Owner: Pediatric Department	Protocol Code: PR-PED- 001
Title of the Protocol: Acute Adrenal insufficiency	

Background:

Adrenal insufficiency may result from a wide variety of congenital or acquired disorders of hypothalamus, pituitary, or adrenal cortex. Destruction or dysfunction of the adrenal cortex is the cause of primary adrenal insufficiency, while secondary adrenal insufficiency is a result of pituitary or hypothalamic disease. Timely diagnosis and clinical management of adrenal insufficiency are critical to prevent morbidity and mortality.

Causes of Adrenal Insufficiency:

These can be broadly categorized as follows:

- Primary adrenal diseases (associated with elevated ACTH levels) e.g. Addison's disease, congenital adrenal hyperplasia, congenital adrenal hypoplasia, adrenoleukodystrophy, adrenal hemorrhage …etc.
- Secondary adrenal insufficiency due to ACTH deficiency associated with pituitary & hypothalamic disorders.
- Patients withdrawing from pharmacological doses of corticosteroids rapidly without tapering at risk of central adrenal insufficiency.

Clinical features of adrenal Insufficiency:

- Muscle weakness, lethargy, vomiting (due to cortisol deficiency, electrolyte disturbances).
- Weight loss (due to anorexia, volume depletion).
- Depression, anorexia (due to cortisol deficiency).
- Hyperpigmentation (in primary adrenal insufficiency, due to ACTH excess).
- Hypoglycemia (due to decreased hepatic glucose production).
- Hypotension & shock (due to loss of vasomotor tone & volume depletion).

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Biochemical features:

- Electrolyte disturbances (low Na, high K) due to mineralocorticoids deficiency (Aldosterone).
- Elevated serum urea & creatinine due to associated dehydration.
- Hypoglycemia due to glucocorticoid deficiency.
- Elevated plasma rennin activity (as an index of volume depletion).
- Elevated plasma ACTH.
- Low cortisol before and after adrenal stimulation by synacthen or another test.

Therapy of adrenal crisis (acute adrenal insufficiency):

The rapid recognition and prompt therapy of a salt-losing crisis are critical to survival. Electrolyte and fluid therapy must be instituted as soon as possible. The predominant manifestations of adrenal crisis are hypotension and shock, usually with hyponatremia and hyperkalemia. Patients often have nonspecific symptoms such as anorexia, nausea, vomiting, abdominal pain, weakness, fatigue, lethargy, fever, confusion, and/or coma.

Intravenous Fluids:

- *Give a bolus of D10% normal saline (10% dextrose with 0.9% saline, without potassium), 20 ml/kg intravenously over 30 minutes.* This will improve the hyponatremic dehydration, as well as hypoglycemia if present.
- Continue then with maintenance and deficit fluid correction for next 24 hours.
- In patients with hyponatremia, exercise caution in correction of sodium not more than 10 mmol/l over 24 hours to prevent osmotic pontine demyelination syndrome.

Steroid Replacement: Therapy is urgent

***Give hydrocortisone by IV or IM injection*.**

- *Give IV bolus of 50-100mg/m^2 hydrocortisone (Solu-Cortef) immediately (dose for age: Age 0 - 3 years give 25 mg, 3 to 10 years 50 mg, ages older than 10 years give 100 mg.* If IV access is not immediately available, give IM while establishing intravenous access. Consider repeating the IV/IM hydrocortisone dose if there is a poor response to initial steroid and fluid treatment.

- Repeat another dose of hydrocortisone if hypotension/shock/poor perfusion still present together with another fluid bolus of 0.9% saline 10 ml/kg bolus (Repeat as necessary).

- Continue stress *doses of hydrocortisone at 50- 100 mg/m^2/day, divided into 4-6 hourly intravenously, until clinically stabilized and out of the adrenal crisis.* Hydrocortisone doses then shifted to oral doses. When the child is stable, reduce the IV dose, or if tolerating oral medications, switch to triple dose oral hydrocortisone replacement (~30-50mg/m^2/day).

Mineralocorticoid Replacement:

When the patient tolerates oral fluids and hydrocortisone was shifted to orally, then commence *fludrocortisone (Florinef) at maintenance doses (usually 0.05 - 0.1 mg daily).*

Hypoglycemia:

Give 10% dextrose 2 - 4 ml/kg slowly over 5-10 minutes to avoid reactive hypoglycemia (maximum dextrose concentration in children is 25%) to ensure recovery to > 4.0mmol/l. Maintenance fluids may require up to 10% dextrose in 0.9% saline to maintain normoglycemia.

