Changes of poststimulatory plasma renin activity in women with hyperthyroidism or hypothyroidism in relation to therapy

Czeslaw Marcisz [1], Eugene J. Kucharz [2], Magdalena Marcisz-Orzel [1], Ryszard Poręba [3], Arkadiusz Orzel [1], Urszula Sioma-Markowska [3]

1 Department of Internal Medicine, School of Health Care, Medical University of Silesia, Katowice, Poland
2 Department of Internal Medicine and Rheumatology, School of Medicine, Medical University of Silesia, Katowice, Poland
3 Department of Obstetrics and Gynecology, School of Health Care, Medical University of Silesia, Katowice, Poland

Correspondence to: Czeslaw Marcisz, MD., PhD.
Department of Internal Medicine, Medical University of Silesia
ul. Edukacji 102, PL 43-100 Tychy, Poland.
fax: +48-32-3254287; e-mail: klinwewtychy@poczta.onet.pl

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Abstract

OBJECTIVE: The influence of thyroid hormones upon renin-angiotensin-aldosterone system is poorly understood. Under basal conditions, individuals belong to normal, low or high plasma renin activity (PRA) subjects. The study was designed to evaluate basal and poststimulatory PRA and serum aldosterone (Aldo) level in patients with hyperthyroidism or hypothyroidism during therapy.

MATERIAL AND METHODS: We examined 73 women with hyperthyroidism, 27 women with hypothyroidism and 36 healthy controls. The patients were investigated before initiation of therapy and after attainment of euthyroid state. All subjects were investigated under basal conditions (normal-sodium diet) and after application of a low-sodium diet for three days and upright position for 3 hr. PRA, serum Aldo level, blood pressure, serum sodium, potassium and thyroid hormone levels were determined in all subjects. The subjects were classified as low PRA (<1.0 ng/ml/h), normal PRA (1.0–4.0 ng/ml/h) and high PRA (>4.0 ng/ml/h) individuals according to results obtained under basal conditions.

RESULTS: Relatively higher poststimulatory enhancement in PRA was found in patients with hyperthyroidism, especially those with low basal PRA, than in those with hypothyroidism. In women with thyroid dysfunctions poststimulatory increase in Aldo were relative lower than poststimulatory enhancement of PRA. After therapy these difference disappeared. The poststimulatory changes in PRA depended on the basal PRA.

CONCLUSIONS: Poststimulatory PRA is higher in hyperthyroid women, especially those with low basal PRA. In women with hypothyroidism, poststimulatory PRA is low. Blood pressure and severity of thyroid dysfunction was found to be similar in the patients with low, normal or high basic PRA. In women with thyroid dysfunctions, serum Aldo level and its relative poststimulatory increments are inadequate to changes of PRA; it is suggested that the dissociation in the renin-angiotensin-aldosterone system occurs in hyperthyroid and hypothyroid women.

ORIGINAL ARTICLE

INTRODUCTION

Thyroid hormones exert a profound influence upon the cardiovascular system (Klein & Danzi 2007; Danzi & Klein 2003). The mechanism of this effect is complex and is still poorly understood. Renin-angiotensin system is one of the important regulatory factors of hemodynamics. Renin is produced in the kidneys and is responsible for cleavage of angiotensinogen to angiotensin I as well as stimulates indirectly production of aldosterone (Aldo) in the suprarenal glands. Plasma renin activity (PRA) is stimulated with application of a low-sodium diet and upright position. Sodium supply should be taken into consideration in evaluation of PRA. It has been shown that PRA determined under basal conditions is different in healthy individuals and subgroups of subjects with normal, low or high PRA have been found.

