

Diabetic ketoacidosis in children and adolescents

P. Raghupathy

Professor of Paediatric Endocrinology, Indira Gandhi Institute of Child Health and Senior Consultant in Paediatric Endocrinology Sagar Hospitals, Bangalore, Karnataka, India

ABSTRACT

Diabetic ketoacidosis (DKA) is considered to be a common presentation of both type 1 diabetes mellitus and type 2 diabetes mellitus in children and adolescents. DKA arises due to lack of adequate insulin in the body. Insulin stops the use of fat as an energy source by inhibiting the peptide hormone glucagon. Without insulin, glucagon levels rise resulting in the release of free fatty acids from adipose tissue, as well as amino acids from muscle cells. Neurological observations should be made for warning signs and symptoms of cerebral edema, and capillary blood glucose concentration should be measured on an hourly basis. Every 2-4 h electrolytes, blood gases, and beta-hydroxybutyrate should be measured. Cerebral edema occurs in 0.5-0.9% of all episodes of DKA. It is considered to be a major cause of death in childhood DKA. Treatment of cerebral edema should be prompt and immediate. Successful DKA management in children depends upon swift diagnosis, meticulous monitoring of clinical and biochemical parameters with prompt intervention.

Key words: Cerebral edema, diabetic ketoacidosis, type 1 diabetes mellitus

INTRODUCTION

Diabetic ketoacidosis (DKA) is considered to be a common presentation of type 1 diabetes mellitus (T1DM) and occasionally, type 2 diabetes mellitus (T2DM) in children and adolescents. DKA arises due to lack of adequate insulin in the body. Insulin stops the use of fat as an energy source by inhibiting the peptide hormone glucagon. Without insulin, glucagon levels rise resulting in the release of free fatty acids from adipose tissue, as well as amino acids from muscle cells.

The biochemical criteria for DKA diagnosis include hyperglycemia (blood glucose [BG] higher than 11 mmol/L or ≥ 200 mg/dL) with a venous pH of < 7.3 and/or a bicarbonate (HCO_3^-) level of < 15 mmol/L; ketonemia

and ketonuria. Although not universally available, blood β -hydroxybutyrate concentration should be measured whenever possible, and a level of ≥ 3 mmol/L is indicative of DKA. Urine ketones, of moderate or large size (typically $\geq 2+$), are also indicative of DKA.

The clinical signs of DKA include dehydration (may be difficult to detect), tachycardia, tachypnoea (may be mistaken for pneumonia or asthma), deep sighing (Kussmaul) respiration with a typical smell of ketones in the breath (variously described as the odor of nail polish remover or rotten fruit), nausea, vomiting (may be mistaken for gastroenteritis), abdominal pain (may mimic an acute abdominal condition), confusion, drowsiness, progressive reduction in level of consciousness, and eventually loss of consciousness.

Risk factors for DKA in newly diagnosed cases include younger age (< 2 years), delayed diagnosis, and lower socioeconomic status with limited access to medical services. Risk factors for DKA in patients with known diabetes include insulin omission, poor metabolic control, previous episodes of DKA, acute gastroenteritis with persistent vomiting and inability to maintain hydration,

Access this article online

Quick Response Code:



Website:
www.ijem.in

DOI:
10.4103/2230-8210.155403

Corresponding Author: Dr. P. Raghupathy, Indira Gandhi Institute of Child Health Hospital, South Hospital Complex, Near NIMHANS, Hombegowda Nagar, Bengaluru - 560 029, Karnataka, India. E-mail: drp.raghupathy@gmail.com

psychiatric (including eating) disorders, challenging social and family circumstances, peripubertal and adolescent girls, those with limited access to medical services and insulin pump therapy failure.

The severity of DKA is categorized by the degree of acidosis: Mild DKA is characterized by a venous pH of <7.3 and/or a HCO_3^- level of <15 mmol/L, moderate DKA is characterized by a venous pH of <7.2 and/or a HCO_3^- level of <10 mmol/L and in severe DKA, venous pH is <7.1 with or without a HCO_3^- level <5 mmol/L.

