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Review Article

Diabetic Ketoacidosis: A Comprehensive Review of Evaluation and Management Strategies

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ABSTRACT

Diabetic ketoacidosis (DKA) is a critical complication of diabetes mellitus, primarily type 1, but increasingly reported in type 2 diabetes. It presents with hyperglycemia, ketosis, and metabolic acidosis and continues to pose significant risks of morbidity and mortality. This review explores the epidemiology, pathophysiology, clinical presentation, diagnosis, and current management protocols for DKA, with special focus on recent updates in treatment guidelines and prevention strategies.

INTRODUCTION

Diabetic ketoacidosis (DKA) is a potentially life-threatening acute complication of diabetes mellitus that results from an absolute or relative deficiency of insulin. It is primarily associated with type 1 diabetes but may also present in individuals with type 2 diabetes under stressful conditions. The condition is characterized by hyperglycemia, metabolic acidosis, and increased total body ketone concentration. Despite advancements in diabetes management, DKA remains a leading cause of morbidity and mortality, especially in young individuals with type 1 diabetes and in those with poor adherence to insulin therapy. DKA may be the initial presentation of diabetes in some cases and is a common cause of hospitalization in persons with diabetes. Recognizing the early signs and providing timely treatment are essential to improve patient outcomes. This review provides an updated understanding of the epidemiology, pathophysiology, diagnosis, treatment, and prevention of DKA based on current guidelines and literature.[1] DKA remains a life-threatening metabolic disorder despite advancements in diabetes care. It accounts for a considerable number of emergency hospital admissions, especially in patients with type 1 diabetes mellitus, and occasionally in those with type 2 diabetes exhibiting ketosis-prone diabetes.[2]

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Epidemiology

DKA affects individuals across all age groups. In a study of 4,807 episodes, 36% were reported in individuals under 30 years. [3]Another large study of over 28,000 young diabetics showed a 6% incidence of DKA, with highest rates among adolescents aged 11–15. Females and patients with migration backgrounds are at greater risk

Pathophysiology

Diabetic ketoacidosis (DKA) is primarily caused by absolute or relative insulin deficiency, often combined with increased levels of counterregulatory hormones such as glucagon, cortisol, catecholamines, and growth hormone. These hormonal changes lead to a cascade of metabolic events:

1. Decreased Glucose Utilization: In the absence of adequate insulin, glucose uptake by insulin-sensitive tissues is reduced, resulting in hyperglycemia. Simultaneously, hepatic glucose production via gluconeogenesis and glycogenolysis increases.

2. Increased Lipolysis: Insulin deficiency activates hormone-sensitive lipase, leading to enhanced breakdown of triglycerides in adipose tissue into free fatty acids (FFAs). These FFAs are transported to the liver.[4]

3. Ketogenesis: In the liver, FFAs are converted into acetyl-CoA, which exceeds the capacity of the Krebs cycle and is shunted toward the production of ketone bodies—acetoacetate, β-hydroxybutyrate, and acetone. The accumulation of these acidic ketone bodies leads to metabolic acidosis.[5]

4. Osmotic Diuresis and Dehydration: Hyperglycemia increases plasma osmolality, causing an osmotic diuresis that results in polyuria, electrolyte loss (particularly sodium, potassium, and phosphate), and severe dehydration.[6] Volume depletion contributes to hypoperfusion and impaired renal function, further worsening hyperglycemia and ketone accumulation.

5. Electrolyte Imbalances: Potassium shifts from intracellular to extracellular compartments due to acidosis and insulin deficiency, but total body potassium is depleted through urinary losses. Phosphate and magnesium are also often depleted.[7]

6. Acidosis: The net effect of increased ketogenesis, decreased clearance, and bicarbonate consumption results in high anion gap metabolic acidosis.[8] This acidosis is partially compensated by respiratory alkalosis through deep, rapid breathing (Kussmaul respiration).
In summary, the pathophysiology of DKA is a complex interplay of insulin deficiency and hormonal dysregulation, leading to hyperglycemia, ketosis, acidosis, and profound dehydration.[9]

Clinical Presentation

The classic triad includes polyuria, polydipsia, and weight loss. Additional symptoms may include fatigue, dyspnea, vomiting, abdominal pain, fruity breath, and altered mental status. Kussmaul respirations are a hallmark of metabolic acidosis.[10]