Investigations of PRA in patients with excess or deficiency in thyroid hormones provided inconsistent results. In most of the reports, sodium and potassium dietary supply was not taken into consideration as a factor affecting PRA. Thus, it is difficult to compare the obtained results. It was shown that PRA (Ogihara *et al.* 1980; Karner *et al.* 2004; Koukoulis *et al.* 2002) or plasma renin level (Asmah *et al.* 1997) was enhanced in patients with thyrotoxicosis and renin activity response to stimulation with a low-sodium diet and upright position (Hauger-Klevene *et al.* 1972; Cain *et al.* 1973) or after intravenous furosemide (Asmah *et al.* 1997) was higher than that in the controls. Other reports revealed contradictory results, PRA in patients with hyperthyroidism under basal conditions was found to be unaltered (Kato *et al.* 2009; Marcisz *et al.* 2001). Hypothyroidism is associated with low PRA and the response of PRA to stimulation is also lower than that in the controls (Hauger-Klevene *et al.* 1972; Saruta *et al.* 1980). Unaltered basic PRA was also reported in patients with hypothyroidism (Koukoulis *et al.* 2002).

The present study was undertaken to evaluate basal and poststimulatory PRA and serum Aldo level in patients with hyperthyroidism or hypothyroidism during therapy and the obtained results were analyzed in relation to the basal PRA level in the patients before the initiation of therapy.

MATERIAL AND METHODS

Studies were carried out in 136 women, all ageing before menopause. The patients with hyperthyroidism were 73 women aged 33.1 ± 9.3 yr. (mean ± SD). Hyperthyroidism was caused by Graves' disease in 61 patients and by toxic nodular goiter in remaining 12 patients. Diagnosis was made on the base of clinical examination including clinical index of Crooks (Crooks *et al.* 1960) as well as determination of serum free thyroxine (fT_4) and free triiodothyronine (fT_3) as well as serum thyreotropin (TSH). The hyperthyroid patients were investigated before the initiation of the treatment, two weeks after the initiation of the therapy (a short-term treatment), and after attainment of the euthyroid state (a long-term therapy). Two weeks period was chosen because usually after this period the serum thyroid hormone levels return to the normal values. The mean period between the first and the last evaluation of the patients was 9 months. Patients were treated with thiamazole (1-methyl-2-mercapto-imidazole, Metizol, Polfa, Poland) in a daily dose of 45–60 mg (X ± SD = 52.5 ± 7.3 mg) applied within two weeks and followed by reduction of the dose according to clinical symptoms and laboratory data of the patients. The therapy was continued after attainment of the euthyroid state with a daily dose 5–10 mg of thiamazole.

The group with hypothyroidism included 27 women aged 37.2 ± 7.9 yr. (mean ± SD). All had primary hypothyroidism. The diagnosis was made on the base of clinical examination including clinical index of Murray (Kuhlencordt 1972) and determination of the same hormones as in patients with hyperthyroidism. The patients were treated with L-thyroxine (Eltroxin, Glaxo, UK) in a daily dose 100–250 μg (mean = 179 μg). The dose was adjusted to clinical state and laboratory data indicating the state of euthyreosis. The patients with hypothyroidism were investigated twice, before the initiation of the therapy and after attainment of the euthyroid state. The mean period between the first and the second investigation was 12 months.

Patients with cardiac insufficiency, heart rhythm disturbances other than sinus tachycardia or bradycardia, cardiac defects, hepatic or renal disorders, metabolic and endocrine disease, acute inflammatory states as well as pregnant women were excluded from the study. The control group consisted of 36 women aged 32.8 ± 8.6 yr. (mean ± SD). The controls were investigated only once. The study protocol was approved by Ethics Committee of Medical University of Silesia, and informed consent was obtained from all participants.

PRA, serum Aldo level and serum sodium and potassium levels were measured in all investigated individuals under basal conditions and after stimulation with a low-sodium diet application and upright position. Basal conditions included application of a normal-sodium diet. The diet contained 120 mmol of sodium and 70 mmol of potassium, daily. Blood was sampled in horizontal position after 8 hr night bed rest. After application of a normal-sodium diet, the investigated subjects were receiving a low-sodium diet (10 mmol of sodium, 70 mmol of potassium) for three days. The measurements were done after application of a low-sodium diet and 3 hr upright position. Compliance of the patients to the diet with low or normal sodium content was evaluated with urine sodium and potassium measurement. Arterial blood pressure was measured in all investigated subjects under basal conditions.

