Doxazosin and Captopril in Mildly Hypercholesterolemic Hypertensive Patients

The Doxazosin-Captopril in Hypercholesterolemic Hypertensives Study

L. Aldo Ferrara, Lucrezia Di Marino, Ornella Russo, Teodoro Marotta, and Mario Mancini
on behalf of the DoCHH Study Group

The evidence linking hypertension and hypercholesterolemia is strong and has fueled research into possible adverse effects of some antihypertensive agents on serum lipid profile. This multicenter, open, parallel study compares the effects of doxazosin and captopril on blood pressure, serum lipid levels, and quality of life in 224 hypercholesterolemic hypertensive patients. Blood pressure was significantly reduced in both treatment groups (p<0.001) and was normalized (standing diastolic pressure ≤90 mm Hg) in 73% of the doxazosin patients and 67% of the captopril group. Serum total cholesterol level was favorably reduced by both doxazosin (from 238 to 223 mg/dl, p<0.001) and captopril (from 245 to 233 mg/dl, p<0.001), whereas high density lipoprotein cholesterol concentration increased only in the doxazosin group (from 33 to 36 mg/dl, p<0.001). The calculated 10-year risk for the development of coronary heart disease was reduced significantly (p<0.001) by 28% in the doxazosin group and by 19% in the captopril group. The quality of life evaluation showed beneficial changes in both treatment groups. As a result of proven antihypertensive efficacy and a lack of unfavorable effects on lipid parameters and health status measures, these findings support the use of both doxazosin and captopril as agents of first choice in the treatment of hypertensive patients with associated lipid abnormalities. (Hypertension 1993;21:97-104)

KEY WORDS • captopril • hypertension, essential • hypercholesterolemia • coronary disease • risk factors • quality of life • doxazosin

There is a growing awareness that antihypertensive therapy should be selected on the basis of more than a simple reduction of blood pressure. Clinicians must consider the full range of benefits and risks associated with treatment. For example, patients with hypertension and elevated serum total cholesterol levels are known to have an increased risk of coronary heart disease (CHD) developing.1,2 The antihypertensive agent selected should not adversely affect the serum lipid profile and unfavorably alter CHD risk.3 The effects of antihypertensive agents on a patient’s quality of life are also becoming important considerations in the selection of an appropriate therapy.4

Selective α1-inhibitors and angiotensin converting enzyme (ACE) inhibitors offer many advantages in the treatment of hypertension. Selective α1-inhibitors, unlike many traditional antihypertensive agents, do not adversely affect serum lipid levels.5 ACE inhibitors have been shown to score more favorably than either methyldopa or propranolol on “an improvement in well-being” scale in the measurement of quality of life.4 However, no comparative studies with selective α1-inhibitors and ACE inhibitors have focused on serum lipid levels, quality of life parameters, and the overall changes in CHD risk. The present study was designed with such an aim in mind.

Doxazosin, a quinazoline derivative and a selective postsynaptic α1-adrenergic receptor antagonist, lowers blood pressure by reducing peripheral vascular resistance while causing little or no reflex tachycardia. It is used on a once-daily basis because of its long elimination half-life (approximately 22 hours) and long duration of action.6 Captopril is an ACE inhibitor that reduces blood pressure primarily by inhibiting the conversion of endogenous angiotensin I to the vasoconstrictors angiotensin II and angiotensin III. Captopril is administered twice daily; the apparent elimination half-life is less than 3 hours.7

This multicenter, parallel study was designed to compare the effects of doxazosin and captopril in terms of efficacy, toleration, and effect on lipid profile and quality of life in patients with hypertension and elevated serum cholesterol levels.

