

Screening for Conn's Syndrome (Primary Aldosteronism)

1.0 Background

Primary aldosteronism is characterised biochemically by a low plasma renin with a raised plasma aldosterone. This guideline describes the recommended initial testing procedures when primary aldosteronism is suspected. Abnormal results do not necessarily confirm a diagnosis and should be referred for specialist opinion.

2.0 Indications

Consider testing for primary aldosteronism when

- Hypertension and hypokalaemia (not diuretic-induced)
- Resistant hypertension
- Adrenal incidentaloma and hypertension
- Severe hypertension (SBP >160, DBP >100)

3.0 Patient Preparation

It is best to take samples for renin and aldosterone estimation under standard conditions. The hormone measurements will not be made unless the following conditions are adhered to or have been modified after discussion - contact the Duty Biochemist.

Discontinue spironolactone and amiloride at least 2 weeks before measurement. Other antihypertensive drugs can make interpretation difficult and ideally should also be discontinued. However – some useful information may be derived from testing in patients taking ACE inhibitors, diuretics, beta blockers and ARBs (see 6.0)

Low serum potassium levels per se can inhibit aldosterone secretion, and ideally the serum potassium should be not less than 3.5 mmol/L at the time of analysis. Potassium supplements should be used to achieve this level, but these should be discontinued 12 hours before blood sampling.

Ensure a normal diet with adequate sodium intake has been taken in the few days prior to sampling.

4.0 Procedure

- The patient should be seated for 30 minutes prior to blood sampling. A change in posture may cause a rise in aldosterone levels (false positive result), or a rise in renin levels (false negative).
- Venous blood specimens are then taken and transported IMMEDIATELY to the Biochemistry Department. **Do not use ice** for transportation as this may cause cryoactivation of renin. **You should phone the lab to say the specimens are arriving.**

Specimen tubes are:

RENIN & ALDOSTERONE: 4 mL Potassium EDTA Vacutainer (367869) (Lilac top)

5.0 Interpretation

Aldosterone (pmol/L) to renin (mIU/L) ratio of greater than 30 where the aldosterone is greater than 300 pmol/L suggests primary aldosteronism (99% sensitivity, 79% specificity). Patients with a positive screening test first require a repeat confirmation ensuring the patient is not receiving beta-blockers. If the repeat test is positive then a more detailed investigation is required (ie salt loading test) to confirm the presence of primary hyperaldosteronism.

6.0 Effect of medication on renin and aldosterone

ACE inhibitors, ARBs and diuretics may “falsely elevate” plasma renin activity; therefore the finding of a normal aldosterone:renin ratio would not exclude the diagnosis of primary aldosteronism. However, a low plasma renin activity in such circumstances means primary aldosteronism is highly suspect.

Adrenergic inhibitors (eg beta blockers and central alpha 2 agonists) suppress renin more than aldosterone, and may cause a falsely elevated ratio. An elevated aldosterone, with an elevated ratio means primary aldosteronism remains suspect in such patients.

Drug	Renin	Aldosterone	Effect
Nifedipine/verapamil	Minimal	Minimal	No effect
Amlodipine	Minimal	Decreased/minimal	Nil/false negative
Alpha blockers	Nil	Nil	No effect
Hydralazine	Minimal	Minimal	No effect
ACE inhibitors	Increased	Decreased	False negative
Diuretics	Increased ++	Increased	False negative
Minoxidil	Increased	Minimal	False negative
AR blockers	Increased	Decreased	False negative
Beta blockers	Decreased	Minimal	False positive
Alpha-methyl dopa	Decreased	Minimal	False positive

7.0 References

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3. Lim PO, Jung RT, MacDonald TM. Raised aldosterone to renin ratio predicts anti-hypertensive efficacy of spironolactone: a prospective cohort follow-up study. *Br J Clin Pharmacol* 1999; 48:756-760.
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5. Doi, SR et al Optimal use and interpretation of the aldosterone renin ratio to detect aldosterone excess in hypertension. *J Hum Hypertension* 2006; 20; 482-9.
6. Manolopoulou J, Fischer E, Dietz A *et al*. Clinical validation for the aldosterone-to-renin ratio and aldosterone suppression testing using simultaneous fully automated chemiluminescence immunoassays. *J Hypertens* 2015; 33: 2500-2511.