Royal United Hospitals Bath
NHS Foundation Trust

Information for Clinicians

Department of Clinical Biochemistry

Aldosterone and renin: guidance for investigation of primary hyperaldosteronism

Amendment History

Issue	Status	Date	Reason for Change	Authorised
V1.0	Approved	May 2024	New Guideline	Moya O'Doherty

Background

Primary hyperaldosteronism (PA) results from the renin-independent overproduction of aldosterone. The most common causes are adrenal adenoma and unilateral or bilateral adrenal hyperplasia. Other subtypes include glucocorticoid suppressible aldosteronism and aldosterone-producing adrenocortical carcinoma.

Indications for requesting aldosterone:renin ratio

Recent studies suggest that more than 10% of hypertensive patients have primary hyperaldosteronism, which is potentially treatable and therefore should be screened for.

Screening for PA using aldosterone:renin ratio (ARR) is advised in the following circumstances (see Endocrine Society Clinical Guideline 2016):

- patients with sustained blood pressure (BP) above 150/100 mmHg on each of three measurements obtained on different days
- with hypertension (BP >140/90 mmHg) resistant to three conventional antihypertensive drugs (including a diuretic)
- controlled BP (<140/90 mmHg) on four or more antihypertensive drugs
- hypertension and spontaneous or diuretic-induced hypokalaemia
- hypertension and adrenal incidentaloma
- hypertension and sleep apnoea
- hypertension and a family history of early onset hypertension or cerebrovascular accident at a young age (<40 years)

- all hypertensive first-degree relatives of patients with PA

NB: a significant proportion of patients with primary hyperaldosteronism are normokalaemic.

Patient preparation

Correct hypokalaemia if present (aim is >3.5 mmol/L).

Do not restrict salt intake.

If safe to do so, withdraw spironolactone, eplerenone, amiloride, triamterene, potassium wasting diuretics and liquorice (for 6 weeks prior to test).

If safe to do so (and especially if a previous ARR screen has been equivocal), withdraw β-blockers and NSAIDS (for 2 weeks prior to test).

If alternative antihypertensive medications are required verapamil, hydralazine, doxazosin and prazosin may be used.

Sample requirements

Aldosterone and plasma renin activity must be measured in the same sample and the aldosterone:renin ratio calculated.

Plasma renin activity and aldosterone:
EDTA plasma preferred.
Do NOT chill sample on collection.
Transport to lab immediately at ambient temperature to prevent cryoactivation of plasma renin activity.
Freeze in lab **within 4 hours of collection**.

Please also send a yellow top SST sample for potassium.

Ideally, primary care patients should be bled at the RUH phlebotomy room for this test to ensure rapid transport to the lab.

If patient is unable to travel to the RUH, this test can be done at the GP surgery, though there is a risk that the sample may not reach the lab in time. The sample should be sent in a red bag or marked as URGENT, and please call specimen reception (01225 824740) on the day of collection so the reception team are aware that an urgent sample is coming. The blood test must be done as close to the time of the transport collection as possible.

Reference ranges

These ranges are for adult hypertensive patients (random, ambulant sample):

Plasma Renin Activity: 0.5-3.5 nmol/L/h
Aldosterone: 90-700 pmol/L
NB: Aldosterone may still be within the reference range in Conn's syndrome but is >275 pmol/L

Aldosterone / Renin ratio	<680	Conn's unlikely
(Note: only relevant in presence	>850	Conn's syndrome possible
of low or suppressed PRA)	>1700	Conn's syndrome very likely

Paediatric samples: please ring and discuss with duty biochemist (01225 824050).

Factors affecting interpretation of results

Biological factors	Effect on Aldosterone	Effect on Renin	Effect on Ratio
Hypokalaemia	↓	↑	↓
Low salt intake	↑	↑	↑
Salt Loading	↓	↓	↓
Age	↓	↓	↓
Renal impairment	↔	↓	↑
Malignant Hypertension or renovascular disease	↑	↑	↓
Pregnancy	↑	↑	↓
Luteal phase	↑	↔	↑
Spironolactone	Variable effect	↑	
β-blockers	↓	↓	↑
NSAIDs	↓	↓	↑
ACEi or ARBs Diuretics Calcium antagonists	↓	↑	↓

Additional investigations

A repeat test is advised in the first instance when an abnormal ARR is obtained. Ideally, patients should be off all medication for any repeat sample, or discussed with the endocrine team if that is difficult to achieve.

Following a second abnormal result, the patient should be referred to endocrinology for further investigations, e.g. saline infusion test (to see if the raised aldosterone is suppressible by salt and water loading) and imaging.

The latest Endocrine Society guidelines (2016) recommend the following further investigations: CT imaging, adrenal venous sampling to distinguish between unilateral and bilateral adrenal disease and potentially genetic testing in patients with a family history of PA or stroke at a young age. These further investigations would be arranged by the endocrine team if indicated once a biochemical diagnosis has been confirmed.

References

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