Initial Management of Diabetic Ketoacidosis

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Key Points

First step in management is fluid resuscitation with normal saline.

- Emergency lab evaluation should include blood glucose, electrolytes, assessment of acid-base status.
- Do not administer IV bolus insulin to patients with DKA.
- Do not administer IV bicarbonate to patients with DKA unless treating documented significant hyperkalemia or hemodynamic instability refractory to catecholamine infusions.
- Cerebral edema is the most common life-threatening complication.

Epidemiology

- Overall, in the U. S. about 29% of new cases of Type 1 diabetes (T1DM) present with diabetic ketoacidosis (DKA) at time of diagnosis; this is more common in children 6 - 10 years of age and in children without private insurance. Further, in a recent study, misdiagnosis continues to contribute to late diagnosis and the development of DKA in children who had previously presented to their primary care physicians or to an ED with classic signs of diabetes.
- In patients with known T1DM, DKA can be related to deliberate or inadvertent omission of insulin.
  Though some children present with infections related to their DKA – most (69%) do not. Further, only a small percentage of patients (3.2% in one study) presented with a serious infection such as pneumonia
- DKA is present at the time of diagnosis in type 2 diabetes (T2DM); however, this varies with ethnicity.

Introduction

Children are not small adults.

- May be unable to give a reliable typical history
- Higher metabolic rate and increase ratio of body surface area to body mass require greater accuracy and precision when replacing fluid and electrolytes.
- Immature cerebral and other auto regulatory mechanisms increase the risk for cerebral edema.

Definitions

- DKA is defined as (need all 3 criteria)
  - Hyperglycemia: >200 mg/dl
  - Venous pH <7.3 or HC03 ≤15 m Eq/l
  - Ketones in serum or urine
- Severity of DKA is primarily determined by the degree of acidosis

Table. Categories of Acidosis

To view a larger image on your device, please click or touch the image.

	Mild	Moderate	Severe
Arterial PH	7.2 - 7.3	7.1 - 7.2	<7.1
Serum Bicarbonate	10 - 15 mmol/L	5 - 10 mmol/L	<5 mmol/L
Glucose	>200 mg/dl	>200 mg/dl	>200 mg/dl
Urine Ketones	+	+	+
Serum Ketones (B-OH Butyrate)	3 or > mmol/L	3 or > mmol/L	3 or > mmol/L

- Hyperosmolar Hyperglycemic Syndrome (HHS)
  - A form of hyperglycemic crisis found usually in patients with Type 2 Diabetes. The differentiation of HHS from DKA is critical as therapeutic strategies differ.
  - Plasma glucose >600mg/dl
  - Arterial pH >7.3
  - Serum bicarbonate >15mmol/L
  - Small urine ketones and absent or minor serumketones
  - Calculated serum osmolality >330 mOsm/kg
  - Altered mental status

Pathophysiology of DKA

- Absolute or relative insulin deficiency combined with the effects of counter-regulatory hormones; catecholamines, glucagon, cortisol, growth hormone (increased during stress e.g., sepsis, trauma)
    - Increased glucose production by liver through gluconeogenesis and glycogenolysis and reduced peripheral glucose utilization resulting in hyperglycemia and hyperosmolarity and osmotic diuresis
    - Lipolysis results in increase free fatty acids that are oxidized to generate acetoacetate and hydroxybutyrate (ketones) which overwhelm the buffering capacity resulting in metabolic acidosis.
- Dehydration, hyperosmolarity, acidosis, and electrolyte abnormalities stimulate further production of counter-regulatory stress hormones resulting in a self-perpetuating cycle.
- This cycle will progress until interrupted by treatment with insulin and fluid and electrolyte replacement.

Evaluation

- Signs and Symptoms
    - Polyuria, polydypsia

        Caused by osmotic diuresis secondary to hyperglycemia
        Osmotic diuresis with excess urine output will continue until dehydration is severe enough to impair glomerular filtration rate or insulin treatment initiated; obligatory electrolyte loss accompanies excess urine output.
- Dehydration
    - Assessing degree of dehydration is difficult and imprecise.
    - For moderate DKA assume 5-7% dehydration and for severe DKA assume 7-10%.
    - Dehydration in DKA rarely causes hypovolemic shock or hemodynamic instability.
- Kussmaul breathing
    - Rapid, deep breaths that may mimic respiratory distress from other causes
    - If long standing, may be associated with chest wall discomfort
    - Compensation for metabolic acidosis by lowering pCO_2
- Malaise
- Nausea, vomiting, and abdominal pain
- Altered mental status
    - Neurologic examinations should be documented using Glascow Coma Scale (GCS) at least every hour until clearly improved and stable.
    - Patients commonly display drowsiness and irritability.
    - Should be arousable with GCS >12
    - Mental status should not deteriorate with treatment.
    - Carefully evaluate for other signs of clinically important cerebral edema and intracranial hypertension (bradycardia, hypertension, slowing respirations, anisocoria, enuresis).

