral supplements. Dietary intake was recorded in a diary, which was reviewed by dieticians as part of the continued life-style modification program. In addition, patients were required to perform exercise on a bicycle for a minimum of 30 min on 4 days each week as recommended by the American Association of Clinical Endocrinologists for intensive diabetes self-management (24). Exercise compliance was discussed with the patient at each clinic visit.

After an initial 4-week, placebo wash-out period, patients were randomized to receive once-daily telmisartan 40 mg, eprosartan 600 mg, or placebo for 12 months. Patients were instructed to take their medication in the morning after breakfast, except on the days of clinic visits. On these occasions, the assigned drug was taken after blood pressure mea-
asurements had been performed at the clinic. This was to ensure that trough blood pressures (i.e., at the end of the dosing interval) were recorded.

At the end of the placebo wash-out phase (baseline) and after 6 and 12 months of randomized treatment, body mass index (BMI; 12 months only), fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), fasting plasma insulin (FPI), homeostasis model assessment of insulin resistance (HOMA-IR), seated trough systolic blood pressure (SBP), seated trough DBP, and lipid profile (plasma TC, low-density lipoprotein cholesterol [LDL-C; 12 months only], HDL-C and TG concentrations) were evaluated. Patients were also assessed for evidence of macroangiography (by electrocardiography and Doppler examination), microalbuminuria and neuropathy (vibration perception threshold) during the baseline visit.

Blood pressure was measured using a standard mercury sphygmomanometer (Korotkoff I and V) with a cuff of appropriate size on the right arm. Measurements were always taken by the same investigator in the morning after the subject had been seated and resting for 10 min in a quiet room and before the once-daily intake of the randomized medication. The average of three successive measurements obtained at 1-min intervals was recorded. Heart rate was monitored at each clinical visit after the patient had been seated for at least 10 min.

Adverse events, intercurrent diseases, and patient compliance to the dosing regimen (assessed by counting the number of pills returned at the clinic visits) were monitored at 12-week intervals during the randomized, double-blind treatment phase. Safety monitoring included physical examination, vital signs assessment, weight and height measurement, and laboratory tests.

Laboratory Evaluations

The patients entered the research unit between 8:00 and 9:00 AM, after a 12-h overnight fast. All samples collected were transported within 4 h to a central laboratory at the authors’ hospital. A total of 15 ml blood (3 ml for HbA1c, 2 ml for FPG, 5 ml for FPI and 5 ml for lipid profile) was collected.

Plasma was obtained by centrifugation at 1,000 g for 25 min at 4°C and was assayed for TC and TG using enzymatic methods (TC, CHOD-PAP (colorimetric method); TG, TG without free glycerol; HITACHI 737; Hitachi, Tokyo, Japan). Determination of HDL-C was performed after the precipitation of 1.006 g/ml infranatant with dextran sulfate–magnesium chloride (26). LDL-C was measured by subtracting the HDL-C value from the infranatant TC value. The interassay coefficients of variation were 2.7% for TC, 9.1% for HDL-C and 2.0% for TG. Plasma glucose was assayed by the hexokinase/glucose-6-phosphate dehydrogenase method using a COBAS Mira Plus autoanalyzer (Hoffmann-La Roche, Basel, Switzerland). The interassay coefficient of variation for glucose was 3.0%. Insulin was determined using Phadi-aseph Insulin radioimmunoassay (Pharmacia, Uppsala, Sweden). HbA1c was measured by aminophenylboronic acid affinity chromatography (DIAMAT, Bio-Rad, Richmond, USA; normal values 4.2–6.2%), with intra- and interassay coefficients of variation of <2% (27), and plasma insulin concentrations were assayed using a radioimmunoassay kit (CEA Sorin, Saluggia, Italy). The HOMA-IR was calculated using the following formula as described by Matthews and coworkers (28):

\[
\text{HOMA-IR} = \frac{\text{FPI} (\mu U/ml) \cdot \text{FPG} (\text{mmol/l})}{22.5}
\]

Statistical Analysis

Data analysis was performed by means of the SPSS statistical software package for Windows (version 9.0; SPSS Inc., Chicago, USA); results were expressed as the mean ± SD. One-way analysis of variance (ANOVA) was used to compare baseline data. Change was calculated as the value obtained at the end of 12-month treatment minus the value obtained at baseline. ANOVA was also used to assess the significance within and between groups. A one-sample Student’s t-test was used to compare values obtained before and after treatment, and two-sample t-tests were used for between-group comparison. Values of \( p < 0.05 \) were considered significant.

