Plasma Renin Activity and Aldosterone Concentration of Patients with Hyperthyroidism and Hypothyroidism

TOSHI OGIHARA, TOSHIHIDE YAMAMOTO, KIYOSHI MIYAI, AND YUICHI KUMAHARA

The Central Laboratory for Clinical Investigation, Medical School of Osaka University, Fukushima-ku, Osaka

Synopsis

Simultaneous measurements of plasma renin activity (PRA), aldosterone concentration and serum potassium were carried out in 27 hyperthyroid, 10 hypothyroid patients and 22 normal controls. In 16 hyperthyroid patients these analyses were done after 90 mg propranolol administration for 6 to 12 days. In both hyper- and hypothyroid patients the studies were repeated after euthyroid achievement. Increased PRA (1.43 ± 0.14 ng/ml/hr, m ± S.E., on recumbent, 2.27 ± 0.2 ng/ml/hr on upright position) and aldosterone concentration (149 ± 20 pg/ml, 236 ± 30 pg/ml) were observed in hyperthyroidism. These values were both significantly high compared with normal controls (PRA: 0.29 ± 0.03, 0.74 ± 0.08, aldosterone: 67 ± 8, 110 ± 5). Increased PRA and aldosterone concentration in hyperthyroid patients were both significantly reduced after propranolol administration, but the extent of reduction was much greater in PRA than in aldosterone concentration. In hypothyroidism both PRA (0.23 ± 0.05, 0.27 ± 0.06) and aldosterone concentration (23 ± 3, 36 ± 8) were significantly low. Those increased and reduced PRA and aldosterone concentration were normalized after achievement of euthyroid states. Serum, potassium levels in these 3 groups were all within normal range and there was no significant difference among these groups. Changes of plasma aldosterone concentration were considered to be secondary to changes of PRA because of parallel changes of these parameters. Clinical significance of altered plasma aldosterone is discussed.

Functional state of the thyroid gland is one of the factors which affect secretion and metabolism of steroid hormones. Luetscher et al. (1963) as well as Kono et al. (1966) observed that aldosterone secretion was increased in hyperthyroidism and reduced in hypothyroidism, though plasma aldosterone concentration (PAC) calculated from secretion and metabolic clearance rate was normal in hyper- and hypothyroidism.

Recently Hauger-Klevene et al. (1972) reported changes in plasma renin activity (PRA) in hyper- and hypothyroidism, which was positively correlated with functional states of thyroid glands. Increased PRA in hyperthyroidism was suppressed by adrenergic blockade. The elevated PRA in hyperthyroidism was presumed to be one of the manifestations of augmented adrenergic activity in hyperthyroidism. Because of reduced pressor sensitivity to infused angiotensin II, they further concluded that the elevated PRA had little to do with maintenance of the arterial hypertension.

It is anticipated that the altered PRA may have any relation with aldosterone secretion and a consequent effect on electrolyte homeostasis. In the following study, we measured PRA and plasma aldosterone concentration (PAC) in patients with hyper- and hypothyroidism before and after treatment. In addition, PAC and PRA were measured after

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adrenergic blockade with propranolol in patients with hyperthyroidism. Plasma potassium concentration of the same samples were measured as well. Correlation among these measurements were sought.

Materials and Methods

PRA, PAC and plasma potassium levels were measured in 27 hyperthyroid, 10 hypothyroid patients and 22 normal controls. In 16 hyperthyroid patients these analyses were done after the administration of propranolol 90 mg/day p.o. for 6 to 12 days. In both hyper- and hypothyroid patients the studies were repeated after euthyroid achievement. The venous blood was drawn on two occasions, i.e., on their appearing in clinic (in the upright position) and after their taking recumbent (supine) position for 1 hr. The patients received an unrestricted diet containing normal amounts of sodium and potassium. PRA was measured by the radioimmunoassay described by Haber et al. (1969). PAC was determined by a modified radioimmunoassay method described by Bayard et al. (1970), using the antibody prepared from the National Institutes of Health, USA. Serum potassium level was determined by flame photometry. Statistical analyses were made using Student's test. All values are expressed as the mean ± standard error of the mean (SEM).

