Home Blood Pressure and Circadian Variation of Blood Pressure in the Evaluation of Hypertensive Patients

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Clinic blood pressures measured at clinic by physician were higher than home blood pressures measured at home by patients in the majority of untreated patients with essential hypertension, but equivalent or lower in some patients. Clinic minus home blood pressure (ΔP) were correlated with the levels of clinic blood pressure ($r = 0.51$, $p < 0.005$ for systolic; $r = 0.35$, $p < 0.02$ for diastolic blood pressure, respectively). The systolic ΔP might be greater in the middle-aged women, especially in the fifties of females than the age-matched males ($p < 0.05$). The ΔP could not be altered by any antihypertensive drugs with the exception of systolic ΔP with diuretic alone.

The blood pressure tended to remain more stable throughout the 24-hour period in proportion as the severity of hypertension increased. The observation of circadian variation in blood pressure disclosed that the blood pressure was lower in the morning, but increased gradually, resulting in the relatively high blood pressure between the afternoon and evening in the low renin and volume expanded type of hypertension. On the contrary, the blood pressure was already high in the early morning in hypertensive patients characterized by the accelerated renin-angiotensin system and contracted volume factor.

SINCE the raised blood pressure increases the morbidity and mortality due to cardiovascular complications (VA cooperative studies), the primary aim of antihypertensive therapy is to reduce blood pressure by all means. In most cases the decision to treat hypertension depends largely upon the level of pressure at a few points.

Key Words:

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Essential hypertension
Secondary hypertension

However, there is a circadian variation in blood pressure and also a great variability in any individual patient. Therefore, an understanding of blood pressure variation is desirable to any therapeutic regimen for the inpatients. It is also natural for us to want to know the levels of blood pressure at home, because the outpatients used to spend most of times at their houses.

In recent years, much reliable equipment for self and automatically measuring blood pressure has been developed and is available for clinical use.

Using some of these equipments, we studied

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Fig.1. Clinic minus home blood pressure (ΔP) correlated with the level of blood pressure recorded at the outpatient clinic. The dotted line represents the equality between home and clinic blood pressure.

in order to elucidate whether or not the home blood pressure differs from the major clinic blood pressure and whether or not the circadian variation of blood pressure is different among the various pathophysiological backgrounds.

I. Discrepancy Between Home and Outpatient Clinic Blood Pressure

METHODS

All subjects were volunteers who had been consulted and/or treated for their high blood pressure at the hypertension clinic, National Cardiovascular Center, Osaka, Japan.

In the beginning, each subject's blood pressure manometer was tested for accuracy. After they were taught how to measure their own blood pressure using already checked manometer, the blood pressure readings were compared with those by the well-trained nurse to assure that the subject's procedure was correct.

Sphygmomanometers were considered acceptable if the difference was not over 4 mmHg from the correct value of 200mmHg. Subjects who could not measure their blood pressure correctly

were eliminated from the present studies. Most of such patients were old people.

The home blood pressure was taken at home by the patients themselves in the sitting position, and then its reading was recorded on a given sheet. The arithmetic average of home blood pressures in the morning between two days ago and the day just before the visit to the hospital was regarded as the representative, and then compared to the casual blood pressure, measured by physicians in the outpatient clinic, which was taken also in the sitting position.

RESULTS

In the 46 untreated patients with essential hypertension, the differences between clinic and home blood pressure (ΔP) were correlated with the levels of clinic blood pressure (Fig. 1). This correlation was more remarkable for systolic rather than diastolic blood pressure. As a whole, systolic and diastolic blood pressures at clinic were higher by 14 and 12%, respectively, as compared to those at home. However, there are some patients whose home readings were higher or equivalent as shown in Fig. 1.

Fig.2. Clinic blood pressure was compared with home blood pressure in each age- and sex-matched group, and in the age-matched female and male group. Each column represents the mean $\pm$ one standard deviation of the mean.

