Analysis of Current State Regarding the Use of Antihypertensive Drugs to Outpatients at Internal Medicine Departments of General Hospital

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The purpose of antihypertensive therapy is not only to normalize the blood pressure but also to prevent severe or fatal complications of the cardiovascular system. Since the presence or absence of target organ failure and major dangerous factors influence the prognosis of hypertension, an appropriate evaluation of these risk factors is important. It is therefore necessary to consider such complications when evaluating antihypertensive therapy.

In this investigation, we examined the current state regarding the use of antihypertensive drugs and their associated complications in Takarazuka City Hospital, to establish a more effective and safer pharmacotherapy from the pharmacist's viewpoint.

A total of 312 patients (138 males, 174 females) who received antihypertensive drugs at the Department of Internal Medicine in our hospital between August 23rd and 27th, 1999 were included in this study. The patients' records were examined with regard to age, the medication received and the complications observed. The most common form of treatment, regardless of age, was calcium channel blockers (Ca blockers), followed by angiotensin converting enzyme inhibitors (ACE-I), and finally \( \alpha \)- and \( \beta \)-adrenergic blockers (\( \alpha \) and \( \beta \) blockers, respectively).

The rates of congestive heart failure (CHF) and ischemic heart disease (IHD) tended to increase with age. On the other hand, those of endocrine metabolic diseases such as diabetes mellitus (DM), hyperlipidemia and gout were either unaffected or tended to decrease with age.

The peculiar use ratio of diuretics in patients with CHF was higher than that in non-CHF (p<0.05). The use of \( \beta \) blockers was slightly higher in IHD. The ratio of \( \alpha \) blockers correlated with the rates of DM (p<0.05) and hyperlipidemia (not significant).

In conclusion, due to the variety of the patient profiles and the clinical backgrounds antihypertensive drug therapy has thus become a complex issue. In addition, GL is not applicable in all cases. However, the results of this study suggest that the current state regarding the use of antihypertensive drugs and their associated complications in our hospital was similar to that in previous reports. It is therefore necessary to further accumulate and analyze such findings including the types of treated diseases, the indications and dosage of each applied drug to establish more effective and safer antihypertensive pharmacotherapies.

Keywords — antihypertensive drugs, complication, hypertension, internal medicine, general hospital
Introduction

In recent years, treatments based on the concept of "evidence-based medicine" has been proposed, and the introduction of guidelines (GL) for various diseases has been suggested for clinical use\(^1\). In 1990, the Ministry of Health and Welfare and the Japan Medical Association published the "Guidelines for vetting of hypertension"\(^2\), but it has not subsequently been revised. Therefore, GL which incorporate the new concept are desirable. On the other hand, GL are determined in the Japanese Society of Hypertension, while in the rest of the world the reports of the World Health Organization/International Society of Hypertension (WHO/ISH) and Joint National Committee (JNC) are widely used. In these GL, standard treatment procedures and appropriate medications are determined based on the presence or absence of cardiovascular risk factors and complications\(^3,4\). Therefore, it is necessary to consider such complications when evaluating antihypertensive therapy.

Previously, there have been a number of reports concerning the use of various antihypertensive drugs, but few studies have analyzed their use with regard to associated complications\(^5\). Moreover, few reports recognize the spread of GL to general hospitals such as ours.

In this study, we analyzed the current state regarding the use of antihypertensive drugs and their associated complications in Takarazuka City Hospital, to establish more effective and safer pharmacotherapy from the pharmacist's viewpoint.

Methods

1. Patients

A total of 312 patients (138 males, 174 females) who received antihypertensive drugs at the Department of Internal Medicine, Takarazuka City Hospital between August 23\(^{\text{rd}}\) and 27\(^{\text{th}},\) 1999 were included in this study. Patients were separated into groups depending on age; "give age groups". The patients' case records were examined with regard to age, the medication received and the complication observed. Diagnosis was confirmed based on a review of their records. The diagnostic names of complications were from insurance diagnostic procedures. Data from cases showing more than one complication were processed along with those of each applicable disease group. And it examined the diseases which showed more than 5% of all the cases.

