# Diabetic Emergencies

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Diabetic emergencies consist of hyperglycemic conditions such as diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar state (HHS) and hypoglycemic emergencies.

Insulin deficiency, increased insulin counter-regulatory hormones (cortisol, glucagon, growth hormone, and catecholamines), and peripheral insulin resistance leading to hyperglycemia, dehydration, ketosis, and electrolyte imbalance underlie the pathophysiology of DKA. DKA usually occurs in young patients with type 1 diabetes who are insulin dependent, and HHS usually occurs in the elderly with type 2 diabetes on either oral hypoglycemic agents or on insulin. The basic pathophysiological difference is absence of circulating insulin in DKA and presence of some residual insulin function in HHS, which prevents lipolysis, and ketosis.

## Hyperglycemic Emergencies

### DKA and HHS (Table 5.1)

A 18-year-old female patient presents to the emergency department with high grade fever, tachypnoea and altered mentation. She had diarrhoea for 3 days that was watery and large in volume. On examination, she was found to be febrile with a temperature of 101 °F. Her pulse rate was 130/min regular, and blood pressure was 90/70 mmHg. She had a Glasgow coma score of 9. Her random plasma glucose on arrival was 480 mg/100 mL. She was not known to have diabetes.

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**Table 5.1** Differences between DKA and HHS

| | Diabetic ketoacidosis | Hyperglycemic hyperosmolar syndrome |
|---|---|---|
| Ketoacidosis | Profound | Minimal or none |
| Glucose | ~250–600 mg/dL | Often >900 mg/dL |
| $HCO_3$ | <15 mEq/L | >15 mEq/L |
| Osmolarity | 300–325 mOsm | Often >350 mOsm |
| Age | Young | Elderly |
| Onset | Acute; over hours to days | Chronic; over days to weeks |
| Associated diseases | Uncommon | Common |
| Seizures | Very rare | Common |
| Coma | Rare | Common |
| Insulin levels | Very low to none | May be normal |
| Mortality | 0–10% (depends on underlying conditions) | 20–40% |
| Dehydration | Severe | Profound |

## Step 1: Start Initial Resuscitation (Refer to Chap. 23, Vol. 2)

- Urgently insert two wide-bore intravenous peripheral catheters for volume resuscitation.
- Blood samples for a complete metabolic profile and other relevant tests are drawn.
- A central line should be inserted in the presence of severe hypotension, lack of peripheral access, need for multiple infusions, severe acidosis, and impaired cardiorespiratory or renal parameters.
- Infuse 1 L of 0.9% NS over 1 h.
- Serum potassium should be >3 mEq/L before Insulin therapy is started.

## Step 2: Take Focused History and Perform Physical Examination

- History of insulin omission in a diabetic patient is common and often points toward a diagnosis of DKA or HHS. The table below points to general differences between the two syndromes.
- DKA could also be the first presentation in young individuals.
- A thorough physical examination helps in finding the precipitating cause/or possible focus of infection, which is often a trigger for the hyperglycemic crisis.
- History of SGLT2 inhibitors (Capaglifozin, Empaglifozin or Dapaglifozin) any of these may lead to euglycaemic diabetic ketoacidosis due to continuous renal elimination of glucose in ketotic state leading to euglycaemia.

## Step 3: Send Essential Investigations

- Metabolic panel to include electrolytes along with Serum Magnesium and Phosphates.
- Blood urea nitrogen and plasma creatinine (may be spuriously high due to chemical analysis interference with ketones).
- Arterial blood gas with Anion Gap.
- Complete blood count with differential count.
- Urinalysis and urine ketones by dipstick.
- Serum ketones.
- Electrocardiogram, Chest X-ray.
- Screening for a possible infective cause as a trigger for the hyperglycemic crisis.

### Management

1. Fluid resuscitation and correction of electrolyte disturbances.
2. IV Insulin therapy.
3. Watch for complications.
4. Treat precipitating cause.