In order to know which groups of subject are more likely to have large differences between their clinic and home readings, the ΔP was evaluated in each age- and sex- matched group, and then, compared between females and males in the same-aged groups. In general, the systolic ΔP might be larger in female patients, especially in the fifties of females ($p < 0.05$) (Fig. 2). The diastolic ΔP also showed almost similar trend, but not statistically significant (Fig. 3).

Secondly, the ΔP in the essential hypertensives under the treatment of diuretic alone, beta adrenergic blockade alone, diuretic plus beta blocker and the latter combination plus vasodilator was compared to that in the control, e.g., age- and sex-matched patients without antihypertensive therapy. These control cases were selected from the previously mentioned subjects. The present results showed that the antihypertensive therapy could not alter the ΔP with the exception of diuretic alone. Only systolic ΔP was decreased significantly in the patients treated with diuretic alone ($p < 0.05$) (Fig. 4).

Fig.3. For explanation see Fig.2.

Fig.4. Effect of antihypertensive treatment on the blood pressure discrepancy between home and clinic in patients with essential hypertension. Each column represents the mean of $\Delta P \pm 1$ SEM during the therapy with various antihypertensive drugs.

DISCUSSION

It has been reported that the clinic blood pressures are higher,¹⁻³ equivalent⁴ or lower⁵ than self-recorded home pressures. However, the present studies revealed that there are some variation between individuals. This finding agreed with the Laughlin's report⁶

Our preliminary studies disclosed that any tranquilizer did not always alter the direction and degree of ΔP , that is, ΔP may not be affected by any drugs except for the inhibitory effect of diuretic alone on the systolic ΔP . The decreased ΔP with diuretics may be due to the decreased vascular reactivity produced by body fluid depletion.

There is a tendency for the forties and fifties of women to have the higher blood pressure at clinic than home blood pressure. In fact, some patients are so apprehensive about their blood pressure that they have extremely high levels of clinic blood pressure frequently despite of little or no organ damages. Physician, therefore, should pay attention to the probable discrepancies between clinic and home blood pressure in some cases, especially in the referred middle-aged woman. The measurement of blood pressure at home should be tried for such patients.

However, it is still controversial whether clinic or home blood pressure should be used for deciding the indication of the antihypertensive therapy and dosage of drugs. Although the casual blood pressure have been used in many epidemiological studies confirming the advantages of antihypertensive treatment, home recordings may be also valuable for avoiding the side effects induced by the over-dosage of drugs. But, it is advisable from our experience that the blood pressure should not be measured at home if patient's characteristic is unstable and neurotic.

II. Circadian Variation of Blood Pressure

METHODS

Twenty-four hours continuous blood pressure monitoring was completed in 8 patients with borderline and moderate essential hypertension. Blood pressure was recorded *via* a polyethylene catheter (Hakko 21G) inserted into brachial artery and attached to a transducer (Statham P-50) coupled to a telemetric blood pressure manometer (San-Ei 270) and trend recorder (San-Ei 6135A). In the same cases the blood pressure was measured noninvasively by automatic sphygmomanometer/printer (Nippon Corlin BP-203X) a few days apart. Both measurements were carried out in almost similar condition except for the different methodology, and the order of each method was randomized.

In the preliminary studies, blood pressure levels were compared simultaneously between

the above mentioned direct (Y) and indirect method (X), because blood pressures by direct method are reported to be usually higher than those by indirect method.⁷ In systolic and diastolic blood pressure, there were correlations between the two methods ($p < 0.001$), the regression equations for the respective pressures being $Y = 1.07 X - 4.9$ and $Y = 0.96 X + 8.3$. According to these regression equations, blood pressure levels by direct method were higher by 6 to 9 mmHg around 150 to 200 mmHg in systolic blood pressure and by 4 to 3 mmHg around 100 to 130 mmHg in diastolic blood pressure as compared to the values by indirect method.