2. Use of antihypertensive drugs with regard to each complication

The peculiar use ratio of each drug with regard to each complication was calculated by the following equation:

\[
\text{Peculiar use ratio} = \frac{\text{use rate of each antihypertensive drug in cases with each complication}}{\text{use rate in cases without the complication}}
\]

A peculiar use ratio of 1 indicates use of the antihypertensive drug irrespective of the presence or absence of the disease. On the other hand, a value greater than 1 indicates use at an especially high rate in the presence of the disease.

The peculiar use ratios of antihypertensive drugs for each complication were analyzed for statistical significance by the chi-square test, with p-values less than 0.05 considered indicate significance.

Results

In this study, 357 patients were initially included, but 45 were excluded as the review of their case records did not indicate a diagnosis of "hypertension". Therefore, the study population included a total of 312 patients. The patient characteristics are shown in Table 1.

Rates of prescription of several antihypertensive drugs divided according to age are shown in Fig. 1. With the exception of the 20-39 age group, the most commonly prescribed antihypertensive drugs were Ca channel blockers (Ca blockers), followed by angiotensin converting enzyme inhibitors (ACE-I). In the case of \(\alpha\)-adrenergic blockers (\(\alpha\) blockers), its rate of use was higher in the younger age groups.

The rates of various complications in each age group are shown in Fig. 2. The rates of congestive heart failure (CHF) and ischemic heart disease (IHD) tended to increase with age. On the other hand, those of endocrine metabolic diseases such as diabetes mellitus (DM), hyperlipidemia and

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Males</th>
<th>Females</th>
<th>Mean ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>6</td>
<td>7</td>
<td>66.3± 7.4</td>
</tr>
<tr>
<td>40-49</td>
<td>7</td>
<td>14</td>
<td>65.4± 8.6</td>
</tr>
<tr>
<td>50-59</td>
<td>31</td>
<td>55</td>
<td>66.8±10.0</td>
</tr>
<tr>
<td>60-69</td>
<td>46</td>
<td>48</td>
<td>65.2± 8.9</td>
</tr>
<tr>
<td>70-79</td>
<td>32</td>
<td>39</td>
<td>60.7± 9.5</td>
</tr>
<tr>
<td>≥80</td>
<td>16</td>
<td>11</td>
<td>59.5±10.5</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; IHD, ischemic heart disease; DM, diabetes mellitus. Age represents Mean ± S.D. (years old).
The peculiar use ratios of antihypertensive drugs in each complication are shown in Fig. 3. In CHF, the peculiar use ratio of diuretics was 3.96 (p<0.05) and that of ACE-I was 1.66 (not significant). Also, the use ratio of β-adrenergic blockers (β blockers) in arrhythmia patients (not
Discussion

The purpose of antihypertensive therapy is not only to normalize the blood pressure but also to prevent severe or fatal complications of the cardiovascular system. Also, the presence or absence of target organ failure and major dangerous factors influence the prognosis of hypertension. Therefore, an appropriate evaluation of these risk factors is important. The WHO/ISH GL and JNC VI outlined standard treatment procedures on the presence or absence of coronary vascular risk and complications, and indicated appropriate antihypertensive treatment regimens based on these parameters. It is necessary to consider such complications when evaluating antihypertensive therapy. In this study, we examined the current state regarding the use of antihypertensive drugs and their associated complications from the pharmacist’s viewpoint.

Firstly, we investigated the prescription rates of various antihypertensive drugs according to patient’s age. With the exception of the 20-39 age group, in which the number of patients was small, the most commonly prescribed antihypertensive drugs were Ca blockers. Ca blockers were reported to be used in more than 70% of cases at large special facilities (e.g. the National Cardiovascular Center, Japan). Our results were in agreement with this previous report. The specific hypotensive actions of these drugs facilitate their use. Also, severe side effects or internal organ dysfunction such as renal failure were seldom reported, making it comparatively simple to determine appropriate dosage regimens for large numbers of patients. However, these agents were reported to cause recurrence and mortality of myocardial infarction to increase in hypertensive subjects or subjects with coronary artery disease. There is some degree of controversy regarding their use. It is, therefore, necessary to perform further large scale clinical trials to reevaluate the position of Ca blockers.

