

## RECENT ADVANCEMENT IN THE MANAGEMENT OF DIABETIC KETOACIDOSIS

### ABSTRACT

Diabetic ketoacidosis (DKA) is a condition of diabetes mellitus that is life-threatening and occurs whenever blood sugar levels rise, ketones are produced and the body begins to get acidosis. The issue of timely and appropriate management is critical to avoid the development of fatal conditions. Over the years, two main approaches to DKA management have emerged: slow and fast. The conventional way of treating DKA attacks is through a gradual improvement of the hyperglycemia and metabolic abnormalities, which may span up to 24 to 48 hours. This procedure mainly involves intravenous fluid replenishment, insulin infusion, and the correction of electrolyte imbalance. However, this method has certain shortcomings. The disadvantage includes the long time that the patient has to stay in hospital, which results in extra costs for treatment and inconvenience for the person. Moreover, overcorrection may heighten the chance of cerebral edema, a rare but fatal issue that may occur during or after DKA treatment. In the last few years, there has been a lot of attention around fast management methods which are aimed at getting rid of excessive blood sugar levels as well as other abnormalities within a shorter time range typically of 6 to 12 hours. Aggressive approaches to quick control include higher insulin infusion rates, intensive fluid resuscitation, and close checks on electrolytes, acid-base status, and other parameters. Supporters of fast treatment say that it shortens the length of hospitalization, makes it less costly, and minimizes brain edema, which is one of the complications. Nevertheless, the negative impacts may involve the incidence of hypoglycemia, hypokalemia, and rebound hyperglycemia by rapid correction. Many studies have demonstrated that the therapeutic and medicinal efficacy and safety levels of both slow and rapid management

approaches to DKA are almost similar. In some instances, trials may reveal similar outcomes of the two strategies, on the other hand, conflicting results have also been reported. This review shall reflect on both the slow and fast management of diabetic ketoacidosis and enlist the ways that have been decided as per the guidelines to help manage the patients on urgent basis in the emergency room.

**Keywords:** diabetic ketoacidosis, fast management, slow management, aggressive management, reversal of DKA, improved patient outcomes.

## INTRODUCTION

Hyperglycemia, acidosis, and ketoacidosis - collectively known as diabetic ketoacidosis (DKA), is a serious complication of diabetes mellitus.(1) While it transcendentally influences people with type 1 diabetes, examples among type 2 diabetes patients are normal. The triggers for DKA frequently incorporate new-beginning diabetes, contaminations, or rebelliousness with treatment regimens.(2)

The precipitating factors for DKA include a wide range of factors, ranging from intense sicknesses to drug-related impacts. Diseases such as pneumonia and urinary tract infections, act as normal triggers, close to intense ailments like injury, medical procedure, and respiratory embolism. (3)

Furthermore, substances like excessive alcohol consumption and certain drugs, including corticosteroids and sympathomimetic specialists, may add to DKA occurrence. Notably, the risk is exacerbated further by substance abuse and compliance issues, particularly among urban Black populations.(4)

The reported incidence rates of DKA range from about 56 per 1000 person-years across geographical regions. (5)These rates are higher among women and non-White people, and people

who use injectable insulin are more likely to get sick than people who use subcutaneous insulin infusion pumps. Also, the incidence of DKA deteriorates essentially with age limits, trance-like state, hypotension, and extreme comorbidities, especially among Black people.(6)

Hospitalization rates for DKA have increased, particularly among individuals under the age of 45, despite improvements in diabetes management. In any case, death rates connected with hyperglycemic emergencies have declined generally speaking in the US.(7)

The geriatric populace faces interesting difficulties concerning hyperglycemic emergencies, credited to expanded insulin opposition and diminished thirst systems. Thus, this segment is especially powerless against hyperglycemia and drying out, basic parts of DKA. With upgraded diabetes observation and early mediation methodologies, grimness and death rates related with intense diabetic emergencies among geriatric people can be significantly relieved.(8)

DKA remains a significant clinical issue that requires extensive treatment plans. In order to decrease the incidence of DKA and improve patient outcomes in a variety of demographic groups, it is essential to have a thorough understanding of the various risk factors that are associated with its onset and to implement specific interventions.(1) To better understand the underlying mechanisms and improve preventative measures for this potentially fatal diabetes mellitus complication, additional research is required.

