Management of Diabetic Ketoacidosis

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Abstract Diabetic ketoacidosis (DKA), a life-threatening complication of diabetes mellitus (DM), occurs more commonly in children with type 1 DM than type 2 DM. Hyperglycemia, metabolic acidosis, ketonemia, dehydration and various electrolyte abnormalities result from a relative or absolute deficiency of insulin with or without an excess of counter-regulatory hormones. Management requires careful replacement of fluid and electrolyte deficits, intravenous administration of insulin, and close monitoring of clinical and biochemical parameters directed towards timely detection of complications, including hypokalemia, hypoglycemia and cerebral edema. Cerebral edema may be life threatening and is managed with fluid restriction, administration of mannitol and ventilatory support as required. Factors precipitating the episode of DKA should be identified and rectified. Following resolution of ketoacidosis, intravenous insulin is transitioned to subcutaneous route, titrating dose to achieve normoglycemia.

Keywords Cerebral edema · Hyperglycemia · Insulin therapy · Ketosis · Pediatric

Diabetic ketoacidosis (DKA) is an important complication of diabetes mellitus, accounting for a majority of deaths related to diabetes in children [1]. Diagnosis is challenging, particularly when children present with DKA at onset of disease. Careful monitoring and appropriate management are critical in order to optimize outcome, prevent complications such as cerebral edema, and reduce mortality. Herein, we present a protocol for evaluation and management of DKA in children based on current recommendations.

Definition and Classification

Diabetic ketoacidosis (DKA) in children is defined as hyperglycemia (serum glucose concentration >200–300 mg/dL) in the presence of metabolic acidosis (blood pH<7.3 with serum bicarbonate level <15 mEq/L) and ketonemia (presence of ketones in blood) [2, 3]. As measurement of ketones in blood is not readily available, ketonuria is used as a marker of ketonemia. When measured, serum ketones (ß hydroxybutyrate plus acetoacetate) exceed 31 mg/dL with or without ketonuria >80 mg/dL [4]. Euglycemic ketoacidosis is observed rarely, occurring in patients with prolonged vomiting, very poor oral intake, known type 1 diabetes mellitus (T1DM) with insulin administered prior to emergency visit, and during pregnancy [5, 6]. Infrequently, adolescents with type 2 diabetes mellitus (T2DM) may present with hyperglycemc hyperosmolar state (HHS), defined by blood sugar >600 mg/dL and increased serum osmolality >320 mOsm/kg in the absence of significant acidosis or ketonemia/ketonuria [7].

The severity of DKA is defined by the degree of acidosis. Mild DKA is defined by venous pH between 7.2 and 7.3 or bicarbonate between 10 and 15 mEq/L; moderate by pH between 7.1 and 7.2 or bicarbonate between 5 and 10 mEq/L; and severe by venous pH below 7.1 or bicarbonate below 5 mEq/L [2, 3].

Clinical Features

Children with DKA classically present with polyuria, polydipsia, dehydration, weight loss, Kussmaul respiration and fruity breath odor. However, the presentation may mimic pneumonia, asthma, bronchiolitis or acute abdomen. A high index of suspicion is required to allow diagnosis in children without past history of diabetes. Hemodynamic
instability or shock is rare as intravascular volume is preserved at expense of intracellular dehydration. One should be alert to the development of cerebral edema, particularly if fluid replacement has already been started. Table 1 enlists common presentations and important pointers in history and examination.

Epidemiology and Risk Factors

The risk of presentation as DKA at onset of disease varies inversely with the incidence of diabetes in the population, reflecting the difficulty in recognizing symptoms of diabetes in areas with low disease prevalence [8]. DKA is the presenting manifestation of diabetes in 25% (15–83%) of children with T1DM and in 5–33% children with T2DM [3, 9, 10]. DKA at diagnosis is encountered more commonly in children younger than 5 years of age and those belonging to families without ready access to medical care [6, 9, 11].

