SHORT COMMUNICATION

Studies on the renin–angiotensin–aldosterone system in elderly hypertensive patients with an angiotensin II antagonist

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Summary

1. To characterize the renin–angiotensin–aldosterone system in elderly hypertensive patients, an angiotensin II antagonist, [Sar₁,Ile₈]angiotensin II, was infused into individuals 60 years old and older with and without hypertension.

2. After infusion of [Sar₁,Ile₈]angiotensin II in all of the elderly patients and subjects an agonistic pressor response was observed that was greater than in middle-aged hypertensive patients.

3. Pre-infusion plasma renin activity and plasma aldosterone concentration in hypertensive and normotensive elderly groups were suppressed in comparison with those in middle-aged hypertensive subjects. The increased agonistic effects of [Sar₁,Ile₈]angiotensin II infusion on blood pressure in the elderly are presumably due to their hyporeninemia.

4. The angiotensin–aldosterone system in elderly essential hypertensive patients is suppressed and is presumably not responsible for their elevated blood pressures.

Key words: aldosterone, angiotensin II antagonist, hypertension, renin.

Abbreviations: ANGII, angiotensin II.

Introduction

To clarify the pathophysiology of essential hypertension in the elderly as well as to improve management of the disease, we studied the renin–angiotensin–aldosterone system in individuals with and without hypertension using an angiotensin II antagonist, [Sar₁,Ile₈]angiotensin II ([Sar₁,Ile₈]-ANGII).

Materials and methods

Twenty-two individuals 60 years old or older were studied. Twelve had hypertension (six men and six women, age 74 ± 3 years (mean ± SEM) and 10 were normotensive (five men and five women, age 75 ± 3 years). Ten patients less than 60 years old with hypertension were also studied (five men and five women, age 42 ± 2 years). All hypertensive patients had blood pressures greater than 160 mmHg systolic and/or 90 mmHg diastolic after lying supine for 2 min. Patients with secondary hypertension or severe cardiovascular complications were excluded.

Antihypertensive medications were discontinued at least 2 weeks before the study. Diets were unrestricted. The subjects were kept supine during the test. [Sar₁,Ile₈]ANGII (Dai-ichi Pharmaceutical Co. Ltd, Tokyo) was infused at a rate of 600 ng min⁻¹ kg⁻¹ for 30 min 1 h after intravenous injection of 40 mg of frusemide (Ogihara, Hata,
Maruyama, Mikami, Nakamaru, Okada & Kumahara, 1978). Infusion of [Sar\(^1\), Ile\(^8\)]ANGII at a rate of 600 ng min\(^{-1}\) kg\(^{-1}\) causes no appreciable change in mean blood pressure (the sum of the diastolic and one-third of the pulse pressure) in frusemide-treated normal subjects (Yamamoto, Doi, Ogihara, Ichihara, Hata & Kumahara, 1976), whereas in patients with angiotensinogenetic hypertension there is a decrease in mean blood pressure of more than 10 mmHg (Ogihara, Hata, Mikami, Nakamaru, Mandai & Kumahara, 1976). Blood pressure was monitored before and during the infusion with an automated device (Non-stetho, Parama Ltd, Tokyo). The mean of five readings before the infusion of [Sar\(^1\), Ile\(^8\)]ANGII was used for the control blood pressure. The blood pressure during the infusion was expressed as the mean of the blood pressures 10, 20 and 30 min after beginning the infusion. The change in the mean blood pressure was calculated as the difference between the control blood pressure and that during the infusion.

Blood was drawn from each subject just before the infusion of [Sar\(^1\), Ile\(^8\)]ANGII for assay of plasma renin activity and plasma aldosterone concentration ([aldosterone]). Blood samples were drawn in cold vacuum tubes containing disodium EDTA to provide 1 mg/mL. Plasma renin activity and [aldosterone] were measured by radioimmunoassays with commercial kits (Ogihara, Yamamoto, Doi, Omori & Kumahara, 1973; Ogihara, Iinuma, Nishi, Arakawa, Takagi, Kurata, Miyai & Kumahara, 1977). Statistical significance was assessed by the analysis of variance, correlation coefficients and Student's t-test (Siegel, 1956).

The Ethical Committee of the Department of Medicine and Geriatrics approved the protocol and informed consent was obtained from each subject after full explanation.

Results

Blood pressure rose significantly higher during the infusion of [Sar\(^1\), Ile\(^8\)]ANGII in the elderly normotensive and hypertensive patients than it did in the middle-aged hypertensive patients \((P < 0.01)\) (Fig. 1).

Plasma renin activity and [aldosterone] were markedly suppressed in the elderly, compared with the middle-aged hypertensive patients: mean plasma renin activity, \(0.9 \pm 0.3\) vs \(4.4 \pm 0.6\) ng h\(^{-1}\) ml\(^{-1}\) \((P < 0.01)\); mean [aldosterone], \(38 \pm 6\) vs \(112 \pm 6\) pg/ml \((P < 0.01)\). The two values were similar \((P > 0.1)\) in the elderly with and without hypertension.

Large correlation coefficients were observed between age, plasma renin activity, [aldosterone] and the change in mean blood pressure \((\Delta \text{mean B.P.})\) with [Sar\(^1\), Ile\(^8\)]ANGII infusion: age vs plasma renin activity \(-0.85\), age vs \(\Delta \text{mean B.P.} -0.55\); plasma renin activity vs \(\Delta \text{mean B.P.} -0.72\); age vs [aldosterone] \(-0.79\); [aldosterone] vs \(\Delta \text{mean B.P.} -0.58\); plasma renin activity vs [aldosterone] 0.71. All correlations were highly significant \((P < 0.01)\).

![Fig. 1. Changes in mean blood pressure during the infusion of [Sar\(^1\), Ile\(^8\)]ANGII (600 ng min\(^{-1}\) kg\(^{-1}\)). SEM values are indicated by vertical bars. ○, Aged hypertensive patients; △, aged normotensive subjects; ●, younger hypertensive patients.](image-url)
Discussion
A reduction in blood pressure after infusion of an angiotensin II antagonist implies that blood pressure is maintained at least partially by the renin–angiotensin system (Haber, 1976). On the other hand, angiotensin II antagonists cause agonist pressor responses in low reninaemic states such as low renin essential hypertension and primary aldosteronism (Ogihara et al., 1976; Carey, Vaughan, Ackerly, Peach & Ayers, 1978).

Plasma renin activity and [aldosterone] decrease with age (Hayduk, Krause, Kaufmann, Huenges, Schillmoeller & Unbehau, 1973; Weidmann, de Chatel, Schiffmann, Backmann, Beretta-Poccioli, Reubi, Ziegler & Vetter, 1977). Our data agree with these earlier reports. The pressor responses observed in our elderly hypertensive patients and normotensive subjects may be due to their hyporeninaemia. These results indicate that the renin–angiotensin–aldosterone system in elderly patients with essential hypertension does not differ from that in the non-hypertensive elderly subjects and is presumably not responsible for elevation of their blood pressure.

References