Results

Results of PRA, PAC and serum potassium levels are summarized in Table 1. In hyperthyroidism PRA was 1.32 ± 0.14 ng/ml/hr in the recumbent position and increased to 2.27 ± 0.2 ng/ml/hr in the upright position. These results are both significantly greater than those of the normal controls, 0.29 ± 0.03 ng/ml/hr and 0.74 ± 0.08 ng/ml/hr, respectively. Those increased PRA in hyperthyroidism were suppressed nearly to the normal range after propranolol administration and normalized after euthyroid achievement. In hypothyroidism both recumbent and upright PRA were slightly lower, i.e., 0.23 ± 0.05 ng/ml/hr and 0.27 ± 0.06 ng/ml/hr, than the normal controls, statistically significant (p < 0.001) in upright. Those lower PRA in hypothyroidism reached to normal range after the remission to euthyroid condition.

PAC of the hyperthyroid subjects, 149 ± 20 pg/ml in the recumbent and 236 ± 30 pg/ml in the upright position were significantly greater than those of the normal subjects, 67 ± 8 pg/ml and 110 ± 5 pg/ml respectively (p < 0.001). Those increased levels were lowered after propranolol administration (p < 0.1 in recumbent, p < 0.01 in upright). PAC of the hyperthyroid subjects were nearly normalized after euthyroid achievement. In hypothyroidism PAC were significantly low, i.e.,

<table>
<thead>
<tr>
<th>Subjects</th>
<th>(N)</th>
<th>Recumbent m±SEM</th>
<th>p</th>
<th>Upright m±SEM</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal control</td>
<td>(22)</td>
<td>0.29±0.03</td>
<td></td>
<td>0.74±0.08</td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism before treatment</td>
<td>(27)</td>
<td>1.32±0.14</td>
<td>0.001</td>
<td>2.27±0.20</td>
<td>0.001</td>
</tr>
<tr>
<td>Hyperthyroidism treated with propranolol</td>
<td>(16)</td>
<td>0.77±0.13</td>
<td>0.01*</td>
<td>1.22±0.16</td>
<td>0.001*</td>
</tr>
<tr>
<td>Euthyroidism after treatment of hyperthyroidism</td>
<td>(13)</td>
<td>0.37±0.05</td>
<td>N.S.</td>
<td>0.92±0.11</td>
<td>N.S.</td>
</tr>
<tr>
<td>Hypothyroidism before treatment</td>
<td>(10)</td>
<td>0.23±0.05</td>
<td>N.S.</td>
<td>0.27±0.06</td>
<td>0.001</td>
</tr>
<tr>
<td>Euthyroidism after treatment of hypothyroidism</td>
<td>(8)</td>
<td>0.53±0.15</td>
<td>N.S.</td>
<td>0.93±0.21</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

p value: compared with the normal control, *: compared with hyperthyroidism
23 ± 3 pg/ml and 36 ± 8 pg/ml (p < 0.001) compared with the normal controls and reached to normal range after thyroid treatment. Serum potassium levels of all groups were in the normal range and there were no significant differences among them.

Discussion

Alterations of plasma aldosterone concentration in different thyroid states remain to be clarified. Altered PRA and aldosterone secretion (as well as metabolic clearance rate thereof) have been reported separately, which were related to the functional states of the thyroid glands (Luetscher et al., 1963, Kono et al., 1966, Hauger-Klevene et al., 1972). The implication of these changes to electrolyte homeostasis, especially of potassium, is totally unknown. Only one report described hyperreninemia, “secondary aldosteronism” with hypokalemia in dogs in the thyrotoxic state by the administration of excess thyroxine (Shahawy et al., 1971). Fukuchi et al. reported increased PRA and PAC in subjects with hyperthyroidism (1973). Increased PRA and reduced PAC were noted in hyperthyroidism by Cain et al. (1973). Results were confusing.