Results

Patient Demographics

Baseline characteristics of the 119 enrolled patients with long-standing type 2 diabetes mellitus controlled by an intensive diabetes self-management scheme (24) randomized to double-blind treatment with telmisartan 40 mg, eprosartan 600 mg, or placebo for 12 months were comparable (Table 1). The patients were non-smokers, had adequate glycemic control (HbA1c <7.0%), were not taking hypocholesterolemic drugs and did not have any evidence of macroangiopathy, nephropathy (albumin excretion rate <30 mg/24 h, performed on overnight urine collections) or neuropathy. Hypertension was recently diagnosed in >40% of the patients, but the self-management scheme for 3–6 months had failed to lower blood pressure sufficiently. The study participants who had received prior antihypertensive therapy (24 in the telmisartan group, 26 in the eprosartan group, and 21 in the placebo group) were taken off their medication for at least 4 weeks to avoid carry-over effects. Prior treatment consisted predominantly of calcium channel blockers, \( \beta \)-blockers, antiadrenergic agents or diuretics; the nature of the medication did not differ between the treatment groups.

Blood Pressure Control

After 6 months of treatment, both telmisartan and eprosartan significantly (\( p < 0.05 \)) reduced SBP compared with baseline (Table 2). There was also a significant (\( p < 0.05 \)) decrease in
DBP in telmisartan-treated patients compared with baseline. At the end of the 12-month double-blind treatment, both telmisartan and eprosartan brought about a significant reduction ($p<0.01$) in seated trough SBP compared with baseline, whereas no significant reduction was observed in the placebo group. The mean ± SD reductions in SBP were 8 ± 2 mmHg for telmisartan and 7 ± 2 mmHg for eprosartan. Significant reductions in trough DBP compared with baseline were also noted with telmisartan ($p<0.01$) and eprosartan ($p<0.05$), but not with placebo. The mean ± SD reductions in SBP were 8 ± 2 mmHg for telmisartan and 4 ± 1 mmHg for eprosartan. The post-treatment trough DBP was significantly lower ($p<0.05$) in the telmisartan group compared with the eprosartan group. No significant changes in heart rate compared with baseline were observed in any of the treatment groups.

### Glucose Metabolism

Telmisartan, eprosartan, or placebo administration for 6 and 12 months did not result in any changes in BMI, HbA1c, FPG, FPI, or HOMA-IR compared with baseline, and there were no significant differences in any of these parameters for patients receiving the active treatments compared with those in the placebo group (Table 3).

### Lipid Profile

After 6-month telmisartan treatment, there was a significant reduction in plasma TC (Table 4). At 12 months, telmisartan treatment resulted in a significant reduction in plasma TC ($p<0.01$), LDL-C ($p<0.01$) and TG ($p<0.05$) compared with baseline. By contrast, there were no significant changes compared with baseline in the lipid profile of patients who had received eprosartan or placebo for 12 months. The reductions in lipid levels achieved with telmisartan were significantly greater ($p<0.05$) than those by eprosartan.

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**Table 1.** Demographics and Baseline Characteristics (Mean ± SD) of Hypertensive Patients with Type 2 Diabetes Mellitus Randomized to Treatment with Telmisartan 40 mg, Eprosartan 600 mg, or Placebo for 12 Months

<table>
<thead>
<tr>
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<th>Telmisartan</th>
<th>Eprosartan</th>
<th>Placebo</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>6 months</td>
<td>12 months</td>
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<tr>
<td>SBP (mmHg)</td>
<td>143 ± 5</td>
<td>139 ± 4**</td>
<td>135 ± 4**</td>
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<tr>
<td>DBP (mmHg)</td>
<td>92 ± 3</td>
<td>87 ± 4</td>
<td>84 ± 3**</td>
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* $p<0.05$ vs. baseline. ** $p<0.01$ vs. baseline. \(^* p<0.01\) vs. placebo at 6 months. \(^\ddagger p<0.01\) vs. placebo at 12 months.

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**Table 2.** Effect of Telmisartan 40 mg, Eprosartan 600 mg and Placebo Administration for 6 and 12 Months on Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)

<table>
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Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)

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<tr>
<td><strong>Telmisartan</strong></td>
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<td>140 ± 5**</td>
<td>137 ± 5**</td>
<td>143 ± 4</td>
<td>142 ± 4</td>
<td>141 ± 4</td>
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<tr>
<td><strong>Eprosartan</strong></td>
<td>92 ± 3</td>
<td>87 ± 4</td>
<td>84 ± 3**</td>
<td>91 ± 4</td>
<td>89 ± 5</td>
<td>87 ± 5**</td>
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* $p<0.05$ vs. baseline. ** $p<0.01$ vs. baseline. \(^* p<0.01\) vs. placebo at 6 months. \(^\ddagger p<0.01\) vs. placebo at 12 months.
Table 3. Effect of Telmisartan 40 mg, Eprosartan 600 mg and Placebo Administration for 6 and 12 Months on Body Mass Index (BMI) and Glucose Metabolism in Hypertensive Patients with Type 2 Diabetes Mellitus

