Hyperaldosteronism

Primary hyperaldosteronism is present when there is excess secretion of aldosterone from a functional tumor (aldosterononoma) independent of a physiologic stimulus. Secondary hyperaldosteronism is present when increased circulating serum concentrations of rennin, as associated with renovascular hypertension, stimulate the release of aldosterone. The prevalence of primary hyperaldosteronism is less than 1% in patients with essential hypertension.

ANESTHETIC CONSIDERATIONS:

1. Perioperative electrolyte abnormalities
   - Hypokalemia
   - Hypernatremia
   - Hypomagnesemia
   - Abnormal glucose tolerance
2. Hypertension
   - Resistant to routine therapy
3. Increased sensitivity to neuromuscular blockade.
   - Modified responses to non depolarizing muscle relaxants and prolonged neuromuscular blockade

ANESTHETIC GOALS:

1. Preoperative optimization of hypertension
2. Preoperative and perioperative correction of volume and electrolyte abnormalities

HISTORY (SPECIFIC SIGNS AND SYMPTOMS)

- **SYSTEMIC HYPERTENSION**
  - headache
  - elevated BP reading
  - hypertensive urgency/emergency
    - angina
    - pulmonary edema
    - hemorrhagic stroke
    - retinal hemorrhage and blurred vision
  - evaluate for end organ dysfunction secondary to hypertension
    - cardiovascular function
      - diastolic dysfunction
      - LVH
    - renal function
      - hypertensive nephrosclerosis
    - ophthalmologic changes
- **HYPOKALEMIA**
  - polyuria
  - nocturia
  - skeletal muscle cramps
  - skeletal muscle weakness
- **HYPERNATREMIA AND SODIUM RETENTION**
  - increased ECF vvolume
  - resistant hypertension

PHYSICAL

- **VITALS**
  - Orthostatic hypotension may herald unexpected hypovolemia
- **CNS**
  - Stroke and associated neurological deficits
  - Visual changes associated with severe hypertension
- **CVS**
  - LVH
    - Displaced apex on precordial examination
  - diastolic dysfunction
  - hypervolemia and increased ECF secondary to Na retention
- **RESP**
  - routine
- **GI**
  - routine
- **GU**
  - Nocturia and polyuria
- **MSK**
  - Peripheral muscle weakness secondary to hypokalemia

INVESTIGATIONS

- **Labs**
  - CBC
  - Lytes, BUN, creatinine
  - Plasma renin
    - Suppressed in almost all patients with untreated primary aldosteronism
    - High plasma renin activity in patients with secondary hyperaldosteronism
  - NB: a syndrome exhibiting all the features of hyperaldosteronism (htn, hypok, suppression of RAS) can result from chronic licorice ingestion
- **Imaging**
  - CXR if indicated
  - ECG if indicated – LVH
  - Echo if indicated

OPTIMIZATION

- Preoperative blood pressure control
- Preoperative correction of electrolyte abnormalities

ANESTHETIC OPTIONS

- None
- Regional
- Neuraxial
- General

ANESTHETIC SETUP

- **Drugs**
  - Standard emergency drugs
  - Perioperative steroids
    - Not indicated for surgical excision of solitary adenoma in adrenal cortex
    - Bilateral mobilization of adrenal glands to excise multiple function tumors may require exogenous cortisol administration (100mg IV q24h)
- **Equipment**
  - Twitch monitor

MANAGEMENT OF ANESTHESIA

- **Induction**
  - Succinylchline is OK
- **Maintenance**
  - Inhaled or IV maintenance are both acceptable
  - Caution with sevoflurane if patient already has hypokalemic nephropathy and polyuria (high inorganic F concentrations with prolonged sevoflurane use)
- **Emergence**
  - If hypoK, at increased risk for prolonged NMB

DISPOSITION & MONITORING

COMPLICATIONS

- Prolonged neuromuscular blockade

PATHOPHYSIOLOGY

Aldosterone is the principal mineralocorticoid in man. Its functions include regulation of extracellular volume and potassium homeostasis through its effects on the renal distal convoluted tubule. Extra-renal actions of aldosterone on cardiovascular tissues, the colon and salivary glands are also well established. Excess production of aldosterone, due to either primary or secondary disorders, is prevalent in the general population, and is an important cause of morbidity and mortality.