Hyponatremia & Hyperkalemia management:

- Hyponatremia in adrenal insufficiency is rapidly corrected by cortisol and volume repletion, which shuts off ADH release and allows excess water to be excreted as mentioned above.

- The choice of hyperkalemia therapy is dependent on the urgency of therapy based on the severity of hyperkalemia and its potential to be life-threatening.
- Children with potassium > 6.0mmol/l should have an ECG and to be on cardiac monitoring. If hyperkalemic ECG changes are present (e.g. peaked T waves ± wide QRS complex ± flattened P waves), treat with calcium gluconate in order to protect the heart (10 % solution) is given at *a dose of 0.5 ml/kg (maximum dose 20 ml) by IV infusion over five minutes.*
- **Insulin and Glucose Therapy:** Glucose is given concomitantly to prevent hypoglycemia. The effect of insulin begins in 10 to 20 minutes and peaks at 30 to 60 minutes. *(Regular insulin dose of 0.1 units / kg, maximum dose of 10 units is given along with a dextrose (10%) dose of 0.5 g/kg over 30 minutes.*
- **Inhaled Beta-Adrenergic Agonists:** is an alternative to IV insulin and glucose infusion in children. Several case reports have demonstrated a decrease of serum potassium of 1 to 1.5 mmol/L within an hour of administration of inhaled beta-adrenergic agonists. *Doses: neonates – 0.4 mg in 2 mL of saline, infants and small children <25 kg – 2.5 mg in 2 mL of saline, children between 25 and 50 kg to give 5 mg in 2 mL of saline.*
- **Cation Exchange Resin (Sodium Polystyrene Sulfonate):** *Give sodium polystyrene sulfonate (keyxlyate) at a dose of 1 g/kg (maximum dose of 30 g) orally, through nasogastric tube, or as a retention enema. Onset is approximately 1 to 2 hours; may repeat dose after 4 to 6 hours based upon repeat serum potassium.*
- **Important notice:** *Sodium polystyrene sulfonate should not be used in preterm neonates, term neonates with intestinal hypomotility and/or those at risk for necrotizing enterocolitis, postoperative patients, or those with bowel obstruction or ileus. Sorbitol can cause intestinal necrosis and should be avoided.*

Management of metabolic acidosis:

Sodium Bicarbonate (for both metabolic acidosis & hyperkalemia): indicated to be used in the management of hyperkalemia together with metabolic acidosis but not just hyperkalemia. In children, *a dose of bicarbonate is 1 mmol/kg (maximum dose 50 mmol) administered intravenously over 20 to 30 minutes.*

Maintenance Therapy of Adrenal Insufficiency (AI):

- *Life - long replacement of glucocorticoid therapy. For primary AI other than CAH, hydrocortisone at 8–12mg/m2 /day in 3 divided doses is recommended. For CAH, the consensus dosing is 10–15mg/m2 /day. Patients with secondary AI may be maintained on 6-8 mg/m^2/day. Doses usually adjusted according to the clinical symptoms and ACTH level.*

- Requirement for glucocorticoid increases with stress (fever, vomiting, diarrhea, surgery & anesthesia) to 2-3 times the usual doses.

- A challenge with hydrocortisone therapy is its short median elimination half-life, especially in children with CAH allowing most of the hydrocortisone dose to be eliminated from the body within 4–7hours. *Hydrocortisone should be administered in at least 3 divided doses.*

- Long-acting glucocorticoids such as dexamethasone, prednisone and prednisolone *are not recommended* for maintenance glucocorticoid therapy in growing children.

- Replacement of mineralocorticoids deficiency in primary disease is by giving *fludrocortisone 0.05 - 0.3 mg / day*.

- The fludrocortisone dose is usually adjusted according to blood pressure, electrolytes and plasma rennin activity.

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Adrenal insufficiency, protocol for children who require surgery, procedure or dental extractions

Background:

Patients with congenital adrenal hyperplasia (CAH), primary and secondary adrenal insufficiency or those who are at risk of suppression from more than one week of glucocorticoid therapy are at risk of adrenal insufficiency and need glucocorticoid cover for surgery.

According to the recommendations published by the Pediatric Endocrine Society Drug and Therapeutic Committee:

Minor Surgery / Day Case:

- *Intravenous hydrocortisone doses are 30-50 mg/m2* at time of anesthesia induction (stat dose) together with intravenous maintainace fluid of dextrose 5% in 0.9 saline until the oral intake is allowed post-operative. Oral hydrocortisone usual dose should be doubled for next 24-48 hours depending on the clinical status of the child.