Methods

Study Design

Clinical investigations were performed in an open trial in 12 hypertension outpatient clinics in Italy (five in...
Northern Italy, two in Central Italy, three in the south, and two in the isles). The study included 224 patients with mild-to-moderate hypertension and concomitant elevated cholesterol. Each patient gave informed consent before entering the study. At or within 1 month of the screening visit, male and female patients (18–65 years of age) provided a medical history and were given a physical examination. Patients were either newly diagnosed as hypertensive (supine and standing diastolic blood pressure [DBP] >95 and <115 mm Hg) or had been previously treated. All patients were to have fasting serum total cholesterol levels >200 mg/dl (5.2 mmol/l) and <300 mg/dl (7.8 mmol/l).

The protocol excluded patients with any of the following: 1) malignant or secondary hypertension; 2) target organ damage of hypertensive disease (CHD, cerebrovascular disease, renal failure); 3) other heart disease; 4) other chronic diseases such as liver failure, diabetes mellitus, marked hypertriglyceridemia (triglyceride >400 mg/dl; 4.51 mmol/l), or concomitant medications, and quality of life were also made during phase 1. A 12-lead electrocardiogram was conducted within 3 months of a patient entering the study. On entering phase 2, patients were randomly assigned to receive either doxazosin or captopril, according to an open, parallel design. During the 10-week dose-adjustment period (phase 2), clinic visits were scheduled at 2-week intervals. At these visits, dose adjustments were made based on the standing DBP, measured approximately 3–8 hours after the morning dose of medication. Captopril therapy, administered once daily, was initiated at 1 mg and could be sequentially increased to 2, 4, 8, or 16 mg/day. Captopril, administered twice daily, was initiated at 25 mg and could be sequentially increased to 50, 75, 100, or 150 mg/day.

Upward dose adjustment continued until one of the following occurred: 1) control of blood pressure was achieved (standing DBP ≤90 mm Hg), 2) a maximum daily dose of 16 mg doxazosin or 150 mg captopril was administered, or 3) clinically significant adverse events precluded further dose increases. Patients whose DBP was reduced by at least 5 mm Hg proceeded into the maintenance period (phase 3), receiving the same dosage of doxazosin or captopril as the last visit of phase 2. At the end of phase 2, patients with a standing DBP reduction of <5 mm Hg from baseline were considered treatment failures and were withdrawn from the study.

Phase 3 was a 4-week maintenance period. At the final visit, standing and supine blood pressures and heart rates were measured in conjunction with body weight, compliance with medication, serum lipid levels, and pharmacologic and biochemistry parameters. In addition, patients completed the quality of life questionnaire, and treatment toleration was assessed. The investigator provided a global assessment of efficacy and toleration for each patient. Efficacy success was defined in terms of the standing DBP response: 1) a reduction in DBP to ≤90 mm Hg (i.e., "normalized"), with at least 5 mm Hg reduction from baseline, or 2) at least a 10 mm Hg reduction from baseline but no achievement of ≤90 mm Hg.

Quality of Life Questionnaire

A modified version of the questionnaire described by Croog et al was used. It consisted of four main measures: a General Well-Being Adjustment Scale (GWBAS), a Physical Symptoms Scale (PSS), a Sexual Dysfunction Scale (SDS), and a Work Performance Scale (WPS). The scoring conventions adopted were consistent with Croog et al. Patients completed the quality of life questionnaire at the end of both phase 1 and phase 3.

The GWBAS was designed to assess levels of anxiety, depression, general health, positive well-being, self-control, and vitality. The individual items were assigned a value from 1 to 6 such that higher scores represented a more positive perception for that trait. For an individual patient, the GWBAS scores could range from 22 to 132. The GWBAS was computed if, and only if, the
patient gave an assessment of all items in the baseline and follow-up questionnaires.

The PSS assessed the degree to which patients experienced sixteen specific symptoms or conditions (e.g., nausea, difficulty sleeping, headaches, numbness or tingling, coughing, skin rash, faintness on standing up quickly, wheezing, and loss of taste). The available alternative responses were "not at all," "a little bit," "moderately," "quite a bit," and "extremely." These were numerically coded on a five-point scale from 0 to 4. The score for the PSS was the sum of the sixteen items and could range from 0 to 64. Lower scores on this scale were more favorable.

