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The Reaction About Anti-Hypertensive Drugs According to Plasma Renin-Aldosterone States

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Abstract

With recent studies, hypertension has not only a simple pathophysiology, thus it can classify details more about and establishing drug therapy strategies compatible with it is a very important method to improve the organ predictive of patients. The purpose of this study is to compare the responsibility of some anti-hypertensive drugs in hypertensive patients according to plasma renin-aldosterone levels, which becomes the background factor of hypertension. We investigated 71 hypertensive men. We included patients whose official hypertensive is 150/100 mmHg over, but we excluded patients with secondary hypertensions with target organ disorders, with unclear blood pressure measurement because of arrhythmia. We applied DRC (direct renin concentration), PAC (plasma aldosterone concentration) tests for 14 days in all the members. The tests are performed with blood samples that can be obtained at the rest site using with JL12316 measurement instrument. We administrated 5 drug therapy (hypothiazide 25 mg/d, Losartan 50 mg/d, amlodipine 5 mg/d, hypothiazide and Losartan12.5/50 mg, amlodipine and Losartan 5/50 mg) to the hypertensive patients. We set 14 days as the drug therapy duration until drug effect estimation, and administered all drugs between 6 and 8 A.M. After drug therapy, we compared with responsibility of anti-hypertensive drugs according to plasma renin and aldosterone levels. The response to anti-hypertensive drugs in hypertension patients is regulated by plasma aldosterone concentration, and the PAC is higher, the responsibility of anti-hypertensive drugs is lowered.

Keywords: Plasma renin activity (PRA), plasma aldosterone level, low renin hypertension, autonomic aldosterone release, anti-hypertensive therapy

INTRODUCTION

Recent points of view indicate that hypertension does not have simple pathogenesis, therefore, it should be classified in detail, and establishing the therapeutic policy is major issue in clinics. A classification of hypertension is one depending on the plasma renin level [1–7].

Renin is a basic component in the renin-angiotensin system and plays a critical role in the activation of this system [6]. Renin and its precursor, prorenin, interact with protein receptors and induce hypertrophy and fibrosis in target organs [6]. A lot of hypertension types are associated with renin activation [6].

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Hypertensive patients could be divided into low-, normal, or high-renin hypertension based on plasma renin activity [1–10]. This classification is rational and popularized widely because it can be related to many pathophysiologic mechanisms (increase of vascular resistance or blood volume increase), even to predict results of different antihypertensive therapies [7].

Many rates of hypertensive patients are included in low-renin hypertension, therefore, we need

appropriate diagnosis and treatment [7]. In essential hypertension, responses on the secretory regulation of PRA (plasma renin activity) are mainly in the normal range (normal renin group), but 20–30% of them show low activities (low renin) and 10–20% with over activities (hyper renin group) [11]. These groups each renin group have different predictions and therapies [11]. Some indicate different PAC (plasma aldosterone concentration) according to PRA in the case of classifying the essential hypertension depending on renin activity [11]. In other words, in some cases, there is no parallel between PRA and PAC, thus, the dissociation between plasma renin activity and plasma aldosterone concentration is important [11].

Primary aldosteronism is interpreted as suppression of renin production by the mechanism of negative feedback because of overproduction of aldosterone [12]. Low PRA under normal range causes difficulties for salt restriction, standing gate, and responses to renin-inducing stimulation [12].

Since Conn has reported hyperkalemic primary aldosteronism, PRA suppression has been an important item in diagnostic criteria for primary aldosteronism, especially [12]. LRH includes essential, secondary, and genetic types, and low-renin primary hypertension and primary aldosteronism are more frequent [7]. In general, 20–30% of all hypertensive patients have low-renin hypertension, including essential hypertension, with the highest rate, some secondary and genetic subtypes [7]. Though low-renin hypertension has been recognized as a moderate phenotype at first, but recent reviews indicated this state has been related to the increase of cardiovascular events both in essential hypertension and primary aldosteronism [7].