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<td></td>
<td>Baseline</td>
<td>6 months</td>
<td>12 months</td>
<td>Baseline</td>
<td>6 months</td>
<td>12 months</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.9 1.2</td>
<td>26.7 1.1</td>
<td>26.5 1.0</td>
<td>26.4 1.3</td>
<td>36.3 1.2</td>
<td>26.2 1.2</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.4 0.2</td>
<td>6.4 0.4</td>
<td>6.3 0.3</td>
<td>6.3 0.3</td>
<td>6.2 0.3</td>
<td>6.2 0.4</td>
</tr>
<tr>
<td>FPG (mg/dl)</td>
<td>128 14</td>
<td>125 16</td>
<td>123 15</td>
<td>130 16</td>
<td>131 17</td>
<td>128 7</td>
</tr>
<tr>
<td>FPI (µU/ml)</td>
<td>19.4 3.8</td>
<td>19.3 4.0</td>
<td>19.1 3.9</td>
<td>19.2 4.1</td>
<td>19.1 3.9</td>
<td>19.0 4.0</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>5.1 3.6</td>
<td>5.0 3.6</td>
<td>4.9 3.5</td>
<td>5.3 3.8</td>
<td>5.2 3.7</td>
<td>5.1 3.6</td>
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HbA1c, glycosylated hemoglobin; FPG, fasting plasma glucose; FPI, fasting plasma insulin; HOMA-IR, homeostasis assessment model of insulin resistance.

Table 4. Effect of Telmisartan 40 mg, Eprosartan 600 mg and Placebo Administration for 6 and 12 Months on Serum Lipid Profile in Hypertensive Patients with Type 2 Diabetes Mellitus

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<td>6 months</td>
<td>12 months</td>
<td>Baseline</td>
<td>6 months</td>
<td>12 months</td>
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<tr>
<td>TC (mg/dl)</td>
<td>195 18</td>
<td>186 19*</td>
<td>180 20**</td>
<td>193 20</td>
<td>192 21</td>
<td>190 19**</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>130 11</td>
<td>122 17*</td>
<td>119 18**</td>
<td>125 22</td>
<td>127 19</td>
<td>124 20</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>42 5</td>
<td>44 5</td>
<td>43 4**</td>
<td>42 4</td>
<td>40 5</td>
<td>41 5</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>125 32</td>
<td>112 31</td>
<td>94 30*</td>
<td>129 30</td>
<td>126 29</td>
<td>121 28</td>
</tr>
</tbody>
</table>

*p<0.05 vs. baseline. **p<0.01 vs. baseline. 0.05 vs. placebo at 12 months. 0.05 vs. eprosartan at 12 months. TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides.

Safety

During the initial 4-week, placebo wash-out period, three patients experienced mild adverse events: fatigue in two patients and headache in one patient. During the 12-month double-blind treatment period, five patients reported mild adverse events: fatigue in one in the telmisartan group and one in the placebo group, dizziness in two in the eprosartan group and headache in one in the placebo group.

Compared with placebo, no serious adverse effects occurred in patients in the telmisartan or eprosartan group. No event resulted in withdrawal from the study.

Discussion

In patients with type 2 diabetes mellitus, the aim is to prevent the emergence of insulin resistance, maintain a favorable lipid profile, and control hypertension in order to minimize cardiovascular complications and improve patient prognosis. This may be achieved using an intensive system of diabetes self-management, with a diabetes management team including dieticians playing a critical role (24). The coordinated efforts of the team are reflected in the normalization of the patients’ glycosylated hemoglobin and free plasma glucose by intensive life-style modification in the patients at baseline, despite the patients having been diabetic for at least 2 years. This approach was continued during the study, with regular counseling sessions to reinforce the benefits of the required exercise and diet.

Nevertheless, pharmacological intervention may be necessary to control blood pressure and minimize cardiovascular complications. The present study comprised patients who were mildly hypertensive. The importance of angiotensin II in the pathophysiology of cardiovascular disease is well known (6), and there is evidence that overactivity of the RAAS may impair the intracellular response to insulin signaling (29). The ACE inhibitors have been shown, in addition to providing effective blood pressure control, not to have any negative effect on glycemia or insulin sensitivity (30). Recently, the relationship between cardiovascular disease, the metabolic syndrome, diabetes and hypertension and the role of peroxisome proliferator-activated receptor-γ (PPARγ) has been demonstrated (31). Preliminary data suggest that the ARB telmisartan increases PPARγ activity and may provide additional benefits in the treatment of type 2 diabetes (32).