The next most prescribed drugs were ACE-I. These have mild effects, various organ protective actions and few severe side effects. Therefore, they are widely used as the first choice of antihypertensive therapy in Japan. On the other hand, ACE-I has sometimes seen restricted use in patients with renal failure. Renal function generally declines with age, which may have been responsible for the observed tendency for its use to decrease in older subjects. But, in this study, we were unable to discuss this relationship in detail, because of the lack of considerations to its function. Only one patient was treated with angiotensin-II (AT-II) antagonists during this investigation period, but in a preliminary survey, treatment with ACE-I was changed to AT-II antagonists in a few cases. One of the reasons for this switch was the appearance of a cough. Further studies in

significant), and, that of α blockers in DM were significantly higher (p<0.05) than those in patients without these complications.
larger numbers of patients are, therefore, necessary to evaluate the effects of AT-II antagonists.

In the present study, the frequency of α blockers use was low in older patients. It is difficult to use these agents in the elderly because of their major side effect, orthostatic hypotension[20]. β blockers have been suggested to reduce the incidence of coronary vascular system diseases in various large scale clinical trials, and to be a good first choice in antihypertensive therapy[25]. However, the study of these agents in larger numbers of cases is necessary. In our results, the rates of use of β blockers were much lower than those of Ca blockers and ACE-I.

Next, we studied the distributions of each complication with regard to age. The rates of cardiac diseases such as CHF and IHD increased with age. In the younger age groups, those of endocrine metabolic diseases such as DM and hyperlipidemia were relatively high, which was consistent with recent epidemiological reports[40].

Moreover, we examined the peculiar use ratios of antihypertensive agents in patients with each of the various complications. The ratio of diuretics in patients with CHF was higher than that in non-CHF, confirming the role of diuretics in the treatment of CHF. In WHO/ISH GL and JNC VI, it was reported that diuretics showed “compelling indications” against CHF, and our results were consistent with these GL. Also, ACE-I, which has an organ protecting action[10], was used at a higher rate in patients with CHF than in those with other complications. The ratio of β blockers showed a correlative tendency with the rate of IHD. This was in agreement with the previous reports, i.e. β blockers improved the coronary artery disease and prevented the myocardial infarction[10]. On the other hand, in heart diseases such as CHF and rest angina, and endocrine metabolic diseases such as DM and hyperlipidemia, the ratio of β blockers was relatively low (but, not significant). Previously, β blockers had “contraindications”, because these agents can adversely affect carbohydrate and lipid metabolism. However, in recent GL[3,4], the use of these agents could be dependent on the status of the patient’s clinical condition in these diseases. The ratio of α blockers was correlated with the rates of DM (p<0.05) and hyperlipidemia (not significant). α blockers were reported to have little effect on sugar metabolism, and a favorable affect on lipid metabolism[15,16].

As mentioned above, in this study, we could not indicate completely the characteristic use of these agents, i.e. β and α blockers. In the present study, we used the patients’ diagnosis based on a review of their clinical records. This used the insurance diagnostic names, which don’t reveal the patient’s condition precisely, because of diagnosis not only in definite cases but also in suspected. Therefore, this approach might possibly have led to inappropriate patients’ groups. This was a major limitation of the present study. In future, “prospective” rather than “retrospective” studies should be performed after taking up “proper” patients’ groups which had “proper” diagnosis.

In conclusion, due to the variety of the patient’s profiles and the clinical backgrounds antihypertensive drug therapy has thus become a complex issue. In addition, the GL is not applicable in all cases. However, the results in this study suggested that the current state regarding the use of antihypertensive drugs and their associated complications in our hospital was similar to previous reports. This was considered to be basic knowledge in further investigations. It is necessary to accumulate and analyze findings including the types of treated diseases, the indications and dosage of each applied drug to establish more effective and safer antihypertensive pharmacotherapies.

References