The SDS consisted of four gender-specific questions about the patient's sexual functioning. The scoring and interpretation of this scale was the same as that described for the PSS. The individual composite score could range from 0 to 16, with 0 being the most desirable.

The WPS consisted of five sets of extremes that related to the patient's performance in the work situation. Responses were coded on a scale from 1 to 7, with higher numbers representing a more positive feeling about the work situations. The composite WPS scores could range from 5 to 35. As with the other scales, the WPS was computed only if patients responded to all items at baseline and follow-up.

**Coronary Heart Disease Risk Analysis**

The Framingham CHD equations were used to calculate the probability of CHD developing in a patient within 10 years.\(^9\)

**Biochemical Methods**

Cholesterol and triglyceride levels were measured by automated enzymatic methods as previously described.\(^6,10\) Low density lipoproteins (LDL) and very low density lipoproteins were precipitated in 400 \(\mu\)l serum by adding 20 \(\mu\)l of 2 M MgCl\(_2\) after 12 hours at 4°C, samples were centrifuged at 2,000g for 30 minutes, and HDL cholesterol concentration was measured in the supernatant using the CHOD-PAP method.\(^11\) LDL cholesterol concentration was calculated by the Friedewald formula\(^12\) as follows:

\[
LDL \text{ cholesterol}=\text{total cholesterol} - (\text{HDL cholesterol}+1/5 \times \text{total triglycerides})
\]

Apolipoprotein A\(_1\) and B concentrations were measured by the immunodiffusion method.\(^13,14\)

**Statistical Methods**

Data are given as mean±SEM or SD, except for lipid parameters, which are expressed as geometric mean and 95% upper and lower confidence limits. Two-tailed statistical tests were performed throughout the data analysis with a value of \(p<0.05\) considered significant. Unpaired \(t\) tests were used to assess the baseline comparability of the treatment groups with respect to age, weight, duration of hypertension, and blood pressure. Fisher's exact and \(\chi^2\) tests were used to assess comparability of categorical data in the treatment groups, for example, sex, concurrent diseases, and concomitant medications.

Mean changes in blood pressure (systolic and diastolic) and heart rate were calculated for all efficacy-evaluable patients for each visit by subtracting the respective baseline values; paired \(t\) tests were computed to evaluate the significance of within-groups changes. Between-group differences for blood pressures and heart rates were evaluated by unpaired \(t\) test.

Similar analyses were applied to the lipid data (i.e., both within- and between-group comparisons). Within-group changes in body weight were assessed using paired \(t\) tests. To normalize the distribution, lipid parameters were logarithmically transformed before \(t\) tests were applied.

The change from baseline in quality of life characteristics was defined as the follow-up score minus the corresponding baseline value for each individual patient. Percent change scores were computed for PSS and SDS. The significance of within- and between-group changes was assessed using paired and unpaired \(t\) tests, respectively.

**Results**

**Patient Population**

Of the 224 patients in the study, 112 were randomly assigned to receive doxazosin and 112 to receive captopril. There were no statistically significant between-group differences in the treatment groups with regard to sex, concomitant medications, or concurrent diseases. Table 1 provides detailed distributions for age, sex, body weight, blood pressure, and serum lipid levels.

Of the 224 patients, 27 doxazosin patients and 25 captopril patients did not meet one or more of the protocol requirements but were included in the blood pressure efficacy assessment at the discretion of the investigators. Of the doxazosin patients, 24 had cholesterol levels <200 mg/dl (5.2 mmol/l), one had no follow-up cholesterol determination, two had triglyceride levels >400 mg/dl (4.5 mmol/l), one had a glucose value of 120 mg/dl, and one was receiving a concomitant antihypertensive medication. Of the captopril patients, 21 had cholesterol levels <200 mg/dl, two had triglyceride levels >400 mg/dl, and two were receiving concomitant antihypertensive medications.