Many studies have been done, but the exact cause of low-renin hypertension is not clear [5]. Some of the formal research has described some factors to suppress PRA in low-renin hypertensive patients [5]. Some of the low-renin hypertensive patients had low PRA, and differentiating low-renin hypertension and primary aldosteronism is very crucial without any consideration of which mechanisms are actually associated with suppressing PRA [7].

Several studies have been performed to observe PRA and the clinical responsiveness to different antihypertensives [7]. In recent years, the role of aldosterone in the occurrence and maintenance of hypertension has been regarded as important, with active studies on hypertension.

Primary mineralocorticoid, aldosterone, is synthesized in the outer region of the adrenal cortex as a zona glomerulosa [4]. Aldosterone production is controlled mainly by levels of angiotensin II and circulating potassium [4]. Aldosterone plays a key role in maintaining intravascular volume and blood pressure through sodium retention in the kidney [4–7]. But excess aldosterone can cause hypertension and cardiovascular complications [4].

The dates have shown that plasma aldosterone had a positive relation with PRA in normotensives but no relation in patients with hypertension [10].

In the past, the others have regarded incidence of primary aldosteronism among hypertensive patients was low (0.5–1%), but recent reviews have reported 8–15% of essential hypertensive patients have been fell in the biochemical diagnosis criteria of primary aldosteronism [9]. Many cases among these had mild hyperaldosteronism and generally idiopathic bilateral dysplasia [9]. Most of the patients had no hypokalemia [9]. Therefore, a normal potassium level cannot exclude primary aldosteronism [9]. Recent studies have confirmed abnormal conditions where the aldosterone level was increased unsuitably without any relationship with biological regulating mechanisms were closely associated with the onset of hypertension, and their therapeutic methods have been established.

Independent autonomous release with no relation to Angiotensin II and sodium is called primary aldosteronism (PA) [4]. PA is the most common cause of endocrine-related hypertension [1–4]. And its incidence is 5–10% in hypertensive patients and about 20% in refractory hypertension [3, 4].

Early detection and targeted therapy is recommended because the risk of cardiovascular complications would be increased in PA [4]. In recent years, rather mild forms of autonomous and renin-independent aldosteronism can be recognized in even people with normal blood pressure [8].

Prospective multicenter studies on aldosterone-producing adenoma and primary aldosteronism have suggested screening for all hypertensive patients diagnosed newly [3].

The more important issue is that responses to the antihypertensives rely on which level of plasma renin or aldosterone is mostly.

We, hence, studied the responses of patients with hypertension to main hypertensives according to plasma renin and aldosterone levels (Table 1).

METHODS

Subjects

We subjected 71 male patients with hypertension.

- *Inclusion:* patients with over 150/100 mmHg of office blood pressure.

Table 1. Features of the subjects before therapy.

Age (Year)	BMI (kg/m^2)	BP (mmHg)		Comorbidity (%)		RAAS Activity		
		SBP	*DBP*	*DM*	*HU*	*DRC (pg/mL)*	*PAC (pg/mL)*	*PAC/ DRC*
45.8 ± 8.0	26.6 ± 3.2	158.4 ± 12.9	108.1 ± 10.6	6/71(8.5)	21/71(29.6)	0–113	0–416	0–2.6

Note: $\bar{X}$ ± SD, n = 71. BMI: Body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, DM: diabetes mellitus, HU: hyperuricemia.

METHODS

Raas Test

We tested DRC and PAC with 14 14-day of placebo. The blood tests were performed 8~9 a.m. after resting for 20 minutes using JL12316 device. Normal range of DRC: 5.2~20.8 pg/mL, PAC: 22~300 pg/mL.

Administration

We applied for 5 drug regimens. The duration of therapy was 14 days, and all drugs were administered in the morning between 6–8 a.m.

Hypothiazide monotherapy (25 mg/d), losartan monotherapy (50 mg/d), CCB monotherapy (amlodipine 5 mg/d), thiazide-ARB combination: hypothiazide-losartan 12.5/50 mg/d, CCB-ARB combination: amlodipine-losartan 5/50 mg/d.

