Pediatric Diabetic Ketoacidosis (DKA) Guidelines for Management

General Guidelines and Definitions:

Disclaimer: These are guidelines—not hard and fast rules. Some patients, such as younger children (<5 y.o.) and poorly controlled diabetics (HbA1c >10%), may not adhere to the usual course and guidelines may need to be modified. The below categorizations of mild, moderate, and severe are not the consensus-statement published definitions, but are more "real-world" categorizations.

DKA: A state of *insulin deficiency* and characterized by *severe depletion of water and electrolytes*. The primary goals are to treat the insulin deficiency (the severity of which is manifest by the degree of ketosis and acidosis, *NOT* by the degree of hyperglycemia) and to gradually replace fluids and electrolytes while avoiding excessive rates of fluid administration so as to not exacerbate the risk of cerebral edema.

Mild DKA: Urine ketones large, +/- vomiting, pH >7.3, Bicarb >15 (published definition: pH <7.3, bicarb <15)

- Management:
  - Oral or IV hydration, depending on vomiting, ability to tolerate PO
  - Supplemental insulin (Novolog, SQ: 0.1-0.2 units/kg every 4 hours)
  - Often managed as outpatient at home or in Emergency Unit
  - In established patient with good family support, sometimes managed at home by phone under guidance from on-call physician who has no knowledge of laboratory results other than self-monitored blood glucose and urinary ketones

Moderate DKA: Mild DKA with persistent vomiting *OR* Large Urine Ketones, pH 7.2-7.3, Bicarb 10-15 (published definition: pH <7.2, bicarb <10)

- Management:
  - Oral or IV hydration (usually IV)
  - Supplemental insulin should be used (Novolog SQ 10% of total daily insulin dose or 0.1-0.2 units/kg every 2-4 hours[*]) in addition to the patient's usual long-acting insulin (Lantus)
  - May require admission and management on inpatient unit with IV regular insulin infusion

Severe DKA: Urine Ketones Large, pH <7.2, Bicarb <10 *OR* mild/moderate DKA with other organ system impairment (altered mental status, impaired renal function, respiratory distress, compromised circulation) (published definition: pH <7.1, bicarb <5)

- Management
  - Admit to hospital for therapy and intensive monitoring
  - PICU status may be appropriate in some cases (altered mental status, hypokalemia, hyponatremia (after sodium corrected for glucose[†]), young age (<5 y.o.), hypotension, per admitting physician)
  - IV hydration (no more than 3 $L/m^2/day$)[¥]
  - IV insulin (0.1 units/kg/hour)
  - Intensive monitoring
  - Follow guidelines as given in the remainder of this protocol

Some useful formulas:

[*]Total daily insulin dose approx. = Lantus dose x 2 (In general, Lantus dose is 50% of pt's total daily insulin)

[†]Corrected sodium = [((Glucose -100)/100) x 1.6] + Pt's Na [glucose is mg/dl]

[¥]BSA (m^2)= sq root [(wt(kg) x ht(cm))/3600]; estimated BSA = (wt(kg) x 4 + 7)/(90 + wt(kg))

[‡]Anion Gap = Na – (Cl + HCO_3); normal is 12 +/- 2 mmol/L

[€]Effective osmolality = 2 x (Na + K) + glucose/18 [glucose is mg/dl]

Guidelines for the management of severe DKA

Fluid Management (2 bag system)

