

PEDIATRIC HYPERGLYCEMIC HYPEROSMOLAR SYNDROME (HHS) TREATMENT PROTOCOL

GENERAL CONCEPTS

- Both HHS and DKA present with hyperglycemia, however, there are several important physiologic and treatment differences between HHS and DKA.
- The criteria for diagnosis of HHS include all of the following:
 - Plasma glucose concentration greater than or equal to 600 mg/dL
 - Venous pH greater than 7.25 OR arterial pH greater than 7.30
 - Serum bicarbonate greater than 15 mmol/L
 - Minimal or absent ketosis
 - Serum osmolality ($2 \times [\text{Na}] + \text{glucose} / 18$) + $\text{BUN} / 2.8$ greater than 325 mOsm
- Patients with HHS are profoundly dehydrated and intravascular volume typically declines during treatment as the glucose level declines and the osmotic effect of hyperglycemia is decreased. Patients with HHS require more aggressive fluid resuscitation than DKA patients. Patients with HHS also have ongoing osmotic diuresis for more prolonged periods than in DKA and may require fluid replacement for urine output – careful monitoring of I & O is essential.
- Patients with HHS also often have very large deficits in potassium and phosphorus due to prolonged hyperglycemia with resultant ion loss. Anticipating large K and Phos replacement is important.
- In HHS, the goals of initial fluid therapy are to expand the intra- and extravascular volume, restore normal renal perfusion and promote a gradual decline in corrected serum sodium concentration and serum osmolality. Differences in treatment strategy between HHS and DKA include the volume of fluid administered, the timing of administration of insulin, and monitoring

of the corrected sodium decline.

- In HHS, insulin is started later and at a lower dosage than in DKA.
- ** For patients with known diabetes that use an insulin pump, please ensure that the insulin pump and infusion site are disconnected from the patient.

ED/PICU MANAGEMENT

INITIAL RESUSCITATION/REHYDRATION

- Use actual body weight for fluid calculations (not ideal body weight)
- Initial bolus: 20ml/kg 0.9% NaCl over 30 minutes. (maximum of 1 liter per bolus)
 - Should be repeated if persistent evidence for inadequate organ perfusion on reassessment – many patients will require a second bolus based on clinical exam.
 - Assume 12 to 15% dehydration.
- After bolus, start 0.45% NaCl at 3.5 X maintenance rate (maximum fluid rate of 500mL/hr). This estimates a rate calculated to replace the deficit (minus initial bolus(es)) plus maintenance requirements over 24 hours (see below). Give IN ADDITION to urinary replacement (described below in “IV Fluid Rate Calculations” section). When “2 bags” are available (see below), PICU orders will transition to 2 bag system at this same rate.

INSULIN

- Use actual body weight for fluid calculations (not ideal body weight) (Maximum initial insulin infusion 5 units/hr; infusion rate may be adjusted as needed later during treatment)
- **Insulin infusion should not be started until the glucose levels are declining at a rate less than 50 mg/dL/hr with fluids alone.
- Start insulin at 0.05 Units/kg/hr. Reduce insulin administration if glucose declines more rapidly than 50-75 mg/dL/hr to 0.03 Units/kg/hr.
- Anticipate a more rapid decline in potassium and phosphorus levels after insulin is started –

consider increasing K and/or Phos concentration in IV fluids when insulin is started if K and/or Phos levels are borderline or trending down.

IV FLUIDS – “TWO-BAG” SYSTEM

- Begin fluid replacement as soon as possible.
- Start 0.45% NaCl until the 2 bags are available. PICU will place admission orders for 2 bag fluids as below (ED may order these specialized fluids if anticipated delay in PICU orders).
- Start potassium replacement at 40mEq/L (equal mixture KPhos and Kacetate) as soon as possible (HHS patients have very large potassium deficits). Potassium and/or Phosphorus may need to be repleted – monitor potassium and phosphorus trends carefully. (For PIV administration, do not exceed 60mEq/L potassium in a single site)
- Do not start the potassium-containing fluids if:
 - K greater than 5.5 on admission. If K greater than 6, obtain ECG
 - Urine output/renal function have not been ensured
- Consider using 0.9% NaCl fluids if patient is hemodynamically unstable or if corrected Na less than 140 or Na falls rapidly with treatment. Do not use hypotonic fluids if corrected Na is less than 130 (very rare in HHS).
 - $\text{Na corrected} = \text{Na measured} + 1.6 \times [(\text{Glucose}-100)/100]$; should normalize with treatment
- Nurse to titrate each bag as patient glucose decreases

Blood glucose (mg/Dl)	BAG #1	BAG #2
	0.45% NaCl with 20mEq K Acetate + 20mEq K Phos (13.6Mm) Rate (% of total)	D10 0.45% NaCl with 20mEq K Acetate + 20mEq K Phos (13.6Mm) Rate (% of total)
More than or equal to 300	100%	0%
200 – 299	50%	50%
less than 200	0%	100%

IV FLUID RATE CALCULATIONS

- For simplicity, use 3.5 x maintenance IVF rate
- Maintenance fluid rate calculation: 4ml/kg for the first 10kg, 2ml/kg for the next 10kg, 1ml/kg for each kg over 20kg
- Assume 12-15% dehydration and aim to replace deficit over 24h
 - Deficit (12%) = weight (kg) x 120 (b) _____ ml
 - Remaining deficit = (b) – volume of resuscitation (c) _____ ml
 - Replacement rate = (c) / 24hr (d) _____ ml/hr
 - FINAL CALCULATED IVF rate = (a) + (d)
- Urinary replacement is usually necessary in HHS until glucose level is less than 300 mg/dL
- Every 4h, replace each 1mL of urine with 0.5mL of 0.45% NS and give over 4 hours. Re-evaluate fluid status q4h to achieve progressively positive fluid balance.

MONITORING

- Vitals q1h, continuous Intake/Output, Neuro checks q1h (q30min if headache and/or altered mental status), Daily Weight
- Laboratory Monitoring (should be obtained with STAT priority)

Admission	Q1h	Q2h	Q4h
VBG or ABG BMP, Mg, Phos Hemoglobin A1c Diabetes antibodies (new onset only): Islet Cell Cytoplasmic Ab Insulin Ab Glutamic Acid Decarboxylase Ab Zinc Transporter Infectious workup as indicated: (CBC, inflammatory markers, cultures, urine studies)	POC glucose	BMP, Phos	VBG or ABG Mg

TRANSITION TO SUBCUTANEOUS INSULIN

- Criteria:
 - Mental status normal
 - Able to tolerate sips of clears
 - Measured Na less than 155
- Process:
 - Administer the first subcutaneous insulin dose (Lantus and/or NovoLog) If possible, give just prior to breakfast or dinner; however, depending on clinical scenario can be given at any time
 - Stop the insulin infusion ONE HOUR after administering subcutaneous basal (Lantus) insulin
 - Allow the patient to start eating
 - Discontinue IVF when the insulin infusion is discontinued and the patient is able to maintain adequate oral hydration Dextrose should be removed from IVF when insulin infusion is discontinued
 - Consider continuing IVF at maintenance (without Dextrose) if substantial portion of calculated fluid deficit has not been replaced OR Potassium/Phos are persistently low.
 - Transition to new lab frequency: POC glucose before meals, nightly, at 2-3am (qAC, qHS and PRN)

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