Laboratory Evaluation

- Presence of acidosis is necessary for the diagnosis of DKA and the degree of acidosis is important in determining the severity of DKA (see Definitions).
- Arterial or venous pH (blood gas) and serum bicarbonate should be measured emergently.
- Bicarbonate should be measured every 2 hours until stable, then can measure every 4 hours until DKA is resolved to determine response to therapy.

Potassium

- Total body potassium depletion is present and requires replacement in essentially all patients with DKA.
- Potassium should be measured emergently at presentation.
- At presentation, potassium levels may be low, normal, or high.
- Potassium levels should be measured every 2 hours until stable, then can measure every 4 hours until DKA is resolved.

  Never begin insulin therapy without potassium replacement in IVF – fatal arrhythmias may occur

Phosphorus

- Phosphorus levels are typically low at presentation and should be followed as treatment progresses.

Sodium

- Measured sodium levels are artifactually depressed by elevated blood sugar.
- As blood glucose levels fall, sodium levels should rise.
- Persistently low or falling sodium levels increase the concern for rapid shifts in osmolality that may increase the risk for cerebral edema.

Laboratory Evaluation at Presentation

- Arterial or venous blood gas
- Renal panel and Magnesium, then

  - Serum osmolality
  - Serum ketones (beta hydroxybutyrate)
  - Urinalysis (ketones)
  - CBC, blood culture, urinalysis (UA), Chest X-ray (CXR) if febrile or concerns for infection
  - Hemoglobin A1C
  - Amylase/lipase if abdominal pain is out of proportion to DKA
  - Pregnancy test for adolescent girls unless pregnancy is otherwise excluded
  - For the new diabetic: C-peptide, GAD-65, islet cell antibody
    - Additionally: Free T4, thyroid-stimulating hormone (TSH), thyroid antibodies (includes thyroid peroxidase and antithyroglubulin antibody), fasting cholesterol, and Celiac panel – 24 hours after admission (after DKA has resolved)
  - If suspect Type 2, in addition to the above, order a spot urine micro albumin/creatinine ratio and hepatic function panel in the morning 24 hours after admission (after DKA has resolved).

Corrected Sodium: Na (measured) + (1.6 X ([Glucose-100]/100))

Calculate Osmolality: 2Na+ Glucose/18+ BUN/2.8

Anion Gap: [Na+] – {[Cl] + [HCO3]} (Normal: 12 ± 2 mmol/L)

Goals of Initial Management

- Reestablish circulating volume and then gradually correct dehydration
- Correct the insulin deficiency
- Correct acidosis and reverse ketosis
- Normalize blood glucose levels
- Correct electrolyte abnormalities

- Minimize risk of DKA complications
- Identify and treat any precipitating causes

Initial treatment should focus on fluid resuscitation to restore tissue perfusion and correction of acidosis with a gradual controlled correction of serum glucose levels.

Fluid resuscitation to restore tissue perfusion ─ Administer normal saline 20ml/kg (up to 1 liter) IV over 1 hour; this may be repeated based upon the severity of dehydration.

Begin an infusion of normal saline (Potassium added if patient is known to have urine output, and potassium level is <6)

- Rate of 2.5 times usual calculated maintenance (max rate is 250 ml/hr or 4L/M2/ day whichever is less)
- Rate should not exceed 4 liters/m^2 in the first 24 hours including fluid boluses for resuscitation.
- Potassium is ideally added as 40 mEq/liter, half potassium acetate and half potassium phosphate; however, fluid administration should not be delayed if this is not easily available.

A continuous infusion of regular insulin should begin at 0.1 units/kg/hour; **do not administer bolus IV insulin**.

Blood sugar must be monitored at least every hour; serum glucose should not decrease by more than 100 mg/dl/hr after initial rehydration with fluid bolus.

If the serum glucose decreases more rapidly than 100 mg/dl or if it decreases below 350 mg/dl, dextrose should be added to the IV fluid.

- This may be in the form of D_5NS with potassium, initially.
- As treatment progresses, the glucose infusion rate will vary and is best managed with a standardized protocol.

Arkansas Children's Hospital employs a 2-bag IV fluid system

- Initial 6 hours of treatment
  - Normal saline (NS) with 20 mEq K acetate/L and 20 mEq KPhos/L and D10NS with 20 mEq K acetate/L and 20 mEq KPhos/L
  - For serum glucose >350mg/dl administer entire IV fluid rate as NS with potassium additives.
  - For serum glucose between 250 and 350 mg/dl administer half of IV fluid rate as NS with potassium additives and half of the IV rate as D_{10}NS with potassium additives.
  - For serum glucose <250mg/dl administer full IV fluid rate as D_{10}NS with potassium additives.
- After 6 hours of treatment IV fluids should be changed to ½ NS with potassium additives and D_{10}½NS with potassium additives.
- The same serum glucose guidelines are used to determine the ratio of the 2 fluids.

Occasionally, patients will have lower-than-desired serum glucose (< 70 mg/dl) even when full IV fluid rate is administered as IV fluid containing 10% dextrose.

- This may be managed by increasing the IV fluid rate if this will not exceed the 4 liters/m2/24-hour maximum rate.
- The dextrose concentration may be increased to 12.5% dextrose.

