**Insulin in Special Situations: Diabetic Ketoacidosis**

K.M. Prasanna Kumar*, Rekha V. Bhat**

Ketoacidosis is a potential life-threatening metabolic complication of diabetes mellitus. Although it is commonly associated with type 1 diabetes, it can also occur in patients with type 2 disease during catabolic periods of stress. In contrast with the widespread belief, diabetic ketoacidosis (DKA) is more common in adults than in children. Inspite of impressive advances in its understanding and management, DKA still has a mortality of 2 - 5%. It is the most frequent cause of death in children and adolescents with type 1 diabetes, and accounts for more than half of all deaths in diabetics younger than 24 years of age.

**Criteria for diagnosis and classification**

DKA consists of the biochemical triad of hyperglycemia, ketonemia and acidemia (Fig. 1). The most widely used diagnostic criteria for DKA is arterial pH of <7.3, serum bicarbonate<15mEq/L, blood glucose >250 mg/dl and a moderate degree of ketonemia &/or ketonuria. Table 1 shows an empirical classification for DKA. Its severity can also be modified by the underlying illness.

**Precipitating events**

Discontinuation of insulin, infection and new-onset diabetes are among the most frequently encountered precipitating events leading to DKA. The infections usually originate from the urinary tract and lungs. Other common factors are listed in Fig. 2. In some patients with known diabetes, DKA develops without a clear precipitating condition.

**Pathogenesis**

The basic underlying mechanism for DKA is insulin deficiency, either relative or absolute, along with elevation of counterregulatory hormones such as glucagon, catecholamines, cortisol and growth hormone. This results in the cascade of events depicted in Fig 2.

**Clinical features**

Symptoms of poorly controlled diabetes may be present for several days. But the metabolic alterations typical of DKA usually evolve within 24 hours. The history often includes polyuria, polydipsia, polyphagia, weight loss, vomiting, abdominal pain, dehydration, weakness, clouding of sensoria and finally coma. Physical findings include poor skin turgor, Kussmaul respirations/ tachycardia, hypotension, alteration of mental status, shock and coma. Hypothermia may be

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*Head of the Department of Endocrinology, M S Ramaiah Medical College, Bangalore- 560043. **Consultant Endocrinologist, Chennai*

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**Table 1 : Empirical classification of DKA**

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma glucose (mg/dl)</td>
<td>&gt;250</td>
<td>&gt;250</td>
<td>&gt;250</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.25-7.30</td>
<td>7.0-7.24</td>
<td>&lt;7.0</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/L)</td>
<td>15-18</td>
<td>10-15</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Anion gap</td>
<td>&gt;10</td>
<td>&gt;12</td>
<td>&gt;12</td>
</tr>
<tr>
<td>Sensorium</td>
<td>Alert</td>
<td>Alert/ drowsy</td>
<td>Stupor/ coma</td>
</tr>
</tbody>
</table>

**Fig. 1: The biochemical triad in DKA**

**Fig. 2: Precipitating factors of DKA**

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Diabetes Mellitus

- Uncontrolled
- Discontinuation of insulin
- Newly diagnosed

Acute illness

- Infections
- Myocardial infarction
- Cerebrovascular accident
- Gastrointestinal bleed
- Renal failure
- Severe burns
- Trauma
- Acute pancreatitis

Drugs

- Thiazides
- Glucocorticoids
- Beta blockers
- Phenytoin
- Didanosine

Substance abuse

- Alcohol
- Cocaine
present and is a poor prognostic sign. Breath may have a fruity odor due to the presence of volatile acetone.1,4

Laboratory evaluation

The initial laboratory evaluation of any patient with suspected DKA should include immediate determination of arterial blood gases, blood glucose, blood urea, serum electrolytes, creatinine and ketones, urine analysis and a complete blood count. Bacterial cultures of urine, blood and other tissues must be obtained. A chest X-ray should also be obtained if indicated. Blood glucose must be monitored every 1-2 hours during treatment. Serum electrolytes and arterial pH should be measured every 2-6 hours depending on the patient’s clinical response.

Useful formulae for the evaluation and treatment of DKA

1. Anion gap = [Na+] – [Cl- + HCO3-]
   Normal = 7-9 mEq/L
   Because serum potassium concentrations may be altered by acid-base disturbances and by total body stores, it is not routinely used in the calculation of anion-gap.

2. Total serum osmolality =
   \[
   2 \times [\text{Na}^+] + \frac{(\text{glucose in mg/dl})}{18} + \frac{\text{BUN in mg/dl}}{2.8}
   \]
   Normal = 290±5 mOsm/kg H2O

3. Corrected [Na+] = [Na+] + 1.6\times\frac{[\text{glucose in mg/dl}] - 100}{100}

Given in Table 2 is a typical example of water and electrolyte deficits in a patient with DKA.8,9

**Management**

The management of DKA can be divided into the following categories:

1. Replacement of fluid losses.
2. Correction of hyperglycemia and metabolic acidosis.
3. Replacement of electrolyte losses.
4. Detection and treatment of precipitating causes and complications.
5. Conversion to a durable regimen following recovery from DKA.