The investigated subjects were divided into subgroups on the base of PRA determined under basal

conditions. The subgroup with low PRA comprised of those with PRA ≤ 1.0 ng/ml/h, the subgroup of normal PRA comprised of individuals with PRA higher than 1.0 ng/ml/h and lower than 4.0 ng/ml/h. The subjects with PRA ≥ 4.0 ng/ml/h were classified to the high PRA subgroup.

All blood sampling were done between 7.30–8.00 AM. PRA and hormone levels were determined with radioimmune methods using the kits commercially available from the Institute for Research, Production and Application of Radioisotopes, Prague, Czech Republic (for PRA and Aldo), Amersham, UK for fT_4 and fT_3, and Farmos Diagnostica, Finland for TSH. Sodium and potassium were measured with ionselective electrode method.

Statistical analysis was carried out with the Student's "t", Fisher's "F" and Satterthwaite's tests. A *p*-value of less than 0.05 was considered as statistical significant.

RESULTS

Table 1 summarizes results of PRA measurement under basal conditions and after stimulation with a low-sodium diet and upright position with regard to low- normal- and high-renin activity. There was no difference in PRA under basal conditions in the patients with hyperthyroidism or hypothyroidism and in the controls. Stimulation resulted in an increase in PRA in all investigated subjects. Higher poststimulatory enhancement of PRA was found in patients with hyperthyroidism than in those with hypothyroidism.

When the patients were divided according to the basal PRA into low PRA, normal PRA, and high PRA subgroups, a different effect of the treatment of hyperthyroidism on PRA was shown (Table 1). Attainment of the euthyroid state in the patients with hyperthyroidism with a low basal PRA was associated with a significant increase in PRA. On the contrary, in the hyperthyroid patients with a high basal PRA the attainment of euthyroid state was associated with a decrease in PRA. Poststimulatory PRA was shown to be diminished after the treatment of hyperthyroidism, the most pronounced decrease was found in the subgroup of the patients with a low basal PRA. PRA was shown to be significantly enhanced in a low PRA patients with hypothyroidism after attainment of euthyroid state. Serum Aldo levels determined under basal conditions in normal-renin patients with hyperthyroidism and hypothyroidism were shown to be higher than in the normal-renin healthy controls (Table 2). The highest relative increase in poststimulatory PRA i.e. expressed in per cent of the basal PRA was found in hyperthyroid patients with low basal PRA before treatment and accounted 1 264% (Table 3). The lowest (= 162%) was shown in hypothyroid patients with low basal PRA also before treatment. Attainment of euthyroid state in both above mentioned groups of patients resulted in normal relative increase in poststimulatory PRA, i.e. 603% and 436%, respectively. These values were comparable to the increase in healthy low PRA individuals (523%). In hyperthyroid patients with high PRA before treatment, an increase in poststimulatory PRA was 168% and after successful treatment of hyperthyroidism was 438%. Proportionally increase in poststimulatory serum Aldo level was not differentiated in all investigated groups (Table 3).

Table 4 summarizes the thyroid function parameters (serum fT4, fT3 and TSH levels, and clinical index), systolic and diastolic blood pressure and serum electrolytes concentration in the patients with hyperthyroidism or hypothyroidism divided into subgroups with

Tab.1. Influence of treatment of hyperthyroidism and hypothyroidism on plasma renin activity (PRA) with regard to low-, normal- and high-renin activity (x ± SEM).