Circadian variation of blood pressure obtained by direct method was essentially same to the patterns in the previous reports,⁸⁻¹¹ but that by indirect method did not always show such a typical pattern, which is characterized by nocturnal fall of blood pressure during sleep (Fig. 5). Even if we consider the existence of some differences between these two methods, the most important factor for this discrepancy could be explained by the following. The direct method forced the increased sympathetic tone continuously especially in a day of awake state, whereas the indirect method forced less sympathetic tone at least in a day. This explanation was also justified by the increased pulse rate in a day when in use of the invasive direct method.

Although the acute inflation of cuff and the printer noise by indirect method may cause frequently some sleep disturbance to a certain extent in the bed-in time and midnight, the intra-arterial technique also may interrupt sleep during a night. In addition, the direct method might run a risk against patients, while the indirect method is safe

Fig. 5. Circadian variation in blood pressure and pulse rate obtained by the direct (left) and indirect method (right).

for them. It is therefore possible for the automatic sphygmomanometer to measure circadian variations of blood pressure repeatedly. As far as we checked the reliability of this method, the circadian variation could be obtained by this noninvasive equipment with reproducibility and the noninvasive method is more useful in view of clinical application.¹²

RESULTS

Comparison of circadian variation in blood pressure among the different grades of essential hypertension

Patients with essential hypertension were first divided into borderline and arterial hypertension according to the WHO definition,¹³ and then, the latter was again subdivided into mild, moderate and severe hypertension according to the criteria advocated by Tokyo University.¹⁴ These classifications were made at the beginning of recording of the circadian variation of blood pressure.

The hourly averaged circadian variation in each group were demonstrated in Figure 6. The nocturnal fall of blood pressure were found in all groups, but slight in borderline, moderate and severe hypertension with the exception of mild hypertension. As usual, most of our patients got up around 6:00 and went to bed around 21:00. However, some patients lay awake in the late

evening, and therefore, there were appreciable rises of blood pressure between 22:00 and 1:00. Despite of these facts, it also appears that the widest variations of systolic blood pressure were those of the patients with mild hypertension.

On the contrary, in patients with borderline, moderate and severe hypertension the blood pressure remained stable throughout the 24-hour reading and was not so influenced by sleep, etc. These findings agreed with those of Pessina, A.C. et al.¹⁵ using the intra-arterial technique, although their grading of hypertensive state were different from ours. Our mild and moderate hypertension may be rather close to moderate and severe hypertension, because our grading was performed by the use of stabilized blood pressure levels following admission.

Relationship between the circadian variation of blood pressure and the pathophysiology of hypertension

Seventy-five patients with essential hypertension were divided into high, normal and low renin group according to the basal plasma renin activity (PRA) in the morning of the fourth day following strict restriction of salt less than 3g per day.

The blood pressure was not low even in the morning and remained stable throughout a day in the high and normal renin group, whereas it was

Fig. 6. Comparison of circadian variation in blood pressure between the different severities of essential hypertension.

Fig. 7. Circadian variation of blood pressure in essential hypertension with high, normal and low plasma renin activity.

Fig.8. Circadian variation of blood pressure in 9 untreated patient with renovascular hypertension (left) and 5 patients undergoing the operation (right).

Fig.10. Circadian variation of blood pressure in primary aldosteronism. A small adenoma was found and removed recently in the patient (KH; left).

Fig.9. Circadian variation of blood pressure in patients with pheochromocytoma. A tumor was found and removed recently also in the left case (KK).

lower in the morning than afternoon, but rised gradually after 15:00 and remained still high during the evening in the low renin group (Fig. 7).

The circadian variation of blood pressure was therefore evaluated in a few kinds of secondary hypertension in order to confirm whether or not the renin-angiotensin-aldosterone system is involved in determining the circadian variation of blood pressure.

The blood pressure remained high throughout the 24 hours reading in patients with renovascular hypertension, whose PRA were indeed high. This pattern was the same as that in the high and normal renin group of essential hypertension, but it changed into the pattern seen in the low renin type of essential hypertension after surgical treat-

Fig.11. Effect of salt depletion on the circadian variation of blood pressure and pulse rate.

ment (Fig. 8).

In 2 cases with pheochromocytoma the blood pressure was high in the morning, but relatively lower in the afternoon and evening. Both patients had also high values of PRA. This particular pattern disappeared after treatment, especially after the removal of tumor (Fig. 9).