## **THE FAST AND SLOW MANAGEMENT OF DIABETIC KETOACIDOSIS IN ADULTS: CURRENT UPDATED PROTOCOLS**

The management of diabetic ketoacidosis (DKA) consists of several therapeutic goals aimed at optimizing patient outcomes. These goals include the optimization of:

**Volume Status:**

Addressing volume depletion is crucial in the management of DKA to restore intravascular volume and improve tissue perfusion.(9)

### **Hyperglycemia and Ketoacidosis:**

Rapid correction of hyperglycemia and reversal of ketoacidosis is essential to prevent life-threatening complications associated with DKA.(2)

### **Electrolyte Abnormalities:**

Correcting electrolyte imbalances, particularly potassium levels, prevents cardiac arrhythmias and other complications.(3)

### **Potential Precipitating Factors:**

Identifying and addressing underlying precipitating factors such as infection or non-compliance with insulin therapy are essential to prevent recurrent episodes of DKA.(10)

As most patients with DKA present to the emergency room, prompt management initiation is crucial. Emergency physicians should begin the management of hyperglycemic crises while simultaneously conducting a physical examination, obtaining basic metabolic parameters, and confirming the diagnosis.(11) The basic early management steps in DKA include:

- Collecting blood for metabolic profiling before initiating intravenous fluids to assess baseline electrolyte and glucose levels accurately.(2)
- Infusing 1 L of 0.9% sodium chloride over 1 hour after drawing initial blood samples to address volume depletion and improve tissue perfusion.
- Ensuring a potassium level of  $>3.3$  mEq/L before initiating insulin therapy. If potassium levels are below this threshold, potassium supplementation should be administered intravenously to prevent the risk of hypokalemia.(9)

- Initiating insulin therapy only after completing the aforementioned steps. This ensures that electrolyte imbalances are corrected and intravascular volume is optimized before initiating treatment, thereby reducing the risk of complications associated with insulin therapy in the setting of hypokalemia or volume depletion.

By adhering to these early management steps and therapeutic goals, healthcare providers can effectively address the acute metabolic derangements associated with DKA and improve patient outcomes. Early intervention is paramount in preventing the progression of DKA to more severe complications and promoting timely resolution of the condition.(12)

## **THE CURRENT MANAGEMENT PROTOCOLS OF DIABETIC KETOACIDOSIS IN ADULTS**

In the case of patients with hyperglycemic emergencies that include diabetic ketoacidosis (DKA) as a complication, therapeutic goals are directed at managing several aspects that can stabilize the patient's condition and prevent any further complications. (13)

These goals include increasing the circulating volume and tissue perfusion and gradually lowering the serum glucose and osmolality. Also, it is important to restore the electrolyte balance and to identify and manage any other comorbid or precipitating causes. (2)

The treatment of DKA is only deemed successful when the patients are closely followed up to confirm that such targets are achieved using clinical and laboratory parameters.

### **Fluid Therapy:**

DKA manifests with a significant loss of total body water, around 6 liters, in a situation of volume depletion. First-line treatment is focused on raising the intravascular volume and ensuring that the urine is flowing normally. (14)

Isotonic saline is usually the most common fluid used for resuscitation, with the initial bolus set at 15-20 ml/kg of body weight over the first hour or 1 -1.5 liters. The optimal rate of initial fluid administration in the management of diabetic ketoacidosis (DKA) has been a subject of investigation in prospective randomized controlled studies. (15)

A study comparing two fluid administration rates of isotonic fluid, either 500 mL/hour or 1 L/hour, found no significant differences in the resolution of DKA, mortality rates, or occurrence of complications. This suggests that the rate of fluid administration may not significantly impact clinical outcomes in DKA management.(16)

Most DKA management protocols advocate for an initial bolus of isotonic crystalloid solution, typically 0.9% saline, administered at a starting rate of 15–20 mL/kg/hour (1–1.5 L/hour) during the first hour of treatment. (14)

Following the initial hydration phase, fluid administration rates can be adjusted to a range of 4–14 mL/kg/hour based on the patient’s hydration status, electrolyte balance, and urine output. The choice of subsequent fluid tonicity is highly important, as rapid correction of serum sodium and osmolality by hypotonic fluids may elevate the risk of cerebral edema.(15)

However, continuous isotonic fluid therapy in pediatric patients has been associated with an increased risk of non-anion gap hyperchloremic acidosis, potentially leading to prolonged hospital stays due to misdiagnosis of persistent ketoacidosis. (14)

Therefore, safe fluid resuscitation practice in DKA patients involves the provision of an initial bolus of isotonic saline at 15–20 mL/kg/hour, followed by the administration of hypotonic saline solution (0.45% saline) at a rate of 4–14 mL/kg/hour as long as the patient remains hemodynamically stable and corrected serum sodium levels are within normal to high ranges.(15)

In cases where a patient develops hyponatremia based on corrected serum sodium levels, the initiation of 0.9% saline at a rate of 150–250 mL/hour is recommended until eunatremia is achieved. It's important to note that the replacement of water deficit using high rates of intravenous fluids has not been extensively studied in pediatric patient populations, and thus, this approach cannot be universally recommended for the management of pediatric DKA.(17)

Overall, fluid administration in DKA management requires careful consideration of fluid tonicity, administration rates, and patient-specific factors to optimize outcomes while minimizing the risk of complications, particularly in vulnerable populations such as pediatric patients.(17)

The amount of fluid replacement needed further depends on the degree of hydration, serum electrolyte levels, and urine output, with approximately half of the expected sodium and water deficit corrected over 12-24 hours.