- *Total* fluids should not exceed 3500 ml/m^2/day (1.5 – 2 x maintenance)
- Volume expansion (Fluid bolus) should be initiated prior to insulin administration, but insulin should be initiated 1 hour after the fluid administration has begun
    - Initial bolus of NS or LR with 10 ml/kg over 1-2 hours (sometimes 20 ml/kg)
    - May skip this phase or limit to 10ml/kg if good perfusion and no circulatory compromise
    - If poor peripheral perfusion, hypotension, or shock persist after the initial 10ml/kg, it may be appropriate to repeat the 10 ml/kg NS bolus
- Rehydration (calculate fluid deficit if possible or can assume 5-10% dehydration and plan to replace the deficit *evenly* over 36-48 hours (including the initial volume expansion and eventual PO intake)
    - This can usually be accomplished by running IV fluids at 1.5 x maintenance or 3000 ml/m^2/day
    - Initial IVF with either NS (or ½ NS) + 20meq/L K-phosphate + 20 meq/L K-acetate (or KCl if K-acetate is not available) **note, there is zero dextrose in this fluid
        - NS is used if 1) measured Na level is low and does not rise with the fall in glucose or if corrected Na level is low (<135) or 2) corrected Na is high (>145) and therefore the osmolality[€] is high
        - If K is >6, repeat the BMP or Istat and add the K to the fluids when the K is <6; If K is low, may need up to 60 meq/L K total (typically 30 and 30 of the two types of K solution)
    - "Y-in" D10 NS (or ½ NS) + 20meq/L K-phosphate + 20 meq/L K-acetate (or KCl) when the serum glucose is less than 250 mg/dl (or if glucose falls faster than 100mg/dl per hour)
    - 2 bag method: Use 2 separate bags of IV rehydration fluid with identical electrolyte composition; one bag has no dextrose and the other has 10% dextrose. Increase and decrease the rate of each bag reciprocally so that the total rate is constant at the desired rehydration rate (ie, 3 L/m^2/day) and the glucose is maintained between 150 and 250.
        - Typically, when the BG is ≤ 250, run the 2 fluids at 50/50 rates and when the BG is <200, stop running the fluid without the dextrose and run the D10 fluid at 100% of the desired rate
        - DO NOT REDUCE INSULIN INFUSION RATE BECAUSE OF FALLING BLOOD GLUCOSE UNTIL THE REDUCTION IS INDICATED BASED ON RESOLUTION OF KETOACIDOSIS; *If the patient is still acidotic, he/she still needs the insulin*—increase the dextrose content instead (can use D12.5)
- **Do not administer sodium bicarbonate to correct the acidosis** (***cautious*** administration may be ***considered*** if pH <6.9 and the acidosis is so profound as to adversely affect the action of epinephrine during resuscitation, decreased cardiac contractility, impaired tissue perfusion from vasodilation, or life-threatening hyperkalemia; dose should be 1-2 mmol/kg over 60 minutes)

Insulin Therapy

- "Low-dose continuous IV insulin infusion" = 0.1 units/kg/ hour regular insulin, IV (conc. 1 unit/mL)
    - Start insulin 1 hr after initial fluids have been started but do not further delay in starting insulin
- Do not give intravenous insulin bolus or subcutaneous insulin bolus when starting the continuous infusion (*if a delay in starting the insulin infusion is expected to be longer than 1 hour (i.e., more than 2 hours after IVF have been started), then a SQ insulin dose may be warranted)
- CONTINUE IV INSULIN INFUSION AT 0.1 UNITS/KG/HR UNTIL THE KETOACIDOSIS IS RESOLVED bicarb >18, the anion gap is closed (AG <12)[‡], and the patient is awake and can tolerate PO fluids
- Usually, Lantus (insulin glargine) should be given at the usual time, even if the patient is on an insulin infusion (Lantus is most frequently given at bedtime; its onset of action is approx. 1-2 hrs)
    - Administering Lantus while on the insulin infusion allows us to d/c the insulin infusion when it is appropriate (see above) without waiting for subcutaneous insulin to be given; it also provides background insulin so that DKA does not recur after the insulin infusion is discontinued (remember: without SQ insulin, once the IV insulin infusion is stopped, the patient has no other insulin on board!)
    - In new-onset diabetes, the usual starting total daily dose of insulin is 0.5-1 units/kg/day, 50% of which should be given as Lantus; in known diabetes, the patient's home dose of Lantus can be used.