On the contrary, the blood pressure was lower in the morning, whereas it remained high between afternoon and evening in the patients with primary aldosteronism. This preoperative pattern bore a resemblance to that of essential hypertension with low PRA, but such a typical pattern

Fig.12. Effect of single administration of captopril (12.5–100 mg in the morning) on the duration of hypertensive effect. Figures in the rectangular squares mean the dose of captopril administered.

disappeared after the treatment (Fig. 10). These changes of pattern in the circadian variation of blood pressure were also recognized before and after the salt depletion (Fig. 11). The reduction of volume factor seems to inhibit the pressor responses to some stimuli, which might occur especially during the afternoon and evening.

Clinical application of circadian variation in blood pressure

One of the most important roles of recording blood pressure over the 24-hour period is to determine the dosage of an anti-hypertensive agent and the timing of its administration. These evaluation should be unavoidable especially in the use of a newly developed antihypertensive drug. The present studies were therefore designed to assess the influence of the angiotensin I converting enzyme inhibitor, captopril,¹⁶ on the duration of its hypotensive effect and the circadian variation of blood pressure.

In 3 patients with essential hypertension the mean arterial pressure fell later than one hour and continued to fall for 6 to 8 hours following the single administration of captopril 100 mmHg (Fig. 12). When captopril was administered 25 to 100 mg TID, the blood pressure was controlled fairly over 24 hours period in patients with moderate and severe essential hypertension. But, this hypotensive effect might be decreased slightly in the midnight (Fig. 13).

DISCUSSION

The present studies indicated that the more

Fig.13. Effect of captopril on the circadian variation of blood pressure and pulse rate in patients with moderate and severe essential hypertension.

the severity of hypertension developed, the more stable the blood pressure remained throughout the 24-hour period. Since the nocturnal fall of blood pressure was slight in patients with severe hypertension, the blood pressure should be noticed carefully and controlled even during the night in such patients. However, there were some patients with severe hypertension whose nocturnal blood pressure fell remarkably. In these cases with the organ damages due to ischemia, their blood pressure should not be lowered so much through the night by an antihypertensive drug. The dangers of pronounced iatrogenic hypotension should be avoided by all means.

The blood pressure in the morning was rather high in the patients with high and normal PRA as well as severe hypertension and extremely high in the patients with pheochromocytoma. The present results suggested that the severe hypertension was associated with renin-angiotensin system to a great extent as compared to the less severe hypertension, although the values of PRA were disregarded in classifying the severities of hypertension.

The common pathophysiological backgrounds of the above high renin type of hypertensive states might be characterized by the contracted plasma volume. To the contrary, the plasma volume might be expanded in the essential hyper-

tension with low PRA and especially in the primary aldosteronism.^{17,18} On the other hand, it is well known that these human physiological functions involved in the regulation of blood pressure possess their own circadian variation. In fact, it is reported that PRA and angiotensin II were decreased at the late evening, tended to increase throughout the midnight and then reached to the peak early in the morning in normal human subjects.^{19,20} In contrast, the urinary output and natriuresis were usually decreased in the night as compared to those found in a day.^{21,22} However, the nocturnal natriuresis and diuresis were also demonstrated in a patient with primary aldosteronism.²³ These previous findings may support the present results concerning the circadian variation of blood pressure. Namely, the renin-angiotensin system might be stimulated to a great extent, resulting in the relatively higher blood pressure in the morning in the high renin and volume contracted type of hypertension. On the other hand, the renin-angiotensin system might be still suppressed in the morning, in which time the volume factor might have just altered from the expanded state to the near-normal state in the low renin type of hypertension. But, as the volume factor tended to increase gradually after meals, the pressor responses to exogenous stimuli might be increased, resulting in the relatively higher blood pressure in the afternoon and evening in such patients.

Since the hypotensive effects of captopril were considerably different between individual patients, the correct dose and timing of its administration should be decided individually with the utmost care.

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