- If the patient has normal mental status and is no longer vomiting, glucose containing oral liquids may be given.
- As a last resort, the insulin infusion rate may be temporarily decreased to 0.05units/kg/hour.

Complications

Hypokalemia

- Avoid by inclusion of potassium in rehydration fluid as soon as urine output is documented and K is <6 mEq/L.
- Potassium level should be monitored frequently (every 2 hours until stable, then every 4 hours until acidosis is corrected).

Hypoglycemia

Insulin replacement

Insulin replacement is essential for correcting DKA; however, insulin will decrease blood glucose to dangerous levels unless dextrose infusions are appropriately increased as blood sugar falls.

- Monitor for signs and symptoms of hypoglycemia including
  - Somnolence
  - Headache
  - Confusion
  - Fatigue
  - Seizures
  - Loss of Consciousness
  - Palpitations
  - Anxiety
  - Tremors
  - Diaphoresis

Treating Mild Hypoglycemia

- Treat mild hypoglycemia (< 70 mg/dl) by increasing the rate of glucose (D10) infusion, or
  - If able to tolerate PO, may follow hypoglycemia protocol with Rule of 15.
- Obtain and record capillary blood glucose measurements every 15 minutes until stable.

Treating Severe Hypoglycemia

- Treat severe hypoglycemia (e.g. seizures, loss of consciousness, or altered mental status) with 1 ml/kg D50 IV push OR Glucagon (see below). Ensure IV site infuses easily as infiltrates will harm patient.
  - The insulin infusion may be temporarily decreased (to as little as 0.025 units/kg/hr) or briefly (< 10 minutes) turned off until hypoglycemia is corrected
  - Avoid holding the insulin infusion for longer periods; ketosis will get worse almost immediately.
  - Glucagon 1 mg emergency kit is to be available in emergency situations of limited IV access for treatment of severe hypoglycemia.
    Infants and children < 20 kg receive 0.5 mg SQ
    Children > 20 kg receive 1 mg SQ
    Glucagon is rarely needed in an inpatient setting with IV glucose available.

- Obtain and record capillary blood glucose measurements every 15 minutes until stable.
- Restart insulin infusion once hypoglycemia is corrected at a lower rate and/or increase the glucose infusion rate if possible.
- For patients who are awake, alert and not vomiting, 15 grams of simple carbohydrates can be offered in the form of juice or equivalent to treat symptomatic lows. Follow Rule of 15.

Hypophosphatemia

Hypophosphatemia can be prevented by including phosphorus in resuscitation fluid usually in the form of potassium phosphate.

Specific Care to Avoid

- Bolus IV insulin
- Administration of sodium bicarbonate
- Over-aggressive IV fluid administration

Concurrent Conditions

- Infection
  - May be present and may occasionally play a role in precipitating or accelerating DKA by increasing counter-regulatory hormones
  - Should be evaluated and ruled out early in the evaluation
- Pancreatitis
  - May be a complicating factor in DKA; however, elevated pancreatic enzymes are common in DKA even if clinically significant pancreatitis is not present.
  - Elevated amylase and lipase alone without clinical evidence of pancreatitis should not prevent use of enteral nutrition.

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

References

References

1. Dunger, D., Sperling, M., Acerini, C. L., Bohn, D. J., Daneman, D., Danne, T. P..... Lawson Wilkins Pediatric Endocrine Society. (2004). Consensus statement on diabetic ketoacidosis in children and adolescents. *Pediatrics, 113,* e133-140.
2. Fiordalisi, I., Novotny, W. E., Holbert, D., Finberg, L., Harris, G. D., & Critical Care Management Group. (2007). An 18-yr prospective study of pediatric diabetic ketoacidosis: An approach to minimizing the risk of brain herniation during treatment. *Pediatric Diabetes, 8,* 142-149.
3. Felner, E. I., & White, P. C. (2001). Improving management of diabetic ketoacidosis in children. *Pediatrics, 108,* 735-740.
4. White, P. C., & Dickson, B. A. (2013). Low morbidity and mortality in children with diabetic ketoacidosis treated with isotonic fluids. *Journal of Pediatrics, 163,* 761-766.

5. Wolfsdorf, J., Glaser, N., & Sperling, M. (2006). Diabetic ketoacidosis in infants, children and adolescents: A consensus statement from the American Diabetes Association. *Diabetes Care 29,* 1150-1159.
6. Wolfsdorf, J., Craig, M., Daneman, D., Dunger, D., Edge, J., Lee, W., Rosenbloom, A. Hanas R. (2007). Diabetic ketoacidosis in children and adolescents with diabetes. *Pediatric Diabetes, 10 (suppl. 12),* 118-133.
7. Zeitler, P. et al. (2011). Hyperglycemic Hyperosmolar Syndrome in Children: Pathological Considerations and Suggested Guidelines for Treatment. Journal of Pediatrics, 158(1), 9 – 14.
8. Mencher S.R., Frank, G, Fishbain, J. (2019). Diabetic Ketoacidosis at the Onset of Type 1 Diabetes: Rates and Risk Factors Today to 15 Years Ago. Glob Pediatr Health, 6, 1 – 9.