Current Status of Lipid Management of Hypertensive Patients

Koichi MATSUBARA, Yasutaka YAMAMOTO, Kazuhiko SONOYAMA, Go IGAWA, Masako FURUSE, Toru YATSUHASHI, Toshihiro HAMADA, Kazuhide OGINO, Osamu IGAWA, Ichiro HISATOME, and Chiaki SHIGEMASA

Hypertensives, in addition to requiring strict blood pressure control, need lipid management to prevent cardiovascular disease. To assess the current status of lipid management of hypertensives, we reviewed the profiles of 830 hypertensives. The quality of lipid management was assessed using the Japan Atherosclerosis Society (JAS) Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults announced in 1997. Hyperlipidemia was diagnosed in 45.2% of hypertensives and in 56.6% of patients in category C (a group of patients with coronary heart disease). Lipid-lowering drugs were used in 63.5% of all hypercholesterolemic patients and in 78.1% of category C patients. Statins were administered to more than 80% of hypercholesterolemic patients. Only 39.4% of hypertensives achieved the target total cholesterol level and only a very small percentage (17.1%) of patients in category C reached the target levels. The elderly hypertensives were the single largest group (42.2% of all hypertensives) in this study population, and the target cholesterol level for this group has been elevated from 200 mg/dl to 220 mg/dl in the JAS Guidelines for Diagnosis and Treatment of Atherosclerotic Cardiovascular Diseases announced in 2002 (new guidelines). In conclusion, in hypertensives requiring lipid management, the lipid-lowering approach appeared insufficient, as the target achievement rate was relatively low despite a high treatment rate. This was most marked for patients in category C. (Hypertens Res 2003; 26: 699–704)

Key Words: hypertension, hyperlipidemia, lipid-lowering therapy

Introduction

According to the Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH-2000), hypertensive patients require not only control of their hypertension, but also management of risk factors such as hyperlipidemia and diabetes mellitus in order to prevent cardiovascular disease. It has also been proposed that the degree of control should be individualized for each patient (1). Among the many risk factors, the relationship between hypercholesterolemia and cardiovascular diseases has been well established. It has been shown that a lipid-lowering therapy is useful both for the primary and the secondary prevention of cardiovascular diseases (2–9). In the Atorvastatin versus Revascularization Treatment (AVERT) study, strict low density lipoprotein (LDL)-cholesterol lowering therapy by atorvastatin was shown to be of greater benefit in decreasing coronary artery events than coronary interventions (10). In Western countries, where there is a higher incidence of coronary artery disease than in Japan, strict cholesterol management is thought to be essential. National Cholesterol Education Program (NCEP) and European Atherosclerosis Society (EAS) guidelines, which emphasize the importance of lipid-lowering therapy, are utilized in Western countries (11–13). In Japan, the Japan Atherosclerosis Society (JAS) Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults had been utilized since 1997 (14), but parts of these
guidelines were not considered to be practically applicable in certain clinical cases. Thus, after taking into account the results of the Kyushu Lipid Intervention Study (KLIS) (15), the pravastatin anti-atherosclerotic trial in the elderly (PATE) (16), and the Japan Lipid Intervention Trial (J-LIT) (17), the Japan Atherosclerosis Society (JAS) Guidelines for Diagnosis and Treatment of Atherosclerotic Cardiovascular Diseases—which included new lipid management goals—were published in July 2002. Recently, we reported the current status of blood pressure management in hypertensive patients in Japan (18), and in this report, we have assessed the status of lipid management in the same population. The aim of this study was to clarify the current status of lipid management of hypertensive patients and to identify problems that warrant improvement.

Methods

Study Design

The details of our method were described in our previous paper (18). This investigation utilized a cross-sectional analysis of 907 hypertensive patients who were treated by 34 cardiologists in Tottori University Hospital and associated facilities (11 general hospitals and 10 private practices) for more than 6 months. Hypertensive patients treated for at least 6 months prior to this survey were included in this study. The investigational period was from October 2000 to March 2001. A maximum of 30 cases were enrolled by each cardiologist. We collected information on age, gender, body height, body weight, prescriptions, risk factors (blood pressure, serum lipids, fasting blood sugar, uric acid, and current smoking), past history (coronary heart disease (CHD), cerebrovascular disease, and arteriosclerosis obliterans) and family history. The latest data available was used (n = 830). Questions for which information or data was unavailable could be left blank.