## Step 4: Fluid Therapy

- Patients with DKA and HHS usually have severe hypovolemia due to absolute or relative deficiency of insulin leading to osmotic diuresis.
- Average fluid loss in DKA and HHS is 8–10 L. HHS may result in fluid losses exceeding 10 L sometimes. The goal is to replace the total volume loss within 24–36 h with 50% of resuscitation fluid being administered during the first 8–12 h.
- In hypotensive patients, use crystalloids to restore circulating volume.
- Crystalloids are initial fluids of choice irrespective of sodium levels. Fluid resuscitation is initiated with 15–20 mL/kg/h of 0.9% NS for the first couple of hours.
- After initial bolus, fluid replacement rates can be reduced to 4–14 mL/kg/h. Type of fluid will be decided by hemodynamic stability, sodium levels and urine output.
- One-half isotonic saline (0.45%) at a rate of approximately 250–500 mL/h if the serum sodium is normal or elevated.
- Isotonic saline is continued at a rate of 250–500 mL/h if hyponatremia is present.
- In patients with HHS, comorbidities like renal and cardiac dysfunctions warrant more close monitoring of hemodynamics.
- Rapid correction of sodium and osmolality may risk cerebral edema.

- Large volumes of 0.9% NS can cause non anion gap metabolic acidosis which may confuse the clinical picture.
- Hypotonic (0.45%) saline infusion may be appropriate after volume correction in hemodynamically stable and hypernatremic patients (after correcting for high blood glucose) as hypotonic saline does not correct hypovolemia rapidly. This might also be appropriate in patients with concomitant potassium infusion to maintain isotonicity of infusion fluid. Calculate free water deficit to assist fluid replacement in patients with hypernatremia (see Chap. 56, Vol. 1) and replace with dextrose or enteral water.
- Volume resuscitation will enable renal losses of glucose and enhance peripheral action of insulin.
- Replace total body water losses slowly with 5% glucose solution (50–200 mL/h) once circulating volume and serum sodium are restored (usually when the blood glucose falls to <200 mg/dL). This is in order to avoid sudden osmolarity changes, which may lead to cerebral edema and convulsions, seen more frequently in the pediatric age group.

## Step 5: Correct Electrolyte Abnormalities

Hyperglycemia may cause dilutional hyponatremia, so measured serum sodium is corrected by adding 1.6 mEq/L (1.6 mmol/L) for each 100 mg/dL (5.6 mmol/L) elevation of serum glucose over 100 mg/dL (5.6 mmol/L). On average, patients with DKA/HHS may have the following deficit of water and key electrolytes per kg of body weight: free water 100 mL/kg; sodium 7–10 mEq/kg; potassium 3–5 mEq/kg; chloride 3–5 mmol/kg; and phosphorus 1 mmol/kg.

- Replacement of serum potassium should begin early in the management of DKA as serum potassium concentration does not reflect total body potassium accurately.
- Potassium replacement should begin as soon as serum potassium concentration is less than 5.5 mEq/L. Target potassium concentration is 4–5 mEq/L.
- Ensure adequate urine output before replacing intravenous potassium.
- Guideline for replacing potassium is as follows:
  - If S. potassium is less than 3.5 mEq/L, give potassium at 20–40 mEq/h as a controlled infusion, through central venous line with continuous cardiac monitoring.
    - Start insulin infusion only after potassium replacement is started.
  - If S. potassium is 3.5–5.0 mEq/L, give potassium at 20 mEq/h.
  - If S. potassium is more than 5.0 or patient is anuric, no supplements are required.
- Potassium should be added to 0.45% saline instead of 0.9% saline to avoid hypertonicity of infused fluid. Correction of hypovolaemia and insulin treatment lead to intracellular shift in potassium.