PRA (ng/ml/h)		INVESTIGATED GROUPS							
		Hyperthyroidism (n = 73)				Hypothyroidism (n = 27)			Healthy (n = 36)
		n	Before treatment	After 2 weeks treatment	After attainment of euthyroid state	n	Before treatment	After attainment of euthyroid state	n
Low PRA	B	31	0.77 ± 0.02	1.24 ± 0.14†	1.16 ± 0.17*	15	0.69 ± 0.05	1.34 ± 0.18*	11 0.68 ± 0.15
	S		8.88 ± 0.62#	7.79 ± 0.54#	5.56 ± 0.61‡		1.56 ± 0.13	6.46 ± 1.31†	3.68 ± 1.10
Normal PRA	B	35	2.12 ± 0.10	1.83 ± 0.18	1.80 ± 0.21	12	1.81 ± 0.11	1.42 ± 0.16	24 1.97 ± 0.11
	S		11.02 ± 0.78#	8.90 ± 0.69*	9.35 ± 0.89		4.62 ± 0.88¶	7.02 ± 1.03	7.30 ± 0.92
High PRA	B	7	5.23 ± 0.29	2.87 ± 0.26‡	2.40 ± 0.69†	–	–	–	1 4.50
	S		13.35 ± 1.46	10.38 ± 1.98	10.00 ± 3.04		–	–	17.00

B – basal, S – poststimulatory, **p*<0.05, †*p*<0.01, ‡*p*<0.001 for the comparison with before treatment
¶*p*<0.05, #*p*<0.01 for the comparison with the healthy individuals

Tab.2. Influence of treatment of hyperthyroidism and hypothyroidism on serum aldosterone level with regard to low-, normal- and high-renin activity (x ± SEM).

PRA (ng/ml/h)		INVESTIGATED GROUPS							
		Hyperthyroidism (n = 73)				Hypothyroidism (n = 27)			Healthy (n = 36)
		n	Before treatment	After 2 weeks treatment	After attainment of euthyroid state	n	Before treatment	After attainment of euthyroid state	n	
Low PRA	B	31	145.6 ± 15.9	144.0 ± 16.7	130.0 ± 15.4	15	157.8 ± 19.0	189.3 ± 27.9	11	138.7 ± 13.7
	S		433.1 ± 31.5	397.0 ± 23.5	363.8 ± 31.4		374.8 ± 0.13	338.1 ± 47.6		381.2 ± 45.2
Normal PRA	B	35	163.5 ± 13.5¶	147.6 ± 12.7	152.7 ± 13.8	12	192.6 ± 31.6¶	167.6 ± 37.6	24	119.8 ± 10.7
	S		450.6 ± 29.9	380.0 ± 26.7	355.3 ± 28.8		373.5 ± 54.6	355.2 ± 46.8		390.8 ± 53.9
High PRA	B	7	206.3 ± 36.6	177.3 ± 29.2	203.3 ± 58.3	–	–	–	1	192.0
	S		482.3 ± 71.5	437.1 ± 72.3	520.7 ± 63.3		–	–		443.0

B – basal, S – poststimulatory, ¶$p<0.05$ for the comparison with the healthy individuals

low, normal or high PRA evaluated under basal conditions. There was no difference in the thyroid function indices and blood pressure between subgroups of the patients with various basic PRA both in patients with hyperthyroidism or hypothyroidism.

DISCUSSION

The basal PRA in patients with hyperthyroidism was found to be similar to that of the healthy controls. This finding is concomitant with report authors who did not show enhanced PRA under conditions of excess of thyroid hormones (Kato *et al.* 2009). Other reports indicate for enhanced basal PRA in patients with hyperthyroidism (Ogihara *et al.* 1980; Karner *et al.* 2004; Koukoulis *et al.* 2002). Sodium intake has been shown to be an important factor affecting PRA. Cain *et al.* (1973) reported that intravenous infusion of saline reduced the enhanced PRA in hyperthyroid patients to normal level. The same results were reported after increase in dietary potassium to 200 mmol daily. In our study, the serum sodium and potassium level in the patients and controls was similar and remained within the normal range. It can be concluded that sodium and potassium affect upon PRA was similar in the patients and controls. PRA is controlled by a number of pathophysiological mechanisms. Enhanced blood volume and blood perfusion influence upon decrease in PRA in patients with hyperthyroidism. On the other hand, an increase in PRA in these patients is resulted from enhanced sympathetic nervous system activity, a common feature associating hyperthyroidism (Levey & Klein 1990). In our previous report, a negative correlation between basal PRA and cardiac output was shown (Marcisz *et al.* 1999).

