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EDITORIAL

Diabetic ketoacidosis: Treatment in the intensive care unit or general medical/surgical ward?

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Abstract

Diabetic ketoacidosis (DKA) is defined as an acute metabolic disorder, which is characterized by an increased presence of circulating ketones, and the development of ketoacidosis in the presence of hyperglycemia. This syndrome occurs as a result of insulin deficiency. Patients can be dramatically ill, however, with aggressive treatment, most patients recover rapidly. Despite being a low-risk condition, the development of acidosis, is one of the admission criteria to the intensive care unit (ICU) for these patients, in order to provide close monitoring, and recognize complications that could result from the use of aggressive therapy, such as continuous infusions if insulin. In some institutions, DKA is treated in the emergency department and general medical/surgical wards to avoid ICU overcrowding.

Key words: Diabetic ketoacidosis; Diabetes; Hyperosmolar non-ketotic state; Clinical outcomes; Serum ketones

Core tip: Diabetic ketoacidosis is a complication for some patients with insulin-dependent diabetes mellitus as well as for non-insulin dependent. It is treated commonly in the intensive care unit (ICU), even though clinical data from many studies support management in regular (medical/surgical) wards, avoiding expensive critical care unit costs and preventing bed crisis in these higher level of care units for sicker patients. Once the patient is treated, adequate follow up and education is mandatory. Noncompliance remains the primary concern for repeated admissions.

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INTRODUCTION

Patients with diabetes mellitus (DM) have health care costs 2.3 times higher than others without this diagnosis[1]. In a prevalence-based study, by the American Diabetes Association, in the United States in 2012, the total cost for diagnosed DM was $245 billion United States dollars, and of it, $176 billion was used for direct medical care costs[1]. In addition, and even more concerning, is the fact that hospitalizations for patients with DM have being increasing[2]. The National Surveillance of Diabetes Public Health Resources, reported that diabetic ketoacidosis (DKA) admissions increased from 80000/year in 1988 to 140000/year in 2009[2].

DKA causes an acute metabolic disorder, which is primarily characterized by an increased presence of circulating ketone bodies, and the development of severe ketoacidosis in the presence of prolonged uncontrolled hyperglycemia, usually due to insulin deficiency[3]. It is more commonly seen in patients with insulin-dependent diabetes mellitus (IDDM), especially among children and young adults. Occasionally, patients with insulin resistant DM can present this complication; especially those that are noncompliant with insulin therapy or who present severe infection[3]. DKA has arbitrarily been classified by some as mild, moderate and severe, according to the initial diagnostic criteria (which includes plasma glucose, arterial pH, serum bicarbonate, urine and serum ketones, serum osmolality and anion gap; and the alteration in the mental status)[4].

EPIDEMIOLOGY

In 2012, 29.1 million Americans or 9.3% of the population were estimated to suffer from DM, according to the American Diabetes Association and the Center for Disease Control and Prevention[2]. Of them, approximately 1.25 million American children and adults have IDDM. This clinical condition has a cumulative incidence of 1.4 million Americans per year and it remains the 7th leading cause of death in the United States since 2010[2]. As noted above, the number of cases of DKA has steadily increased over the past 2 decades[2,3]. In one study in the United States, DKA presentations to the emergency department (ED) increased 35% from 1996 to 2006[3]. When compared to other countries like England, Austria and Germany, the United States has the highest rates of DKA in children with IDDM[5]. Mortality rates for patients with hyperglycemic syndromes (DKA and hyperosmolar non-ketotic states) have been reported as 0.02% in patients with diabetes who are 45 years or younger, and 0.014% among older adults[6]. In some studies, the average length of stay in the hospital for patients with DKA has decreased from 5.7 to 3.4 d, being longer for patients categorized in the "severe" group[2,7]. In the authors' experience, some patients can even be discharged within 23 h of hospital admission despite an initial severe acidemia.

IS DKA A CRITERION FOR ICU ADMISSION?

In many institutions, and for decades, DKA has been routinely treated in ICU environments, including recommendations by the American Diabetes Association guidelines for DKA treatment[3,4,7-9]. The primary reason for these level of care requirements, has been the presence of severe metabolic acidosis, even if patients are grouped as mild or moderate in severity[10]. Frequent blood glucose monitoring, the need for intravenous insulin infusions, and the requirement of frequent vital signs is cited as the hospital structural requirements for this ICU level of care[11]. However, several studies have shown that DKA can be safely treated in the ED or even in medical wards (Table 1)[12-17]. By taking this lower level of care approach, we can potentially avoid ICU hospitalization rate and higher costs, bed overcrowding and reserving the beds for patients who present complications such as hypotension, coma, acute myocardial ischemia, or those with several comorbidities (*i.e*., end-stage renal disease, congestive heart failure) and anyone categorized as suffering severe DKA[12,18,19]. In some observational studies DKA patients admitted to the ICU have a shorter length of stay when compared to non-diabetic mellitus ICU patients[20,21]. A recent retrospective cohort study of 156, 842 hospitalizations among 94 acute-care hospitals, analyzed the adjusted cost of hospitalizations in lower and higher ICU utilizations groups, and concluded that the overuse of ICU only increases the cost and the utilization of invasive procedures but with no improvement in hospital mortality[22].