OBSERVATION

The patients were admitted to the clinic and checked their office blood pressures-based blood pressure checking guidelines after sufficient rest once 14 days. Observation indices: blood pressure

- *Significant decrease:* More than 20/10 mmHg lowering (mean BP 13 mmHg).
- *Goal of BP lowering:* 130/90 mmHg for all patients.

Statistical Estimation

All parameters were noted to $\bar{X}$ ± SD and estimated by t-test using SPSS16.0. significance level defined $p < 0.05$. Also, we applied ANOVA analysis when the pretreatment blood pressures in two groups were different significantly.

RESULTS

Responses to Antihypertensives According to Plasma Renin Level

At first, blood pressure lowering effect for hypothiazide on plasma renin level had no significant difference between low renin and normal-high renin groups in regards with systolic of diastolic pressures after treatment (SBP 151.7 ± 12.5 mmHg versus 148.5 ± 13.8 mmHg, p = 0.354, DBP 103.8 ± 11.6 mmHg versus 103.5 ± 10.5 mmHg, p = 0.930, Tables 2 and 3).

Table 2. Differences of responses on DRC in hypothiazide monotherapy.

Index	n	DRC (pg/mL)	BP Before Therapy (mmHg)		BP After Therapy (mmHg)		Difference (mmHg)	
			SBP	***DBP***	***SBP***	***DBP***	***⊿SBP***	***⊿DBP***
Low renin	22	3.0 ± 1.6	156.8 ± 9.2	107.8 ± 11.0	151.7 ± 12.5	103.8 ± 11.6	–5.1 ± 9.3	–4.0 ± 6.3
Normal-high renin	49	23.5 ± 26.1	158.5 ± 13.7	107.9 ± 10.5	148.5 ± 13.8	103.5 ± 10.5	–10.0 ± 10.2	–4.4 ± 7.0
p		<0.001	0.532	0.952	0.354	0.930	0.055	0.816

Note: $\bar{X}$ ± SD.

It showed same results in calcium antagonist monotherapy (amlodipine 5 mg/d), that is, systolic pressure after treatment was 139.0 ± 8.1 mmHg in low rennin group and 140.4 ± 13.1 mmHg in normal-high renin group (p = 0.750) and diastolic pressure after treatment was 93.0 ± 12.0 mmHg in low renin group and 94.6 ± 10.5 mmHg in normal-high renin group (p = 0.690) (Table 4).

Table 3. Differences of responses on DRC in calcium antagonist monotherapy.

Index	n	DRC (pg/mL)	BP Before Therapy (mmHg)		BP After Therapy (mmHg)		Difference (mmHg)	
			SBP	***DBP***	***SBP***	***DBP***	***⊿SBP***	***⊿DBP***
Low renin	10	2.3 ± 1.5	157.3 ± 5.7	102.9 ± 10.8	139.0 ± 8.1	93.0 ± 12.0	–18.3 ± 8.1	–9.9 ± 7.8
Normal-high renin	33	25.4 ± 28.3	158.5 ± 13.7	108.6 ± 12.0	140.4 ± 13.1	94.6 ± 10.5	–18.1 ± 11.3	–14.1 ± 9.3
p		<0.001	0.694	0.184	0.750	0.690	0.954	0.207

Note: $\bar{X}$ ± SD.

In ARB monotherapy (losartan 50 mg/d), systolic pressure was 148.3 ± 16.2 mmHg in low-renin group and 145.0 ± 16.1 mmHg in the normal-high-renin group (p = 0.567), and diastolic pressure was 99.9 ± 10.7 mmHg in the low-renin group and 94.3 ± 10.3 mmHg normal-high-renin group (p = 0.134) (Table 5).

Table 4. Differences of responses on DRC in ARB monotherapy.

Index	n	DRC (pg/mL)	BP Before Therapy (mmHg)		BP After Therapy (mmHg)		Difference (mmHg)	
			SBP	***DBP***	***SBP***	***DBP***	***⊿SBP***	***⊿DBP***
Low renin	12	3.0 ± 1.7	153.8 ± 12.9	101.8 ± 11.5	148.3 ± 16.2	99.9 ± 10.7	–5.4 ± 16.0	–1.8 ± 11.9
Normal-high renin	25	25.3 ± 28.3	151.9 ± 13.8	99.8 ± 8.8	145.0 ± 16.1	94.3 ± 10.3	–6.1 ± 11.3	–5.5 ± 6.6
p		<0.001	0.706	0.566	0.567	0.134	0.745	0.337

Note: $\bar{X}$ ± SD.

