

## GUIDELINES (JSH 2009)

# Chapter 3. Principles of treatment

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### POINT 3

1. The objectives of treatment are to control hypertension and prevent the occurrence of cardiovascular diseases due to sustained high blood pressure, thereby reducing mortality. In patients who have already developed cardiovascular disease, treatment is aimed at preventing their progression or recurrence, reducing mortality and improving the quality of life (QOL).
2. Treatment is necessary for all patients with hypertension (blood pressure  $\geq 140/90$  mm Hg) and for those with a blood pressure of  $\geq 130/80$  mm Hg if they have diabetes, chronic kidney disease (CKD) or myocardial infarction. The recommended target for blood pressure control is  $< 130/85$  mm Hg in young and middle-aged people. It should be  $< 130/80$  mm Hg in those with diabetes mellitus, CKD or myocardial infarction and  $< 140/90$  mm Hg in elderly people and patients with cerebrovascular diseases.
3. Antihypertensive treatment consists of lifestyle modifications (step 1) and antihypertensive drug therapy (step 2). Lifestyle modifications include restriction of salt intake and, if the patient is obese, weight control and exercise, restriction of alcohol intake, promotion of fruit and vegetable consumption, restriction of intake of saturated fatty acids and total lipids, and cessation of smoking (see Chapter 4). To prevent hypertension, one has to modify his or her lifestyle. The time of initiating antihypertensive drug therapy should be determined according to the level of blood pressure and the presence or absence of risk factors for cardiovascular disease and organ damage.
4. In principle, antihypertensive drug therapy should be started with a low dose of a long-acting drug once a day. If the dose must be increased, twice-daily administration may be considered. Appropriate combinations of drugs (combination therapy) are recommended to prevent adverse effects and enhance antihypertensive effects. Combination therapy should be considered from the outset for grade II or more severe hypertension.
5. Home blood pressure measurement is useful not only for the diagnosis of white coat hypertension and masked hypertension, but also for evaluating the effectiveness of antihypertensive treatment. It is also important to maintain good patient concordance (adherence) (see Chapter 2). Patients with white coat hypertension should be followed up periodically (every 3–6 months) even without treatment.
6. The QOL of patients with hypertension is affected by physical and psychological problems due to hypertension itself, the effects of antihypertensive drug therapy (including adverse effects) and the doctor–patient relationship.
7. In addition to sufficient communication, information, and consideration of the QOL and adverse effects, reducing the amount and frequency of medication is effective in improving adherence and controlling blood pressure.
8. The attending physician must eventually determine treatment by comprehensively evaluating the results of epidemiological and clinical studies, the clinical background of the patient, the pharmacological actions and cost of antihypertensive drugs, and also the long-term cost-effectiveness of antihypertensive treatment.

### 1) OBJECTIVES OF TREATMENT

The objectives of antihypertensive treatment are to prevent the occurrence of cardiovascular disease due to damage to the heart and blood vessels caused by sustained high blood pressure, and consequent functional impairment and death. In patients who have already developed cardiovascular disease, treatment is aimed at preventing progression or recurrence, reducing mortality and, thus, helping patients with hypertension to lead their lives as do healthy people.

The higher the risk of cardiovascular disease, the greater the effect of hypertension treatment.<sup>178</sup> The results of randomized case–control comparative studies provide the best scientific basis for evaluating the effects of antihypertensive treatment (lifestyle modifications and drug therapy). However, the effects of antihypertensive drug therapy are often underestimated in randomized case–control comparative studies, and the duration of such studies is only a few years, whereas hypertension is treated over a lifetime. Therefore, the significance of the results of randomized case–control comparative studies is limited.<sup>60</sup>

Evaluating the therapeutic effects on hypertension through clinical trials of a few years' duration is easy as the patients are likely to experience more bouts during the study. Therefore, many recent studies have been conducted using elderly and high-risk patients.