The role of sympathetic nervous system stimulation in enhancement of PRA in patients with hyperthyroidism seems not to be supported. In general, it is well known that β-adrenergic stimulation leads to increased renin secretion although in patients with hyperthyroidism there is no data indicating for increased density or sensitivity of the adrenergic receptor of the juxtaglomerular apparatus. Moreover, blood catecholamine level was found to be normal (Coulombe *et al.* 1977) or even decreased (Premel-Cabic *et al.* 1986) in the hyperthyroid patients. A decrease in PRA resulted from β-adrenergic or α-adrenergic receptor blockade was similar to that shown in healthy individuals (Hauger-Klevene *et al.* 1972; Cain *et al.* 1973). Kobori *et al.* (1997) reported that adrenergic system is not involved in increase of PRA in rats receiving thyroid hormones.

In our study PRA level in patients with hyperthyroidism was found to be normal in 48% of the investigated patients, and in the remaining ones was low (42%) or high (10%). There was no relationship between severity of hyperthyroidism and PRA. The subgroups with different PRA have similar level of free thyroid hormones and thyreotropin as well as they have similar severity of clinical symptoms. There was also no difference in systolic and diastolic blood pressure and serum sodium and potassium level in hyperthyroid patients subgroup with various PRA. An increase in PRA in one-tenth of our patients is believed to be resulted from reduced blood volume. This reduction is caused by enhanced perspiration and increased defecation or even diarrhea, a common features of hyperthyroidism. An increased PRA is a compensatory phenomenon in these patients and facilitated a normal blood pressure and organ perfusion in the patients with decreased blood volume. The

Tab. 3. Relative increase in plasma renin activity (%ΔPRA) and serum aldosterone level (%ΔAldo) under the influence of low-sodium diet and upright position in women with hyperthyroidism and hypothyroidism and in healthy controls classified according to the low-, normal- and high-renin activity. The PRA and Aldo under basal conditions is taken as 100% (x ± SEM).

PRA		INVESTIGATED GROUPS								
		Hyperthyroidism (n = 73)				Hypothyroidism (n = 27)				Healthy (n = 36)
		n	Before treatment	After 2 weeks treatment	After attainment of euthyroid state	n	Before treatment	After attainment of euthyroid state	n	
Low PRA	%ΔPRA	31	1264 ± 167#	850 ± 139*	603 ± 105‡	15	162 ± 41¶§	436 ± 142*	11	523 ± 142
	%ΔAldo		316 ± 55	267 ± 33	229 ± 37		168 ± 43	139 ± 64		187 ± 27
Normal PRA	%ΔPRA	35	459 ± 50	539 ± 67	569 ± 96	12	182 ± 50¶	482 ± 94*	24	359 ± 45
	%ΔAldo		245 ± 39	209 ± 36	139 ± 17		123 ± 25	170 ± 39		256 ± 39
High PRA	%ΔPRA	7	168 ± 48	358 ± 182	438 ± 108	–			1	378
	%ΔAldo		200 ± 92	156 ± 40	234 ± 67					142

*p<0.05, ‡p<0.001 for the comparison with before treatment
¶p<0.05, #p<0.01 for the comparison with the healthy individuals
§p<0.001 for the comparison with the patients with hyperthyroidism before treatment

Tab. 4. Thyroid function parameters in patients with thyroid disorders and healthy controls with regard to low-, normal- and high-renin activity (x ± SEM).