- Hypomagnesemia occurs early in the course of DKA and requires correction. Monitor serum magnesium levels.
- Phosphorous depletion is common in DKA. Replacement is advised when it is severely depressed (<1 mg/dL) and in patients with respiratory failure, cardiac failure and hemolytic anemia.
- Sodium bicarbonate infusion: metabolic acidosis improves with restoration of intravascular volume and tissue perfusion. There is a limited role of bicarbonate therapy as it has not been shown to improve outcome in DKA. Moreover, bicarbonate therapy is associated with adverse effects such as increased paradoxical intracellular and cerebrospinal fluid acidosis, increased $CO_2$ production, adverse effect on tissue oxygenation, and post resuscitation metabolic alkalosis.
- Bicarbonate therapy may be considered in the following situations:
  - When pH is persistently less than 7.0 after 2–3 h of treatment.
  - When hypotensive shock is unresponsive to rapid fluid replacement and persistent severe metabolic acidosis exists.
  - In the presence of severe hyperkalemia.
- Even in these circumstances, bicarbonate can only "buy time" until other treatment corrects acidosis.
- Bicarbonate may be given as an infusion of 100 mEq over 4 h in sterile water till pH > 7.1.

## Step 6: Start Intravenous Insulin Infusion

- Insulin therapy should be started only after fluid and electrolyte resuscitation is underway.
- Use regular (rapid acting) insulin at 0.1 U/kg body weight as a bolus dose and then 0.1 U/kg/h as a continuous infusion or 0.14 U/kg body weight as a continuous infusion without a bolus dose.
- When plasma glucose reaches 200–250 mg/dL, the insulin rate can be decreased by 50% or to the rate of 0.02–0.05 U/kg/h. If the blood glucose level does not decrease by 50–75 mg/dL/h, the rate of insulin infusion should be doubled.
- Rate of reduction of blood glucose should be less than 50–75 mg/dL/h.
- Rapid correction of blood glucose levels could lead to cellular edema seen mainly in pediatric population, which can lead to convulsion and electrolyte disturbances (hypokalemia, hypomagnesemia, and hypophosphatemia).

## Step 7: Monitor Effectiveness of Therapy Clinically and Biochemically

- The following features indicate clinical improvement:
  - Increased sense of well-being, reduced tachycardia and tachypnoea.
  - Improved mental status, able to eat orally.

- The following biochemical parameters suggest resolution of DKA/HHS:
  - Serum glucose below 200 mg/dL in DKA and below 250–300 mg/dL in HHS.
  - Serum bicarbonate more than 18 mEq/L.
  - Venous pH more than 7.30.
  - Serum anion gap less than 12 mEq/L.
  - Decreasing urine sugar.
  - Urine or serum ketones by nitroprusside test are not reliable parameters to follow as this test predominantly measures acetoacetate and acetone, whereas β-hydroxybutyrate is the predominant ketone in severe DKA, which is not measured usually in the laboratory. There may be a paradoxical rise of serum or urinary ketones as patients improve due to conversion of beta-hydroxybutyrate to acetone and acetoacetic acid.
  - Direct estimation of beta hydroxybutyrate.
  - Plasma effective osmolality (exclude urea in osmolality calculation) below 315 mOsmol/kg.
  - Delta Anion Gap/Delta Bicarbonate: to detect combined metabolic disorders like anion gap and non anion gap metabolic acidosis and metabolic alkalosis.

## Step 8: Switch to Subcutaneous Insulin When Stable

- Maintain IV insulin until biochemically stable and the patient has taken at least two meals.
- Switch to subcutaneous regular insulin with half dose of total intravenous insulin requirement either as a fixed dose or sliding scale insulin as per protocol (see Chap. 2, Vol. 2).
- IV infusion should be stopped 2 h after the first dose of subcutaneous insulin.

## Step 9: Identify Precipitating Factors

- Precipitating factors should be sought and treated. Common precipitants include the following:
  - Missed insulin therapy.
  - Infections—pneumonia, sepsis, urinary tract infection.
  - Trauma.
  - Pancreatitis.
  - Myocardial infarction.
  - Pregnancy.
  - Stroke.
  - Steroid use.

