CLIN. AND EXPER.-THEORY AND PRACTICE, A11(SUPPL.2), 535-544 (1989)

ANGIOTENSIN CONVERTING ENZYME INHIBITION, PULSE WAVE VELOCITY AND AMBULATORY BLOOD PRESSURE MEASUREMENTS IN ESSENTIAL HYPERTENSION

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Key Words : Essential hypertension, Angiotensin converting enzyme inhibition, Ambulatory blood pressure recordings

ABSTRACT

Ambulatory blood pressure measurements are better at predicting the outcome of hypertension than single measurements. Since cardiovascular morbidity and mortality are mainly related to large artery damage in hypertensive patients, non-invasive indices of arterial distensibility, such as pulse wave velocity, have been proposed for the evaluation of cardiovascular risk. Indeed, pulse wave velocity is positively correlated with blood pressure (BP) when measured by ambulatory recordings, while there is no correlation with clinical mercury sphygmomanometer readings. Angiotensin converting enzyme (ACE) inhibitors such as perindopril not only reduce high blood pressure, but also increase arterial compliance and distensibility. This latter effect could lead to a more marked decrease in systolic blood pressure than diastolic blood pressure following long-term treatment with ACE inhibitors. This has been demonstrated using ambulatory blood pressure monitoring in hypertensive patients treated with perindopril for three months. The correlation coefficient between ambulatory systolic and diastolic blood pressure before ($r = 0.82$) and after ($r = 0.76$) perindopril was significant. Comparison of the corresponding slopes indicated that, for any given value of diastolic blood pressure, systolic blood pressure was significantly lower after perindopril than before perindopril. The action of the drug on the arterial wall may therefore explain the more marked effect on systolic blood pressure than on diastolic blood pressure.

INTRODUCTION

There is a general consensus that casual and office blood pressure recordings are predictive of subsequent cardiovascular damage. Unfortunately, they are somewhat unsatisfactory predictors, especially when blood pressure is in the so-called "mild hypertension" range (1). Several studies have shown that ambulatory blood pressure correlates more strongly than casual and office blood pressure recordings with echocardiographic indices of left ventricular hypertrophy (2-4) or with indices of target organ damage in the heart, optic fundi and kidney (5-7). However, since cardiovascular morbidity and mortality of patients treated for hypertension are mainly related to large artery damage (1, 8), non-invasive indices of arterial disease may be more suitable than echocardiographic findings and target organ damage for the evaluation of cardiovascular risk. In the present study, the relationships between ambulatory blood pressure monitoring and pulse wave velocity, used as an index of arterial distensibility, are analysed, in particular with respect to the effect of the angiotensin converting enzyme inhibitor, perindopril (9), on both parameters.

PULSE WAVE VELOCITY, ARTERIAL DISTENSIBILITY AND AMBULATORY BLOOD PRESSURE MONITORING IN UNTREATED HYPERTENSIVE PATIENTS

Recent studies have shown that, in patients with essential hypertension, the alterations concern not only the resistance vessels, but also the large arterial vessels, the compliance of which is significantly reduced (10). The determination of vascular impedance, which reflects the resistance, capacitive and inertial components of the

vessels, is certainly the most accurate index for the study of the arterial modifications in hypertension (11). In particular, impedance characteristics have been widely used to evaluate arterial distensibility (10, 11). This parameter is directly related to the corresponding pulse wave velocity in the arterial segment studied and inversely related to the cross-sectional area of the artery (11-13). Since this last factor is only slightly modified according to the blood pressure level, pulse wave velocity is the parameter most widely used as a non-invasive index of arterial distensibility (10-12). Regional pulse wave velocity can be easily determined from the time delay between the pulse wave recorded simultaneously from proximal and distal sites and is related to the distance between the recording sites. Pulse wave velocity, used as an index of arterial distensibility, can be measured in hypertensive patients and related to the level of blood pressure measured by ambulatory blood pressure recordings.