Table 1. (a) Japan Atherosclerosis Society (JAS) Guideline for Diagnosis and Treatment of Hyperlipidemia (Previous Guidelines) and (b) Japan Atherosclerosis Society (JAS) Guidelines for Diagnosis and Treatment of Atherosclerotic Cardiovascular Diseases (New Guidelines.)

<table>
<thead>
<tr>
<th>Category</th>
<th>CHD</th>
<th>Risk factors*</th>
<th>Target total cholesterol level (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>( - )</td>
<td>( - )</td>
<td>&lt; 220</td>
</tr>
<tr>
<td>B</td>
<td>( - )</td>
<td>( + )</td>
<td>&lt; 200</td>
</tr>
<tr>
<td>C</td>
<td>( + )</td>
<td></td>
<td>&lt; 180</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>CHD</th>
<th>Risk factors**</th>
<th>Target total cholesterol level (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>( - )</td>
<td>0</td>
<td>&lt; 240</td>
</tr>
<tr>
<td>B1</td>
<td>( - )</td>
<td>1</td>
<td>&lt; 220</td>
</tr>
<tr>
<td>B2</td>
<td>( - )</td>
<td>2</td>
<td>&lt; 220</td>
</tr>
<tr>
<td>B3</td>
<td>( - )</td>
<td>3</td>
<td>&lt; 200</td>
</tr>
<tr>
<td>B4</td>
<td>( - )</td>
<td>4 or more</td>
<td>&lt; 200</td>
</tr>
<tr>
<td>C</td>
<td>( + )</td>
<td></td>
<td>&lt; 180</td>
</tr>
</tbody>
</table>

* Positive risk factors for coronary heart disease (CHD) include age (≥45 years for males; after menopause for females), family history of CHD, smoking, hypertension, obesity (body mass index≥ 26.4), and impaired glucose tolerance. Atherosclerotic diseases other than CHD are treated as in category B. ** Positive risk factors for CHD include age (≥45 years for males; ≥55 years for females), hypertension, diabetes mellitus, smoking, family history of CHD, and low high density lipoprotein-cholesterol (HDL-C) (< 40 mg/dl). Cerebral infarction and arteriosclerosis obliterans are treated as in category B4. Diabetes mellitus without other risk factors is treated as in category B3.

Definition

Hypertension was defined by using the JSH-2000. Patients receiving antihypertensive therapy were defined as being hypertensive. The JAS Guideline for Diagnosis and Treatment of Hyperlipidemia in Japanese Adults (1997) (previous guidelines) were used to define hypercholesterolemia. Hypercholesterolemia was defined as a total cholesterol ≥220 mg/dl or treatment with cholesterol-lowering drugs. We utilized the previous guidelines (Table 1-a) and the JAS Guidelines for Diagnosis and Treatment of Atherosclerotic Cardiovascular Diseases (2002) (new guidelines; Table 1-b) to assess the quality of the lipid management. Diabetes mellitus was defined using criteria developed by the Japanese Diabetes Society (1999).

Statistical Analysis

All values were expressed as the means ± SD. All statistical analyses were performed with the program StatView 4.5 for Windows (Abacus Concepts Inc., Berkeley, USA). Comparisons among the groups were performed with analysis of variance (ANOVA) or χ² test. Values of p < 0.05 were considered to indicate statistical significance.
Results

Characteristics of Patients

Data of 907 hypertensive patients were collected. After excluding the cases for whom lipid data were unavailable, we analyzed the data of 830 patients (383 males and 447 females). The mean age of these patients was 66.8 ± 10.6 years old. Their mean systolic blood pressure was 141 ± 15 mmHg and their mean diastolic blood pressure was 80 ± 11 mmHg. The mean total cholesterol level was 205 ± 32 mg/dl. Table 2-a shows the number of patients in each category according to the previous guidelines and the percentage of hypercholesterolemic patients. There were 701 patients (84.5%) in category B and 129 patients (15.5%) in category C. Forty-five point two percent of all hypertensive patients were diagnosed as having hypercholesterolemia. There was a significant difference between the percentage of hypercholesterolemic patients in category C (56.6%) and that in category B (43.1%) ($p = 0.0046$).

Drug Treatment of Hypercholesterolemia

Table 2-b shows the percentage of patients receiving lipid-lowering therapy. Lipid-lowering drugs were administered to 63.5% of all hypercholesterolemic patients. Of note, 78.1% of hypercholesterolemic patients in category C were treated for hypercholesterolemia; this was significantly different when compared with patients in category B ($p = 0.0039$).