All patients had a diagnosis of essential hypertension. The mean known duration of hypertension for doxazosin and captopril patients was 5.5 years (range, 0.17–28 years) and 4.2 years (range, 0.08–20 years), respectively. Based on standing DBP, 61% of doxazosin patients and 60% of captopril patients had mild hypertension (95–104 mm Hg) at baseline; 37% of doxazosin patients and 38% of captopril patients had moderate hypertension (105–114 mm Hg). Fifty-six (50%) doxazosin and 44 (39%) captopril patients had one or more concurrent illnesses at baseline, predominantly diseases of the circulatory, digestive, respiratory, or endocrine/metabolic systems.

Four (4%) doxazosin and six (5%) captopril patients were receiving concomitant medications at entry into the study; most were either central nervous system or cardiovascular agents. Five (4%) doxazosin and five (4%) captopril patients started concomitant therapies during the study, the majority of which were benzodiazepines, analgesic, or antiulcer drugs.
TABLE 1. Sex, Age, Body Weight, Blood Pressure, Heart Rate, and Serum Lipid Distribution in Doxazosin and Captopril Groups

<table>
<thead>
<tr>
<th>Measurement</th>
<th>n</th>
<th>Doxazosin</th>
<th>Captopril</th>
<th>Between-group comparison</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n)</td>
<td>55</td>
<td>55</td>
<td>58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (n)</td>
<td>56</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td>51.5±7.9</td>
<td>52.4±7.2</td>
<td></td>
<td>0.36</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td></td>
<td>72.8±9.2</td>
<td>71.5±10.9</td>
<td></td>
<td>0.34</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td></td>
<td>161.3±14.9</td>
<td>164.2±12.8</td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td></td>
<td>102.3±5.2</td>
<td>102.5±4.5</td>
<td></td>
<td>0.82</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td></td>
<td>73.7±8.2</td>
<td>75.5±8.4</td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>67</td>
<td>238.5</td>
<td>245.1</td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td></td>
<td>231.7-245.6</td>
<td>238.9-251.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>67</td>
<td>123.2</td>
<td>139.6</td>
<td></td>
<td>0.18</td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td></td>
<td>108.4-140.0</td>
<td>122.2-159.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>67</td>
<td>32.8</td>
<td>33.8</td>
<td></td>
<td>0.57</td>
</tr>
<tr>
<td>95% Confidence interval</td>
<td></td>
<td>30.6-35.3</td>
<td>31.7-36.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BP, blood pressure; bpm, beats per minute; HDL-C, high density lipoprotein cholesterol. Age, body weight, blood pressure, and heart rate are expressed as mean±SD. Data for cholesterol, triglycerides, and HDL-C are log normalized and expressed as geometric mean with 95% confidence interval.

Ninety-five (85%) doxazosin and 90 (80%) captopril patients completed the study. Of the 17 doxazosin and 22 captopril patients who discontinued treatment, six (5%) doxazosin and 14 (13%) captopril patients were withdrawn because of an inadequate antihypertensive response, six (5%) doxazosin and five (4%) captopril patients were withdrawn because of adverse events, four (4%) doxazosin and two (2%) captopril patients were lost to follow-up, and one patient in each treatment group was withdrawn because of poor compliance with the dosage schedule. There were no statistically significant between-group differences with regard to study completion or early withdrawal.

Dose and Duration of Therapy

The mean duration of therapy for all patients receiving either doxazosin or captopril was 96.5 days (range, 16–139 days) and 96.4 days (range, 3–151 days), respectively. The mean doses at the final visit were 5.3 and 89.7 mg/day for doxazosin and captopril, respectively. The mean baseline standing blood pressures for doxazosin patients and captopril patients were 108.4±5.2 and 164.2±14.9 mm Hg, respectively. At the final visit, patients treated with doxazosin and captopril showed a statistically significant (p<0.05) reduction standing systolic/diastolic pressure by 18.6/14.7 mm Hg. Captopril significantly (p<0.05) reduced standing blood pressure by 20.0/13.2 mm Hg. Figures 1 and 2 show changes in supine and standing blood pressures.