The carotid-femoral pulse wave velocity (PWV) was evaluated in 22 patients with sustained essential hypertension together with 3 different methods of blood pressure recording : mercury sphygmomanometer, semi-automatic blood pressure recording using the Dinamap apparatus and 24-hour ambulatory blood pressure monitoring with the Spacelabs monitor (13). Although PWV was not correlated with blood pressure measured by mercury sphygmomanometry, it was strongly and positively correlated with blood pressure measurements using the other two techniques. The best correlation was observed with ambulatory measurements and exclusively concerned systolic blood pressure ($r = 0.69$; $p < 0.001$; Figure 1). Finally, although PWV is positively correlated with blood pressure measured by mercury sphygmomanometry in large populations (11, 12), this correlation is only observed with ambulatory blood pressure recordings in smaller groups of subjects.

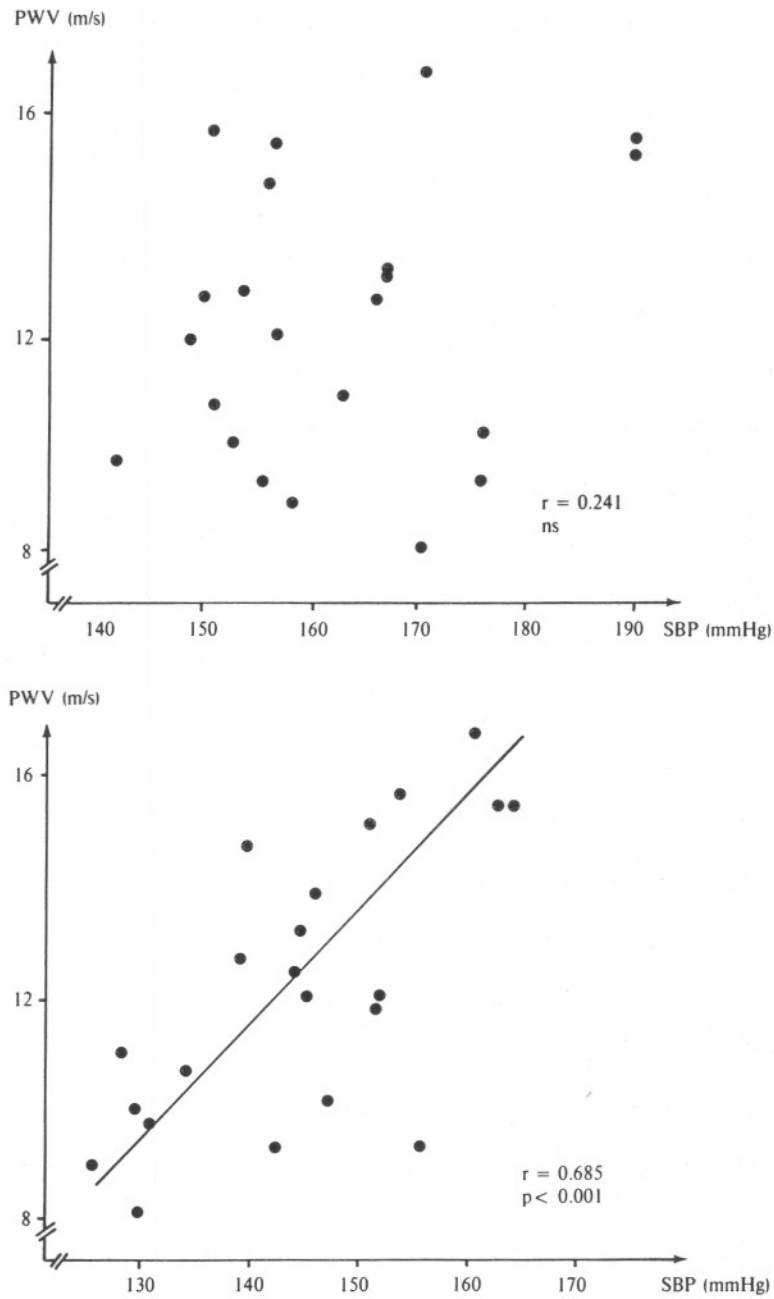

FIG. 1 : Relationship between carotid-femoral pulse wave velocity (PWV) and systolic blood pressure (SBP) measured either by conventional methods (on the upper panel) or by 24-hr ambulatory blood pressure recording (on the lower panel).
[(13) (with permission)].