Prescriptions by medication type for hypercholesterolemic patients are shown in Fig. 1. Hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) were administered to 85.7% of treated hypercholesterolemic patients, and 95.1% of patients who were administered a statin received monotherapy. In category B, 88.4% of treated hypercholesterolemic patients were treated with a statin, and 96.9% of patients who were treated with a statin received monothera-
target total cholesterol level. However, the achievement rate for treated hypercholesterolemic patients decreased to 26.5%. Hypercholesterolemia was diagnosed in 56.6% of the patients in category C, and 78.1% of these patients were treated with lipid-lowering drugs. These percentages in category C were much higher than those in the other categories of patients. Despite the well-established benefit of lipid-lowering therapy and the high treatment rate in these patients, the target achievement rate of treated patients in category C was extremely low at 15.8%. A similar tendency toward low target achievement rates was also observed in the

### Table 3. Number of Patients According to Risk Factors (New Guidelines)

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk factor</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>HT</td>
<td>46</td>
</tr>
<tr>
<td>B2</td>
<td>HT + age</td>
<td>350</td>
</tr>
<tr>
<td></td>
<td>HT + low HDL-C</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>HT + smoking</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>HT + family history</td>
<td>2</td>
</tr>
<tr>
<td>B3</td>
<td>HT + DM</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>HT + age + low HDL-C</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>HT + age + smoking</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>HT + age + family history</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>HT + low HDL-C + smoking</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>HT + low HDL-C + family history</td>
<td>1</td>
</tr>
<tr>
<td>B4</td>
<td>HT + CI and/or ASO</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>HT + age + low HDL-C + smoking</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>HT + age + smoking + family history</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>HT + DM + age + low HDL-C</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>HT + DM + age + smoking</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>HT + DM + age + low HDL-C + smoking</td>
<td>2</td>
</tr>
<tr>
<td>C</td>
<td>HT + CHD</td>
<td>129</td>
</tr>
</tbody>
</table>

HT, hypertension; HDL-C, high density lipoprotein-cholesterol; DM, diabetes mellitus; CI, cerebral infarction; ASO, arteriosclerosis obliterans; CHD, coronary heart disease.

In category C, 77.2% of treated patients were treated with a statin, and 88.6% of patients who were treated with a statin received monotherapy.

Fibrates were administered to 10.5% of treated hypercholesterolemic patients, and 80% of patients who were administered fibrate received monotherapy. The percentages of patients who were administered fibrate were 8.8% and 15.8% in categories B and C, respectively.

Combination therapy with two or more medications was more often observed in category C (12.3%) than in category B (2.8%).

### Target Achievement Rate of Total Cholesterol

The percentages of patients who achieved the target total cholesterol level in each category are shown in Table 2a and b. Thirty-nine point four percent of all hypertensive patients achieved the target level. The achievement rate for category B was 43.5%. However, the rate of target achievement was extremely low in category C (17.1%), and was significantly different from that in category B ($p < 0.0001$).

When the data for hypercholesterolemic patients were analyzed, the achievement rate for treated hypercholesterolemic patients was 26.5%. Notably, the rate in category C was an extremely low 15.8%, and this rate was significantly different from that in category B (29.8%) ($p = 0.0361$).

When the results were analyzed with respect to cardiologist age (30–39 years old or more than 40 years old), there were no significant differences in the target achievement rates (data not shown).

### Evaluation Using the New Guidelines

The relationship of major coronary risk factors and the number of patients in each category of the new guidelines is shown in Table 3. Category B2 has the largest number of patients. The patient group with two risk factors, the elderly hypertensives (HT + age), made up 98.0% of the category B2 group, which was the single largest group (42.2% of all hypertensives) in this study. In category B3, 44.9% of patients had diabetes mellitus (DM). Furthermore, there were large numbers of aging, low high density lipoprotein (HDL) -cholesterolemia, and smoking patients in category B3. As for category B4, about 70% of patients had a past history of cerebral infarction (CI) and/or arteriosclerosis obliterans (ASO).

Fifty-three point four percent of all hypertensives achieved the target total cholesterol level when they were assessed by the new guidelines. The cholesterol target achievement rates were calculated in patients of categories B1, B2, B3, and B4, because the target cholesterol levels of these categories changed from those in the previous guidelines. The achievement rate for categories B1, B2, B3, and B4 were 58.7%, 68.6%, 48.3%, and 52.5%, respectively. When the data for hypercholesterolemic patients were analyzed, the achievement rate for treated hypercholesterolemic patients was 39.9% for the new guidelines. The rates in categories B1, B2, B3, and B4 were 14.3%, 56.2%, 37.8% and 37.5%, respectively.