The results of large placebo-controlled randomized comparative studies conducted in foreign countries have established that antihypertensive drug therapy has many beneficial effects on patients with hypertension. Antihypertensive drug therapy clearly reduces the incidence and mortality rate of cardiovascular diseases.<sup>179</sup>

According to the analysis of the results of clinical studies conducted abroad, the relative risk of stroke decreases by 30–40% and that

of ischemic heart disease decreases by 15–20%, with a reduction of 10–20 mm Hg in the systolic blood pressure and 5–10 mm Hg in the diastolic blood pressure. In these studies, the decrease in absolute risk due to antihypertensive drug therapy was greater with increasing blood pressure level and age pre-treatment. Analysis of the results of studies of patients with systolic hypertension also showed that stroke and ischemic heart disease are reduced by 30% and over 20%, respectively, by a decrease of 10 mm Hg in the systolic blood pressure.<sup>116</sup>

As the incidence of stroke and ischemic heart disease in Japan differs from that in Western countries, the above results cannot be applied directly to the Japanese population. However, antihypertensive drug therapy is considered to be more effective in patients with high blood pressure and older patients regardless of ethnicity.

The relative risk is higher in young and middle-aged patients with hypertension than in normotensive individuals of the same age, but absolute risk is low compared with elderly patients. In addition, a decrease in the absolute risk due to treatment is lesser in younger than in elderly patients. Therefore, the necessity of long-term antihypertensive treatment in young and middle-aged hypertensive patients should be recognized.

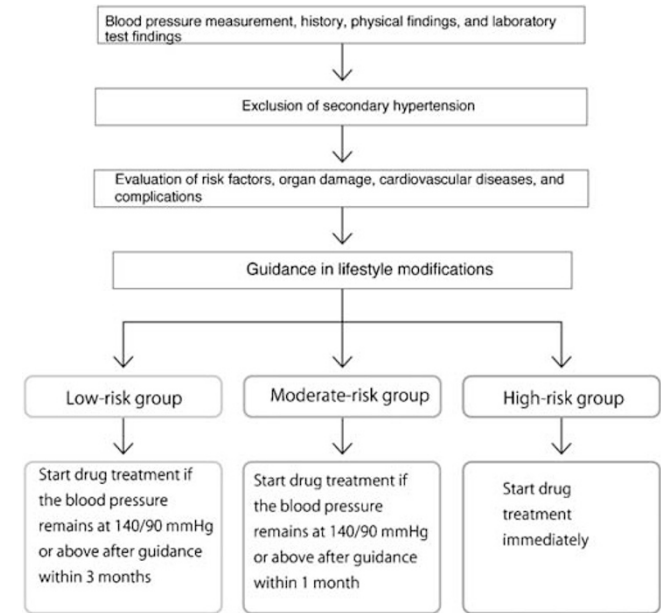
As the incidence of stroke is several times higher than that of ischemic heart disease in Japan, unlike in Western countries, antihypertensive drug therapy is expected to be more effective in Japan. According to a meta-analysis of the preventive effect of antihypertensive drug therapy on the occurrence of cardiovascular disease, the decrease in risk due to treatment did not differ between men and women.<sup>180</sup>

## 2) PLANNING OF HYPERTENSION MANAGEMENT AT INITIAL EXAMINATION

If blood pressure is high at initial examination, it is usually measured several times on another day. In addition, the patient is instructed to measure home blood pressure to eliminate white coat hypertension, white coat phenomenon and masked hypertension, and the overall risk of the patient developing cardiovascular disease, including the presence or absence and severity of organ damage, is assessed.

Lifestyle modifications must be made by all patients particularly those in high-risk groups. Patients with metabolic syndrome (MetS) that has markedly increased recently and is considered an important risk factor for hypertension, diabetes mellitus, chronic kidney disease (CKD) and cardiovascular disease, strict and sustained lifestyle modifications should be practiced rigorously. The prevention and management of MetS and support for patients with MetS are core issues in the Specific Health Screening and Health Guidance initiated in April 2008, in Japan. In addition, if home blood pressure or ambulatory blood pressure monitoring (ABPM) (covered by health insurance since April 2008, in Japan) differs widely from clinic blood pressure, it is appropriate to determine a therapeutic strategy by attaching greater importance to home blood pressure or ABP than to clinic blood pressure. After evaluating the overall risk of cardiovascular disease, the evaluation, therapeutic strategy and target control levels of clinic and home blood pressures should be explained to the patient until the patient sufficiently understands them.