Since the cardiovascular morbidity and mortality of patients treated for hypertension is mainly related to large artery damage, the determination of pulse wave velocity, together with ambulatory blood pressure measurements, can therefore be proposed for the evaluation of the effect of antihypertensive treatment.

ACE INHIBITION, ARTERIAL DISTENSIBILITY AND AMBULATORY BLOOD PRESSURE MONITORING

In previous studies (14-16), angiotensin converting enzyme inhibitors have been shown to be more effective for reducing systolic blood pressure than beta antagonists, for the same reduction in diastolic blood pressure. The design of these studies failed to determine whether the difference observed between the two drugs was due to a greater efficacy of the ACE inhibitor or to a lesser efficacy of the beta blocking agents. This result is potentially important in relation to angiotensin converting enzyme inhibitors. While diastolic blood pressure is predominantly influenced by the caliber of small arteries, systolic blood pressure is influenced by many other factors, such as the rate of ventricular ejection and the compliance and distensibility of large arteries. Ventricular ejection is not modified by ACE inhibitors, while arterial compliance and distensibility are significantly enhanced both in the acute and the long term (17). The increased arterial compliance and distensibility induced by long-term treatment with perindopril (Table 1) may therefore affect systolic blood pressure more than diastolic blood pressure, which would explain why angiotensin converting enzyme inhibitors decrease systolic blood pressure to a greater degree than diastolic blood pressure.

TABLE 1

Changes in blood pressure, heart rate and brachial artery hemodynamics before (T0) and after (T1) perindopril and following a second placebo period (T2) (18) (with permission).

	T0 (placebo)	T1 (active treatment)	T2 (placebo)
Mean blood pressure (mmHg)	128.9 ± 2.5	112.4 ± 3.6**	127.6 ± 2.4
Pulse wave velocity (m/sec)	10.09 ± 0.53	8.75 ± 0.24**	9.99 ± 0.43
Arterial compliance (dynes/cm^4/10^{-7})	1.29 ± 0.21	1.84 ± 0.15*	1.37 ± 0.18

Values are expressed as mean ± SEM
* $p < 0.05$, ** $p < 0.01$ in comparison with T0 and T2.

To assess this possibility, non-invasive ambulatory blood pressure monitoring was performed in 21 patients with sustained essential hypertension before and after 3 months of treatment with perindopril (19). The drug was administered at a dose of 4 or 8 mg once a day in the morning. Systolic and diastolic blood pressure decreased significantly ($p = 0.002$) over the entire 24-hour period. Comparison of the correlation coefficient between systolic and diastolic blood pressure recorded by the Spacelabs monitor before ($r = 0.82$) and after ($r = 0.76$) perindopril, indicated that these correlation coefficients were significantly different. Corresponding slopes were calculated and were equal to 1.13 ± 0.04 and 0.99 ± 0.04 respectively ; comparison of these slopes showed that, after treatment, the slope was significantly lower ($p < 0.01$) than before treatment, indicating that angiotensin converting enzyme inhibition by perindopril modifies the relation between systolic and diastolic blood pressure and may therefore decrease systolic blood pressure to a greater extent