Major Surgery:

- *Intravenous hydrocortisone dose is 100 mg/m2 at time of anesthesia induction* (stat dose) together with intravenous maintainace fluid of dextrose 5% in 0.9 saline, followed by intravenous hydrocortisone dose of 100 mg/m2/day divided into 6 hourly.

- As soon as oral intake is allowed and tolerated, oral hydrocortisone, the usual dose should be doubled for next 3-5 days depending on the clinical status of the child. The stress doses of hydrocortisone are tapered back to physiologic dose based on the pace of clinical improvement usually within 3-5 days.

- Fludrocortisone dose is the same in stress situation or surgery.

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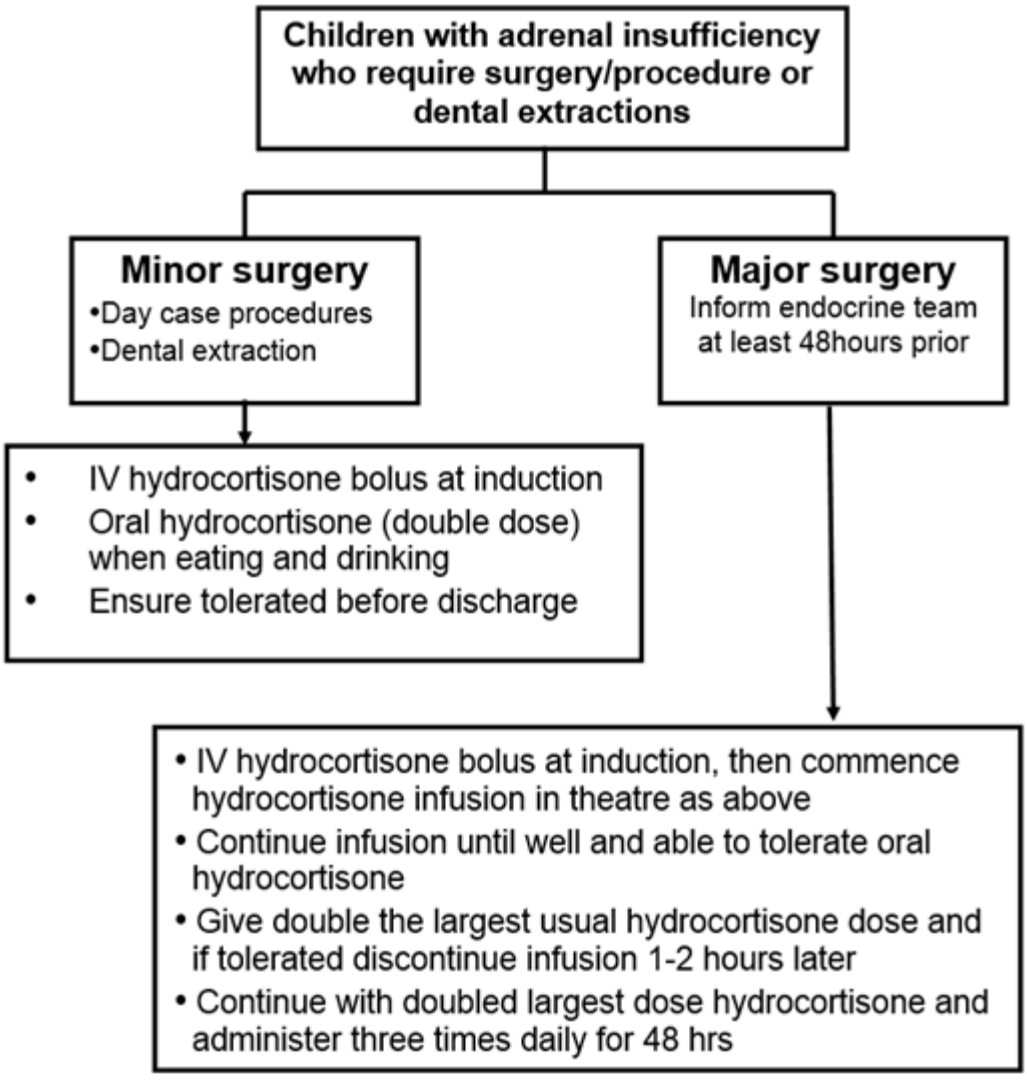

Reference:

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