
بنام خداوند جان و خرد

Treatment of Acute Adrenal Insufficiency

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TABLE 15.19 Clinical and Laboratory Features of an Adrenal Crisis

Dehydration, hypotension, or shock out of proportion to severity of current illness
Nausea and vomiting with a history of weight loss and anorexia
Abdominal pain, so-called acute abdomen
Unexplained hypoglycemia
Unexplained fever
Hyponatremia, hyperkalemia, azotemia, hypercalcemia, or eosinophilia
Hyperpigmentation or vitiligo
Other autoimmune endocrine deficiencies, such as hypothyroidism or gonadal failure

Frequencies of Etiologies of Primary Adrenal Insufficiency

ETIOLOGY	%	AGE AT DIAGNOSIS
Congenital adrenal hyperplasia	59	Infancy
Autoimmune	16	Childhood-adolescence
APECED (autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy)	6	Childhood-adolescence
Adrenoleukodystrophy	4	Childhood-adolescence
Isolated glucocorticoid deficiency	4	Infancy
Idiopathic	4	Childhood
Syndromes	3	Infancy
X-linked adrenal hypoplasia congenita	2	Infancy-childhood
Hemorrhage	1	Infancy

Secondary Causes: Central Hypoadrenalism

- Exogenous glucocorticoid therapy
- Hypopituitarism
  - Selective removal of ACTH-secreting pituitary adenoma
  - Pituitary tumors and pituitary surgery, craniopharyngiomas
  - Pituitary apoplexy
  - Granulomatous disease (tuberculosis, sarcoid, eosinophilic granuloma)
  - Secondary tumor deposits (breast, bronchus)
  - Postpartum pituitary infarction (Sheehan syndrome)
  - Pituitary irradiation (effect usually delayed for several years)
- Isolated ACTH deficiency
  - Idiopathic
  - Lymphocytic hypophysitis
  - TPIT *(TBX19)* gene mutations
  - *PCSK1* gene mutation (POMC processing defect)
  - *POMC* gene mutations
- Multiple pituitary hormone deficiencies
  - *HESX1* gene mutations
  - *LHX4* gene mutations
  - *SOX3* gene mutations
  - *PROP1* gene mutations

TOPICAL CORTICOSTEROID POTENCIES

Potency	Class	Generic (Brand)	Strength (%)
High	1	Betamethasone dipropionate	0.05
		Clobestasol propionate	0.05
		Halobetasol propionate	0.05
	2	Desoximetasone	0.05, 0.25
		Fluocinonide	0.05
Medium	3	Betamethasone valerate	0.1
		Triamcinolone acetate	0.1, 0.5
	4	Flurandrenolide	0.05
	5	Fluticasone propionate	0.05
Low	6	Desonide	0.05
	7	Hydrocortisone	0.5-2.5

Generally limit high-potency TCS to <2 weeks duration

	PATHOPHYSIOLOGIC MECHANISM	(%)*
SYMPTOMS		
Fatigue	Glucocorticoid deficiency	90
Anorexia, weight loss	Glucocorticoid deficiency	90
Nausea, vomiting	Glucocorticoid deficiency, mineralocorticoid deficiency	90
Salt craving (primary adrenal insufficiency only)	Mineralocorticoid deficiency	20
Myalgia or joint pain	Glucocorticoid deficiency	
SIGNS		
Low blood pressure, orthostatic hypotension	Mineralocorticoid deficiency, glucocorticoid deficiency	70–100
Skin or mucosal hyperpigmentation (primary adrenal insufficiency only)	Excess of proopiomelanocortin-derived peptides	70
LABORATORY FINDINGS		
Hyponatremia	Mineralocorticoid deficiency, glucocorticoid deficiency (leading to decreased free water excretion)	90
Hyperkalemia (primary adrenal insufficiency only)	Mineralocorticoid deficiency	50
Hypoglycemia	Glucocorticoid deficiency	30
Ketosis	Glucocorticoid deficiency	30
Low random cortisol level	Glucocorticoid deficiency	80
Eosinophilia, lymphocytosis	Glucocorticoid deficiency	
High ACTH level (primary adrenal insufficiency only)	Glucocorticoid deficiency	100
High plasma renin activity (primary adrenal insufficiency only)	Mineralocorticoid deficiency	100

Adrenal crisis can be triggered by

- significant physical stress
- illness
- fever, gastroenteritis,…
- undergo surgery with general anesthesia
- trauma
- Levothyroxine
- GH therapy

IV fluid therapy

- *Treatment of acute adrenal insufficiency must be immediate and vigorous*.
- An intravenous solution of 5% glucose in 0.9% saline should be administered to correct hypoglycemia, hypovolemia, and hyponatremia.
- Hypotonic fluids (e.g., 5% glucose in water or 0.2% saline) must be avoided because they can precipitate or exacerbate hyponatremia.

