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PICU Diabetic Ketoacidosis Protocol

Background: Diabetic Ketoacidosis (DKA) is a life-threatening emergency that requires appropriate and timely treatment. The primary defect is inadequate or complete **lack of insulin**, the key hormone that allows cellular glucose utilization for energy. Glucose instead remains in the bloodstream, leading to glucosuria, dehydration and loss of essential electrolytes. In the absence of insulin, fatty acids become the predominant energy source for cells, with the accumulation of ketone byproducts and resulting metabolic acidosis. The degree of dehydration, estimated to be ~10% in patients with new onset insulin-dependent diabetes mellitus (in whom the diagnosis is often delayed), and metabolic derangements are second only to those seen in patients with severe burn injuries.

Unlike the "healthy" child with acute gastroenteritis and dehydration from vomiting, diarrhea, and inability to tolerate oral intake, children with DKA have *hyperosmolar dehydration* which requires a more conservative approach to fluid replacement in order to decrease the risk of the most serious and potentially lethal complication: cerebral edema.

The key to successfully reversing DKA without adverse events lies in understanding the pathophysiology of the condition. Insulin, isotonic fluids, and electrolytes are required, along with close monitoring of the patient's unique response, to optimize the time to improvement and avoid complications.

The protocol that follows provides a guideline for treatment of DKA and does not replace clinical judgement.

Initial Fluid Resuscitation

- For a **Patient in Shock** (hypotension, pallor, mottling of skin, cool extremities, obtunded mental status):
    - The patient must have two large bore peripheral IV catheters: one reserved for blood sampling **only** and one for administering fluids and insulin*
    - Administer 10-20 mL/kg of Normal Saline (NS) or Lactated Ringers (LR) via rapid IV bolus
    - Reassess the patient post-bolus; repeat ONLY if needed to establish adequate perfusion
        - Patients with DKA have persistent tachycardia due to high stress hormone levels even when intravascular volume is adequate. Tachycardia is not a reliable sign of hypovolemia in DKA.
        - Do NOT correct dehydration completely with the initial fluid boluses

- For a Patient **NOT in Shock**
    - Administer 20 mL/kg Normal Saline IV over 30 minutes
    - Reassess the patient post-bolus
        - Most patients require only ONE bolus
        - Do not administer additional boluses just because the patient looks dry or is tachycardic
        - If blood pressure and urine output are satisfactory, rely on continuous fluid infusions rather than boluses to avoid inadvertent administration of excessive fluids

Assessing the need for further therapy following Initial Fluid Bolus(es)

Consider the following:

- Indications for further DKA treatment:
    - The patient appears ill
    - The patient can't tolerate oral fluids and can't eat
    - The presence of metabolic acidosis: pH <7.25, HCO3 < 18

- If, after initial hydration, the patient does not have significant acidosis and can eat, he/she may be managed with subcutaneous insulin. Consider continuing NS at the maintenance rate to help clear ketones

- If the patient has continued utilizing an insulin pump during hydration, the basal rate may be continued with additional bolus dosing via the pump for meals and correction

*Fluids and insulin should be infused through the same catheter so that if it malfunctions, the patient will not receive one without the other. Either scenario (severe hyper or hypoglycemia) will both delay time to resolution and complicate the patient's course.

Administering Replacement Fluids After Initial Bolus(es)

- Patients with **pH <7. 25, HCO3 < 18**
  - Maintain the rate of **all** fluids at less than or equal to 2.5 times maintenance or 250 mL/hour (whichever is less)
  - This corresponds to a limit of 4 liters/meter squared (L/m^2) over 24 hours.
  - If this rate is used, it is not necessary to explicitly calculate and replace deficits
  - The volume of the insulin infusion need not be included in calculating the total fluid rate since it is usually quite small
  - Small amounts of ice chips may be offered if the patient is alert and not vomiting

- Continue the initial fluid rate of 2.5 x maintenance or 250 mL/hour until the acidosis is resolved (pH > 7.25 and/or HCO3 > 18) and the patient can tolerate oral fluids

- After acidosis is resolved, consider transitioning to oral rehydration. Otherwise continue 1-1.5 x maintenance non-dextrose containing IV fluids to clear urine ketones

- Ongoing administration of IV fluids (versus oral rehydration) may be more appropriate for patients admitted late at night who do not wish to be awakened frequently to drink

- Once the acidosis has resolved, fluid restriction may be discontinued

- For any of the following conditions, continue fluid restriction (total fluid 1-1.5 x maintenance) for 48 hours from the time the initiation of fluid resuscitation:
  - Signs or symptoms of increased intracranial pressure (ICP)/cerebral edema
  - Initial serum glucose > 1,000 mg/dL
  - Initial corrected serum Na > 150 mEq/L

- A serum sodium (Na) level that does not increase as the serum glucose decreases is an indication of severe hyponatremia and an ominous sign
  - Pseudohyponatremia (a low serum sodium in the presence of severely elevated glucose) is common in patients presenting with DKA. In most instances, the sodium normalizes with treatment of hyperglycemia
  - Persistent hyponatremia may indicate the presence of excess free water and an increased risk of cerebral edema
  - Further fluid restriction to 1- 1.5 x maintenance is usually an effective treatment, but in rare instances of extreme hyponatremia with altered mental status, hypertonic saline may be needed until symptoms resolve

Managing Fluid Content

SODIUM (Na)

- Use 0.9% NaCl (NS) or Lactated Ringers for the initial bolus and all fluids thereafter
    - This may help keep the serum Na stable as the serum glucose decreases

$$CorrectedNa = MeasuredNa + 1.6\left(\frac{glucose - 100}{100}\right)$$

POTASSIUM (K)

NOTE: In the context of metabolic acidosis, patients with DKA often present with high or high normal serum K levels. However, they are usually **total body K depleted,** due to excessive urinary losses.

