

## 1.1 Saline Loading in the Investigation of Primary Aldosteronism (PAL) Policy

### 1.1.1 Background & Rationale

Saline loading is used to determine whether patients with elevated aldosterone to renin ratio (greater than 70) have autonomous aldosterone production, as part of the investigations for suspected primary aldosteronism (PAL). Aldosterone is produced by the adrenal glands, normally under the regulation of angiotensin 2 and the serum potassium concentration. Angiotensin 2 and potassium both stimulate aldosterone production (hypokalaemia suppresses aldosterone).

In the condition known as primary aldosteronism, the adrenal gland produces aldosterone independently (autonomously), with little regulation by angiotensin 2 or potassium. Excess aldosterone circulating in the blood leads to hypertension by the reabsorption of sodium and water from the kidney.

Saline loading is one way of determining whether the adrenal glands are indeed autonomous or normal. The intravenous infusion of 2 litres of saline in a normal individual switches off renin secretion from the kidneys, and lack of renin leads to reduction in angiotensin 2 and therefore reduction in aldosterone. This would be a normal response and hence the aldosterone level should fall after 2 litres of saline, below 150 pmol/L.

When a patient has primary aldosteronism, the saline loading study should fail to suppress aldosterone. Patients with primary aldosteronism often have low renin and low angiotensin levels anyway, as the sodium and water retention in this condition will suppress renin excretion from the kidneys. Hence the aldosterone level will NOT fall significantly after 2 litres of saline in a patient with typical primary aldosteronism.

Of course this technique is not perfect and false positives and false negatives can occur. This particular test is susceptible to a false negative study (that is, a patient who in fact does have primary aldosteronism has a normal saline loading study and their aldosterone falls below 150). Drugs interfere with this test as well, beta-blockers suppress renin, ACE inhibitors, diuretics and angiotensin blockers stimulate renin release. These drugs should be withdrawn 1 week prior to a saline loading study under supervision of a physician (i.e. if medication withdrawal is safe). Prazosin and calcium channel blockers do not affect results of this test to a significant degree.

### 1.1.2 Indications

Saline loading is indicated as a screening tool for primary aldosteronism in the presence of:

- Hypertension with unexplained hypokalemia / metabolic alkalosis
- Resistant hypertension (with or without unexplained hypokalaemia).
- As part of secondary hypertension screen.

The initial screening includes two elevated resting plasma aldosterone/ renin ratios.

### 1.1.3 Expected Outcomes

- Registered Nurses administering intravenous saline loading will have a thorough understanding of the procedure.
- Registered Nurses will safely and effectively administer intravenous saline loading using the recommended procedure.

### 1.1.4 Limitations for Practice

- Saline loading should only be administered by Registered Nurses who have read the policy and have a clear understanding of the correct administration procedure.
- Patients must withdraw (or reduce if not possible to withdraw) from beta blockers (where there is no coexistent ischaemic heart disease), diuretics, ACE inhibitors and vasodilators, as ordered by the treating medical officer. Suitable replacement drugs include Prazosin and Hydralazine.
- The cut off value for an abnormal ratio will differ according to different laboratories and their methods for measuring renin.

### 1.1.5 Procedure

In addition to the following procedure, all relevant St George Hospital and Community Health Service policies must be adhered to when administering saline loading.

- Medical officer to take patient's history. If a family history of primary hyperaldosteronism is found, patients should be screened for the disorder 'FHI', (familial aldosteronism type – 1 OR glucocorticoid remediable aldosteronism) by collecting blood (in 2 x 5ml EDTA tube) to test for the presence of the hybrid FHI gene. At present this is sent to a laboratory in Queensland (Prof M Stowasser).
- Inform patient of procedure.
- Baseline observations, including blood pressure, pulse and temperature are to be recorded pre-procedure.
- Collect blood after 30 minutes of bed rest. Blood is tested for plasma renin and aldosterone concentration, as well as plasma sodium, potassium and creatinine levels.
- Wash hands.
- Establish intravenous access.
- 2 litres of intravenous normal saline is administered over four hours, as ordered by a medical officer. The patient is to remain on bed rest throughout the duration of the normal saline infusion.
- Blood is again collected and tested for renin and aldosterone at the completion of the infusion.
- Blood samples should be collected into ONE EDTA tube (5mls) AND ONE YELLOW/RED TOPPED TUBE (ie total two tubes). Blood needs to be kept at room temperature (no ice) and transferred to the laboratory. In the laboratory, blood is spun at room temperature, then snap frozen in ethanol/ dry ice prior to assay.
- A normal result is where the aldosterone concentration suppresses below 150 pmol/L.
- A positive result is where aldosterone does not suppress below the above cut off. Autonomous production of aldosterone is confirmed and a diagnosis of PAL can be established.
- For patients with proven aldosteronism, adrenal vein sampling (AVS) should be arranged with Radiology. Samples are drawn from peripheral blood, IVC, left and right adrenal veins.
- Adrenal CT scan may help identify an adrenal adenoma in some cases and may assist the Radiologist in localisation of the glands during AVS.
- Of patients diagnosed with PAL:
  - Approximately 1/3 will have unilateral production of aldosterone (adenoma)
    - ½ of these will be cured by surgery
    - ½ will require less medication after surgery
  - Approximately 2/3 will have bilateral production of aldosterone, which should be treated with medication.

### 1.1.7 References

St George Hospital Renal and Hypertension Unit Clinical Protocols – Investigation of suspected aldosteronism (PAL). Location: St George Hospital Intranet Site.

Accessed 26<sup>th</sup> July 2005.

Personal Communication, Dr George Mangos (Nephrology Consultant, St George Hospital). 19<sup>th</sup> January 2006.