In a prospective, randomized clinical trial in India, Karoli and coworkers reported that once the DKA patient is evaluated in the ED, and categorized in the severity score, direct admission to a regular ward provided no additional mortality and the only complication noted was hypoglycemia. Other groups have used other classifications to allocate resources for patients with DKA[15]. In a retrospective study, Marinac and Mesa, using laboratory criteria (serum bicarbonate, anion gap, base excess and serum osmolality), and diastolic blood pressure, patients were grouped in 5 grades (Grade 0 - Ⅳ)[19]. ICU admission was recommended only for those who had grade Ⅳ DKA[19] (Table 2).

TREATMENT OPTIONS IN THE ED OR ICU

The treatment of acute DKA includes restoration of fluid

Table 1 Clinical trials comparing care in the intensive care unit *vs* the emergency department or medical ward for patients with diabetic ketoacidosis

Ref.	Country	Patients enrolled	Site of management	Therapy used	Outcome	Length of stay
Dunbar *et al*[12] Retrospective study (January 1994 - March 1995)	United States	61	15: ICU 46: Regular floor	Not mentioned	Mortality due to sepsis in only 1 patient with initial pH < 7.00	ICU: 2 d Regular floor: Not mentioned
Umpierrez *et al*[14] Prospective randomized open trial	United States	45	15: ICU 30: ED	ICU: Intravenous insulin drip ED: 15 subcutaneous insulin aspart Q1H ED: 15 subcutaneous insulin aspart Q2H	Hypoglycemic event presented in each group in only 1 patient per group. No complications, no recurrence of ketoacidosis and no mortality	ICU: 4.5 ± 3 d ED with SC Q1H: 3.4 ± 3 d ED with SC Q2H 3.9 ± 3 d
Karoli *et al*[15] Prospective randomized open trial (January 2009 - June 2010)	India	50	25: ICU 25: ED	ICU: 25 intravenous regular insulin ED: 25 subcutaneous insulin lispro	Hypoglycemic event presented, 2 patients in the ICU group and 1 patient in the ED group. No complications, no recurrence of ketoacidosis and no mortality	ICU: 6.6 ± 1.5 d ED: 6.0 ± 1.2 d
Ersöz *et al*[16] Prospective randomized open trial	Turkey	20	20: ICU	ICU: 10 intravenous regular insulin ICU: 10 subcutaneous insulin lispro	No need to switch to IV regular insulin, no hypoglycemic events, no complications, no recurrence of ketoacidosis and no mortality	Not mentioned
Umpierrez *et al*[18] Prospective randomized open trial	United States	20	10: ICU 10: MW	ICU: 20 intravenous regular insulin IMU: 10 subcutaneous insulin lispro Regular floor: 10 subcutaneous insulin lispro	Hypoglycemic event presented in each group in only 1 patient per group, no complications, np recurrence of ketoacidosis and no mortality	IMU and Regular floor: 4 ± 2 d ICU: 4 ± 1 d
Sotiropoulos *et al*[25] Prospective study (June 2007 - May 31 2008)	Greece	21	21: ED	ED: 21 intravenous regular insulin	Myocardial infarction in only 1 patient - Mortality 4.7%	Not mentioned
Della Manna *et al*[26] Controlled clinical trial (June 2001 - June 2003)	Brazil	60	3: ICU 57: ED	ICU: 3 intravenous regular insulin ED: 27 intravenous regular insulin ED: 30 subcutaneous insulin lispro	Hypoglycemic event on 10 patients, 6 patients due to regular insulin and 4 due to lispro; no complications, no recurrence of ketoacidosis and no mortality	Not mentioned

IMU: Intermediate care unit; SC: Subcutaneous; Q1H: Every hour; Q2H: Every two hours; ICU: Intensive care unit; ED: Emergency department; MW: Medical ward; DKA: Diabetic ketoacidosis.

Table 2 List of conditions requiring admission of patients with diabetic ketoacidosis in the intensive care unit

Myocardial infarction
Congestive heart failure
Acute renal failure
Acute respiratory failure
Altered mental status
Coma
Shock
Hypothermia
Sepsis
Pancreatitis
Gastrointestinal bleeding
Uncontrolled hypertension
End stage renal disease
Hyperkalemia

deficits in the first 24 to 36 h, electrolyte replacement and insulin therapy, which is administered slowly to decreased plasma glucose[23,24]. As noted above, a few randomized, open label trials have proved good outcome and non-inferiority for patients who are managed on regular medical/surgical wards while using with rapid acting insulin, aspart or lispro[13,15,17,25-29].

By establishing a rapid diagnosis and starting treatment in the ED, clinicians can help patients to decrease their costs and hospital stay.

The primary issue in patients with DKA remains the need for repeated hospital admissions. Non-compliance in these patients makes the outcome and prognosis worst. Indeed, medical non-compliance and adherence to the outpatient treatment is the most common precipitating factor leading to the development of moderate-to-severe DKA, requiring ICU admission secondary to complications (*i.e.*, cerebral edema, sepsis) and making the management in the ED and/or ICU very complex[21,25,30]. Life-support care, such

as mechanical ventilation, vasopressors, intravenous antibiotic therapy and mortality rates are higher in these patients, when compared to patients not requiring these interventions[30].

CONCLUSION

The benefit of ICU level of care for patients with DKA rather than regular medical/surgical wards is not well established for patients with mild-to-moderate DKA. Many studies suggest the utilization of the ED or the regular (medical/surgical) wards in the management of these patients. There is significant cost-benefit in managing DKA in the ED and regular wards instead of the ICU, where only patients that require life-supportive intervention should go. Once patients are discharged from the hospital adequate follow up is necessary to avoid readmissions and assure compliance.

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