Monitoring and Other Guidelines

- Strict monitoring of Intake and Output is essential (Strict I/O)
- The patient should remain NPO until acidosis is resolved
    - This is so that total intake can be strictly monitored to avoid excessive fluid administration and decrease the risk for cerebral edema; additionally, all patients in DKA are at risk for cerebral edema and are therefore at potential risk of aspiration should consciousness be altered
- Check urine ketones every void until negative twice
- Check blood sugar (bedside glucose) every hour while on insulin infusion
    - After transition to SQ insulin and PO feeds, BS can be checked QAC, QHS, and 0200
- BMP, Magnesium, Phosphorous initially and Q8 hours
- I-Stat-7 Q2 hours until pH >7.25, then Q4 hours
- Vital Signs Q1 hour for at least first 12 hours, then Q2 hours; HR monitor and pulse oximetry
- Neuro checks/GCS Q1 hour
- Mannitol 1 gm/kg at bedside (and ready to be given for acute change in mental status)
- STAT Head CT for an acute change in mental status (if serious consideration of cerebral edema, do not wait for the head CT to give the mannitol)
- Initial labs should include: Hemoglobin A1c, BMP, Mg, Phos, Beta-hydroxybutyrate, diabetes autoantibodies (islet cell antibody, insulin antibody, glutamic acid decarboxylase (GAD-65) antibody), celiac panel (total IgA and TTG), TSH and free T4 (if patient is very ill, the TSH and free T4 should wait until he/she is more stable to avoid abnormalities of "sick euthyroid syndrome"), insulin and c-peptide (if there is a question that the patient may have type 2 diabetes), CBC, cultures if indicated (fever, etc; **leukocytosis is a common finding in DKA and does not alone indicate infection)
- A flow sheet with lab results and clinical response can be a useful guide to therapy

Cerebral Edema in DKA

- The most common cause of death during DKA in children is cerebral edema, which occurs in ~ 0.5-0.9% of cases; mortality rate is 21-24%. It usually occurs during the first 4-12 hours of treatment and when it is clinically apparent, the prognosis is usually poor. The pathogenesis is still incompletely understood, but risk factors include:
    - Younger age; New-onset diabetes; Longer duration of symptoms
    - ***Sodium bicarbonate treatment for correction of acidosis***
    - *Greater volumes of fluid given in the first 4 hours*
    - *Administration of insulin in the first hour of fluid treatment*
    - Increased BUN at presentation
    - Greater hypocapnia at presentation after adjusting for degree of acidosis
    - More severe acidosis at presentation
    - An attenuated rise in measured serum sodium concentrations during therapy
- Children with DKA are frequently sleepy, but warning signs and symptoms of cerebral edema include:
    - Slowing of heart rate, rising blood pressure, decreased O_2 saturation
    - *Change* in neurological status (restlessness, irritability, increased drowsiness, incontinence)
    - Headache, focal neurological signs, dilated/unresponsive/sluggish/unequal pupils, papilledema
    - Decreasing urine output without clinical improvement or tapering of fluids
- CEREBRAL EDEMA IS A LIFE THREATENING MEDICAL EMERGENCY REQUIRING IMMEDIATE AGGRESSIVE INTERVENTION AND IMMEDIATE TRANSFER TO AN INTENSIVE CARE UNIT SETTING. Therapy includes:
    - Reduce rate of fluid administration by 30%
    - Give Mannitol 0.5-1 gm/kg over 20 min and repeat if no initial response in 30 min to 2 hrs
        - Hypertonic saline (3% saline) 5-10 ml/kg over 30 min may be an alternative or 2nd line
    - Elevate head of the bed
    - Intubation may be necessary if impending respiratory failure, but aggressive hyperventilation to hypocarbia (pCO_2 <22 mmHg) has been associated with poor outcome and is not recommended
    - Head CT scan should be obtained to rule out other possible intracerebral causes of neurologic deterioration AFTER treatment for cerebral edema has been started (DO NOT DELAY TREATMENT TO GET THE HEAD CT!)

References:
Wolsdorf et al, Ped Diab 2009:10(Suppl 12):188-33
Wolsdorf et al, Diab Care 2006:29(5):1150-59
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