The risk of DKA in established T1DM is 1–10% per person per year [4]. Incorrect dosage or omission of insulin is the factor precipitating DKA in 75% cases; other factors predisposing to DKA in children with known diabetes include poor metabolic control, prior episodes of DKA, peripubertal and adolescent age with female gender, presence of eating disorder, difficult or unstable family circumstances, poor access to medical care and pump failure in children receiving insulin pump therapy [12, 13]. The risk is also increased during stresses such as infections or surgery. Annually, 15–20 children present with DKA in the emergency department in our center; most of these are recent onset diabetic children.

Pathophysiology of Biochemical Derangements in DKA

A balance between insulin and its counter regulatory hormones, including catecholamines, glucagon, growth hormone and cortisol, maintains adequate fuel supply to the brain and other tissues during periods of fasting and physiologic stress. Relative or absolute deficiency of insulin (due to declining insulin production or peripheral resistance to insulin action, in types 1 and 2 diabetes, respectively), with or without elevation of counter-regulatory hormones in response to the stress of an infection, trauma or surgery, tilts this balance, producing a catabolic state [14]. Increased glucose production and impaired peripheral glucose utilization then lead to hyperglycemia, hyperosmolality, glycosuria and osmotic diuresis. Inability of tissues to utilize glucose causes lipolysis with production of ketones which are responsible for metabolic acidosis, ketonemia, ketonuria and fruity odour of acetone in breath. During DKA, intracellular potassium is depleted because of transcellular shifts caused by hypertonicity and in exchange for protons that are buffered intracellularly during metabolic acidosis [15]. In turn, this potassium is lost due to hyperglycemia driven osmotic diuresis, and with recurrent vomiting. Hyperaldosteronism secondary to volume depletion further exacerbates potassium losses. Phosphate is another intracellular ion lost from the body due to osmotic diuresis. Serum sodium is artificially lowered in DKA due to hyperglycemia [16, 17].

Management of DKA

Most children with DKA require admission. Initial resuscitation should be followed by frequent clinical and biochemical monitoring. The goals of therapy in DKA include [18]

1. Correction of dehydration
2. Correction of acidosis and reversal of ketosis
3. Restoration of blood glucose to near normal
4. Avoiding complications of therapy, particularly cerebral edema
5. Identification and treatment of the precipitating event
6. Prevention of recurrent episodes

The management of DKA can be discussed under the following headings.

Initial Assessment and Resuscitation

A diagnosis of DKA is made in presence of serum glucose concentration >200–300 mg/dL, blood pH <7.3, serum bicarbonate level <15 mEq/L and ketonemia [2, 3]. As rapid tests for detection of ketones in blood are usually not available, presence of ketones in the urine is looked for.

Hospital admission is indicated in all cases except those with mild acidosis, no dehydration and preserved ability to take fluids orally. Indications for admission to the intensive care unit include presence of severe DKA or risk factors for cerebral edema such as, age <5 yrs and new onset diabetes [19]. Severe DKA is more common in children with prolonged duration of symptoms, compromised circulation and depressed level of consciousness [16].

A brief general physical examination suffices to ascertain status of airway, breathing and circulation and need for resuscitation (Table 1). Patients with impaired consciousness require the airway to be secured; intubation and nasogastric tube placement are essential if Glasgow coma scale falls below 8. Adequate oxygenation should be maintained using supplemental oxygen as required while monitoring by pulse oximetry. For children presenting with hypotension, immediate fluid resuscitation is carried out with 0.9% normal saline as 10–
20 mL/kg bolus given rapidly [16]. Two large bore peripheral intravenous lines are secured, of which one should preferably be kept heparin locked to allow painless repetitive sampling.