### Discussion

Strict blood pressure control and lipid management are crucial for the prevention of cardiovascular diseases. This study was performed to clarify the current status of lipid management of hypertensive patients. In this study population, a high percentage (45.2%) of hypertensive patients were revealed to have concomitant hypercholesterolemia.

### Control of Total Cholesterol

Thirty-nine point four percent of all hypertensives achieved the target total cholesterol level. However, the achievement rate for treated hypercholesterolemic patients decreased to 26.5%. Hypercholesterolemia was diagnosed in 56.6% of the patients in category C, and 78.1% of these patients were treated with lipid-lowering drugs. These percentages in category C were much higher than those in the other categories of patients. Despite the well-established benefit of lipid-lowering therapy and the high treatment rate in these patients, the target achievement rate of treated patients in category C was extremely low at 15.8%. A similar tendency toward low target achievement rates was also observed in the
other categories of patients. Thus, we concluded that the intensity of lipid-lowering therapy was generally inadequate. We feel that this was due either to the fact that the chosen lipid-lowering agent lacked sufficient efficacy or that these patients were resistant to the agent. Our findings indicate that these patients require more aggressive therapy to protect them from cardiovascular diseases.

Drug Treatment of Hyperlipidemia

When individual prescriptions were reviewed, statins were administered to more than 80% of treated hypercholesterolemic patients, and most of them were treated with statin alone. These results indicate that cardiologists have a deep conviction in the efficacy of statins compared with the other lipid-lowering agents. In addition to their lipid-lowering effect, statins have been reported to improve blood pressure control in hypertensive patients who have concomitant hyperlipidemia; moreover, statins are well known to prevent cardiovascular diseases (19–24). All these beneficial effects have led physicians to consider statins as a useful intervention for atherosclerotic diseases (25). Therefore, when the lipid-lowering effect of the initial lipid-lowering therapy is inadequate, a stronger medicine should be used (26–27).

We found in our study that fibrates were often used for the treatment of hyperlipidemia. In category C, about 16% of treated patients were administered fibrate. It has been reported that fibrates have anti-arteriosclerotic effects which are independent of their lipid-lowering action, and this suggests that they would also be useful in the treatment of arteriosclerotic diseases (28).

Combination therapy was more often observed in category C than in category B. We speculated that lipid management for patients of category C might be more problematic than that for category B patients, and thus cardiologists tried to lower the total cholesterol level with combination therapy. However, the target achievement rate of patients of category C was extremely low, and these patients will all require more aggressive therapy.

It has been reported that younger physicians are more aggressive with respect to lipid-lowering therapy than older physicians (29). However, our study found no significant difference in the target achievement rates between the younger and older cardiologists.

Application of New Guidelines

The results of our study show that the percentage of patients who achieved the target total cholesterol level increased slightly when the revised target levels of the new guidelines were applied. This phenomenon appeared to be mainly due to the increase of the target achievement rate in category B2 patients. In this category, the target total cholesterol level was raised from 200 mg/dl to 220 mg/dl in the new guidelines, and this category had the largest number of patients in our study. In this category, 98.0% of the patients were elderly hypertensives. Clinical trials for elderly hypertensives with hypercholesterolemia are currently ongoing. Thus, in the near future, guidelines for the treatment of elderly hypertensives with hypercholesterolemia will be forthcoming. However, given the lack of current guidelines for the treatment of such patients, physicians need to utilize other data derived from vascular echography, pulse wave velocity, and other examinations to evaluate arteriosclerosis non-invasively on a case-specific basis.

Study Limitations

One of the limitations of this study was the lack of data at the lipid level before the initiation of lipid-lowering therapy. This information might have provided a different perspective on the target achievement rates in each category and thereby influenced our evaluation of the effectiveness of lipid-lowering therapy. We are particularly concerned that patients in category C whose total cholesterol level was within the normal range, that is less than 220 mg/dl, might be prescribed statins in an attempt to prevent secondary CHD. An additional potential limitation of our study is that we may have underestimated the family history of CHD because we only evaluated the family history of premature CHD. According to previous reports, the percentage of patients with a family history of CHD was 15–30% (30–32), but in our category B2, only 0.6% of patients had a family history of premature CHD. Thus, in order to correct for this potential underestimation of the percentage of patients with a family history of CHD, 15–30% of patients in category B2 were assigned to category B3. This reassignment resulted in a decrease of the target achievement rate, but the number of patients in category B2 was still the largest. Thus, careful attention should be given to this large group, as improvement in their management could be expected to significantly decrease the overall atherosclerotic burden.

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