Diagnosis

Diagnostic criteria include:

-Serum glucose >250 mg/Dl
-Arterial pH <7.3
-Serum bicarbonate <18 mEq/L
-Anion gap >10–12 mEq/L

-Positive serum/urine ketones

Venous pH is now an acceptable alternative to arterial pH. Serum β-hydroxybutyrate levels are more reliable than urine ketone tests.[11]

Differential Diagnosis

Differential Diagnoses Include:

- Hyperosmolar hyperglycemic state (HHS)
-Alcoholic ketoacidosis
-Lactic acidosis
- Pancreatitis
-Starvation ketosis
- Myocardial infarction

Management

Management of diabetic ketoacidosis (DKA) involves several critical steps to correct fluid deficits, electrolyte imbalances, hyperglycemia, and the underlying cause.[12]

1. Initial Evaluation:

- Assess airway, breathing, circulation, mental status, and hydration.

- Obtain vital signs and initiate continuous cardiac monitoring.

- Draw blood for glucose, electrolytes, blood urea nitrogen (BUN), creatinine, osmolality, ketones, CBC, and ABG or VBG.[13,14]

- Perform ECG and chest X-ray if infection or cardiac cause suspected.

2. Fluid Replacement:

- Start with 0.9% NaCl at 15–20 mL/kg/hour (~1 L/hr) for the first 1–2 hours.

- Adjust based on corrected sodium: If corrected Na is normal or high, switch to 0.45% NaCl.
• If low, continue with 0.9% NaCl.

- When serum glucose falls to 200 mg/dL, switch to 5% dextrose with 0.45% NaCl to prevent hypoglycemia. [15,16]

3. Insulin Therapy:

- Regular insulin IV bolus: 0.1 units/kg followed by continuous IV infusion at 0.1 units/kg/hr.

- Alternatively, 0.14 units/kg/hr infusion without bolus.

- Decrease insulin rate to 0.05–0.1 units/kg/hr when glucose falls to 200 mg/dL; maintain between 150–200 mg/dL.

- Subcutaneous rapid-acting insulin analogues (e.g., lispro) can be used in mild DKA.[17,18]

4. Potassium Replacement:

- If K+ < 3.3 mEq/L: Hold insulin and give 20–30 mEq/hr until > 3.3.

- If 3.3–5.2 mEq/L: Add 20–30 mEq K+ to each liter of IV fluid.

- If > 5.2 mEq/L: Do not give potassium but monitor every 2 hours.[19]

5. Bicarbonate Therapy:

-Reserved for pH < 6.9.
- Administer 100 mEq NaHCO3 in 400 mL sterile water with 20 mEq KCl over 2 hours.

-Repeat until pH ≥ 6.9.[20]

Phosphate and Magnesium:

- Phosphate replacement if level < 1.0 mg/dL or symptoms present; 20–30 mEq potassium phosphate IV.[21]

- Magnesium replacement if < 1.2 mg/dL or symptomatic; monitor for cardiac arrhythmias.

7. Transition to Subcutaneous Insulin:

- DKA resolution: Glucose < 200 mg/dL, HCO3 ≥ 18 mEq/L, and pH > 7.3.

- Start subcutaneous insulin 1–2 hours before stopping IV insulin.

- For insulin-naïve patients: Total daily insulin 0.5–0.8 units/kg/day in divided doses.[22]

8. Identification and Treatment of Precipitating Cause:

- Treat infections, correct nonadherence, manage myocardial infarction, pancreatitis, or other triggers.

- Provide diabetes education and follow-up.[23]

Complications

1. Potential complications include:[24]
2. Cerebral edema (especially in children)
3. Hypokalemia
4. Hypoglycemia
5. Acute renal failure
6. Thrombosis
7. Arrhythmias
8. Rhabdomyolysis

Prevention Strategies

Education on sick-day rules, early symptom recognition, ketone monitoring, and insulin adjustment during illness is vital. Psychosocial barriers to care, especially in adolescents, must be addressed through counseling and community support.[25]

CONCLUSION

DKA is preventable with appropriate education and timely medical intervention. Effective management requires prompt recognition, aggressive fluid and insulin therapy, and careful monitoring of electrolytes. Long-term strategies must focus on patient education, psychosocial support, and healthcare access.

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