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Clinical application of wave intensity for the treatment of essential hypertension

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Abstract Wave intensity analysis is a method of studying intravascular flow wave propagation, calculated as the product of the rate of change in pressure (dP/t) and the rate of change in velocity (dU/dt). The typical pattern of wave intensity seen during the cardiac cycle has two dominant peaks. The larger first peak (FP) occurs during early systole when a forward traveling compression wave is generated by the left ventricle. The second smaller peak (SP) follows a period of relatively little net wave production during mid-systole. Wave reflection is seen as a small backward-traveling compression wave occurring just after the first peak of wave intensity (NP). In this study, we investigated the usefulness of parameters from the wave intensity for estimating the efficacy of the α-1 blocker, doxazosin, to reduce blood pressure, by the reduction of peripheral vascular resistance. We examined 20 patients with essential hypertension. Patients were included if their diastolic blood pressure was >95 mmHg on at least three separate visits to the clinic. The study consisted of a 2-week baseline phase followed by a 2–4-week dose-adjusted phase with doxazosin. Treatment began with 1 mg/day doxazosin, and the dose was doubled fortnightly until the diastolic blood pressure was <90 mmHg. Blood–pressure measurements and side effects were recorded at intervals of 2 weeks. Before and after 4 weeks of stable treatment with doxazosin, a comprehensive clinical evaluation was given. Doxazosin reduced systolic and diastolic blood pressure. Both FP and SP increased and NP decreased. ΔMBP (change in mean blood pressure) correlated well with NP before and after the antihypertensive therapy. The efficacy of doxazosin was confirmed by the decreased reflection wave of aortic flow from wave intensity analysis. Thus, patients with a significant reflection wave may be good candidates for antihypertensive treatment by a vasodilator, such as doxazosin.

Key words Wave intensity · Hypertension · α-Blocker

Introduction

Wave intensity analysis is a method of studying intravascular flow wave propagation, and is calculated as the product of a change in pressure (dP/dt) and a change in velocity (dU/dt).[1–3] Some clinical applications were attempted in the artery and ventricle.[4–6] The typical pattern of wave intensity seen during the cardiac cycle has two dominant peaks. The larger first peak occurs during early systole when a forward-traveling compression wave is generated by the left ventricle following the opening of the aortic valve and the acceleration of blood in the ascending aorta. The second smaller peak follows a period of relatively little net wave production during mid-systole when the wall motion caused by left ventricular contraction is matched by the movement of blood out of the left ventricle. Also, wave reflection is seen as a small backward-traveling compression wave occurring after the first peak of wave intensity.

Treatment of hypertension is important in the prevention of cardiovascular complications. Therefore, a strategy for effective antihypertensitive therapy is essential for the management of patients with essential hypertension.[7] Most patients with hypertension have an increased arterial pressure that is associated with an increased contractile state or increased mass of vascular smooth muscle in arterioles. Therefore, a major alteration in hypertension is an increased vascular resistance, which is caused by an increase in the tone of vascular smooth muscle in the arteriole. Wave reflection in wave intensity parameters can be useful for the estimation of vascular tone in patients with hypertension. In this study, we tried to estimate the usefulness of wave intensity analysis in assessing the hemodynamic effect of antihy-

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pertensive treatment.[3] We used doxazosin, a quinazoline derivative which acts on postsynaptic α-1 receptors and lowers blood pressure by reducing peripheral vascular resistance. In this study, we investigated the usefulness of parameters from the wave intensity for estimating the efficacy of doxazosin in reducing blood pressure by decreasing peripheral vascular resistance.

Patients and methods

Patients

We examined 20 patients with essential hypertension. Patients were included if their diastolic blood pressure was >95 mmHg on at least three separate visits to the clinic. The study consisted of a 2-week baseline phase followed by a 2–4-week dose-adjusted phase with doxazosin. Treatment began with 1 mg/day doxazosin, and the dose was doubled fortnightly until the diastolic blood pressure was <90 mmHg. Informed consent was obtained from all patients. This study was approved by the ethical committee of our university.

Blood–pressure measurements

Blood pressure was measured in a quiet room after a rest of 15 min in the recumbent position. Brachial blood pressure [systolic blood pressure (SBP), diastolic blood pressure (DBP)] and heart rate were measured in the left arm. A mean of three readings was taken. Mean blood pressure (MBP) was calculated by the formula, DBP + (SBP − DBP)/3. Blood–pressure measurements and side effects were recorded at intervals of 2 weeks. Before and after 4 weeks of stable treatment with doxazosin, a comprehensive clinical evaluation was made and parameters of wave intensity were examined.