The primary functions of aldosterone are to regulate extracellular volume and potassium balance. These effects are mediated through the effects of aldosterone on the distal nephron. Aldosterone binds to the type I mineralocorticoid receptor in the cytosol of distal cortical collecting principal cells. Translocation of the hormone-receptor complex to the nucleus leads to modification of target gene expression, and subsequently increased number of "open" sodium channels on apical cell membranes. The resulting **increase in reabsorption of sodium** generates a negative electrical gradient in the tubular lumen, which promotes **potassium and hydrogen ion excretion** to maintain electrical neutrality

Aldosterone is synthesized in the zona glomerulosa of the adrenal gland. Its production is restricted to this layer of the adrenal cortex because of zonal-specific expression of aldosterone synthase (CYP11B2). Aldosterone secretion is under the control of three primary factors: angiotensin II, potassium, and adrenocorticotropic hormone (ACTH). The renin-angiotensin system (RAS) is a principal regulator of aldosterone secretion. Renin, an enzyme produced in the juxtaglomerular apparatus of the kidney, catalyzes the conversion of angiotensinogen (an inactive precursor peptide) to angiotensin I. Angiotensin I undergoes further enzymatic conversion by angiotensin-converting enzyme (ACE) to produce angiotensin II. Angiotensin II acts via the angiotensin receptor to stimulate the release of aldosterone by increasing the transcription of aldosterone synthase. The RAS serves to regulate two critical functions in the human body: sodium homeostasis and arterial pressure (1). Through complex negative feedback loops (Figure 1), activity of the RAS can be suppressed or enhanced by sodium balance, intravascular volume, and other factors. For example, renin (and consequently aldosterone) production is stimulated by low tubular sodium or low renal perfusion; conversely, renin is suppressed by high sodium content or high perfusion pressure. Angiotensin II and other components of the RAS are also expressed locally in the zona glomerulosa and regulate aldosterone production in a paracrine fashion.

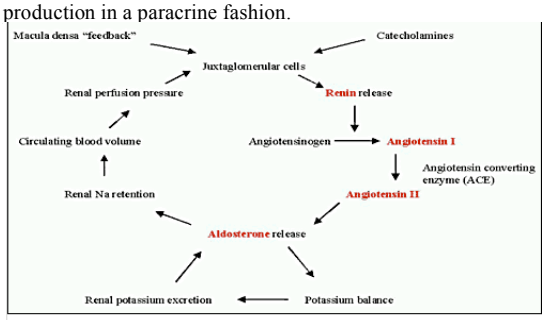

Figure 1. Renin-angiotensin-aldosterone and potassium-aldosterone negative-feedback loops. Aldosterone production is determined by input from each loop. (Adapted and redrawn from Williams GH, Dluhy RG. Disease of the adrenal cortex. In: Fauci AD, Braunwald E, Isselbacher KJ, et al, eds. Harrison's Principles of Internal Medicine. 15th ed. New York: McGraw-Hill, 2001)

- Primary hyperaldosteronism is secondary to an aldosterone secreting tumor (typically an adrenal aldosteronoma) or excess endogenous aldosterone secretion
- Secondary hyperaldosteronism is secondary to increased circulating concentrations of renin, thus stimulating the release of aldosterone.
- Treatment:

- Primary: mineralocorticoid receptor antagonist, steroids, surgery
- Secondary: mineralocorticoid receptor antagonist, ACEI/ARB (caution if bilateral RAS), angioplasty if RAS

Table 1: Mineralocorticoid-Excess States

Mineralocorticoid Excess with low plasma renin activity

- Primary Aldosteronism (PA)
  - Aldosterone-producing adenoma (APA)
  - Idiopathic bilateral hyperplasia (BAH)
  - Unilateral primary adrenal hyperplasia (UAH)
  - Glucocorticoid-remediable aldosteronism (GRA)
  - Aldosterone-producing adrenocortical carcinoma
- Congenital adrenal hyperplasia (e.g., 11beta-hydroxylase deficiency)
- Syndrome of Apparent Mineralocorticoid Excess (AME)*
- Liddle's syndrome*

Mineralocorticoid Excess with high plasma renin activity (Secondary Hyperaldosteronism)

- Usually Hypertensive
  - Renovascular disease (atherosclerotic, fibromuscular hyperplasia)
  - Coarctation of the aorta
  - Renin-secreting tumors
- Usually Normo- or Hypotensive
  - Reduced Circulating Blood Volume:
    - Gitelman's Syndrome
    - Bartter's Syndrome
    - Pseudohypoaldosteronism Type I
    - Diuretic Use (surreptitious or prescribed therapy)
  - Reduced 'Effective' Circulating Blood Volume:
    - Congestive Heart Failure
    - Hepatic cirrhosis
    - Nephrotic Syndrome

*In these disorders, non-aldosterone mediated renal sodium reabsorption results in volume expansion and suppression of both plasma renin activity and plasma aldosterone.

REFERENCES

- Stoeltings's Anesthesia and coexisting disease Chapter 16
- Endotext.org section on hyperaldosteronism