Parameter	INVESTIGATED GROUPS							
	Hyperthyroidism (n = 73)			Hypothyroidism (n = 27)		Healthy individuals (n = 36)		
	Low PRA (n = 31)	Normal PRA (n = 35)	High PRA (n = 7)	Low PRA (n = 15)	Normal PRA (n = 12)	Low PRA (n = 11)	Normal PRA (n = 25)	High PRA (n = 1)
Serum fT_4 level (pmol/l)	60.63 ± 6.09	53.16 ± 5.70	48.99 ± 10.09	4.79 ± 1.07	6.22 ± 1.55	14.72 ± 1.46	15.88 ± 1.05	14.50
Serum fT_3 level (pmol/l)	26.08 ± 1.83	24.74 ± 1.70	27.83 ± 1.06	2.12 ± 0.43	2.35 ± 0.69	5.13 ± 0.58	6.09 ± 0.36	6.04
Serum TSH level (mIU/l)	0.04 ± 0.01	0.08 ± 0.05	0.02 ± 0.02	30.62 ± 6.04	38.08 ± 5.61	1.70 ± 0.33	1.76 ± 0.39	1.01
Clinical disease activity index*	27.8 ± 0.5	27.2 ± 0.5	27.7 ± 1.2	24.4 ± 0.8	23.9 ± 0.6	–	–	–
Systolic blood pressure (mmHg)	131.1 ± 2.4	131.2 ± 2.3	130.7 ± 10.1	123.9 ± 6.1	120.7 ± 5.8	115.3 ± 2.1	115.9 ± 3.5	118.0
Diastolic blood pressure (mmHg)	69.0 ± 1.9	67.2 ± 2.0	70.9 ± 5.1	89.9 ± 3.9	80.9 ± 4.1	71.6 ± 3.0	74.6 ± 2.5	74.0
Serum sodium level (mmol/l)	141.1 ± 0.5	139.6 ± 0.5	140.0 ± 0.6	139.8 ± 0.8	139.1 ± 0.5	138.3 ± 0.8	139.4 ± 0.7	135.0
Serum potassium level (mmol/l)	4.51 ± 0.07	4.39 ± 0.08	4.33 ± 0.04	4.40 ± 0.11	4.52 ± 0.08	4.38 ± 0.09	4.48 ± 0.08	4.30

* = Crooks's index for hyperthyroidism. Murray's index for hypothyroidism

same explanation was provided by Ogihara *et al.* (1980) in the patients with severe hyperthyroidism. Water and sodium retention was attributed to the renin-angiotensin system activity in rats with hyperthyroidism (Garcia-Estan *et al.* 1995).

Attainment of euthyroid state in the patients with low-renin activity under basal conditions was associated with an increase in PRA. On the other hand, in the hyperthyroid patients with high-renin activity, a therapy leading to attainment of euthyroid state caused a decrease in PRA. It may be concluded that both low and high basal PRA in patients with hyperthyroidism is resulted from an excess of thyroid hormones. The detailed mechanisms of these phenomena are unclear and are believed to be complex. Stimulation of PRA with a low-sodium diet and upright position resulted in higher increase in PRA in the hyperthyroid patients than in the healthy controls. This finding is concomitant with results of other studies, including reports of stimulation of PRA with upright position (Hauger-

Klevene *et al.* 1972), application of a low-sodium diet (Cain *et al.* 1973) or after furosemide infusion (Asmah *et al.* 1997) to hyperthyroid patients. An increase in PRA associated with upright position is suggested to be caused by β-adrenergic stimulation (Hauger-Klevene *et al.* 1972; Cain *et al.* 1973). This hypothesis does not agree with lack of changes in blood catecholamine level in hyperthyroid patients after upright position. Under these conditions, the catecholamine level in hyperthyroid patients was similar (Martin 1993) or lower (Premel-Cabic *et al.* 1986) than in the healthy subjects.