Measurement of wave intensity

We used QFM 1100 special version (Hayashi Electric, Kanagawa, Japan) for the measurement of wave intensity. This system was modified according to the method of Niki et al.[8] In this system, blood pressure waveforms were obtained from the diameter of the carotid artery and calibrated by the peak and bottom values measured with a cuff-type manometer applied to the upper arm. $(dP/dt) \times (dU/dt)$ were then calculated simultaneously using an electrocardiogram (Lead II) (Fig. 1). A transducer was placed on the right common cervical artery with the patient in the supine position. All measurements were averaged over 10 beats. All data of blood flow velocity, pressure, and wave intensity measured by the QFM system were also transferred to a personal computer (VAIO, PCG-Z505G, Sony, Tokyo, Japan) and analyzed. The parameters of wave intensity were: FP (mmHg·m/s^3): first positive peak of wave intensity curve; SP (mmHg·m/s^3): second positive peak of wave intensity curve; NP (mmHg·m/s^3): negative peak just after the first peak of wave intensity curve.

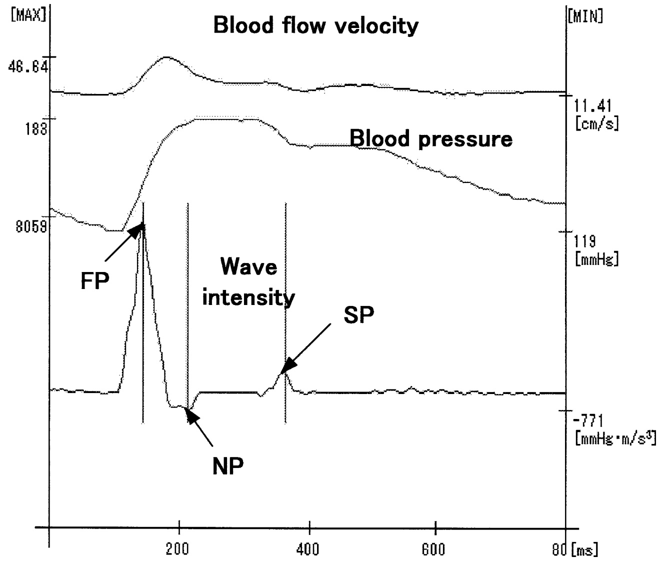

Fig. 1. Recording of wave intensity parameters. *FP*, first positive peak; *SP*, second positive peak; *NP*, negative peak just after first positive peak

Statistical analysis

All data are expressed as the mean ± standard deviation. Linear regression analysis was used to compare blood pressure reduction and NP on wave intensity parameters.

Results

Blood pressure and heart rate

Average administered dose of doxazosin was 2 mg/day. Doxazosin reduced systolic and diastolic blood pressure in casual blood pressure (165 ± 5 vs 127 ± 16 mmHg in systolic blood pressure, $P < 0.01$, 96 ± 17 vs 72 ± 8 mmHg in diastolic blood pressure, $P < 0.01$). However, the heart rate did not change (60 ± 3 vs 60 ± 3 beats/min).

Parameters of wave intensity

After treatment, both FP and SP increased, and NP decreased. ΔMBP (change in mean blood pressure) correlated well with both NP before treatment and ΔNP (change in NP) ($r = -0.92$ and 0.93, $P < 0.01$) (Figs. 2 and 3).

Discussion

We clarified the usefulness of wave intensity parameters, and revealed that suitable cases for vasodilator therapy can

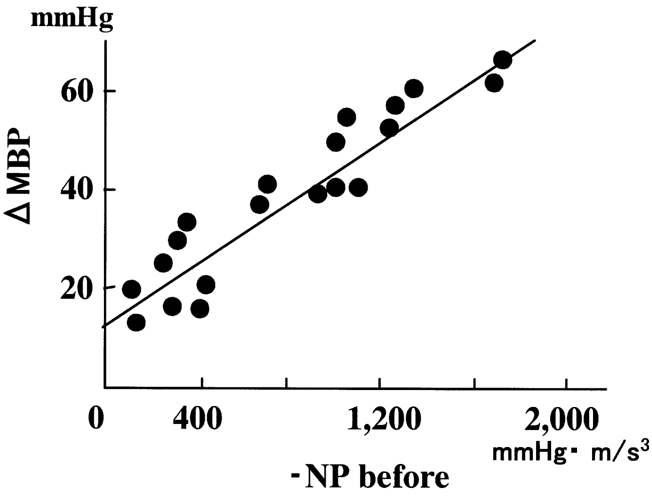

Fig. 2. Relationship between negative peak (*NP*) before treatment and change in mean blood pressure (Δ*MBP*). *NP* and ΔMBP showed a good negative correlation ($r = 0.92$, $P < 0.01$)