Changes in Blood Pressure and Heart Rate

The mean baseline standing blood pressures for doxazosin and captopril patients were 158/104 and 161/104 mm Hg, respectively. At the final treatment visit, doxazosin significantly (p<0.05) reduced standing systolic/diastolic pressure by 18.6/14.7 mm Hg. Captopril significantly (p<0.05) reduced standing blood pressure by 20.0/13.2 mm Hg. Figures 1 and 2 show changes in supine and standing blood pressures.

There were no clinically significant changes in heart rate in either treatment group (range, +2.1 to −2.1 beats per minute), and there were no differences between the groups in terms of blood pressure or heart rate at the final treatment visit. Ninety-three (83.8%) doxazosin and 91 (82.7%) captopril patients showed an improvement in the severity grade of hypertension compared with baseline.

Therapeutic Success Rate

One hundred and eleven (99%) doxazosin and 110 (98%) captopril patients were evaluated for antihypertensive efficacy, with mean durations of therapy of 96.5 and 97.2 days, respectively. Ninety-three (83.8%) doxazosin patients and 86 (78.2%) captopril patients were considered therapeutic successes at mean daily doses of 4.4 and 75.9 mg, respectively. The therapeutic success rate did not differ significantly between the two groups. Standing DBP was "normalized" (≤90 mm Hg) in 81 (73.0%) doxazosin patients and 74 (67.3%) captopril patients at mean daily doses of 3.9 and 67.2 mg, respectively. Standing DBP was reduced by ≥10 mm Hg from baseline (but not to ≤90 mm Hg) in 12 doxazosin and 12 captopril patients at mean daily doses of 8.3 and 129.2 mg, respectively. The efficacy failure rate was 16.2% for doxazosin (at a mean dose of 9.3 mg/day) and 21.1% for captopril (at a mean dose of 135.9 mg/dl). A significantly (p<0.05) greater number of patients demonstrated an inadequate response to the maximum dose in the captopril group than in the doxazosin group.

Serum Lipid Profile

At the final visit, patients treated with doxazosin showed a statistically significant (p<0.001) reduction from baseline in mean serum total cholesterol and in

TABLE 2. Final Dose Distribution of Therapy for Patients Treated with Doxazosin and Captopril

<table>
<thead>
<tr>
<th>Final dose (mg/day)</th>
<th>Doxazosin</th>
<th>Captopril</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>Patients</td>
<td>No.</td>
</tr>
<tr>
<td>1</td>
<td>13</td>
<td>11.6</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>35.7</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>26.8</td>
</tr>
<tr>
<td>8</td>
<td>11</td>
<td>9.8</td>
</tr>
<tr>
<td>16</td>
<td>18</td>
<td>16.1</td>
</tr>
</tbody>
</table>

Total               | 112       | 100       | 112       | 100        |
LDL cholesterol levels, with a statistically significant increase in HDL cholesterol level \( (p<0.01) \) and the HDL/total cholesterol ratio \( (p<0.001) \). Captopril patients also demonstrated a significant reduction in mean serum total cholesterol \( (p<0.001) \) and in LDL cholesterol \( (p<0.01) \) levels. The HDL/total cholesterol ratio was significantly increased \( (p<0.01) \), but unlike patients treated with doxazosin, HDL cholesterol itself was not significantly affected (Table 3). Other lipid changes were not statistically significant. There were no significant differences between the groups in terms of lipid effects, although doxazosin did produce a greater increase than captopril in HDL cholesterol level (11.6\% versus 4.0\%, \( p=0.07 \) between-group difference) and in the HDL/total cholesterol ratio (23.1\% versus 11.1\%, \( p=0.08 \) between-group difference). Table 4 shows data on the difference in mean percent change between the doxazosin and captopril groups. No correlation between the changes in blood pressure and serum lipid levels was observed in either treatment group.