In low-risk patients with a blood pressure of 140–149/90–99 mm Hg (grade I hypertension) but no other risk factors, organ damage or cardiovascular disease, lifestyle is modified, and blood pressure is measured again after a certain period (within 3 months). Risk is stratified by blood pressure on repeat measurement, and therapeutic strategy is determined according to Figure 3-1. As many recent observational studies have shown, the risk of cardiovascular disease



**Figure 3-1** Planning of hypertension management at the initial examination. High-risk patients with high-normal blood pressure should be treated first by lifestyle modification. If their blood pressure does not reach the target level, then drug therapy should be considered.

increases in normal blood pressure (<130/85 mm Hg)<sup>8,9,109</sup> as well as in high-normal blood pressure (130–139/85–90 mm Hg)<sup>17,121–123</sup> compared with optimal blood pressure (<120/80 mm Hg); therefore, the threshold systolic blood pressure for the initiation of antihypertensive drug therapy has been lowered. As a result, even in low-risk patients, if blood pressure is not reduced to <140/90 mm Hg through lifestyle modifications alone, antihypertensive drug therapy is started after a certain period (within 3 months). In contrast, even when blood pressure at initial examination is classed as grade I hypertension, a therapeutic strategy matched to the risk should be established and executed according to Figure 3-1 if the risk is judged to be moderate or high, depending on the number of risk factors and organ damage, including diabetes mellitus and CKD or established cardiovascular disease.

If blood pressure at initial examination is 160–179/100–109 mm Hg (grade II), having excluded white coat hypertension or white coat phenomenon by measuring home blood pressure, and if the overall risk is judged to be moderate by risk assessment, antihypertensive drug therapy should be initiated after a period of lifestyle modification (within 1 month). Antihypertensive drug therapy should be initiated immediately if the risk is judged to be high even in patients showing grade II hypertension at initial examination (Figure 3-1). If blood pressure is  $\geq 180/110$  mm Hg (grade III) at initial examination, the risk is judged to be high and antihypertensive drug therapy must be initiated immediately (within a few days).

Patients with organ damage or other diseases such as diabetes mellitus, CKD, cerebrovascular disorders and heart disease are judged to be high-risk even if their blood pressure is <140/90 mm Hg (Table 2-8). Strict, immediate and adequate antihypertensive drug therapy should be considered if blood pressure does not reach target level despite lifestyle modifications (see Chapters 4, 5, 6 and 7).

Based on the results of large-scale clinical studies, there is no evidence supporting the effectiveness of antihypertensive drug therapy in patients with MetS with a high-normal blood pressure (130–139/

85–89 mm Hg), a fasting blood glucose level of 110–125 mg per 100 ml (not diabetic) and no organ damage. Therefore, the 2007 ESH/ESC Guidelines judged the risk of such patients with MetS to be high, the second rank after ultra-high, but suggested no more than strict lifestyle modifications for their treatment, commenting that aggressive drug therapy cannot be recommended at that stage.<sup>66</sup> The present Guidelines also recommend strict lifestyle modifications as an initial treatment for such patients with MetS (see Chapter 7).

### 3) PATIENTS TO BE TREATED AND TARGET BLOOD PRESSURE

#### a. Patients to be treated

**Age.** Hypertension should be treated in patients of all ages. However, the results of observational studies in elderly people performed in Western countries suggest that hypertension may not be a risk factor for cardiovascular disease in people aged  $\geq 80$  years.<sup>178,181</sup> However, the HYVET,<sup>182</sup> performed recently in people aged  $\geq 80$  years, showed that antihypertensive drug therapy reduces mortality due to stroke and total mortality (see Chapter 8).

**Blood pressure levels.** The results of a meta-analysis of 61 studies prospectively evaluating the relationship between blood pressure and death from cardiovascular disease<sup>9</sup> indicated that cardiovascular mortality increases when blood pressure is  $\geq 115/75$  mm Hg. Long-term observation in the Framingham Study<sup>122</sup> showed that the risk of cardiovascular disease doubles in people with a high-normal blood pressure compared with those with an optimal blood pressure. Therefore, the JNC7<sup>38</sup> recommended lifestyle modifications for patients with prehypertension (120–139/80–89 mm Hg) and antihypertensive drug therapy in combination with lifestyle modifications for those with hypertension ( $\geq 140/\geq 90$  mm Hg).