**Fluid replacement**

Fluid replacement should correct the estimated deficits within the first 24 hours in adults and 48 hours in children. Rapid fluid administration can produce cerebral edema in children. In patients with renal or cardiac compromise, monitoring of serum osmolality and frequent assessment of
renal, cardiac and mental status must be performed during fluid resuscitation to avoid iatrogenic fluid overload. Fig. 4 shows the protocol for fluid replacement in adults. Fig. 5 shows the protocol for fluid replacement in children.

**Insulin therapy**

Insulin of choice in DKA is regular insulin. It must be given as a continuous intravenous infusion unless the episode of DKA is mild. If the serum potassium level is low, insulin should be withheld until it is elevated to >3.3mEq/L. The insulin infusion must be continued until acidosis has resolved. This typically takes longer to clear than hyperglycemia. Criteria for resolution of DKA includes blood glucose <200mg/dl, serum bicarbonate >18mEq/L and a venous pH of >7.3. Venous pH is 0.03 units lower than arterial pH. Fig. 6 depicts insulin therapy in adults. Initial intravenous bolus is not recommended in children. They may be directly started on continuous insulin infusion.

**Electrolyte correction**

Guidelines for replacement of potassium in adults with DKA is shown in Fig. 7. Usually 20-30mEq of potassium in each litre of IV fluid is sufficient to maintain the levels in the normal range. In children, potassium concentration in the IV fluid may be adjusted according to the serum concentration, as shown in Table 3.

Phosphate replacement may sometimes be indicated in patients with cardiac dysfunction, anemia or respiratory depression and in those with serum phosphate concentration <1.0mg/dl. When needed, 20-30meq/L potassium phosphate can be added to replacement fluids.

**Treatment of precipitating factors**

Possible sources of infection should be sought and aggressively treated with antibiotics. Even if a source of infection cannot be identified, antibiotic therapy must be considered because of the high mortality associated with it. Electrocardiographic tracings should be reviewed for possible ischemia or infarction whether the patient is symptomatic or not.

**Complications**

The most common complications of DKA include hypoglycemia, hypokalemia and hyperglycemia. They can be avoided by strictly following the guidelines recommended. Hyperchloremia can also occur, but is transient and not

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**Table 3: Potassium replacement in children with DKA**

<table>
<thead>
<tr>
<th>Serum potassium (mEq/L)</th>
<th>IV fluid potassium (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>40-60</td>
</tr>
<tr>
<td>3-4</td>
<td>30-40</td>
</tr>
<tr>
<td>4-5</td>
<td>20-30</td>
</tr>
<tr>
<td>&gt;5</td>
<td>0-20</td>
</tr>
</tbody>
</table>

**Fig. 5: Fluid replacement in children with DKA**

### Insulin for adults with DKA

- **Regular insulin**
  - IV route
    - 0.15U/kg as IV bolus
    - 0.1U/kg/h IV infusion
    - If plasma glucose does not fall by 50-70% mg/dl in the 1st hour
    - Double the rate of infusion until it falls by 50-70 mg/dl/h
    - When plasma glucose reaches 250 mg/dl
    - IV infusion 0.05-0.1U/kg/h
  - SC/IM route
    - 0.4U/kg ½ as IV bolus & ½ as SC/IM
    - 0.1U/kg/h SC/IM
    - When plasma glucose reaches 250 mg/dl
    - SC/IM 5-10U every 2h

**Fig. 6: Insulin for adults with DKA**

**Potassium replacement in adults with DKA**

- Serum K+<3.3 mEq/L
  - Withhold insulin
    - Give 40 mEq KCl/h (% KCl and ¼ KPO4)
    - until K+≥3.3 mEq/L
  - Maintain value between 4 & 5 mEq/L

- Serum K+<3.3 mEq/L
  - Give 20-30 mEq K+ in every L of IV fluid (% KCl and ¼ KPO4)
  - Maintain value between 4 & 5 mEq/L

- Serum K+≥5 mEq/L
  - Withhold K+
clinically significant. Cerebral edema is seen in 0.7-1% of cases of DKA in children and has a high mortality rate (>70%). The risk of developing cerebral edema is largely negated by the addition of dextrose to intravenous fluids once blood glucose reaches 250 mg/dl and with gradual correction of sodium and water deficits in patients with high serum osmolality. Acute respiratory distress syndrome is a potentially fatal complication of DKA, that fortunately occurs rarely.11

**Long-term management**

Once the ketoacidosis has resolved, and the patient is able to eat, split-dose therapy with short-acting and intermediate-acting insulin can be given. It is easier to make this transition before breakfast and at dinner time. For patients with known diabetes, a return to their previous regimen is usually adequate. For newly diagnosed diabetes, insulin can be initiated at a dose of 0.5–1 units/kg/day. Two-thirds of this total daily dose should be given in the morning and one-third in the evening. If the patient is unable to eat, intravenous insulin infusion must be continued along with an infusion of 5% dextrose in half-normal saline given at a rate of 100 to 200ml/hour. This can be supplemented with subcutaneous regular insulin as needed every 4 hours.1,2,4

**Prevention**

Diabetic ketoacidosis can be prevented to a large extent if the patient understands the importance of continuing insulin therapy, especially during illness.

**References**