If pre-morbid weight is known, current weight helps estimate the degree of dehydration. Signs on physical examination are often inaccurate in estimating the severity of dehydration in these children [20] (Table 1). Due to hyperosmolality, intravascular volume is preserved at the expense of intracellular dehydration. In presence of prolonged capillary refill, dry mucosa, absent tears, sunken eyes, weak pulses and cool extremities, or investigations suggesting moderate ketoacidosis, one should presume moderate degree of dehydration (weight loss of 5–7%) [21]. Severe ketoacidosis can be presumed to indicate 7–10% weight loss, while hypotension or low volume/impalpable pulses indicate severe dehydration (weight loss≥10%) [22].

One should also look for signs of raised intracranial tension and evidence of infection.

Biochemical Assessment

While obtaining intravenous access, the following investigations are sent for: serum glucose, electrolytes [sodium (Na⁺), potassium (K⁺), calcium (Ca²⁺), magnesium (Mg²⁺), phosphorus(PO₄³⁻)], venous blood gas (pH, PCO₂, HCO₃⁻, lactate, base deficit), blood urea, creatinine, hematocrit, and total and differential leukocyte counts. While blood ketones are not measured routinely, urine can be easily examined for ketones by dipstick. If measurement of serum potassium is unavailable or delayed, a baseline electrocardiogram (ECG) is obtained.

The degree of hyperglycemia may predict severity of dehydration; blood glucose >500 mg/dL indicates severe
dehydration usually accompanied by 30–40% reduction in glomerular filtration rate (GFR), while levels above 800 mg/dL indicate fall in GFR by over 50% [23]. Unlike serum sodium, elevations of blood urea nitrogen and hematocrit are expected to correlate with the degree of dehydration [24]. Although total body potassium is decreased, serum levels at presentation may be normal or high due to redistribution in response to acidosis and insulin deficiency [15].

The corrected sodium level, calculated osmolality and anion gap should be computed from the above measurements as suggested in Table 2, since these are useful in guiding therapy. A wide anion gap acidosis is expected, typically between 20 and 30 mmol/L; an anion gap >35 suggests concomitant lactic acidosis [25]. As detailed earlier, the observed hyponatremia is usually artifactual. Effective serum osmolality, which is computed by ignoring the contribution of freely diffusible urea to total osmolality, is often between 300 and 350 mOsm/L and correlates well with abnormalities in mental status [17, 26].

Leukocytosis with leftward shift is common in DKA due to release of cytokines and catecholamines, and does not necessarily indicate infection [27]. Cultures (blood and urine) and chest radiograph are obtained if there is suspicion of infection. Computed tomography to evaluate for cerebral edema is planned in case examination suggests raised intracranial tension.

Water and Salt Replacement

**Calculation of Fluid Deficit** As described above, since clinical estimates of volume deficit are often inaccurate, one should calculate fluid requirements presuming a deficit of 30–50 mL/kg in mild to moderate DKA and 50–100 mL/kg in severe DKA. All intravenous or oral fluids given in another location must be factored into fluid calculations.

**Fluid Bolus** If a patient presents in shock, 20 mL/kg of 0.9% saline (normal saline, NS) or Ringer’s lactate is administered over 15–30 min. Additional fluid boluses of 10–20 mL/kg NS and inotropes may be administered if required to restore circulatory volume. For patients presenting with severe volume depletion without shock, volume replacement is begun with NS at 10–20 mL/kg/h over 1-2 h. The administration of colloids is not recommended [18].

**Subsequent Fluid Management** It is recommended that 0.9% saline or Ringer’s acetate be used in the initial 4–6 h of management. Subsequently, as the blood glucose approaches 300 mg/dL; or earlier, if the fall in blood glucose is precipitous