As for the epidemiological studies in Japan, death from cardiovascular disease increased significantly in the Tanno/Sobetsu Study<sup>183</sup> in Hokkaido, and the incidence of stroke increased significantly in the Hisayama Study<sup>8</sup> in Fukuoka, when blood pressure was  $\geq 140/90$  mm Hg. In these Guidelines, a blood pressure of  $\geq 140/90$  mm Hg is defined as hypertension, similar to the JSH2004 Guidelines.<sup>65</sup> Therefore, patients, including the elderly, with a blood pressure  $\geq 140/90$  mm Hg, should be treated.

If hypertension is complicated by diabetes mellitus, CKD or myocardial infarction, a blood pressure of  $\geq 130/80$  mm Hg is considered to require treatment. Lifestyle should be modified in patients with a high-normal blood pressure and those with a normal blood pressure and diabetes mellitus, CKD, MetS, multiple risk factors, organ damage or cardiovascular disease. In addition, antihypertensive drug therapy is indicated for all types of hypertension and high-normal blood pressure if it is concurrent with diabetes mellitus, CKD or myocardial infarction.

#### b. Target levels of blood pressure control

In the JSH2004 Guidelines, the target level of blood pressure control was  $<130/85$  mm Hg in young and middle-aged individuals,  $<130/80$  mm Hg in those with diabetes or kidney disease and  $<140/90$  mm Hg in elderly people. The results of the HOT<sup>139</sup> and recent FEVER<sup>184</sup> studies suggest that  $<140/90$  mm Hg should be a general target. The 2007 ESH/ESC Guidelines<sup>66</sup> set  $<130/80$  mm Hg as a target, because studies including the *post hoc* study<sup>185</sup> of the PROGRESS,<sup>135</sup> EUROPA,<sup>186</sup> ACTION<sup>187</sup> and CAMELOT<sup>188</sup> suggested that a strict control of the blood pressure leads to a decrease in cardiovascular events, not only in patients with diabetes or kidney disease but also in those with cerebrovascular or coronary artery disease. These Guidelines set a target of blood pressure control of  $<130/$

**Table 3-1 Target levels of blood pressure control**

Young and middle-aged patients	$<130/85$ mm Hg
Elderly patients	$<140/90$ mm Hg
Diabetic patients	$<130/80$ mm Hg
Patients with kidney diseases	
Patients after myocardial infarction	
Patients with cerebrovascular diseases	$<140/90$ mm Hg

85 mm Hg for young and middle-aged people and  $<130/80$  mm Hg for those with diabetes mellitus, CKD or myocardial infarction. In elderly people, the eventual target of control is  $<140/90$  mm Hg. However, as many elderly people aged  $\geq 75$  years have organ damage, antihypertensive drug therapy may cause ischemia of important organs. Therefore, it is important to conduct antihypertensive therapy by paying careful attention to changes in symptoms and laboratory test results (Table 3-1).

### 4) SELECTION OF TREATMENTS

Genetic and environmental factors are intricately involved in the occurrence and progression of essential hypertension. Therefore, treatment for hypertension cannot be considered without the correction of lifestyle-related problems (non-drug therapy), many of which are environmental factors. However, as mentioned in treatment I of Chapter 4, few patients achieve the target of blood pressure control through lifestyle modifications alone, and drug therapy is necessary in most cases. For each patient with hypertension, an outline of the treatment plan is formulated according to stratification of the risk by comprehensive evaluation of the severity of hypertension, risk factors for cardiovascular disease and cardiovascular complications (Figure 3-1).

Patients with hypertension can be classified using the risk profile into low-, moderate- and high-risk groups, but antihypertensive drug therapy is indicated even in patients with high-normal blood pressure if they have diabetes mellitus, cardiovascular disease or CKD.