Clinical studies have indicated that, for ARBs, reductions in blood pressure are comparable to those achieved with ACE inhibitors (33). In addition, the beneficial effects of a low dose of an ARB in the prevention of target organ damage have been demonstrated in mildly hypertensive patients with type 2 diabetes, with prevention of early kidney damage being independent of the antihypertensive activity (34). To date, the ARBs valsartan, losartan, and candesartan cilexetil given for periods of up to 12 weeks have been shown not to affect glucose homeostasis (16, 35, 36) and, when given for a
period of 12 weeks, valsartan and candesartan cilexetil did not adversely affect the lipid profile of diabetic patients with hypertension (16, 36). Only one study has evaluated the longer-term impact on lipid profiles in diabetic patients (17). Derosa et al., comparing the ACE inhibitor perindopril and the ARB candesartan cilexetil after 12-month administration, found that only perindopril produced significant improvements in metabolic parameters.

In the present study, at the end of the 12-month active treatment, once-daily telmisartan provided significantly superior control of trough DBP compared with once-daily eprosartan. However, there was no significant difference in the reduction in SBP achieved with telmisartan or eprosartan. It should be noted that the 40 mg dose was the lower of the two telmisartan monotherapy doses recommended for the treatment of hypertension. The recommended dose range for the former is 400–800 mg; the starting dose is usually 600 mg, with an increase to 800 mg if the response is insufficient to achieve target blood pressure. In the present study, the ARB dose remained unaltered throughout the treatment period.

The significantly greater reduction in trough (i.e., at the end of the dosing interval) DBP with telmisartan compared with eprosartan observed in this study may be attributed to the former’s longer terminal elimination half-life compared with that of eprosartan (18, 20). The advantages of the longer action of telmisartan may extend to the prevention of cardiovascular events, which follow a similar circadian pattern, with an increase in their incidence being associated with the early morning blood pressure surge (37). For a drug with a short half-life taken in the morning, the time of maximal cardiovascular risk is likely to coincide with a period of suboptimal blood pressure control.

The comparable reduction in SBP in both the telmisartan and eprosartan groups observed in the present study may be explained by the SBP being related to sympathetic activity. Preclinical data suggest that eprosartan exerts sympathoinhibitory activity (38). In another study comparing eprosartan 400 mg twice daily with enalapril 10 mg once daily in the treatment of severe hypertension, the effects of the two antihypertensive agents on DBP were comparable, whereas eprosartan brought about a significantly superior reduction of SBP (39).

The importance of aggressive blood pressure control in patients with type 2 diabetes in reducing cardiovascular complications has been demonstrated by the UK Prospective Diabetes Survey (3). In patients achieving a blood pressure of 144/82 mm Hg, risks of heart failure, stroke and any diabetes-related endpoint were all significant reduced. The Hypertension Optimal Treatment study subsequently showed that intensive blood pressure control to 130/85 mm Hg by the use of a combination of antihypertensive drugs resulted in further risk reduction (40). A reduction of blood pressure to such a degree may be difficult to achieve, and a more realistic target is 135/85 mm Hg. In the telmisartan treatment group, after 1-year treatment, the SBP/DBP was 135/4/84 3 mm Hg using the lower recommended once-daily dose of 40 mg compared with values of 137/5/87 5 mm Hg for eprosartan 600 mg given once daily.

The absence of changes in FPG, HbA1c, FPI, or HOMA-IR may be partly attributed to the continuation of a diet and exercise regime that the patients had followed since the diagnosis of diabetes at least 2 years before enrollment into this study. Other studies have not necessarily adopted an intensive regime for the self-management of diabetes as recommended by the American Association of Clinical Endocrinologists (24), and this may impact metabolic parameters.

The plasma lipid profile of diabetic patients is especially important given the high incidence of atherosclerosis in diabetic patients (41). In comparison with once-daily eprosartan 600 mg, telmisartan treatment at a dose of 40 mg once daily resulted in a significant reduction in plasma LDL-C, TC, and TG levels. With eprosartan, lipid levels were similar to those observed in placebo-treated patients maintained on a strict diet with restricted fat intake. This distinction between telmisartan and eprosartan may possibly be explained by the high lipophilicity of telmisartan compared with eprosartan and other ARBs (42) and the PPARγ-modulating effect of telmisartan (34). Other structural differences among the ARBs may also contribute to the possible differences in metabolic profiles; however, other than this study there are currently no head-to-head comparisons of different antihypertensives of this class.

These results suggest that there are differences between ARBs. Telmisartan, after administration for 12 months, conferred significant advantages compared with eprosartan in terms of blood pressure control and plasma lipid levels in diabetic patients with hypertension. No data are available on the relationship between ARB and 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibition. It is possible that telmisartan, because of its long duration of action, may have additive effects on the inhibition of HMG-CoA reductase and other mechanisms controlling metabolic disorders. Further studies are required to assess such possibilities.

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