| Table 2 Monitoring of clinical signs and biochemical investigations and their frequency |
|----------------------------------|----------------------------------|
| **Hourly**                       | **Every 2 to 4 h**               |
| • Heart rate                     | • Electrolytes (Na⁺, K⁺, Ca²⁺, P, Mg²⁺) |
| • Respiratory rate               | • Blood urea                     |
| • Blood pressure                 | • Hematocrit                     |
| • Hydration status               | • Venous blood glucose from laboratory |
| • Neurologic examination         | • Venous blood gas (pH, HCO₃⁻, pCO₂) |
| • Headache                       | • Urinary ketones                |
| • Recurrence of vomiting         | • Electrocardiogram, if laboratory results of potassium are delayed |
| • Glasgow coma scale             | • Calculations:                  |
| • Restlessness or irritability   |   • Corrected sodiumb            |
| • Increased drowsiness           |   Measured[Na] + 1.6× [Glucose(mg/dL)−100] |
| • Incontinence                   |   • Anion gap                    |
| • Cranial nerve examination (for new onset palsies, abnormal pupillary response) |   Na⁺ – (Cl⁻ + HCO₃⁻) |
| • Fluid intake                   |   • Calculated osmolality [25]    |
| • Urine output                   |   2[Na + K] + [Glucose(mg/dL)−100] / BUN(mg/dL) |
| • Insulin administered           |   • Acidosis is likely metabolic alone, if |
| • Capillary blood glucosea       |   pCO₂ = last two numbers of the pH, and |

Na⁺ sodium, K⁺ potassium, Ca²⁺ calcium, P phosphorus, Mg²⁺ magnesium, HCO₃ bicarbonate, pCO₂ partial pressure of carbon dioxide, Cl⁻ chloride, BUN blood urea nitrogen

a Estimates of capillary blood glucose by glucometer must be cross-checked against laboratory venous glucose since the former may be inaccurate in the presence of poor peripheral circulation and acidosis and lack of glucometer calibration

b Other researchers have proposed a correction factor of 2.4 instead of 1.6 [15, 16]
(fall of >90 mg/dl/h), fluid containing 5% dextrose and with
tonicity between 0.45% saline to NS should be used [28].
However, if serum sodium is low (<132 mEq/L) and does
not rise with fall in blood glucose, NS can be used for
subsequent fluid replacement [29].

Replacement of Urinary Losses Replacement of urinary
losses is not required since initial rehydration rapidly
lowers blood glucose levels, decreasing ongoing diuresis.

Monitoring Fluid therapy should be guided by clinical
assessment and serial calculations of effective osmolality
and corrected sodium. Overzealous fluid resuscitation,
depicted by rapid change in corrected sodium (>1-2 mEq/L per
hour) and effective osmolality, is associated with the
development of cerebral edema [3, 30].

Rate of Fluid Administration The total fluid deficit should
be corrected evenly over 48 h at an infusion rate not
exceeding 1.5–2 times the maintenance requirements [3].
One must be mindful to subtract any fluid already
administered as boluses (except for resuscitation) or just
prior to emergency visit [17].

Example We shall calculate the fluid requirement for a boy
weighing 10 kg with severe DKA (assuming 10% dehy-
dration), who received one bolus of 20 mL/kg 0.9% saline
within one hour:

- Maintenance fluid requirement for 48 h=2000 mL
- Fluid deficit (10% dehydration)=1000 mL
- Subtract fluid bolus given over one hr=-200 mL
- Total fluid to be administered in 47 h=2800 mL.
- Therefore, fluid administration rate=59.5 mL/h

Insulin Therapy

Insulin therapy is essential to reverse the metabolic derange-
ments like lipolysis and ketogenesis, and to normalize the
blood glucose.

Timing Therapy with insulin is started after the initial volume
expansion, i.e., 1-2 h after starting fluid replacement [31].

Type Although rapid acting subcutaneously administered
insulins such as lispro and aspart are demonstrated to be
effective, only intravenous regular insulin is used for
management of DKA in children [32, 33].

Bolus Dose Administration of insulin boluses is not
justified [34, 35]. Satisfactory decrease in serum glucose
is achieved with rehydration alone, and use of boluses is
associated with occurrence of cerebral edema [30].

Dose Low dose intravenous insulin therapy at 0.1 Unit per kg
per hour is the standard of care [17, 36]. Higher doses are
associated with increased risk of hypokalemia, hypoglyce-
mia and too rapid a decline in serum osmolality, while lower
rates may be inadequate to suppress ketogenesis [37, 38].

