AJH 1988; 1:103S–105S

Enhanced Brachial Artery Compliance Following Perindopril in Essential Hypertension

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Brachial artery mean arterial pressure (MAP), blood flow velocity (BFV), blood flow (BF), and arterial compliance (AC) were measured using pulsed Doppler systems in patients with sustained essential hypertension. The hemodynamic investigation was performed before (T_0) and after 3 months (T_1) of chronic treatment with the converting enzyme inhibitor Perindopril and after a further month with placebo (T_2). Following treatment with Perindopril, BFV, BF, and AC significantly increased while MAP significantly decreased. The changes in AC and BFV were negatively and significantly correlated both between T_0 and T_1 and between T_1 and T_2. The study showed that the increase in arterial compliance produced by Perindopril was inversely related to the extent of arteriolar dilatation, indicating that factors other than the blood pressure reduction itself were involved in the brachial artery changes. Am J Hypertens 1988;1:103S–105S

KEY WORDS: Large arteries, hypertension, converting enzyme inhibition.

Converting enzyme inhibitors (CEI) are known to produce together a blood pressure reduction and an increase in arterial compliance.[1] Since the mechanical effect of blood pressure reduction may cause "per se" a compliance enhancement,[1] the question is raised to know if the observed changes in compliance are drug or pressure-induced.[1] Indeed CEI might pharmacologically relax the arterial smooth muscle[2] independently of blood pressure reduction. For that reason, we studied the changes in forearm arterial hemodynamics produced by the CEI Perindopril.[3]

MATERIAL AND METHODS

Fifteen patients with sustained essential hypertension (grades I and II of the WHO classification) were included in the study. Mean age was 49 ± 2 years (±1 SEM). Previous treatments were discontinued at last 15 days before the study. Diastolic pressure remained constantly above 100 mm Hg during this untreated ambulatory wash-out period. As detailed elsewhere,[4] the 15 patients were shown to be non-placebo-responders at the end of 4 weeks follow-up (T_0). Then Perindopril was administered orally once a day at the dosage of 2 mg.[3] After 4 weeks, the dosage was increased to 4 mg once a day if diastolic pressure was equal or more than 95 mm Hg. After another 4 weeks, the dosage was increased to 8 mg per day in resistant patients. Active treatment was stopped after a total survey of 12 weeks. At this time (T_1), the active dose was 4 mg in eight patients and 8 mg in seven. A second placebo study was performed within 4 weeks. Then the study was stopped (T_2). Hemodynamic investigations were performed at times T_0, T_1, and T_2: T_0 and T_2 corresponded to the end of the two placebo-periods, and T_1 to the end of active treatment. The hemodynamic study began at 9:00 AM and was carried out with the patients in the recumbent position as follows[4]: arterial blood pressure and heart rate were measured automatically with an oscillometric blood pressure recorder; forearm arterial hemodynamics were obtained with a bidimensional pulsed Doppler system (as previously described and validated[4,5]), which enabled brachial artery diameter (D) and blood flow velocity to be mea-