Responses to the Plasma Renin with Aldosterone Levels

In thiazide monotherapy, systolic pressure after treatment was 146.7 ± 8.5 mmHg in low renin-low aldosterone type and 163.6 ± 8.4 mmHg in low renin-normal aldosterone type (p = 0.009) with significant elevation in low renin-normal aldosterone type and diastolic pressure was 102.3 ± 13.0 mmHg and 105.8 ± 13.7 mmHg, respectively, without significance (p = 0.677).

On other hand, systolic pressure was 144.1 ± 7.2 mmHg in the case of normal renin-low aldosterone type and 153.9 ± 18.1 mmHg in normal renin-normal aldosterone type with mild elevation in normal

renin-normal aldosterone type (p = 0.08) and diastolic pressure was 103.3 ± 6.1 mmHg and 108.3 ± 12.0 mmHg, respectively, without difference (p = 0.277) indicating hypothiazide had weaker respond based on the increment of aldosterone level in the condition of same plasma renin level (Table 6).

Table 5. Differences responses on RAAS in hypothiazide monotherapy.

Index		BP Before Therapy (mmHg)		BP After Therapy (mmHg)		Difference (mmHg)	
Renin	***Aldosterone***	***SBP***	***DBP***	***SBP***	***DBP***	***ΔSBP***	***ΔDBP***
Low	Low	154.5 ± 5.6	105.3 ± 11.2	146.7 ± 8.5	102.3 ± 13.0	–7.8 ± 10.0	–3.0 ± 7.1
	Normal	165.2 ± 7.4	108.6 ± 16.9	163.6 ± 8.4	105.8 ± 13.7	–1.6 ± 2.6	–2.8 ± 5.9
p		0.024	0.709	0.009	0.677	0.196	0.961
Normal	Low	161.4 ± 5.7	108.9 ± 10.1	144.1 ± 7.2	103.3 ± 6.1	–17.3 ± 6.0	–5.6 ± 7.1
	Normal	163.0 ± 13.0	111.7 ± 12.4	153.9 ± 18.1	108.3 ± 12.0	–9.1 ± 12.1	–3.4 ± 8.8
p		0.682	0.582	0.082	0.277	0.092	0.545

Note: $\bar{X}$ ± SD.

Blood pressure lowering effects according to plasma renin-aldosterone level in hypothiazide/losartan combination therapy resulted in 124.7 ± 4.8 mmHg of systolic pressure in low renin-low aldosterone level and 157.6 ± 9.3 mmHg low renin-normal aldosterone level with significant decrease in low renin-low aldosterone level (p = 0.000). Diastolic blood pressure was 87.7 ± 10.9 mmHg and 97.2 ± 22.8 mmHg respectably without significant difference between two groups (p = 0.385).

On the other hand, post treatment systolic pressure was 124.9 ± 10.5 mmHg in normal renin-low aldosterone type and 141.7 ± 18.1 mmHg in normal renin-normal aldosterone type with significant decrease in normal renin-low aldosterone type (p = 0.027) and post treatment diastolic pressure was 85.8 ± 6.0 mmHg and 96.4 ± 15.9 mmHg respectably with significant difference (p = 0.038) (Table 7).

Blood pressure lowering effects according to plasma renin-aldosterone level in ypothiazide/losartan combination therapy resulted in 124.7 ± 4.8 mmHg of systolic pressure in low renin-low aldosterone level and 157.6 ± 9.3 mmHg low renin-normal aldosterone level with significant decrease in low renin-low aldosterone level (p = 0.000). Diastolic blood pressure was 87.7 ± 10.9 mmHg and 97.2 ± 22.8 mmHg respectably without significant difference between two groups (p = 0.385).