- Add K to maintenance fluids unless any of the following conditions is present:
    - Oliguria/anuria
    - Acute renal failure
    - Cardiac arrest
    - Serum K >5.5 mEq/L **and** urine output < 1mL/kg/h

- For routine K replacement: Add 10 mEq/L potassium chloride (KCl) and 30 mEq/L potassium acetate (CH3CO2K) to the maintenance IV fluids (both dextrose containing and non-dextrose containing)
    - NOTE: It is best to order fluids from the pharmacy with K as soon as the initial evaluation is complete, because the serum K decreases with initiation of insulin (due to intracellular shift) and it is usually <5.5 by the time those fluids are available

- Check the initial serum K level before starting fluids that contain K
    - If lab results are delayed longer than one hour, add K unless any of the contraindications mentioned above is present

- Monitor serum K every hour until it is ≤ 5.5 mEq/L

- Serum K decreases with:
    - Administration of both glucose and insulin
    - Correction of acidosis
    - Rehydration which improves glomerular filtration rate (GFR) and increases renal elimination of K

- Monitor for and treat hypokalemia, especially at initiation of fluids and insulin

- Follow bedside cardiac monitor tracing for T-wave changes associated with hyper and/or hypokalemia

PHOSPHATE (PO4)

NOTE: As is true for potassium, patients with DKA are usually total body PO4 depleted despite initial serum levels that appear normal or elevated

Maintain serum PO4 level of 1.5 mg/dL or greater

- Severe hypophosphatemia (<1 mg/dL) is rare in DKA.
- Serum PO4 decreases during treatment of DKA (due to intracellular shifts).
- Hyperphosphatemia may lead to hypocalcemia or metastatic calcification
- Avoid PO4 supplementation in patients with clinical or biochemical evidence of hypocalcemia (ionized calcium < 1.10)

CALCIUM (Ca)

NOTE: Symptomatic hypocalcemia is rare in DKA

- Treat symptomatic hypocalcemia with 100 mg/kg IV Ca gluconate (maximum dose 2 grams [gm])
  - Monitor heart rate and rhythm during Ca administration
  - Administer slowly over 30 minutes to avoid bradycardia
- Do NOT infuse calcium through the same line as potassium phosphate; the solution will form precipitates
- Monitor the IV entry site frequently during the infusion since extravasated calcium solutions may cause tissue necrosis

MAGNESIUM (Mg)

NOTE: Symptomatic hypomagnesemia is rare in DKA

- Correct hypomagnesemia (serum Mg <1.0 mEq/L) before correcting hypocalcemia
- Treat hypomagnesemia with magnesium sulfate (MgSO4) 25-50 mg/kg IV over 1-2 hours or intramuscular (IM)

Administering Insulin and Glucose

- Order the insulin infusion from the pharmacy (100 units of regular insulin in 100 mL NS) as soon as the diagnosis of DKA is confirmed
- Consultation by the Endocrine team is required for all newly diagnosed patients. It is wise to obtain the consult early in the admission so that doses of subcutaneous long-acting and short-acting insulin are available when the patient is ready to transition from IV insulin

- At the same time, order the replacement fluids in two bags: **
    - One as normal saline with potassium (NS + 10 mEq/L KCl + 30 mEq/L CH3CO2K)
    - One as normal saline with dextrose (D10 NS + 10 mEq/L KCl + 30 mEq/L CH3CO2K)

- Start the continuous IV infusion of regular insulin at 0.1 units/kg/hour, within the first hour of treatment, but after the initial fluid bolus (s). The drop in glucose from fluids alone is unpredictable. It's important to know the blood glucose level at the time insulin is started. (Use of the patient's insulin pump will be left to the discretion of the Endocrine team)

- Start the replacement/maintenance fluid combination immediately following the fluid bolus(s).

- Indications for initiating the dextrose-containing solution:
    - Serum glucose decreases by 360 mg/dL in less than 6 hours
    - Serum glucose of 300 mg/dL or less

- Prior to starting the dextrose-containing solution, choose the appropriate **glucose:insulin ratio** (i.e., gm/hour of glucose to units/hour of insulin) for the patient's initial pH. Use a ratio of **3:1** for an initial **pH ≥ 7.1-7.3**, or **2:1** for an initial **pH < 7.1.** Use the electronic DKA calculator for assistance with calculating the correct infusion rates.