Preparation To minimize the risk of computational errors, 50
units of regular insulin is diluted in a volume of 50 mL NS to
arrive at a standard insulin concentration of 1 U/mL [34].

Priming of Tubing Priming of tubing must be performed by
flushing insulin solution through the tubing prior to
infusing into the patient, because insulin binds to glass
bottles, plastic IV bags, syringes and tubing [4].

Duration of Therapy Regular insulin is administered at the
same rate (0.1 U/kg/h) until the resolution of ketoacidosis,
i.e., venous pH>7.3, HCO₃⁻ >15 mmol/L and closure of the
anion gap 4, 28).

Dose Adjustment Following start of insulin therapy, blood
glucose is expected to fall at the rate of 36–90 mg/dl/h [35,
39]. Since blood glucose normalization occurs much before
resolution of ketoacidosis, the concentration of dextrose in
replacement fluid should be increased as required to
maintain glucose between 150–200 mg/dl [4, 27]. If
hypoglycemia occurs despite increase of strength of
dextrose solution up to 12.5% (starting from 5%), the dose
of insulin may be reduced in decrements of 0.02 units/kg/
hour to 0.05 units/kg/h, provided that metabolic acidosis
continues to resolve [4]. Young children with DKA, older
children with established diabetes and those with non
ketotic hyperosmolar states tend to demonstrate marked
sensitivity to insulin [40]. Some suggest the use of two bag
infusion system, wherein identical electrolyte solutions
differing only in the concentration of dextrose (one at 0%,
another at 10%) are simultaneously run through different
cannulae, with the rates of administration titrated as per
results of blood glucose testing [39, 41].

Insulin resistance is suspected if rate of fall of blood
sugar <70 mg/dl/h or acidosis is not improving even though
blood glucose is falling. Rate of infusion can be increased
gradually to 0.3U/kg/h after ruling out errors in insulin
prescription or preparation and extravasation from intrave-
nous line [18].

Clearance of Urinary Ketones Clearance of urinary ketones
is not an end point for therapy with intravenous
insulin. Ketone dipsticks principally detect acetoacetate,
which shall continue to be detected even though ketosis has
resolved as normalization of ketosis is associated with
return of elevated β-hydroxybutyrate to acetoacetate ratio,
from up to 10:1 during ketoacidosis, to 1:1 [42].
Potassium Replacement

Addition of potassium to intravenous fluids is essential in DKA because of an actual deficit in the total body potassium of about 3–6 mEq/kg, primarily from the intracellular pool [43].

Potassium should be added to the fluid at a rate of 40 mEq/L (ideally 50% as chloride and 50% as phosphate) once the child has voided and a normal serum level (<6 mEq/L) has been documented, usually concurrent with start of insulin therapy [18, 44]. If the patient is hypokalemic, potassium replacement is begun at the time of initial volume expansion even before starting insulin therapy [18, 44]. If the patient is hyperkalemic, potassium replacement therapy is deferred until urine output is documented [18, 44]. During administration of potassium, adequate urine output is ensured and potassium and ECG monitored frequently (Table 2), in order to avoid both hyperkalemia (>5.5 mEq/L) and hypokalemia (<3.5 mEq/L) [45]. Recheck K+ every 1-2 h if values are outside normal range.

The maximum recommended rate of intravenous potassium replacement is 0.5 mEq/kg/h (or 80 mEq/L intravenous fluid) [18]. This requires careful monitoring. If hypokalemia persists despite a maximum rate of potassium replacement, then the rate of insulin infusion can be reduced.

Phosphate Replacement

Total body phosphate is depleted in DKA due to movement across the cell wall and osmotic diuresis, but it is unclear whether replacement of phosphate is associated with clear clinical benefits [46, 47]. Serum phosphate levels below 1 mg/dL are associated with adverse impact on tissue oxygenation and cause rhabdomyolysis or hemolytic anemia [48]; hence, intravenous phosphate replacement is reserved for such cases, with close monitoring of serum calcium [49]. Intravenous phosphate preparations are not available readily at present in India.