#### a. Lifestyle modifications

Hypertension is a lifestyle-related disease, and it has been shown to be not only prevented but also managed by lifestyle modifications.<sup>189–191</sup> A high-normal or high blood pressure is an indication for lifestyle modifications in all patients. If hypertension is concurrent with risk factors for cardiovascular disease, such as dyslipidemia and diabetes mellitus, lifestyle modifications are of particular importance as they can reduce these risk factors at minimal cost and effort.

Although many patients fail to achieve the target of blood pressure control through lifestyle modifications alone, they can at least reduce the types and doses of the necessary antihypertensive drugs.<sup>192,193</sup> Lifestyle modifications must be maintained even after the initiation of antihypertensive drug therapy. They include restriction of salt intake, increased fruit and vegetable consumption, restriction of cholesterol and intake of saturated fatty acids, maintenance of an appropriate body weight, restriction of alcohol intake, exercise and cessation of smoking. Lifestyle modifications should be kept in mind for the prevention of hypertension in the future.

#### b. Time to start antihypertensive drug therapy

In low- or moderate-risk patients with hypertension, antihypertensive drug therapy is started if the blood pressure cannot be reduced to  $<140/90$  mm Hg within a given period of time through lifestyle modifications alone. In high-risk patients, that is patients with hypertension complicated by diabetes mellitus, cardiovascular disease or CKD, antihypertensive drug therapy should be initiated simulta-

neously with lifestyle modifications. Emergencies related to hypertension require the immediate initiation of drug therapy, but such patients should be referred to hypertension specialists. Elderly patients should also be treated with drugs if their blood pressure is  $\geq 140/90$  mm Hg, but the blood pressure level at which drug therapy should be commenced is unclear in those aged  $\geq 80$  years (see Chapter 8).

### c. Antihypertensive drug therapy

Many Japanese patients with hypertension require drug therapy. The major antihypertensive drugs used in Japan include calcium (Ca) antagonists (dihydropyridines and diltiazem), renin-angiotensin (RA) system inhibitors such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs), diuretics (thiazide and thiazide-like diuretics, K-sparing diuretics and loop diuretics),  $\beta$ -blockers (including  $\alpha\beta$ -blockers),  $\alpha$ -blockers and drugs with central nervous system actions (methyldopa, clonidine and so on). Antihypertensive drugs with different mechanisms of action also have characteristic adverse effects. From the point of view of the evidence-based selection of drugs, the usefulness of diuretics, Ca antagonists, ACE inhibitors and ARBs has been established by many reports. Recently, the results of large-scale clinical trials indicating the usefulness of ARBs and Ca antagonists have been reported in Japanese patients with hypertension.<sup>194,195</sup>  $\beta$ -blockers have also been shown to be useful, but their inhibitory effects on stroke are reported to be weaker than those of other antihypertensive drugs.<sup>196,197</sup>

According to the results of randomized intervention studies comparing antihypertensive drugs and the meta-analyses of these reports, some drugs are suggested to be more effective for the prevention of certain cardiovascular diseases. Generally, however, the prevention of cardiovascular disease by antihypertensive drugs is ascribed primarily to a decrease in blood pressure rather than to the effects of particular drugs. Although recent large-scale clinical intervention studies in high-risk patients with hypertension<sup>198,199</sup> suggested the importance of an early reduction (1–3 months) in blood pressure, they also suggested the danger of sudden changes in the treatment regimen.

Whatever the antihypertensive drugs chosen, there are principles for their use. (1) Select a drug that is effective by once-a-day administration, in principle. (2) Start drug therapy at a low dose. In particular, commence administration of a thiazide diuretic using half or quarter of the tablet, as the initial dose mentioned for the Japanese drugs is too high. (3) Combination therapy should be considered from the outset for grade II or more severe hypertension ( $\geq 160/100$  mm Hg), and drugs should be combined appropriately to prevent adverse effects and enhance the depressor effect (see Chapter 5). (4) If the first drug shows only a weak depressor effect or is poorly tolerated, replace with a drug showing a different action mechanism. (5) If hypertension is complicated by other diseases, select antihypertensive drugs by paying due attention to indications and contraindications. Also, make sure to verify the interactions of antihypertensive drugs with drugs administered for the treatment of other diseases.