On the other hand, post treatment systolic pressure was 124.9 ± 10.5 mmHg in normal renin-low aldosterone type and 141.7 ± 18.1 mmHg in normal renin-normal aldosterone type with significant decrease in normal renin-low aldosterone type (p = 0.027) and post treatment diastolic pressure was 85.8 ± 6.0 mmHg and 96.4 ± 15.9 mmHg respectably with significant difference (p = 0.038) (Table 7).

Blood pressure lowering effects according to plasma renin-aldosterone level in hypothiazide/ losartan combination therapy resulted in 124.7 ± 4.8 mmHg of systolic pressure in low renin-low aldosterone level and 157.6 ± 9.3 mmHg low renin-normal aldosterone level with significant decrease in low renin-low aldosterone level (p = 0.000). Diastolic blood pressure was 87.7 ± 10.9 mmHg and 97.2 ± 22.8 mmHg respectably without significant difference between two groups (p = 0.385).

On the other hand, post treatment systolic pressure was 124.9 ± 10.5 mmHg in normal renin-low aldosterone type and 141.7 ± 18.1 mmHg in normal renin-normal aldosterone type with significant decrease in normal renin-low aldosterone type (p = 0.027) and post treatment diastolic pressure was 85.8 ± 6.0 mmHg and 96.4 ± 15.9 mmHg respectably with significant difference (p = 0.038) (Table 7).

Generally, In hypothiazide monotherapy group, the rate of the patients whose systolic pressure decreased more than 10 mmHg were 50% (3/6) in the case with low renin-low aldosterone level and 0% (0/5) in cases with low renin-normal aldosterone level and showed significant difference (p = 0.064),

and 100% (8/8) in the cases with normal renin-low aldosterone level and 40% in the cases with normal renin-normal aldosterone level, so it's rate was remarkably low in normal renin-normal aldosterone level (p = 0.005).

Table 6. Differences of responses on DRC in hypothiazide-ARB combination therapy.

Index		**BP Before Therapy (mmHg)**		**BP After Therapy (mmHg)**		**Difference (mmHg)**	
Renin	***Aldosterone***	***SBP***	***DBP***	***SBP***	***DBP***	***⊿SBP***	***⊿DBP***
Low	Low	154.5 ± 5.6	105.3 ± 11.2	124.7 ± 4.8	87.7 ± 10.9	–29.8 ± 9.9	–17.7 ± 5.8
	Normal	165.2 ± 7.4	108.6 ± 16.9	157.6 ± 9.3	97.2 ± 22.8	–7.6 ± 11.7	–11.4 ± 15.6
p		0.024	0.709	0.000	0.385	0.008	0.383
Normal	Low	161.4 ± 5.7	108.9 ± 10.1	124.9 ± 10.5	85.8 ± 6.0	–36.5 ± 9.8	–23.1 ± 12.2
	Normal	163.0 ± 13.0	111.7 ± 12.4	141.7 ± 18.1	96.4 ± 15.9	–21.6 ± 13.2	–15.9 ± 12.2
p		0.682	0.582	0.027	0.038	0.012	0.199

Note: $\bar{X} \pm SD$.

In hypothiazide/losartan combination, the rate of the patients whose systolic pressure were lowered less than 20 mmHg were 83.3% (5/6) in the cases with normal renin-low aldosterone level and 20% (1/5) in the cases with low renin-normal aldosterone level, so there was significant difference (p = 0.036) and it's rates were 100% (8/8) in the case of normal renin-low aldosterone type and 53.3% (8/15) in the case of normal renin-normal aldosterone type, with significant difference (p = 0.021) (Table 8).

Table 7. Differences of responses on RAAS in hypothiazide monotherapy or thiazide-ARB combination therapy (%).

Index		**Thiazide Monotherapy ⊿SBP ≦ –10 mmHg**	**Thiazide-ARB ⊿SBP ≦ –20 mmHg**
Plasma renin	**Plasma aldosterone**		
Low	Low	3/6 (50.0)	5/6 (83.3)
	Normal	0/5 (0.0)	1/5 (20.0)
p		0.064	0.036
Normal	Low	8/8 (100.0)	8/8 (100.0)
	Normal	6/15 (40.0)	8/15 (53.3)
p		0.005	0.021

In amlodipine monotherapy, systolic pressure after treatment was 136.7 ± 7.6 mmHg in low renin-low aldosterone group and 147.5 ± 14.0 mmHg in low renin-normal aldosterone group without significant difference (p = 0.147) and diastolic pressure was 93.3 ± 9.2 mmHg and 100.5 ± 21.1 mmHg, respectively, also without difference (p = 0.476).