Diabetic ketoacidosis results from a deficiency of circulating insulin and increased levels of the counter regulatory hormones: Glucagon, catecholamines, cortisol and growth hormone. Relative insulin deficiency occurs when the concentrations of counter-regulatory hormones markedly increase in response to stress, infection or insufficient insulin.^[1] The combination of absolute or relative insulin deficiency and high counter-regulatory hormone concentrations results in an accelerated catabolic state with increased glucose production by the liver and kidney (via glycogenolysis and gluconeogenesis), and simultaneously impaired peripheral glucose utilization, which combine to result in hyperglycemia and hyperosmolality; increased lipolysis and ketogenesis leading to ketonemia and metabolic acidosis. Hyperglycemia together with hyperketonemia cause osmotic diuresis, dehydration, and obligatory loss of electrolytes. Lactic acidosis from hypoperfusion or sepsis contributes to the acidosis. Thus DKA leads to a vicious life-threatening cycle of events ranging from hyperglycemia, hyperketonemia, osmotic diuresis, severe vomiting, dehydration, and subsequently obligatory loss of electrolytes, greater stress hormone production, and thus more severe insulin resistance. If not interrupted by exogenous insulin, fluid and electrolyte therapy, it would lead to fatal dehydration, hypoperfusion, and ultimately metabolic acidosis.

Ideally, DKA can be managed in any hospital/private unit or in a pediatric inpatient ward in case of children, with adequately trained nursing and medical personnel where lab services are available 24 h throughout the week. However, an intensive care unit (ICU)/pediatric ICU is required for children <2 years of age and in case of severe DKA characterized by compromised circulation, coma, and an increased risk of cerebral edema.

Diagnosis of DKA should be done accurately due to a possibility of a confusing clinical picture such as dehydration, meningitis, acute abdomen, pneumonia, etc. Emergency assessment can be done by following the general guidelines of Pediatric Advanced Life Support. Immediate

measures are a brief history and quick diagnosis, which is essential. Initial immediate assessment or investigation includes evaluation of the severity of dehydration, level of consciousness through Glasgow Coma Scale, body weight and height if the person is mobile. Baseline investigations involve the measurement of BG levels, beta-hydroxybutyric acid, serum electrolytes and renal functions. During physical examination, physician may look for signs of dehydration, acidosis, and electrolyte imbalance, including shock, hypotension, acidotic breathing, central nervous system (CNS) status, etc.

The essential principles of DKA treatment include careful replacement of fluid deficits, correction of dehydration, correction of acidosis and hyperglycemia via insulin administration, maintenance of glucose levels at a normal range, correction of electrolyte imbalance and treatment of any precipitating cause. Successful management of DKA requires constant clinical and biochemical monitoring and timely adjustment of insulin dose, fluid and electrolyte status. Antibiotics, oxygen, and cardiac monitoring can be used if required.

Studies have shown that severe acidosis can be corrected by fluid and insulin replacement. Insulin metabolizes ketoacids and stops further production. However, HCO_3^- administration is shown to have no clinical benefit and may cause paradoxical CNS acidosis. Moreover, rapid correction may cause hypokalemia.

Fluid therapy is initially used for the treatment of DKA, followed by insulin therapy if required. The main objectives of fluid therapy are: Restoration of circulating volume, replacement of electrolytes, improvement of glomerular filtration and clearance of glucose and ketones from the blood. Before starting fluid therapy, the physician should check if the child was treated earlier before the current admission. During fluid therapy, water and salt deficit are replaced using 0.9% normal saline and a 10-20 mL/kg normal bolus may also be used for approximately 1-2 h. If the patient is in shock, several boluses may be given. Subsequent therapy is used for deficit replacement. Normal saline or Ringer lactate is used over a period of 4-6 h. Consequently, maintenance fluids are used. Usually, half normal saline (0.45%) with potassium chloride is given depending on the state of hydration and electrolyte levels. Fluid therapy is usually planned for a period of 48 h. However, a child may improve earlier than 48 h. Normal circulation is often achieved in 12 ± 6 h. When the child becomes stable, fluids can be given orally, and subsequently insulin can be given subcutaneously. In cases of mild DKA, no bolus is needed. The main principle of fluid therapy is to never infuse fluids more than 1.5-2 times the normal

daily requirement. Moreover, constant monitoring and assessment of hydration is absolutely essential.

Potassium replacement therapy is used when the total body potassium deficit is nearly ~3-6 mmol/kg. If the patient is hypokalemic, start potassium replacement at the time of initial volume expansion and before starting insulin therapy. Otherwise, start replacing potassium after initial volume expansion and concurrent with starting insulin therapy. If the patient is hyperkalemic, defer potassium replacement therapy until urine output is documented.