APPROXIMATE RELATIVE POTENCY

Compound (tablet strength, mg)	Anti-inflammatory (glucocorticoid) effect	Sodium-retaining (mineralocorticoid) effect	Equivalent[a] dosage (for anti-inflammatory effect, mg)[b]
Cortisone (25)	0.8	1.0	25
Hydrocortisone (20)	1.0	1.0	20
Prednisolone (5)	4	0.8	5
Methylprednisolone (4)	5	Minimal	4
Triamcinolone (4)	5	None	4
Dexamethasone (0.5)	30	Minimal	0.75
Betamethasone (0.5)	30	Negligible	0.75
Fludrocortisone (0.1)	15	150	Irrelevant
Aldosterone (none)	None	500[c]	Irrelevant

[a]Note that these equivalents are in approximate inverse accord with the tablet strengths.
[b]The doses in the final column are in the lower range of those that may cause suppression of the hypothalamic–pituitary–adrenocortical axis when given daily continuously. Much higher doses, e.g. prednisolone 40 mg, can be given on alternate days or daily for up to 5 days without causing clinically significant suppression.
[c]Injected.

Hydrocortisone

- 10 mg for infants
- 25 mg for toddlers
- 50 mg for older children
- 100 mg for adolescents
- as a bolus and similar doses should be divided q 6-hr
- These doses may be reduced during the next 24 hr if progress is satisfactory.

Management in neonates:

- Hydrocortisone 20 to 30 mg/m2/day divided 3 doses (ie, 2/5mg three times daily) higher doses of hydrocortisone (50mg/m2/day) may be used for initial reduction of markedly elevated adrenal hormones.
- Fludrocortisone 0/1-0/3 mg/daily in 2 divided doses (150µg/m2/daily), and one gram or 4 mEq/kg/day of sodium chloride divided in several feeding.

CAH Management in children & adolescents

- **Children**

Hydrocortisone 10-15 mg/m2/day divided in 3 doses although higher doses are sometimes needed.

- **Older adolescents & adults**
  - Dexamethasone 0/25-0/5 mg at bedtime

    or
  - Prednisolone 5-7/5mg divided in two doses

Fludrocortisone 0/05 to 0/2 mg/day

Monitoring

- Laboratory assessment: 10 to 14 days after starting treatment.
- morning ACTH levels high in the normal range to 3-4 times normal.

TABLE 15.20 Treatment of Acute Adrenal Insufficiency (Adrenal Crisis) in Adults

Emergency Measures

1. Establish intravenous access with a large-gauge needle.
2. Draw blood for immediate serum electrolytes and glucose and routine measurement of plasma cortisol and ACTH. Do not wait for laboratory results.
3. Infuse 2–3 L of 154 mmol/L NaCl (0.9% saline) solution, or 50 g/L (5%) dextrose in 154 mmol/L NaCl (0.9% saline) solution, as quickly as possible. Monitor for signs of fluid overload by measuring central or peripheral venous pressure and listening for pulmonary rales. Reduce infusion rate if indicated.
4. Inject intravenous hydrocortisone (100 mg immediately and every 6 hours).
5. Use supportive measures as needed.

Subacute Measures After Stabilization of the Patient

1. Continue intravenous 154 mmol/L NaCl (0.9% saline) solution at a slower rate for next 24–48 hours.
2. Search for and treat possible infectious precipitating causes of the adrenal crisis.
3. Perform a short ACTH stimulation test to confirm the diagnosis of adrenal insufficiency (if patient does not have known adrenal insufficiency).
4. Determine the type of adrenal insufficiency and its cause, if not already known.
5. Taper glucocorticoids to maintenance dosage over 1–3 days, if precipitating or complicating illness permits.
6. Begin mineralocorticoid replacement with fludrocortisone (0.1 mg by mouth daily) when saline infusion is stopped.

TABLE 15.21 Treatment of Chronic Primary Adrenal Insufficiency in Adults

Maintenance Therapy

Glucocorticoid Replacement

- Hydrocortisone 15–20 mg on awakening and 5–10 mg in early afternoon
- Monitor clinical symptoms and morning plasma ACTH.

Mineralocorticoid Replacement

- Fludrocortisone 0.1 (0.05–0.4) mg orally
- Liberal salt intake
- Monitor lying and standing blood pressure and pulse, edema, serum potassium, and plasma renin activity.
- Educate patient about the disease, how to manage minor illnesses and major stresses, and how to inject steroid intramuscularly.
- Obtain MedicAlert bracelet/necklace, Emergency Medical Information card.

summary

- An intravenous bolus of 10 to 20 mL/kg of normal saline
- An intravenous blous of 2 to 4 mL/kg of 5-10 percent dextrose (significant hypoglycemia)
- Dextrose saline 1/5 maintenance
- Don’t give potassium
- Hydrocortisone 50-100 mg/m2/IV stat then 100mg/m2/day
- Stress dose should be taper rapidly according to the clinical improvement, generally by reducing the dose by 50% each day until the patient receiving his or her usual glucocortoid daily dose.


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