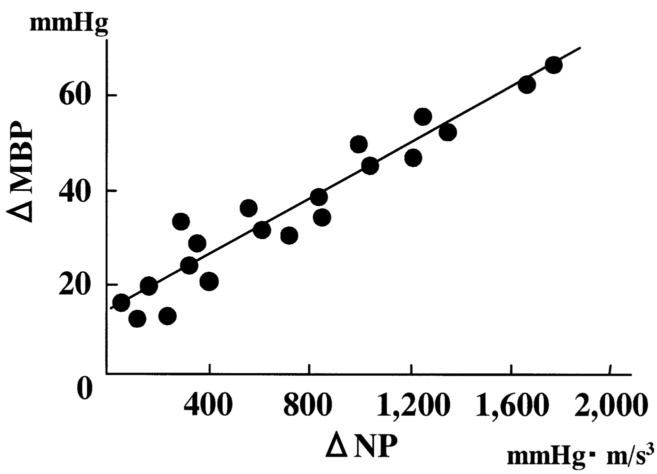

Fig. 3. Relationship between change in negative peak (ΔNP) and ΔMBP. ΔNP and ΔMBP showed a good correlation ($r = 0.93$, $P < 0.01$)

be selected by wave intensity parameters in patients with essential hypertension.

Wave intensity is a newly developed method to measure wave propagation as a physical parameter. There will be some advantages to this method, because it determines the nature of the flow in terms of fluid dynamics in the aorta. This study clarified its usefulness in antihypertensive therapy. Recent studies using wave intensity, have mainly been concerned with the hemodynamic changes associated with pharmacological agents, such as cathecholamines and vasodilators.[9,10] Hyperdynamic effects of catecholamines increase first peak wave intensity, and vasodilators make the second peak decrease. The wave intensity parameter is considered to be useful for analyzing the interaction between the heart and the vessels.

As the changes for wave intensity parameters will be not only for doxazosin but also common for vasodilators other than doxazosin, we would favor using these changes in wave intensity parameters as a guide for selecting suitable candidates for vasodilator therapy. Degrees of first negative peak intensity may represent the efficacy of doxazosin in patients with essential hypertension.

Estimation of efficacy for antihypertensive treatment

Selection of an antihypertensive drug is often done using the clinical experience of the doctor, considering the effects of age and any hemodynamic changes.[11,12] However, the results of our study suggest that the use of vasodilation may be monitored using wave intensity measurement. Increased negative peaks during middle systole correlate well with the clinically observed effects of antihypertensive treatment.

In the present study, we chose those patients indicated for vasodilator therapy. Further studies may also reveal the indication of other drug therapies. It may be possible to select suitable antihypertensive treatments from the point of view of the hemodynamic status of the patient.

The reflection wave from the peripheral artery can be represented by wave intensity parameters. This is measured by the middle systolic negative peak of wave intensity parameters.

In essential hypertension, there are thought to be two types of hemodynamic groups. One is hyperdynamic, and the other is the high vascular resistance group. The hyperdynamic group has low peripheral artery resistance and is usually found in mild essential hypertension. The high vascular resistance group may be a different subgroup of essential hypertension. An augmentation index has been used for the estimation of wave reflection and arterial stiffness. Mahmud and Feely showed that angiotensin II receptor blockade can be considered to have a favorable effect on arterial wave reflection in resistant essential hypertension.[13] Calcium-channel blockers were also shown to have favorable effects on wave reflection in the treatment of hypertension by Pannier et al.[14] O'Rourke also showed that optimization of wave reflection is one of the goals of the treatment of hypertension.[15] Wave intensity analysis may be useful in distinguishing the hyperdynamic group from the high wave reflection group. This analysis may be useful for determining suitable treatments for hypertensive patients in order to control complicating hemodynamic abnormalities.[16] This may also explain the usefulness of wave intensity parameters in analyzing the pathophysiology of patients with essential hypertension.

There were some limitations in this study. We did not evaluate a large number of patients with essential hypertension, although the results are highly significant. A placebo-controlled study would confirm the results of this study. We did not continue to examine patients not indicated for effective treatment by this α-blocker (doxazosin). If the patient were a nonresponder to this antihypertensive treatment it would not be justifiable to continue treatment with this drug. Comparison with the responses to β-blocker therapy might be recommended.

In conclusion, the efficacy of doxazosin was confirmed by the decreased reflection wave of aortic flow indicated by wave intensity analysis. Thus, patients with a significant reflection wave may be good candidates for antihypertensive treatment with vasodilators, such as doxazosin.

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