In DKA, rehydration alone reduces BG. Insulin therapy is used to restore normal metabolism, to suppress lipolysis, ketogenesis and normalize BG. A low dose of intravenous (IV), insulin infusion is considered to be safe and effective. Insulin infusion should be initiated 1-2 h after starting fluid replacement therapy; that is after the patient has received initial volume expansion. The dose of insulin should usually remain at 0.05-0.1 unit/kg/h, at least until resolution of DKA viz. pH <7.30, serum HCO₃ levels <15 mmol/L and beta-hydroxybutyrate levels <1 mmol/L. No IV bolus is required to be given because it may worsen hypokalemia or precipitate cerebral edema. As long as possible, the physician should minimize the time on IV insulin infusion, and optimal doses of insulin should be used to avoid severe hypokalemia. BG should be gradually lowered at a rate of 50-100 mg/dL. When BG level falls to 250 mg/dL, 5% glucose is added to IV fluid. Furthermore, 10% or 12.5% glucose may be needed while continuing insulin infusion to correct metabolic acidosis. Furthermore, 2 hourly subcutaneous or intramuscular short-acting insulin may also be used if facilities for IV infusion are not available.

However, for successful DKA management, meticulous monitoring of the patient's clinical and biochemical response using a flow chart is essential. Neurological observations, for warning signs and symptoms of cerebral edema, and capillary BG concentration should be measured on an hourly basis. Every 2-4 h serum electrolytes, blood gases, and beta-hydroxybutyrate should be measured. The physician should look for any warning signs of cerebral edema viz. restlessness, irritability, increased drowsiness, cranial nerve palsies, abnormal pupillary responses, headache, slow heart rate (HR), rising blood pressure (BP) or recurrence of vomiting.

Cerebral edema occurs in 0.5-0.9% of all episodes of DKA. It is considered to be a major cause of death in childhood DKA. Risk factors include initial pH of <7.1, abnormal baseline mental status, newly diagnosed patients who are <5 years old, patients suffering from dehydration and severe acidosis with lower partial pressure

of carbon-dioxide, rapid rehydration (>50 cc/kg in the first 4 h), insulin given before or within 1st h of fluid initiation, persistent hypernatremia and high blood urea at presentation.

Diagnostic criteria of cerebral edema include abnormal motor or verbal response to pain, decorticate or decerebrate posture, cranial nerve palsy, and abnormal respiratory patterns (grunting, tachypnoea, apnoea, Cheyne-Stokes respirations). Major criteria include altered sensorium, sustained deceleration of HR (decrease by >20 beats/min) and age-inappropriate incontinence. Minor criteria include vomiting, lethargy, diastolic BP < 90 mm Hg, headache, and age <5 years.

Treatment of cerebral edema should be prompt and immediate. 0.5-1 g/kg of mannitol should be administered intravenously over 10-15 min, and should be repeated if there is no initial response in 30 min to 2 h. Hypertonic saline (3%) with suggested dose of 2.5-5 mL/kg, administered over 10-15 min, may be used as an alternative to mannitol, especially if there is no initial response to mannitol.^[2,3]

SUMMARY

Diabetic ketoacidosis is a common presentation of both T1DM and T2DM in children and adolescents. DKA arises due to lack of adequate insulin in the body. For successful DKA management, meticulous monitoring of the patient's clinical and biochemical response using a flow chart is essential. Neurological observations, for warning signs and symptoms of cerebral edema, and capillary BG concentration should be measured on an hourly basis. Every 2-4 h electrolytes, blood gases, and beta-hydroxybutyrate should be measured.

REFERENCES

1. Wolfsdorf J, Glaser N, Sperling MA, American Diabetes Association. Diabetic ketoacidosis in infants, children, and adolescents: A consensus statement from the American Diabetes Association. *Diabetes Care* 2006;29:1150-9.
2. Wolfsdorf JI, Allgrove J, Craig ME, Edge J, Glaser N, Jain V, *et al.* Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes* 2014;15 Suppl 20:154-79.
3. Decourcey DD, Steil GM, Wypij D, Agus MS. Increasing use of hypertonic saline over mannitol in the treatment of symptomatic cerebral edema in pediatric diabetic ketoacidosis: An 11-year retrospective analysis of mortality*. *Pediatr Crit Care Med* 2013;14:694-700.

Cite this article as: Raghupathy P. Diabetic ketoacidosis in children and adolescents. *Indian J Endocr Metab* 2015;19:55-7.
Source of Support: Nil, **Conflict of Interest:** None declared.