Systolic pressure after treatment was 138.0 ± 9.5 mmHg in normal renin-low aldosterone type and 144.1 ± 11.3 mmHg in normal renin-normal aldosterone type without significant difference (p = 0.240) and diastolic pressure was 93.4 ± 5.4 mmHg and 98.0 ± 9.8 mmHg, respectively, also without significant difference (p = 0.270) (Table 9).

Systolic pressure after treatment was 131.3 ± 4.6 mmHg in low renin-low aldosterone type and 140.5 ± 13.7 mmHg in low renin-normal aldosterone type without difference (p = 0.276) and diastolic pressure was 88.3 ± 5.7 mmHg and 87.5 ± 20.9 mmHg, respectively, also without significant difference (p = 0.942).

Systolic pressure after treatment was 124.3 ± 10.8 mmHg in normal renin-low aldosterone type and 135.6 ± 10.3 mmHg in normal renin-normal aldosterone type with significant increase in normal renin-normal aldosterone type (p = 0.034) and diastolic pressure was 83.4 ± 8.9 mmHg and 91.3 ± 11.6 mmHg, respectively, without significant difference (p = 0.138) (Table 10).

Table 8. Differences of responses on RAAS in CCB monotherapy.

Index		BP Before Therapy (mmHg)		BP After Therapy (mmHg)		Difference (mmHg)	
Renin	***Aldosterone***	***SBP***	***DBP***	***SBP***	***DBP***	***△SBP***	***△DBP***
Low	Low	154.5 ± 5.6	105.3 ± 11.2	136.7 ± 7.6	93.3 ± 9.2	–17.8 ± 7.1	–12.0 ± 7.6
	Normal	165.5 ± 8.5	105.8 ± 1890	147.5 ± 14.0	100.5 ± 21.1	–18.0 ± 10.8	–5.3 ± 8.8
p		0.038	0.965	0.147	0.476	0.977	0.230
Normal	Low	160.7 ± 5.8	108.9 ± 10.1	138.0 ± 9.5	93.4 ± 5.4	–22.7 ± 6.6	–16.4 ± 9.7
	Normal	162.1 ± 13.0	111.1 ± 12.3	144.1 ± 11.3	98.0 ± 9.8	–18.0 ± 12.8	–13.1 ± 8.3
p		0.797	0.827	0.240	0.270	0.374	0.427

Note: $\bar{X}$ ± SD.

Table 9. Differences of responses on RAAS in CCB –ARB combination therapy.

Index		BP Before Therapy (mmHg)		BP After Therapy (mmHg)		Difference (mmHg)	
Renin	***Aldosterone***	***SBP***	***DBP***	***SBP***	***DBP***	***△SBP***	***△DBP***
Low	Low	154.5 ± 5.6	105.3 ± 11.2	131.3 ± 4.6	88.3 ± 5.7	–23.2 ± 7.1	–17.0 ± 6.9
	Normal	165.5 ± 8.5	105.8 ± 1890	140.5 ± 13.7	87.5 ± 20.9	–25.0 ± 14.3	–18.3 ± 14.7
p		0.038	0.965	0.276	0.942	0.791	0.858
Normal	Low	160.7 ± 5.8	108.9 ± 10.1	124.3 ± 10.8	83.4 ± 8.9	–36.4 ± 11.6	–26.4 ± 15.5
	Normal	162.1 ± 13.0	111.1 ± 12.3	135.6 ± 10.3	91.3 ± 11.6	–26.5 ± 14.8	–19.8 ± 12.4
p		0.797	0.827	0.034	0.138	0.143	0.309

Note: $\bar{X}$ ± SD.