### **Insulin Therapy:**

Insulin at physiologic doses is the fundamental and most vital aspect of DKA treatment. A rapid intravenous bolus of 0.1 U/kg body weight is used to start the regular insulin followed by the continuous infusion of regular insulin at a rate of 0.1 U/kg/hr. (18)

The insulin infusion rate is now reduced to 0.05 U/kg/hr as the plasma glucose levels are lowered to 200-250 mg/dl. The subcutaneous insulin infusion is, in most cases, the preferred way of administration of regular insulin because of its short half-life and ease of titration. (19)

Recent research has questioned the traditional approach to the initial insulin bolus in diabetic ketoacidosis (DKA) treatment. One study compared the effectiveness and safety of two insulin infusion methods – with and without a priming bolus.(20)The results showed no notable differences in outcomes between patients treated with continuous insulin infusion at a rate of 0.14 U/kg/h without an initial bolus and those given a priming insulin bolus of 0.07 U/kg

followed by continuous infusion at 0.07 U/kg/h. Notably, the effectiveness of a therapeutic approach with an insulin dose of 0.1 U/kg was not evaluated in this study.(21)

Similarly, a recent investigation found no significant variance in various clinical parameters, including hypoglycemia incidence, glucose change rate, anion gap, emergency department stay length, or hospital stay, among patients receiving continuous insulin infusion at a rate of 0.1 U/kg/h with or without an insulin bolus.(15) Despite these findings, no prior studies have directly compared clinical outcomes in pediatric DKA patients treated with and without a priming insulin bolus. Consequently, the use of a priming bolus in pediatric DKA care is not recommended due to the lack of evidence supporting its effectiveness and safety in this patient population.(22)

The rationale for the priming bolus stemmed from a study involving patients with hyperosmolar hyperglycemic non-ketotic diabetes, suggesting that an initial bolus could help address the relative insulin resistance observed in DKA. (23)

However, the relevance of this finding to DKA management remains uncertain, particularly considering the conflicting evidence and the absence of studies specifically examining pediatric patients. (24)

As such, further research is needed to clarify the optimal insulin infusion strategies in DKA management and their impact on clinical outcomes, especially in pediatric populations. Until then, clinicians should use caution and adhere to evidence-based practices when implementing insulin therapy in DKA management.(25)

### **Potassium Therapy:**

The DKA patients most frequently have mild to moderate hyperkalemia because of their acidosis and insulin deficiency. Insulin therapy gives way to a lowering of serum potassium levels.

When serum potassium levels fall below 5.3 mmol/l, we replace this with potassium supplementation, while simultaneously correcting acidosis and volume.(26)

### **Bicarbonate Therapy:**

Bicarbonate therapy has shown no significant benefit in DKA treatment, according to prospective randomized studies. (17)

However, in adult patients with severe acidosis (pH < 6.9), sodium bicarbonate may be administered intravenously at a dose of 100 mmol in 400 ml sterile water with 20 mmolKCl, given at a rate of 200 ml/h for 2 hours until the pH rises to 7.0. Continued treatment may be necessary every 2 hours if pH remains below the target.(27)

### **Phosphate Therapy:**

Phosphate therapy may be considered in individuals with hypophosphatemia, but caution is warranted as it may lead to hypocalcemia when administered in large doses.(28)

## **CONCLUSION**

The management of diabetic ketoacidosis (DKA) is a complex process, requiring careful consideration of insulin, fluid, and electrolyte replacement strategies. While established clinical guidelines provide a solid foundation for DKA treatment, it is essential to recognize the unique characteristics of each patient's presentation, emphasizing the need for personalized approaches. Prioritizing safe and effective strategies to address volume deficit and insulin replacement, alongside regular monitoring for DKA resolution and potential complications, is paramount. Recent research has shed light on new avenues for optimizing DKA care. Studies have demonstrated the efficacy and safety of subcutaneous insulin administration in mild DKA cases, suggesting potential benefits in cost reduction without compromising outcomes. Additionally,

protocol-driven care models have shown promise in streamlining DKA management processes and resource utilization.

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