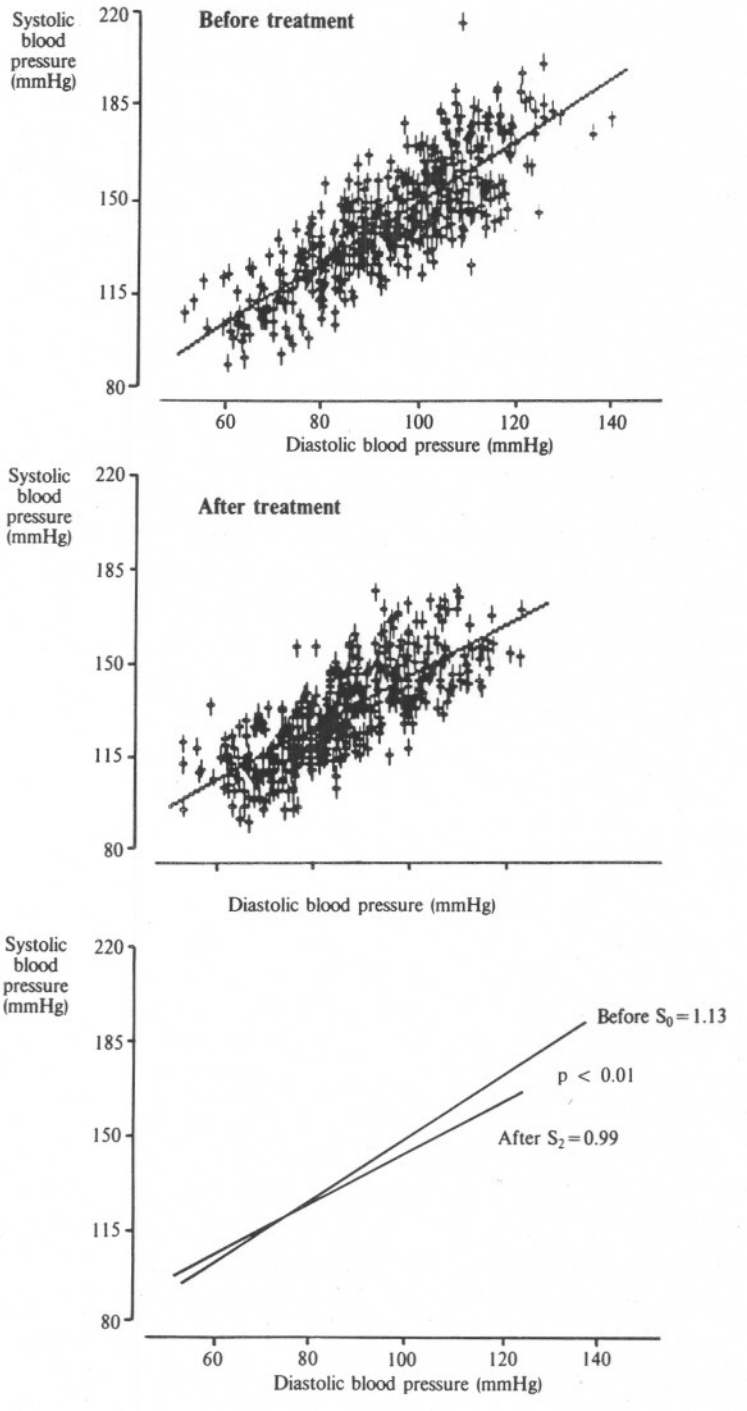

FIG. 2 : Correlation between systolic and diastolic blood pressure before and after perindopril. The correlation coefficient between these two parameters was 0.82 before and 0.76 after treatment. The corresponding slopes were significantly different ($p < 0.01$). [(19) (with permission)].

than diastolic blood pressure. Since perindopril is known to increase arterial compliance and distensibility (18), it seems likely that the more marked decrease in systolic rather than diastolic blood pressure induced by the drug may be related to its effect on the vessel wall of large arteries (Figure 2).

ACKNOWLEDGMENTS

This study was performed with a grant from the Institut National de la Santé et de la Recherche Médicale (INSERM), the Association pour l'Utilisation du Rein Artificiel (AURA), the Association Claude Bernard and the Ministère de la Recherche, Paris. We would like to thank Miss LORIDO and Miss McMORROW for their excellent assistance.

REFERENCES

1. Freis, E.D. Borderline mild systemic hypertension: Should it be treated? Am.J. Cardiol. 1986; 58: 642-645.

2. Rowlands, D.B., Ireland, M.A., Glover, D.R., Mc Leavy, R.A.B., Stallard, T.J.,Littler, W.A. The relationship between ambulatory blood pressure and echocardiographically assessed left ventricular hypertrophy. Clin. Sci. 1981; 61: 101s-103s.

3. Drayer, J.I.M., Weber, M.A., De Young, J.L. Blood pressure as determinant of cardiac left ventricular muscle mass. Arch. Intern. Med. 1983; 143: 90-92.