Table 10. Differences of responses on RAAS in CCB monotherapy and CCB-ARB combination therapy (%).

Index		CCB Monotherapy	CCB-ARB Combination Therapy
Plasma Renin	**Plasma Aldosterone**	**△SBP ≦ –10mmHg**	**△SBP ≦ –20 mmHg**
Low	Low	3/6 (50.0)	5/6 (83.3)
	Normal	0/5 (0.0)	1/5 (20.0)
p		0.064	0.036
Normal	Low	8/8 (100.0)	8/8 (100.0)
	Normal	6/15 (40.0)	8/15 (53.3)
p		0.005	0.021

In amlodipine monotherapy the rates of the patients whose blood pressures lowered less than 10 mmHg were 50% (3/6) in the case of low renin-low aldosterone type and 0% (0/5) in the case of low renin-normal aldosterone type, therefore it showed higher rates in the case of low renin-low aldosterone type than low renin-normal aldosterone type. Its rates were 100% (8/8) in the case of normal renin-low aldosterone type and 40% (6/15) in the case of normal renin-normal aldosterone type, with remarkably higher rates (p = 0.005) in the case of normal renin-low aldosterone type.

In the amlodipine/losartan combination therapy, the rates of the patients whose blood pressures were lowered less than 20 mmHg were 83.3% (5/6) in the case of low renin-low aldosterone type and 20% (1/5) in the case of low renin-normal aldosterone type with higher rates (p = 0.036) in the case of low renin-low aldosterone type and it's rates were 100% (8/8) in the case of normal renin-low aldosterone and 53.3% (8/15) in the case of normal renin-normal aldosterone type with higher rates (p = 0.021) in normal renin-low aldosterone type.

Our results indicated that responses of antihypertensives in the hypertensive patients depended on plasma aldosterone level mainly and decreased the responses with increment of aldosterone level.

DISCUSSION

Renin-angiotensin-aldosterone system is a key regulator in volume and homeostasis of sodium [7]. Relationship between components consisting of renin-angiontensin-aldosterone system is associated with the pathogenesis of hypertension.

Critical issues in recent years are the management for low renin hypertension, in detail, that is, RASS pattern, confirming the responses of antihypertensives on plasma renin-aldosterone.

Low renin phenotype in essential hypertension expresses higher heredity and polymorphism and variation affecting on regulation of sodium play role in this pathogenesis [7].

But most patients with low renin hypertension have essential hypertension and single genetic type is rare as a classic type [7].

And also, essential hypertension is recognized as an acquired state but more than 40% are polygenic, defining by heredity [7].

Low renin hypertension would be divided into low renin/high aldosterone and low renin/low aldosterone empirically [7].

Clinical issue is to see how the detailed plasma renin or aldosterone state effect responses of antihypertensive and search effective methods for drug combination on these states.

Primary aldosteronism is a common cause of secondary hypertension and is characterized by renin independent autonomous aldosterone discharge causing hyperactivity of mineral corticoid receptor and sodium [8].

Autonomous aldosterone secretion is an important issue because the inappropriate activity of mineral corticoid receptor is associated with increasing the morbidity and mortality of cardiovascular disease and its management decreases their risks [8].

Primary aldosteronism is recognized as a rare disease classically which is checked among the patients with severe hypertension and hypokalemia [8]. But recent research indicated that many consecutive processes were involved [8]. For example, the screening and confirming study on primary aldosteronism have performed among large groups with mild-moderate essential hypertension and found that 10% of the patient had primary aldosteronism [8].

Elevation of aldosterone associated with low renin activity is a marker for inappropriate secretion by the adrenal gland [7].

Therefore, primary aldosteronism should be considered in patients with this phenotype [7]. In the case of a hypertensive patient with primary aldosteronism, if they have an aldosterone-release adenoma or unilateral hyperplasia, the option would be adrenalectomy or anti-mineral corticoid, so it is important that this state should be diagnosed or excluded [7].

It has been confirmed that the patients with over-aldosteronism had a higher risk for stroke, myocardial infarction, and arterial fibrillation than essential hypertensive patients with the same risk background, so it is a present problem [7].