This study showed that PRA in patients with hypothyroidism was lower than in healthy subjects. This finding is concomitant with earlier reports (Saruta *et al.* 1980). We have not observed any individuals with hypothyroidism and high PRA; low PRA was found in 56% of the investigated hypothyroid patients. Low PRA in these patients may be related to renin and angiotensinogen synthesis and release. Animal models revealed that hypothyroidism is associated with decreased angiotensinogen synthesis in the liver (Ruiz *et al.* 1987) as well as its lower level in plasma (Ruiz *et al.* 1987; Bouhnik *et al.* 1981). Diminished synthesis was related to thyroid hormone deficiency and was normalized in euthyroid state (Bouhnik *et al.* 1981). Investigations of renin activity provided contradictory results. Some revealed decreased plasma renin level (Jimenez *et al.* 1984), other reports showed normal level with enhanced renal content of renin (Bouhnik *et al.* 1981) or increased plasma renin level (Ruiz *et al.* 1987). It may be concluded that low PRA was resulted from angiotensinogen deficiency and the role of renin level alterations was lower in diminished PRA in patients with hypothyroidism. This concept was suggested by Bouhnik *et al.* (1981) in a disease model in rats. They also suggested that diminished renin level is resulted from decreased sensitivity of β-adrenergic receptors in the juxtaglomerular apparatus.

Application of PRA stimulation with a low sodium diet and upright position in patients with hypothyroidism resulted in lower PRA increase in the patients than in the controls. Similar findings were shown in other reports after PRA stimulation with upright position (Hauger-Klevene *et al.* 1972) or furosemide (Saruta *et al.* 1980). Our results have shown that low PRA response to stimulation was found in the patients with low basal PRA. It is suggested that low response is resulted from impaired hepatic synthesis of angiotensinogen. Similar finding was reported in animals with experimental hypothyroidism (Ruiz *et al.* 1987). Saruta *et al.* (1980) suggested that low response to furosemide in hypothyroid animals is caused by insufficiency of the juxtaglomerular apparatus.

Attainment of euthyroid state resulted in normal poststimulatory PRA and it proofs that low PRA is associated with thyroid hormone deficiency. Park *et al.* (2001) suggested that the marked increase of PRA in myxedema patients after correction of hypothyroidism might be related to a prolonged decrease in plasma volume. This study found that basal Aldo levels were increased in normal-renin patients with hyperthyroidism or hypothyroidism. Others also reported higher serum Aldo level in patients with hypothyroidism (Fommei *et al.* 2002) or hyperthyroidism (Takeda *et al.* 1986) than in healthy controls. Our early study indicates that poststimulatory Aldo levels in patients with hyperthyroidism were lowered (Marcisz *et al.* 2003a), and this finding is concomitant with results reported by Cain *et al.* (1973). On the other hand, in low-renin patients with hypothyroidism the poststimulatory Aldo was found to be relatively higher. It indicates that an excess or deficiency of thyroid hormones lead to uncoupling of the renin-angiotensin-aldosterone system. This suggestion is similar to mechanism reported by other papers (Marcisz *et al.* 2003a; b; Shigematsu *et al.* 1989). In the mechanism contributing to this phenomenon was proposed inhibitory effect of atrial natriuretic peptide on Aldo secretion in hyperthyroid patients (Marcisz *et al.* 2003a).

CONCLUSIONS

In conclusion, our findings show that: (a) poststimulatory PRA is higher in hyperthyroid patients, especially those with low basal PRA, (b) in patients with hypothyroidism, poststimulatory PRA is impaired, (c) in hyperthyroidism or hypothyroidism blood pressure and severity of thyroid dysfunction are similar in patients with low, normal or high basal PRA, (d) in patients with thyroid dysfunctions, serum Aldo level and its relative poststimulatory increment are inadequate to PRA. It is suggested that dissociation in the renin-angiotensin-aldosterone system occurs in patients with thyroid dysfunctions.

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