Correction of Metabolic Acidosis and Bicarbonate Therapy

As discussed above, acidosis in DKA usually responds to fluid and insulin therapy and administration of bicarbonate is seldom considered. Theoretically, therapy with bicarbonate is expected to slow recovery from ketosis through promotion of hepatic ketone synthesis. No clear outcome advantage is demonstrated in patients receiving bicarbonate for DKA [50]. Indeed, therapy with bicarbonate in DKA is linked to adverse outcomes, including increased risk of hypokalemia, hypernatremia, paradoxical worsening of CNS acidosis and increased risk of cerebral edema [51–53]. However, bicarbonate administration may be considered in children with cardiac dysfunction secondary to profound acidosis (pH<6.9) and in those with life threatening hyperkalemia [18, 54]. If administered, it is given at 1-2 mEq/kg over 60 min diluted in 0.45% saline [18].

Monitoring

Successful management of DKA requires meticulous documentation of the patient’s clinical and biochemical response to therapy, on a flow chart. Table 2 provides the desirable frequency of each observation.

Continuous assessment of vital signs in critically ill patients is facilitated by use of a cardiac monitor and placement of arterial catheter for invasive blood pressure monitoring. While persistent tachycardia and hypotension indicate continued hypovolemia, a drop in heart rate with new development of hypertension suggests raised intracranial pressure, as seen with cerebral edema. Patients with depressed consciousness should be catheterized to allow accurate hourly urine output charting. Nursing staff should carefully record all fluids received, including saline boluses, volume administered with injectable medications or as infusions, and any oral intake.

Monitoring corrected serum sodium aids in the assessment of free water deficit, while declining anion gap indicates successful therapy of metabolic acidosis. Presence of pCO2 which is lower than predicted indicates respiratory alkalosis that may be a pointer to sepsis [55].

Continuous noninvasive capnography to measure end-tidal CO2 is suggested to correlate well with the degree of acidosis in DKA; the resolution of ketoacidosis is evident in form of steady increment of ETCO2 towards normal range (35–45 mmHg) [56].

Antibiotic cover is provided if there is fever or other signs of infection.

Transition to Subcutaneous Insulin Therapy

Oral fluids should be introduced only when substantial clinical improvement has occurred, metabolic acidosis has been corrected (though ketosis may persist) and the patient indicates a desire to eat.

As oral feeds are advanced, intravenous fluids are reduced and a change to subcutaneous insulin is planned.

Timing of Switch To Subcutaneous Route The ideal time of begin administration of subcutaneous insulin is just before a meal. In order to avoid rebound hyperglycemia, rapid acting insulins (lispro or aspart) are administered subcutaneously 15–30 min prior and regular insulin 1-2 h prior, to stopping insulin infusion [14, 18]. With intermediate- or long-acting insulin, the overlap should be longer and the IV insulin gradually lowered. For example, for patients on a basal-bolus insulin regimen, the...
first dose of basal insulin may be administered in the evening and the insulin infusion is stopped the next morning.

**Dose of Subcutaneous Insulin** In patients with known insulin dependent diabetes, their usual insulin regimen may be restarted. For patients with DKA at disease onset, the recommended total daily dose (TDD) for pre-pubertal age is 0.75–1 units/kg and for pubertal children is 1–1.2 units/kg [14]. This is conveniently administered as:

- Before breakfast: 2/3 of TDD (1/3 as rapid acting and 2/3 as intermediate acting insulin)
- Before dinner: 1/3 of TDD (1/3 as rapid acting and 2/3 as intermediate acting insulin) [14]

Frequent monitoring of blood glucose is indicated (before breakfast, before lunch, before dinner and at 2 am) to prevent hypo and hyperglycemia and to adjust the insulin requirement in newly diagnosed patients.