- Start fluids at 2.5 x maintenance (total fluid max 250 ml/hr)

- Titrate the glucose infusion rate by increasing or decreasing the rate of the dextrose-containing fluid and adjusting the glucose-free solution rate to keep the total hourly fluid volume constant.

- Maintain the insulin rate at 0.1unit/kg/hr. If the blood glucose level drops too quickly (> 50 - 100 mg/dL/hour), increase the dextrose-containing fluid rate until the total fluid volume reaches 2.5 x maintenance before decreasing the rate of the insulin infusion. Do NOT discontinue the insulin as this will only delay the resolution of DKA.

NOTE: Blood glucose will often fall more rapidly than 50 -100 mg/dL/hour during the first hour of hydration. As intravascular volume expands, the GFR increases which increases glucosuria.

**The two-bag fluid system allows for changes in the glucose concentration at intervals that coincide with blood glucose monitoring without waiting for the Pharmacy to prepare and send a new bag with each needed change. This is accomplished by adjusting the ratio of glucose-containing to non-glucose-containing fluids while maintaining a constant total volume. Note that the bags are identical except for the presence of glucose in one and its absence in the other.

Subsequent Management of Blood Glucose in DKA

- As mentioned above, try NOT to decrease the rate of the insulin infusion while the patient is acidotic since this will delay the clearance of ketones and the correction of the acidosis. Increase the glucose infusion rate instead
  - Usually, the serum glucose corrects before the metabolic acidosis. The degree of acidosis bears little relationship to the degree of hyperglycemia

- Increase the insulin infusion rate to 0.15-0.2 units/kg/hour if hyperglycemia and acidosis have not improved after 3-4 hours of non-dextrose-containing fluids
  - Insulin resistance to this degree is rare

- Aim for a blood glucose level of 150-200 mg/dL while the patient is on insulin
  - Levels > 200 mg/dL may lead to glycosuria and osmotic diuresis
  - Levels < 100 mg/dL increase the risk of hypoglycemia, especially in younger patients and new-onset diabetics who are still very sensitive to insulin

- Increase the glucose infusion rate as treatment progresses to yield a glucose:insulin ratio of as much as 6-8:1, if the patient becomes more sensitive to insulin as the acidosis is corrected

- Occasionally a patient may require dextrose concentrations above 10% (e.g., 12.5%), but this is rare.
  - Dextrose concentrations above 10% are considered hyperosmolar and are not to be used unless clinically indicated
  - Dextrose concentrations up to 12.5% can be administered via a peripheral IV, however please discuss this with fellow or attending
  - Once the pH approaches 7.3, consider decreasing the insulin infusion rate rather than administering very large volumes or high concentrations of dextrose-containing solutions

Transitioning to Subcutaneous Insulin

Consider the following prior to converting to subcutaneous insulin:

- The end point of IV therapy for DKA is correction of the acidosis, NOT normoglycemia

- The criteria for stopping the insulin infusion are essentially identical to the criteria for starting it:
  - The patient must be able to tolerate adequate oral intake
  - The acidosis has resolved; pH >7.25 and/or HCO3 > 18

- Switch to subcutaneous insulin at the next regular meal
  - Insulin dosing, carbohydrate counting, sliding scale, and diet should be provided by the Endocrine team

- A meal tray must be at the bedside or quickly available before proceeding

- Administer subcutaneous insulin
  - Verify insulin dosing schedules with the Endocrine attending or fellow *
  - For patients with known IDDM, utilize the previously established home insulin regimen
  - Give the initial dose of long-acting insulin glargine (Lantus) at bedtime (or when usually given at home) even if IV insulin is still infusion
  - Dosing should have already been provided by the Endocrine team

- Allow the patient to eat and discontinue the IV insulin and glucose solutions immediately following the subcutaneous insulin injection

- The medical team may elect to continue the non-glucose-containing fluids at maintenance if the urine ketones have not cleared. This is not essential since ketonuria may persist despite correction of acidosis

- Initiate diabetes education and training in insulin dosing and administration, management of hypoglycemia, etc. simultaneously with the conversion to intermittent subcutaneous insulin dosing

- The patient and family must be comfortable with the regimen and be provided with the needed prescriptions and follow-up appointments prior to discharge from the hospital. This is best accomplished by transferring the patient to the Endocrine service when he/she no longer meets criteria for ICU admission

Estimating the dose of subcutaneous insulin: *

- Insulin Total Daily Dose (TDD) = Weight (kg) x 0.5 or 0.8
- 0.5 x TDD is usually given as insulin glargine (Lantus) at night
- Insulin Sensitivity Factor (ISF) = 1 unit of insulin aspart (NovoLog) for every (1800/TDD) mg/dL of blood glucose above 120 mg/dL
- Carbohydrate coverage = 1 unit of insulin aspart (NovoLog) for every (500/TDD) grams of carbohydrate eaten

* These calculations are estimates and may vary from patient to patient. All starting doses of insulin must be confirmed by the Endocrine team.

References

1. White PC, Dickson BA. Low morbidity and mortality in children with diabetic ketoacidosis treated with isotonic fluids. J Pediatr 2013. 163(3):761-6.