Pediatric Diabetic Ketoacidosis Guidelines

For new onset diabetes in a pediatric patient NOT in DKA (see criteria below)

- These guidelines may not be appropriate
- Consult endocrine and pediatric admit resident
- Utilize EPIC's Order set labelled **Pedi Diabetes New Onset**

For any pediatric patient in DKA, whether new onset or not

- Initiate the following guidelines
- Consult PICU and endocrine
- Utilize EPIC's order set labelled **Pedi Diabetes DKA**
- Use 2 bag IV fluid system as determined by the excel file **DKA IV fluids and roadmap**

Please remember also, **guidelines and protocols are no substitute for clinical exam and expert opinion**.

If your patient does not continue to improve over the first 3-4 hours of treatment, please re-assess and seek expert opinion from endocrine and/or critical care.

Pediatric DKA Guidelines

- The goal is correction of metabolic acidosis, not euglycemia.

Criteria for diagnosis of DKA.

All 3 must be satisfied

- Hyperglycemic (glucose > 200 mg/dL) **AND**
- Metabolic Acidosis (pH < 7.3, bicarb < 15 mEq/L) **AND**
  - Mild pH 7.2-7.3, bicarb 10-15
  - Moderate pH 7.1-7.2, bicarb 5-10
  - Severe pH <7.1, bicarb <5
- Ketosis – blood and/or urine

Airway / Breathing

- The vast majority of children with DKA will be tachypneic with increased work of breathing but with a very low CO2 and no oxygen requirements.
- Consider intubation only for **respiratory failure** or for children who are comatose (lost airway protection).
- Be very cautious, it is impossible to match the minute ventilation of Kussmaul respirations which is compensating for metabolic acidosis.

Circulation

- While cautious IV rehydration is recommended, you must first aggressively treat shock.
  - If hypotensive or poorly perfused give 20 mL/kg isotonic fluid bolus (Lactate Ringers, Normosol, Normal saline). Repeat as needed until no longer in shock.
  - Consider a 10 mL/kg NS bolus for all other DKA patients (up to 1000mL max).
  - Proceed to slow IV rehydration using the two bag method at 1.5x maintenance rate detailed in the DKA order set or attached.

Disability

- It is not uncommon to have some altered mental status in moderate and severe DKA. The cause is likely multifactorial (osmotic, ischemic and cytotoxic).
- While cerebral edema is a very real possibility (up to 1%), head CT for confirmation is no longer recommended.
- Treat all suspected clinically relevant cerebral edema by decreasing your IV fluid rate and consider 0.5-1 g/kg of mannitol.

Initial Laboratory Studies

- CBC
- BMP + Calcium + Magnesium + Phosphorus
- Urinalysis
- Venous Blood Gas
- If first presentation consider:
  - Thyroid auto Abs (Thyroglobulin Ab screen & Thyroperoxidase Ab)
  - Tissue Transglutaminase (TTG)
  - IgA
  - TSH and T4 are NOT necessary at this time

Monitoring Laboratory Studies

- Q1H glucose while on an insulin infusion
- Q2H DKA panel (lytes, glucose, pH)
- Q-void urine ketones
- If abnormalities found on initial labs, monitor until normalized

Insulin Treatment

- If the child is in DKA, make NPO and begin an insulin infusion at 0.1 U/kg/hour as soon as possible.
- The **only** indication for a bolus of insulin (0.1 U/kg of regular insulin) is an abnormal delay in obtaining the insulin drip from the pharmacy.
- Adjust your fluid management based on attached guide. Hypoglycemia is treated by increasing the dextrose containing fluid rate or potentially increasing to 12.5% dextrose.
- Only decrease the insulin infusion for hypoglycemia not responding to maximal D10% solution infusion rate. Attempt to not lower below 0.05 U/kg/hour unless life threatening hypoglycemia or hypokalemia develop.

Cerebral Edema

- **Clinically significant** cerebral edema occurs in up to 1% of pediatric DKA and accounts for 20% of the mortality.
- The actual incidence of brain swelling may be as high as 50% and the causative mechanism is not fully understood.
- It can take up to 24 hours before it develops so close monitoring and high suspicion are required; Q1H neuro checks.
- Major risk factors are elevated BUN, deceased $PaCO_2$, biacarbonate therapy and sodium not rising as expected.
- Mannitol (0.5-1 g/kg)is the first line for clinically significant cerebral edema with 3% saline (5-10 mL/kg) is second.

End Point

- **DKA is over when the acidosis is finished, not when you achieve euglycemia**.
- If the anion gap is closed, **and** the patient is able to take PO food, consider starting subcutaneous insulin (using the roadmap attached) and switching off the infusion with guidance from endocrine.