Figure 3-1 shows a flow chart of antihypertensive treatment in adults. This is no more than a principle for daily clinical practice; more appropriate treatments should be designed for individual patients depending on condition. Home blood pressure measurement is useful for the diagnosis of white coat hypertension<sup>62</sup> and masked (reverse white coat)<sup>200</sup> hypertension and for the evaluation of the effectiveness of antihypertensive treatments. In patients with white coat hypertension, a decision on whether it should be treated must be made by considering the risk factors and the presence or absence of

target organ damage. Even if drug therapy is not performed, patients must be followed up carefully every 3–6 months. In patients with masked hypertension, its cause must be examined, and the presence or absence of organ damage must be evaluated.

## 5) OTHER POINTS REQUIRING ATTENTION

### a. Initial treatment

The objective of initial treatment is to select antihypertensive drugs effective for reducing blood pressure to the target level and adjust their doses. Therefore, antihypertensive drugs may have to be changed or used in combination, or their doses may have to be increased, until blood pressure decreases to the target level. Generally, antihypertensive drug therapy for grade I hypertension should be started using a single drug at the minimum dose, and if the reduction in blood pressure is insufficient, the dose should be increased or the drug replaced for, or combined with, another drug with a different mechanism of action. For the treatment of grade II–III or high-risk hypertension, combination therapy should be considered from the outset. For combination therapy, the combination of a RA system inhibitor with a diuretic or Ca antagonist or that of a Ca antagonist (dihydropyridines) and a  $\beta$ -blocker are recommended. The combination of a diuretic and a  $\beta$ -blocker should be avoided in patients with obesity or MetS, because new onset of diabetes mellitus is observed more frequently than with other combinations of antihypertensive drugs.<sup>201</sup>

### b. Long-term treatment (continuous treatment)

The objective of long-term treatment is to prevent cardiovascular disease by maintaining a target blood pressure level over a long period and comprehensively managing risk factors other than blood pressure.

As patients with hypertension generally have no marked symptoms or signs, and as the treatment for hypertension continues over a long period, some patients stop visiting medical facilities. It is an important task of the attending physician to devise measures to ensure patients continue coming to the hospital, observe lifestyle modifications and take drugs as instructed. For the satisfactory continuation of treatment, it is important for physicians to maintain a good doctor-patient relationship by continuing close communication with patients and sufficiently explaining hypertension as a disease, the treatment methods, the results expected from treatments and the expected adverse effects of antihypertensive drugs. As patients may misunderstand a reduction of their blood pressure due to antihypertensive drugs to mean their hypertension has been cured and so quit treatment,<sup>202</sup> sufficient explanation is necessary. The sufficiency of communication with the physician and the degree of patient satisfaction with the medical staff markedly affect the patient's QOL.<sup>203</sup> Patient-involved treatment that is formulated by considering the patient's QOL and does not interfere with the patient's daily living or social activities is desirable.

### c. Attention to the QOL

Although impairment of the QOL is milder in patients with hypertension than in those with other serious diseases, QOL has been shown to be impaired by being conscious of hypertension.<sup>204,205</sup> Problems with emotional state and responses, sleep, heart and digestive functions, and sense of satisfaction appear with increases in blood pressure.<sup>206</sup> Age also markedly affects the QOL. The degree of impairment of the QOL increases and individual differences widen as age advances.<sup>207</sup> As QOL is evaluated on the basis of a wide range of aspects, including physical symptoms, psychological state, degrees of mental and physical satisfaction, sense of well-being, work, hobbies, social activities, home

and sex life, these items should be assessed as objectively and comprehensively as possible.<sup>208</sup>

Although sufficient attention must be given to impairment of the QOL due to the adverse effects of antihypertensive drugs, QOL has been reported to improve with treatment of hypertension.<sup>209,210</sup> As treatment for hypertension continues over a long period, consideration not to reduce the QOL of patients with hypertension is important to ensure the continuation of treatment.

#### d. Concordance/adherence

Concordance means the participation of a patient with sufficient knowledge in the management of his or her disease and the implementation of treatment agreed between the physician and patient.<sup>211</sup> As hypertension is often asymptomatic, adherence (continuation of treatment) is poor, it tends to be left untreated and drug therapy is often discontinued. However, treatment with emphasis on concordance is considered to improve adherence and to lead to the prevention of cardiovascular disease.