4. Devereux, R.B., Pickering, T.G., Harshfield, G.A., Kleinert, H.D., Denby, L., Pregibon, D., Jason, R., Kleinert, B., Borer, J.S., Laragh, J.H. Left ventricular hypertrophy in patients with hypertension: Importance of blood pressure response to regularly recurring stress. Circulation 1983; 68: 470-476.

5. Sokolow, M., Werdegar, D., Keim, H.K., Hinman, A.T. Relationship between level of blood pressure measured casually and by portable recorders and severity of complications in essential hypertension. Circulation 1966; 34: 279-298.

6. Pessina, A.C., Palatini, P., Sperti, G., Gordone, L., Libardoni, M., Mos, L., Mormino, P., Di Marco, A., Dal Palu, C. Evaluation of hypertension and related target organ damage by average day-time blood pressure. Clin. Exp. Hypertension 1985; A7: 267-278.

7. Mann, S., Millar-Graig, M.W., Raftery, E.B. Superiority of 24-hour measurement of blood pressure over clinic values in determining prognosis in hypertension. Clin. Exp. Hypertension 1985; A7: 279-282.

8. Safar, M.E., Bouthier, J.A., Levenson, J.A., Simon A. Peripheral large arteries and the response to antihypertensive treatment. Hypertension 1983; 5 (suppl III): 63-68.

9. Laubie, M, Schiavi, P., Vincent, M., Schmitt, H. Inhibition of angiotensin I converting enzyme with S-9490 : Biochemical effects, interspecies differences and role of sodium diet in hemodynamic effects. J. Cardiovasc. Pharmacol. 1984; 6: 1076-1082.

10. Safar, M.E., Simon, A. Hemodynamics in systolic hypertension. In: Handbook of Hypertension, 7, Pathophysiology of Hypertension, Cardiovascular Aspects, Zanchetti, A. and Tarazi, R.C. eds, Elsevier Sci. Pub., 1986, pp 225-241.

11. O'Rourke, M.F. Vascular impedance: The relationship between pressure and flow. In: Arterial Function in Health and Disease. Churchill Livingstone, London, 1982, pp 94-132.

12. Avolio, A.P., Chen, S., Wang, R., Zhang, C., Li, M., O'Rourke, M.F. Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community. Circulation 1983; 68:50-58.

13. Asmar, R., Brunel, P., Pannier, B., Lacolley, P., Safar, M. Arterial distensibility and ambulatory blood pressure monitoring in essential hypertension. Am. J. Cardiol. 1988; 61: 1066-1070.

14. Thind, G.S. Lisinopril versus atenolol alone and with hydrochlorothiazide in the treatment of mild-to-moderate essential hypertension. J. Hypertension, 1986; 4 (suppl 5): S423-S425.

15. Webster, J., Petrie, J.C., Robb, O.J., Trafford, J., Burgess, J., Richardson, P.J., Davidson, C., Fairhurst, G., Vandenhurg, M.J., Cooper, W.D., Arr, S.M., Kimber, G. Enalapril in moderate-to-severe hypertension: A comparison with atenolol. Br. J. Clin. Pharmacol. 1986; 21: 489-495.

16. Helgeland, A., Strommen, R., Hagelund, C.H., Tretli, S. Enalapril, atenolol, and hydrochlorothiazide in mild-to-moderate hypertension. A comparative multicentre study in general practice in Norway. Lancet 1986; 1: 872-875.

17. Safar, M.E., Laurent, S., Bouthier, J.D., London, G.M., Mimran, A. Effect of converting enzyme inhibitors on hypertensive large arteries in humans. J. Hypertension 1984; 4 (supp 5): S285-S289.

18. Asmar, R.G., Pannier, B., Santoni, J.-Ph., Laurent, S., London, G.M., Levy, B.I., Safar, M.E. Reversion of cardiac hypertrophy and reduced arterial compliance after converting enzyme inhibition in essential hypertension. Circulation 1988; 78:941-950.

19. Asmar, R.G., Pannier, B., Santoni, J.-Ph., Safar, M.E. Angiotensin converting enzyme inhibition decreases systolic blood pressure more than diastolic pressure as shown by blood pressure monitoring. J. Hypertension 1988; 6 (suppl 3): S79-S81.