Our present results of PRA in hyper- or hypothyroidism before and after normalization of thyroid functions, PRA changes in hyperthyroidism after moderate dosage of propranolol for one or two weeks were consistent with those of Hauger-Klevene et al. (1972). PAC was altered in the same direction as PRA, i.e., elevated in hyperthyroidism and reduced in hypothyroidism, which was normalized after remission to euthyroid states in both conditions. These results of PAC were different from those reported by Luetscher et al. (1963) and Kono et al. (1966). This difference might be due to different methods used to estimate PAC. The elevated PAC in hyperthyroidism was reduced following administration of propranolol to a lesser degree than PRA was. By in vitro enrichment experiment, propranolol added to serum to a concentration up to 100 µg/ml did not interfere with PRA and aldosterone assay (unpublished data). Bühler et al. (1972) described that propranolol did reduce PRA and, to a lesser degree, aldosterone excretion rate in hypertensive patients with high plasma renin activity. Our finding was consistent with these results.

Parallel changes of PRA and PAC suggest that the altered PAC in hyper- and hypothyroidism is secondary to changes of PRA.

<table>
<thead>
<tr>
<th>Recumbent m±SEM</th>
<th>Upright m±SEM</th>
<th>Serum potassium (mEq/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAC (pg/ml)</td>
<td>p</td>
<td>m±SEM</td>
</tr>
<tr>
<td>67 ± 8</td>
<td>0.001</td>
<td>110 ± 5</td>
</tr>
<tr>
<td>149 ± 20</td>
<td>0.001</td>
<td>236 ± 30</td>
</tr>
<tr>
<td>95 ± 20</td>
<td>0.1*</td>
<td>144 ± 22</td>
</tr>
<tr>
<td>47 ± 7</td>
<td>N.S.</td>
<td>82 ± 10</td>
</tr>
<tr>
<td>23 ± 3</td>
<td>0.001</td>
<td>36 ± 8</td>
</tr>
<tr>
<td>64 ± 17</td>
<td>N.S.</td>
<td>114 ± 20</td>
</tr>
</tbody>
</table>
Despite of this parallelism between PRA and PAC among those three functional states of thyroid, PAC did not show significant correlations with PRA in each of these three conditions both in recumbent and upright postures. This dichotomy is rather unexpected and we can not offer explanations for this at present. Elevated PAC in hyperthyroidism and reduced PAC in hypothyroidism can be normalized by expansion or reduction of body fluid if they are secondary to PRA changes. In this regard, we do not have data.

Other than PRA, other factors such as plasma potassium concentration and/or ACTH are presumed to alter PAC. It is unlikely that the plasma potassium concentration has an influence on PAC because of unchanged plasma potassium concentration among hyper-, eu- and hypothyroidism. ACTH has been known to alter aldosterone secretion. Because of a large dose employed and transient nature of response, its role in aldosterone secretion under physiological conditions has been questioned (Liddle et al., 1956, Crable et al., 1959, Tucci et al., 1967). Augmented or reduced secretion of ACTH has been speculated in hyper- or hypothyroidism (Gallagher et al., 1972), which, nevertheless, might play a role in changing PAC in individual cases.

Serum potassium concentration in different thyroid states remains normal (Ingbar and Woeber, 1968). In a rather acute experiment, Shahawy et al. produced elevated PRA, elevated aldosterone excretion rate and hypopotassemia in dogs made thyrotoxic by the administration of thyroxine. They concluded that thyroxine caused elevation of PRA and induced “secondary aldosteronism” with hypopotassemia (Shahawy et al., 1971). In our study, neither hypo- or hyperpotassemia was found in hyper- or hypothyroidism. If altered PAC had little to do with serum potassium concentration, it might act on intracellular potassium. Total body exchangeable potassium has been reported to be reduced or increased in hyper- or hypothyroidism. In this regard, however, the question remains unsettled whether this is due to reduction or increase in body mass or in intracellular potassium (Aikawa et al., 1953, Munro et al., 1958). Lastly, aldosterone antagonist, for example, progesterone, might be altered in the same direction as aldosterone in the functional disorders of thyroids. Thus far, no actual measurement has been reported of progesterone secretion in thyroid disorders.

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References