According to a questionnaire survey of Japanese patients with hypertension, less than 50% of patients answered that the objective of the antihypertensive treatment was the prevention of cardiovascular disease, which suggests that the objective is not sufficiently understood.<sup>212</sup> In addition, in a questionnaire survey of patients who dropped out from antihypertensive drug therapy, many patients thought that hypertension had been cured when their blood pressure decreased,<sup>202</sup> suggesting a poor understanding of the importance of adherence to antihypertensive treatment. Another questionnaire survey showed that both physicians and patients considered the willingness to listen to patients to be the most important aspect of an ideal physician, but both physicians and patients were aware that the amount of consultation time is insufficient to facilitate this.<sup>212</sup> Providing sufficient information to patients has been shown to improve adherence and the state of blood pressure control.<sup>213,214</sup> Also, as the adverse effects of antihypertensive medication reduce adherence, sufficient attention should be paid to such effects.

According to another questionnaire survey in Japan, few patients were eager to be actively involved in the determination of therapeutic strategy or selection of drugs, but many were interested in the adverse effects and were reluctant to consent to changes in drugs or increases in the dose because of anxiety over these effects.<sup>215</sup> Furthermore, adherence tended to deteriorate with increases in the number of tablets to be taken.<sup>215</sup> A reduction in the number of tablets to be taken, the daily frequency of taking drugs<sup>216</sup> and the use of fixed combinations of two drugs<sup>217</sup> have been reported to be useful in improving adherence. Table 3-2 summarizes the methods for treatment, in which the physician and the patient share an understanding as partners.

#### e. Cost-effectiveness of antihypertensive treatment

Treatment for hypertension is a major problem when considering its proportion of the total medical expenditure, and pharmaco-economic

**Table 3-2 How to conduct treatment for the physician and patient as partners by reaching a shared understanding**

- Talking with the patient about the risk of hypertension and the effects of treatment
  - Clearly explaining the treatment plans orally and in writing
  - Tailoring the treatment plans to the patient's lifestyle
  - Providing information about hypertension and the treatment plans to the patient's partner and family
  - Using methods based on behavioral theories such as measuring the blood pressure at home and devising measures to remember to take drugs
  - Paying attention to adverse effects and changing the dose or the drug if necessary
  - Simplifying the regimen by reducing the number of tablets to be taken and the number of times of taking drugs daily, using fixed combinations and so on
  - Talking with the patient about adherence and his/her problems
  - Providing a system to support the patient to continue to take drugs, visit the hospital and modify the lifestyle
  - Explaining the lifetime costs and effects of treatments
- (Cited with partial modification from the ESH-ESC 2007<sup>85</sup>)

analyses have been carried out to evaluate its effects and cost on the basis of the results of various clinical studies.<sup>218,219</sup>

The effectiveness of antihypertensive treatment is evaluated according to indices including the degree of decrease in blood pressure and preventive effect on the occurrence of cardiovascular disease. In addition to the new onset of diabetes mellitus and metabolic changes such as hyperuricemia, negative effects such as reduction in the QOL are also included.

Cheaper generic formulations are available in some branded hypertensive products. The cost of treatment for hypertension includes the cost of antihypertensive drugs, the cost of treatment for cardiovascular disease due to hypertension and new-onset metabolic disorders. The effects of new-onset metabolic disorders on cardiovascular disease may not be clarified by the results of large-scale clinical trials alone, which are performed over a period of about 5 years;<sup>220</sup> therefore, evaluations using simulation models are being performed for the comprehensive assessment of the cost-effectiveness of long-term treatment for hypertension. Results of these evaluations suggest that antihypertensive drug treatment is more cost-effective than no treatment,<sup>221</sup> and that treatment primarily using diuretics at a standard dose is not necessarily cost-effective in long-term treatment.<sup>222,223</sup>

#### Citation Information

We recommend that any citations to information in the Guidelines are presented in the following format:

The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2009). *Hypertens Res* 2009; **32**: 3–107.

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