Soluble (Pro)renin Receptor Levels in Patients with Graves’ Disease

Tokyo Women’s Medical University, Department of Medicine II, Endocrinology and Hypertension
Yuki Mizuguchi, Midori Yatabe, Junichi Yatabe, Yasufumi Seki, Michita Niyama, Daisuke Watanabe, Kanako Bokuda, Takashi Ando, Satoshi Morimoto, Atsuhito Ichihara

Background

The (pro)renin receptor ([P]RR) is a receptor for renin and prorenin, which regulates the tissue Renin-Angiotensin System (RAS). [P]RR also plays an important role in the assembly and function of vacuolar H⁺-ATPase (V-ATPase), an ATP-dependent proton pump that transports protons across plasma membranes and acidifies intracellular compartment.

[P]RR is cleaved by furin to generate soluble [P]RR [s(P)RR], which is secreted into blood and urine. Recently, we developed s(P)RR ELISA kit to measure the concentration of s(P)RR in blood. We previously reported that high blood concentration of s(P)RR indicates poor organ prognosis in gestational diabetes, chronic renal disease (CKD) and malignant tumor.

Purpose

The regulating factor of (P)RR and s(P)RR remains unclear. Thyroid hormone (TH) directly activate RAS, which suggests that TH might be one of the regulating factor of (P)RR. Therefore, this study was conducted to investigate the relationship between thyroid function and blood s(P)RR levels in GD patients.

Methods

Study in endocrine disease patients

2012.4.1 〜 2015.10.1
61 Untreated Graves’ Disease (GD), 23 Hashimoto disease, 59 normal subject, 16 acromegaly, 13 pheochromocytoma

<Measured parameter>
Serum s(P)RR*, height, body weight, BMI, blood pressure, BUN, Cr, FT4, FT3, TSH, TRAb, HbA1c, blood sugar level IDL-C, HDL-C, TG

<Excretion criteria>
CKD G3 〜 Diabetes mellitus
Malignant tumor
Patients taking RAS inhibitor
Other severe complication

Reexamination in 6-18 month after treatment

Results

s(P)RR levels in endocrine disease patients

<table>
<thead>
<tr>
<th>GD (n=61)</th>
<th>Control (n=59)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.36 (μg/ml)</td>
<td>13.44 (μg/ml)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

FT4 (μg/dl) 21.30 (μg/dl) 21.30 (μg/dl) 0.22
SHP (ng/ml) 117.1 (ng/ml) 122.8 (ng/ml) 0.395
ERP (ng/ml) 67.7 (ng/ml) 75.5 (ng/ml) 0.002
SHP (ng/ml) 0.0000 0.0000 0.0000
FT3 (μg/dl) 4.57 (μg/dl) 4.10 (μg/dl) 0.0003
FTH (μg/dl) 17.22 (μg/dl) 18.20 (μg/dl) 0.0000
C (μg/dl) 1.55 (μg/dl) 0.78 (μg/dl) 0.0004

Summary

1) Serum s(P)RR levels were significantly higher in GD patients than normal subjects.
2) GD patients with high s(P)RR levels showed treatment-resistance.
3) GD patients with low BMI showed higher levels of serum s(P)RR than those with high BMI, while serum s(P)RR levels were positively correlated with BMI in normal subjects.

Conclusion

These results showed that poor nutritional condition caused by GD might induce s(P)RR production to cause organ damages.

Conflict of Interest

We have no conflict of interest with regard to our presentation.

1008—EP
Thyroid (non-cancer)
Yuki Mizuguchi
Poster presented at ECE 2016