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0895-7061/88/$3.50

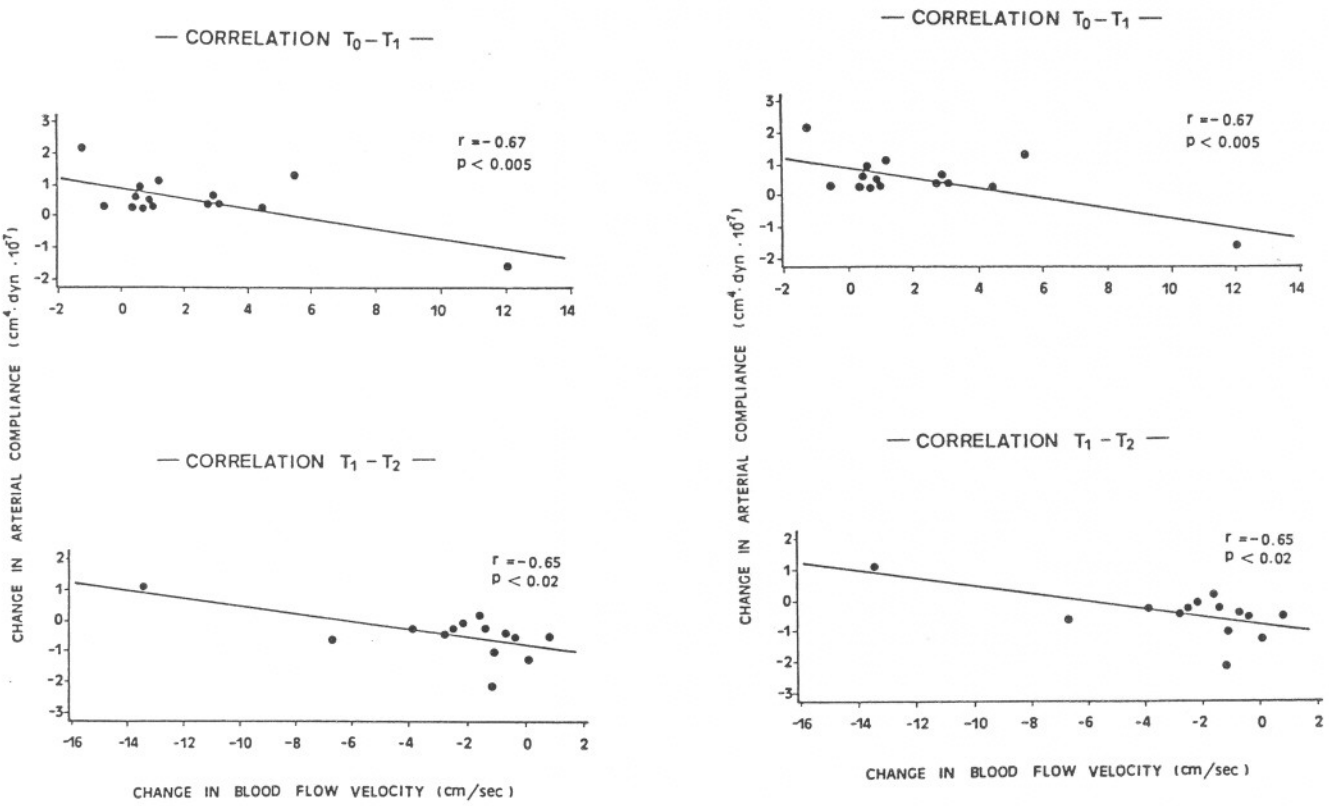

FIGURE 1. *Relationship between changes in blood flow velocity and changes in arterial compliance following Perindopril (see text). Between T_1 and T_2 only 14 data were available.*

sured simultaneously. Then brachioradial pulse wave velocity (PWV) was determined using mecanography, as previously described.[4] Arterial compliance per unit length was calculated as $3.14\ D^2/4\ p\ PWV^2$, with p being the constant blood density.[4] Variance analysis was undertaken by Newman–Keuls tests and was used for statistical evaluation.[6]

RESULTS

Perindopril therapy caused a significant decrease in mean arterial pressure: 112 ± 4 mm Hg versus 128 ± 3 mm Hg at T_0 and T_2 ($P < 0.01$). Blood flow velocity increased: 8.91 ± 1.59 ml/s versus 6.58 ± 0.89 and 6.26 ± 0.77 ml/s at T_0 and T_2 ($P < 0.01$). Arterial compliance significantly increased: 1.84 ± 0.15 cm⁴ · dyn · 10^{-7} versus 1.29 ± 0.21 and 1.37 ± 0.18 cm⁴ · dyn · 10^{-7} at T_0 and T_2 ($P < 0.01$).

Figure 1 shows that the changes in compliance were significantly and negatively correlated with the changes in blood flow velocity both between T_0 and T_1 ($P < 0.005$) and between T_1 and T_2 ($P < 0.02$).

COMMENTS

Vascular resistance is the ratio between mean arterial pressure and blood flow. As blood flow is the product of the brachial artery cross-sectional area by blood flow velocity, any decrease in vascular resistance is associated with an increase in blood flow velocity. Indeed pharmacological studies using the dihydralazine derivative, cadralazine, have shown that vascular resistance and blood flow velocity are inversely related.[7] Thus, any increase in blood flow velocity indicates that arteriolodilatation occurs.[7]

Converting enzyme inhibitor produces a significant blood pressure reduction due to arterial dilatation. Simultaneously, brachial blood flow and blood flow velocity are known to increase while forearm vascular resistance is reduced.[8] In that condition, the observed increase in arterial compliance may be due either to the mechanical effect of the decrease in the distending pressure or to a drug-induced arterial smooth muscle relaxation.[1–4] If the former mechanism was primary involved, the extent of arteriolodilatation (ie, decrease in vascular resistance or increase in blood flow velocity) will be expected to be positively associated with the increase in arterial compliance. In the present study, the opposite result was observed: the higher the increase in blood flow velocity, the higher the degree of arteriolodilatation, the lower the increase in arterial compliance (Fig 1). Such findings strongly suggest that the blood pressure reduction itself could not explain exclusively the compliance enhancement.

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 Ministére de la Recherche, Paris. We thank Mrs. Valérie Boiteau and Mrs. Marie-José Eggers for their excellent assistance.

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