An increase in accident rate for cardiovascular events would probably be predisposed by the effect of aldosterone, which induces inflammation, fibrosis, and necrosis in several target organs [7–9].

These non-epithelial effects become progressive when added to traditional effects on electrolyte balance [12].

The relation between the abnormal effect of aldosterone on target organs and cardiovascular events recognized experimentally would be confirmed by the fact that left ventricular hypertrophy, microalbuminuria, endothelial dysfunction, QT prolongation, and metabolic syndrome are increased in patients with primary aldosteronism compared to patients with controlled hypertension.

We have compared the responses of antihypertensives according to plasma renin-aldosterone activity because plasma renin or aldosterone levels play a critical role in the pathogenesis and maintenance of hypertension.

CONCLUSIONS

First, responses on thiazide monotherapy and thiazide-ARB combination therapy decreased with the increment of aldosterone level.

Second, in contrast with mono or combination therapies with thiazide diuretics, plasma aldosterone level did not affect the responses in mono-combination therapies with CCB on the same plasma renin level.

DECLARATION

Availability of Data and Material

Not applicable.

Conflict of Interest

The author declares that there is no conflict of interest.

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REFERENCES

1. Abe K, Irokawa N, Aoyagi H, Seino M, Yasujima M. Low renin hypertension--is it a stage of essential hypertension? Tohoku J Exp Med. 1977;121(4):347–354. doi:10.1620/tjem.121.347
2. Gouli A, Kaltsas G, Tzonou A, Markou A, Androulakis II, Ragkou D, et al. High prevalence of autonomous aldosterone secretion among patients with essential hypertension. Eur J Clin Invest. 2011 Nov;41(11):1227–1236. doi:10.1111/j.1365-2362.2011.02531.x.
3. Giacchetti G, Mulatero P, Mantero F, Veglio F, Boscaro M, Fallo F. Primary aldosteronism, a major form of low renin hypertension: from screening to diagnosis. Trends Endocrinol Metab. 2008 Apr;19(3):104–108. doi:10.1016/j.tem.2008.01.005.
4. Nanba K, Vaidya A, Rainey WE. Aging and adrenal aldosterone production. Hypertension. 2018 Feb;71(2):218–223. doi:10.1161/Hypertensionaha.117.10391.
5. Honda M, Izumi Y, Tsuchiya M, Ueda Y, Watanabe H, Inoue T, et al. A simplified screening test for differentiating primary aldosteronism from essential hypertension with low plasma renin activity. Jpn Circ J. 1980 Sep;44(9):719–725. doi:10.1253/jcj.44.719.
6. Mukhin NA. Renin as a target of direct pharmacological block in arterial hypertension. Ter Arkh. 2009;81(8):5–9.
7. Mulatero P, Verhovez A, Morello F, Veglio F. Diagnosis and treatment of low-renin hypertension. Clin Endocrinol (Oxf). 2007;67:324–334.

8. Baudrand R, Guarda FJ, Fardella C, Hundemer G, Brown J, Williams G, et al. Continuum of renin-independent aldosteronism in normotension. Hypertension. 2017;69(5):950–956. doi:10.1161/Hypertensionaha.116.08952.
9. Dluhy RG, Williams GH. Aldosterone--villain or bystander? N Engl J Med. 2004;351(1):8–10. doi:10.1056/NEJMp048132.
10. Tolagen K. Aldosterone in primary hypertension: relationship to plasma renin activity and urinary electrolytes and a comparison with normotensive subjects. Scand J Clin Lab Invest. 1978 Sep;38(5):487–493. doi:10.1080/00365517809108455.
11. Tolagen K, Karlberg BE. Plasma and urinary aldosterone and their interrelations with blood pressure, plasma renin activity and urinary electrolytes in normotensive subjects. Scand J Clin Lab Invest. 1978 May;38(3):241–247. doi:10.3109/00365517809108418.
12. Liu Z, Jin L, Zhou W, Zhang C. The spectrum of plasma renin activity and hypertension diseases: utility, outlook, and suggestions. J Clin Lab Anal. 2022;36(11):e24738. doi:10.1002/jcla.24738.