**Calculated Risk of Coronary Heart Disease**

Both doxazosin and captopril significantly \( (p<0.001) \) reduced the calculated risk of a patient developing CHD within 10 years. Doxazosin produced a reduction of 28\% (from 22.7\% to 17.9\%) and captopril reduced the risk of CHD by 19\% (from 23.0\% to 19.7\%). There was no statistical difference between the groups.

**Changes in Body Weight**

There were no significant within- or between-group changes in mean body weight (baseline versus final: 72.7 versus 72.4 kg for doxazosin and 71.4 versus 70.8 kg for captopril).

**Laboratory Tests**

Abnormal biochemical values possibly related to therapy were reported in 19 doxazosin patients and in 20 captopril patients. For both treatment groups, most of the abnormal test values related to uric acid levels or serum albumin. Among the doxazosin patients, 11 values (three uric acid and eight albumin) were either abnormal or at the upper extreme of the normal range at baseline. Of the captopril patients, nine had albumin test values that were either abnormal or at the upper extreme of the normal range at baseline. The laboratory abnormalities in both groups were minor and considered of no clinical significance.

**Adverse Events**

Adverse events were classified into three categories based on the investigators’ assessment of relation to treatment: definitely related to therapy, unknown relation to treatment, and not related to therapy. Thirty-eight patients in the doxazosin group and 30 patients in the captopril group experienced side effects that were related to treatment but were of unknown relation. The total number of adverse experiences was 66 and 38 in the doxazosin and captopril groups, respectively. When only the adverse events related to treatment were considered, patients treated with doxazosin most frequently reported palpitations (8.0\%), headache (6.3\%), and dizziness (1.8\%). Captopril patients most frequently reported coughing (3.6\%), taste loss (1.8\%), and dizziness (1.8\%). One episode of syncope was reported in the captopril group; none were reported in the doxazosin group.

**Quality of Life**

A total of 188 patients (93 in the doxazosin group and 95 in the captopril group) were included in the quality
of life analyses. Thirty-six patients were not included because they either had completed only a baseline or follow-up questionnaire (n=34) or were taking concomitant antihypertensive medication (n=2). Quality of life characteristics for the two treatment groups were found to be homogenous with respect to baseline scale and subscale questionnaire scores according to unpaired t tests.

Table 5 presents the mean changes for the quality of life scales. In general, even though the within-group changes showed significant improvement only in the doxazosin group, and no significant changes in SDS or WPS subscale questionnaire scores according to unpaired t tests.

**Investigators' Overall Assessment**

On completion of the study, the investigators gave a general assessment of clinical effect for each patient.

**Table 4. Difference in Mean Percent Change of Lipid Parameters Between Doxazosin and Captopril**

<table>
<thead>
<tr>
<th>Lipid fraction</th>
<th>Mean difference</th>
<th>95% Confidence interval</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>-1.28</td>
<td>-5.50 - 2.65</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.13</td>
<td>-12.49 - 14.27</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>7.61</td>
<td>-0.48 - 15.21</td>
<td>p=0.07</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>-3.07</td>
<td>-9.77 - 3.23</td>
<td>NS</td>
</tr>
<tr>
<td>Apolipoprotein A_1</td>
<td>1.55</td>
<td>-3.35 - 6.22</td>
<td>NS</td>
</tr>
<tr>
<td>Apolipoprotein B</td>
<td>-0.45</td>
<td>-7.44 - 5.20</td>
<td>NS</td>
</tr>
<tr>
<td>HDL/total cholesterol</td>
<td>10.16</td>
<td>-0.95 - 19.33</td>
<td>p=0.08</td>
</tr>
</tbody>
</table>

HDL, high density lipoprotein; LDL, low density lipoprotein.

**Discussion**

The results of this open, comparative, multicenter trial on a large population of mild-to-moderate hypertensive patients with elevated cholesterol levels confirm the antihypertensive efficacy of once-daily doxazosin and twice-daily captopril.15,16

The completion rate of the patients was high; more than 80% of those recruited were able to complete this clinical trial. This is mostly because of the effectiveness of the drug treatments in lowering blood pressure. DBP was normalized in 81 patients (73%) in the doxazosin group and 74 (67%) in the captopril group using low-to-medium doses of the drugs (mean daily doses of 3.9 and 6.7 mg, respectively). The efficacy failure rate of both monotherapies was low.