Sodium	•Sodium usually increases with therapy as the hyperglycemia corrects. You can estimate the 'corrected' sodium using the equation in this guideline. •The recommended IV fluid components in the two bag system helps to mitigate large swings in sodium levels. •Failure of the sodium to rise as expected can be a sign of cerebral edema
Potassium	•Total body potassium is usually quite low despite initial labs. •Initial hyperkalemia is usually caused by profound acidosis shifting K+ into extracellular space. •Hypokalemia can develop as insulin and acidosis correction drives potassium back into intracellular spaces.
Chloride	•Hyperchloremia is a common iatrogenic finding due to excessive normal saline. •Will cause a secondary metabolic acidosis. •Independent risk factor for acute kidney injury. •Prevention is the goal, avoid excessive 'normal' saline.
Bicarbonate	•Bicarbonate boluses should be avoided. •They are contrainidicated in pediatric DKA and are an independent risk factor for the development of cerebral edema. •Reversal of acidosis together with acetate and glutamate in the IV fluids will slowly reconstitute serum bicarbonate.
BUN / Creatinine	•Likely to be high on admission due to dehydration and protein metabolism •Elevated levels are an independent risk factor for cerebral edema.
Glucose	•Euglycemia is not the priority •If hypoglycemic, follow protocol. If persistent, you may increase dextrose containing IV fluids and/or lower insulin infusion to 0.05 U/kg/hr
Phosphate	•Total body phosphate is usually low despite initial labs •Initial hyperphosphatemia from acidosis and dehydration will be replaced with hypophosphatemia. •Hypophosphatemia can cause weakness, CNS depression, and cardiac and respiratory failure.
Calcium	•Can decrease with phosphate repletion. •Ideally should check iCal as serum calcium levels will be unreliable with fluid shifts. •Hypocalcemia can cause cramping, fatigue, irritability.
Magnesium	•Not a huge concern but can potentially be low after prolonged DKA •Consider repletion if lower than 2 mEq/L
Anion Gap	•**The best indicator of success in your therapy**. •When anion gap is closed (12 +/-3) you can consider switching to subcutaneous insulin, turning off the insulin infusion and starting PO feeds; this should be done in consultation with endocrine.

Impact of DKA

- DKA is the most frequent metabolic disorder encountered in the PICU.
- The mortality rate of DKA is approximately 1%.
- Complications of DKA and/or its therapy include acidosis, cardiovascular collapse, cerebral edema, stroke, pulmonary edema, hypokalemia, hypoglycemia, hypocalcemia, and hypophosphatemia.
- Cerebral edema is a major factor in the morbidity and mortality of DKA accounting for almost 1/4 of the fatalities.

Pathophysiology

- Relative insulin deficiency leads to an inability of glucose to enter cells and a loss of inhibition of the breakdown of fat, protein, and glycogen.
- This results in hyperglycemia and an increase in β-hydroxybutyric acid and acetoacetic acid (ketones) and hyperlipidemia.
- Hyperglycemia above the renal threshold (approximately 200) leads to glycosuria and osmotic diuresis with subsequent loss of water.
- In addition, vomiting adds to the loss of volume
- Subsequent dehydration leads to decreased excretion of ketoacids which results in further increases in these acids and worsening acidosis.

History

- Polyuria, polydypsia, weight loss, abdominal pain, nausea, vomiting, recent viral or bacterial infection

Physical Exam

- Dehydration, Kussmaul respirations, fruity odor.
- Delayed capillary refill, orthostatic hypotension, altered mental status (follow closely, regardless of mental status at the time of admission). Monitor for signs of increased ICP.
- Frequently present with signs and symptoms of an acute abdomen that responds to rehydration.
- Consider sepsis evaluation if febrile.

Useful equations

- Estimated Osmolality = 2(Na+) +(glucose/18) + (BUN/2.8)
- Corrected Sodium (mEq/L) for hyperglycemia = Na+ + [0.016* (measured glucose – 100)]
- * Some report 0.024 as the correction factor.

References

- ISPAD Clinical Practice Consensus Guidelines 2014 Compendium. Pediatr Diabetes. 2014 Sep;15
- Glaser N, Barnett P, McCaslin I, Nelson D, Trainor J, Louie J, Kaufman F, Quayle K, Roback M, Malley R, Kuppermann N, Risk factors for cerebral edema in children with diabetic ketoacidosis. The Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics. N Engl J Med. 2001;344(4):264.
- Vavilala, Monica S. MD. Imaging for Cerebral Edema in Diabetic Ketoacidosis: Time to Zap the CT? Pediatric Critical Care Medicine: March 2017 - Volume 18 - Issue 3 - p 281–282
- Wootton-Gorges SL, Buonocore MH, Kuppermann N, Marcin JP, Barnes PD, Neely EK, DiCarlo J, McCarthy T, Glaser NS. Cerebral proton magnetic resonance spectroscopy in children with diabetic ketoacidosis. Am J Neuroradiol. 2007;28(5):895.
- Roberts JS, Vavilala MS, Schenkman KA, Shaw D, Martin LD, Lam AM. Cerebral hyperemia and impaired cerebral autoregulation associated with diabetic ketoacidosis in critically ill children. Crit Care Med. 2006;34(8):2
- Vavilala MS, Richards TL, Roberts JS, Chiu H, Pihoker C, Bradford H, Deeter K, Marro KI, Shaw D. Change in blood-brain barrier permeability during pediatric diabetic ketoacidosis treatment. Pediatr Crit Care Med. 2010;11(3):332.
- Bonkowsky, JL., Filloux, FM. Extrapontine Myelinolysis in a Pediatric Case of Diabetic Ketoacidosis and Cerebral Edema. Journal of Child Neurology / Volume 18, Number 2, February 2003
- Modi, M. Vora, K. Parikh, G. Shah, V. A Comparative Study of Impact of Infusion of Ringer's Lactate Solution Versus Normal Saline on Acid–Base Balance and Serum Electrolytes During Live Related Renal Transplantation. Saudi J Kidney Dis Transpl 2012;23(1):135-137
- Lobo, D. Awad, S. Should chloride-rich crystalloids remain the mainstay of fluid resuscitation to prevent 'pre-renal' acute kidney injury? Kidney International (2014) 86, 1096–1105