**Preventions of Complications of Therapy**

Complications of DKA are listed in Table 3. Strategies to prevent common dyselectrolytemias, including hypokalemia and hypophosphatemia, have been discussed in relevant sections.

**Cerebral Edema**

While clinically significant cerebral edema is detected in only 0.3–1% individuals presenting with DKA, this complication is responsible for 60–90% of all deaths in DKA [1, 3]. Over a quarter of patients with clinically significant cerebral edema succumb, and another quarter have significant neurological morbidity [1, 3]. The exact pathogenesis and progression are unclear.

Risk factors for development of this complication include: age <5 yrs, new onset diabetes, prolonged duration of DKA symptoms, and presentation with severe acidosis or severe hypocapnia after adjusting for the degree of acidosis [53, 57]. Therapy associated risk factors for cerebral edema include: use of bicarbonate, rapid decline in serum osmolality, attenuated rise in sodium during therapy, higher volumes of fluid infused in first 4 h and early administration of insulin within the first hour of treatment [53, 57].

Clinical signs and symptoms are outlined in Tables 1 and 2. Cerebral edema usually becomes manifest 4–12 h after starting treatment [53]. However, onset before therapy or as late as 24–48 h after treatment are described [58, 59].

**Management of Cerebral Edema**

1. The head end of the bed should be elevated.

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<th>Table 3 Complications of DKA</th>
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<td>Hypoglycemia</td>
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<td>Hypokalemia</td>
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<tr>
<td>Hyperchloremic acidosis</td>
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<td>Cerebral edema</td>
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<tr>
<td>Cerebral venous thrombosis</td>
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<td>Arrhythmia</td>
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<td>- Secondary to dyselectrolyte</td>
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<td>- Prolonged QT interval corrected for heart rate (QTc)</td>
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<td>Pancreatitis</td>
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<td>Renal failure</td>
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<td>Rare complications</td>
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<td>- Deep vein thrombosis</td>
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<td>- Rhabdomyolysis</td>
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<td>- Pulmonary edema</td>
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<tr>
<td>Infections:</td>
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<td>- Mucormycosis (rhinocerebral and pulmonary)</td>
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2. The fluid administration rate should be reduced by 1/3 [18].
3. The air way is secured; if warranted by deterioration in sensorium, the patient should be intubated and mechanically ventilated.
4. During ventilation, aggressive hyperventilation (PCO₂< 22 mm Hg) should be avoided [60].
5. Intravenous mannitol is administered at 0.5–1 g/kg over 20 min; alternatively 3% saline is given as 5–10 ml/kg over 30 min [18, 61].
6. The dose is repeated if no response is perceived within 30 min to 2 h.
7. Following institution of therapy, a cranial CT is ordered to rule out other treatable causes of neurological deterioration like thrombosis or hemorrhage.

**Prevention of Recurrent Episodes**

Infections rarely precipitate DKA. In previously diagnosed patients with diabetes, omission of insulin, whether deliberate or accidental, underlies 75% cases of DKA [12, 13]. One should identify and address the factors underlying this phenomenon, including poor socioeconomic status, poor access to health care and psychosocial concerns, such as lack of parental supervision, eating disorders, psychiatric issues and misconceptions like withholding insulin during stress such as starvation, vomiting or infections.

Newly diagnosed patients and their parents should receive instructions regarding administration of insulin, home glucose monitoring and sick day care. A health care provider should be readily accessible in cases of emergencies.
Awareness among physicians is essential to allow early recognition and management of impending DKA, so that hospital admission, complications like cerebral edema, and ensuing morbidity and mortality can be avoided.

Conclusions

Diabetic ketoacidosis is an important cause of morbidity and mortality in children with diabetes mellitus. Timely diagnosis, appropriate management, careful monitoring and apprehending complications are critical to ensuring a favorable outcome. Management of cerebral edema is challenging and outcome remains unsatisfactory. Strategies for appropriate management of this complication require further investigation.

References