

Relationship Between Hypothalamic-Pituitary-Adrenocortical Axis Activity And Characteristics Of Aldosterone-producing Adenomas

Moe Thuzar^{1,2}, Yu-Chin Lo^{1,2}, Zeng Guo¹, Warrick J Inder^{2,3}, Michael Stowasser¹

1. Endocrine Hypertension Research Centre, The University of Queensland Diamantina Institute & Princess Alexandra Hospital, Brisbane, Australia

2. Department of Endocrinology & Diabetes, Princess Alexandra Hospital, Brisbane, Australia

3. Faculty of Medicine, The University of Queensland, Brisbane, Australia

Background

Aldosterone production can be regulated by adrenocorticotrophic hormone (ACTH) which normally controls cortisol secretion from the adrenal cortex.^{1,2}

Primary aldosteronism, the most common endocrine cause of hypertension, is characterised by excessive production of aldosterone from an adenoma and/or hyperplasia of one or both adrenal glands.^{1,2}

Some cases of aldosterone-producing adenoma (APA) display features which may suggest increased sensitivity to the stimulatory effects of ACTH.³

Aim

To investigate if there is any relationship between the hypothalamic-pituitary-adrenocortical (HPA) axis activity and the characteristics of APAs.

Methods

Study Design & Materials

A single-centre retrospective study involving 41 APA cases which were confirmed on histology including positive immunohistochemistry staining for CYP11B2

Assessments

APA cases were characterised with regards to clinical, biochemical and somatic mutation status.

HPA axis activity was assessed from morning plasma cortisol, ACTH and 1 mg overnight dexamethasone (DEX) suppression test.

Statistical Analyses

Correlations between the characteristics of APAs and the HPA axis activity were analysed by Pearson's correlation coefficient.

The HPA axis activity between APAs with *KCNJ5* mutation and those without was compared using Mann Whitney U-test.

Quantitative data are expressed as median (range). Blood samples for biochemistry were taken before 10 am. *total n=33. **total n=21. DDD, defined daily dose, it is the standardised unit measure reflecting the maintenance dose per day (ref. WHO)

Results

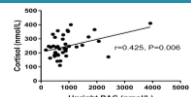
Table 1. Characteristics of APA Cases

Characteristics	APA cases (n=41)
Age (years)	49 (24-69)
Gender	
Female (n, %)	12 (29.3%)
BMI (kg/m ²)	30.6 (19.2-43.3)
Overweight/obese (n, %)	35 (85.4%)
Nodule size (mm)	14 (3-28)
Somatic mutation status (n, %)	
<i>KCNJ5</i> mutation	14 (34.1%)
Other mutations	25 (61.0%)
No mutation detected	2 (4.9%)
Blood pressure parameters	
SBP (mmHg)	153 (124-187)
DBP (mmHg)	92 (68-116)
Anti-hypertensive meds (n)	3 (0-6)
Anti-hypertensive meds (DDD)	2.2 (0-9.9)
Biochemical parameters	
Post-DEX cortisol >50 nmol/L (n, %)*	1 (3.0%)
Plasma ACTH (ng/L)**	19 (10-45)
Plasma cortisol (nmol/L)	
- Recumbent	306 (179-500)
- Upright	240 (110-410)
Plasma aldosterone (pmol/L)	
- Recumbent	590 (203-4275)
- Upright	690 (173-3920)
Plasma direct renin (mU/L)	
- Recumbent	2.0 (0.5-7)
- Upright	3.5 (0.5-15.4)
Plasma potassium (mmol/L)	3.0 (1.7-3.8)
Plasma creatinine (umol/L)	81 (50-130)

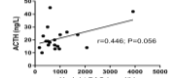
References

1. Stowasser M & Gordon R. *Physiol Rev.* 2016;96(4):1327-84
2. Funder JW. *Front. Endocrinol.* 2016;7:40.
3. Guo Z et al. *J Clin Endocrinol Metab.* 2020.

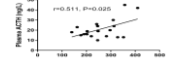
Correlations Between Plasma Aldosterone & HPA Axis Parameters



Plasma Aldosterone Concentration positively correlated with Cortisol

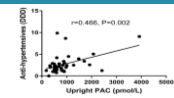


Plasma Aldosterone positively correlated with ACTH

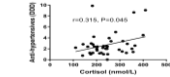


Plasma Cortisol positively correlated with ACTH

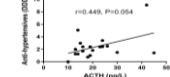
Correlations Between Clinical Characteristics, Plasma Aldosterone & HPA Axis



Plasma Aldosterone positively correlated with Anti-hypertensives dose



Plasma Cortisol positively correlated with Anti-hypertensives dose



Plasma ACTH positively correlated with Anti-hypertensives dose

Other

Plasma Aldosterone also positively correlated with BMI
Plasma cortisol, ACTH, post-DEX cortisol, BMI and DDD of anti-hypertensives were not significantly different between APAs with *KCNJ5* mutation vs other APAs

Conclusions

HPA axis activity correlated with clinico-biochemical characteristics in patients with APAs, but the prevalence of autonomous hypercortisolism was low. The findings suggest a potential role of ACTH in the pathophysiology of APAs.

There was no significant difference in HPA axis activity between those with somatic *KCNJ5* mutation compared to those without.