In addition to the effective control of blood pressure, other findings deserve comment. After treatment with doxazosin and captopril, serum total cholesterol and triglyceride levels and the HDL/total cholesterol ratio improved. In addition, doxazosin had a favorable effect on HDL cholesterol concentration. These results from a wide population of hypercholesterolemic hypertensive patients extend the findings on blood lipids already detected in normolipidemic hypertensive patients using prazosin17,18 or its analogues doxazosin19 and terazosin.20 The effects of captopril on serum lipid profile were even more favorable than the effects observed in normolipidemic hypertensive patients.21-23

Because the serum cholesterol distribution of our sample is truncated at its lower end, the effect of drug
The large number of antihypertensive drugs available means that doctors are faced with the difficulties of selecting the most effective and well-tolerated drugs in long-term treatment. In a recent trial investigating the quality of life of hypertensive patients taking propranolol, methyldopa, or captopril, patients on the ACE inhibitor scored significantly higher than those on methyldopa on measures of general well-being, work performance, and life satisfaction. Even in comparison with those taking propranolol, patients treated with an ACE inhibitor reported fewer side effects and less sexual dysfunction, with a greater improvement on measures of general well-being. In the present study, using a modified version of the questionnaire described by Croog et al, we found that the group treated with doxazosin demonstrated significant improvements in both the GWBAS and PSS, with a reduction in some specific physical symptoms. The captopril group showed an improvement only in GWBAS, although no significant between-group differences were detected. There is no doubt that ACE inhibitors are a cornerstone of antihypertensive therapy in the nineties. Their efficacy, combined with a lack of untoward side effects and an improvement in the quality of life, means they are often the agents of choice. Doxazosin, the selective α-blocker, was comparable in terms of efficacy and scored even better than captopril on parameters of lipid metabolism and quality of life. As a result, doxazosin should be considered in the first-line treatment of hypertension, as are ACE inhibitors.

References


Table 5. Changes from Baseline in Quality of Life Scores in Doxazosin and Captopril Groups

<table>
<thead>
<tr>
<th>Quality of life measure</th>
<th>Doxazosin</th>
<th>Captopril</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Final</td>
</tr>
<tr>
<td>GWBAS (+)</td>
<td>91.3±1.5</td>
<td>96.1±1.4</td>
</tr>
<tr>
<td>PSS (-)</td>
<td>10.8±1.0</td>
<td>8.0±0.8</td>
</tr>
<tr>
<td>SDS</td>
<td>Male (-)</td>
<td>1.8±0.5</td>
</tr>
<tr>
<td></td>
<td>Female (-)</td>
<td>3.1±0.5</td>
</tr>
<tr>
<td>WPS (-)</td>
<td>14.5±0.5</td>
<td>14.6±0.5</td>
</tr>
</tbody>
</table>

GWBAS, general well-being adjustment scale; (+), improvement with an increasing score; PSS, physical symptoms scale; (-), improvement with a decreasing score; SDS, sexual dysfunction scale; WPS, work performance scale.

*Within-group significance, p < 0.05.


35. Samuelsson O, Wilhelmsen L, Andersson OK, Kennett K, Berglund G: Cardiovascular morbidity in relation to change in blood pressure and serum cholesterol levels in treated hypertension: Results from the Primary Prevention Trial in Goteborg, Sweden. *JAMA* 1987;258:1768–1776

Doxazosin and captopril in mildly hypercholesterolemic hypertensive patients. The Doxazosin-Captopril in Hypercholesterolemic Hypertensives Study.
L A Ferrara, L Di Marino, O Russo, T Marotta and M Mancini

Hypertension. 1993;21:97-104
doi: 10.1161/01.HYP.21.1.97

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1993 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/21/1/97

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/