### Step 10: Continue Supportive Care

- The urinary catheter: Consider in persistent hypotension, renal failure, anuria, and impaired consciousness. Maintain strict asepsis during catheterization.
- Measure hemodynamics: static indices like CVP or dynamic indices of volume status should be monitored in patients who present with shock. Also consider in the elderly with concomitant illness, cardiac failure, or renal failure even in the absence of hypotension.
- Thromboembolic complications are common, and DVT prophylaxis should be initiated (see Chap. 21, Vol. 2).
- The nasogastric tube: If consciousness is impaired, insert a NGT to avoid aspiration of gastric contents.
- Start appropriate antibiotics if infection is a possible trigger.

## Hypoglycemia

A 70-year-old male patient, with type 2 diabetes mellitus, was brought to the emergency department with history of feeling unwell, nausea, vomiting for 2 days, sudden onset of giddiness, sweating, palpitations, and altered sensorium. Blood glucose on a glucometer was 42 mg/dL.

Impaired consciousness in diabetic patients is most commonly due to hypoglycemia that is most often drug-induced. Symptoms of hypoglycemia are nonspecific, and this can masquerade as cardiorespiratory, neurological, and even psychiatric problems. A low threshold for checking blood sugar in all diabetic patients to exclude hypoglycemia is warranted as it is an imminently treatable condition and if left unattended leads to severe morbidity and mortality.

### Step 1: Promptly Identify Clinical Features of Hypoglycemia

- Features of hypoglycemia could be autonomic such as diaphoresis, tremor, anxiety, palpitation, hunger, paraesthesia, and tachycardia caused by sympathetic stimulation.
- These may be absent in patients with autonomic neuropathy or on β-blockers.
- In some patients, neuroglycopenic features such as drowsiness, behavioral abnormalities, coma, and seizures predominate.

### Step 2: Check Blood Glucose Immediately

- Urgent capillary sugar should be checked with the bedside glucometer. If possible, a simultaneous venous sample should be sent to the laboratory for glucose analysis. Point of care glucometers generally overestimate glucose values in the

lower range. Whenever hypoglycemia is suspected, always send blood for glucose estimation by glucose analyzer.
- Administration of dextrose should not be delayed if blood glucose checking cannot be done immediately.
- If the blood glucose level is less than 70 mg/dL and symptoms improve with glucose administration, then patient symptomatology may be attributed to hypoglycemia.

### Step 3: Give Intravenous Dextrose

- Reverse hypoglycemia rapidly with 50 mL of 25–50% glucose given intravenously.
- Check blood glucose after dextrose infusion and repeat the injection till the glucose is above 70 mg/dL for at least two consecutive readings and the patient is asymptomatic.
- Start intravenous dextrose infusion 6-h with frequent blood glucose monitoring in patients on long-acting insulin, oral hypoglycemic drugs, or renal impairment as they are prone to recurrent hypoglycemia.

### Step 4: Consider Alternative Agents in Specific Circumstances

- Injection glucagon may be given in a dose of 1 mg intramuscularly or subcutaneously if venous access is not possible.
- Injection octreotide 25–50 mcg may be given subcutaneously or as an intravenous infusion in patients with resistant hypoglycemia, sulfonylurea-induced hypoglycemia, or hypoglycemia induced by drugs like quinine or quinidine.

### Step 5: Consider Precipitating Factors of Hypoglycemia in Diabetic Patients

- Missed meals/inadequate food intake.
- Insulin overdose.
- Change of therapy/dosage of hypoglycemic drugs or insulin.
- Concomitant ingestion of drugs causing hypoglycemia.
- Presence of hepatic or renal failure.

### Step 6: Consider Disorders and Drugs Associated with Hypoglycemia (See Tables 5.2 and 5.3)

- In an intensive care unit, certain disorders are associated with hypoglycemia, and frequent blood glucose monitoring should be done in these patients.
- Hypoglycemia is more common if there is intolerance to enteral feeding and the patient is not started on parenteral nutrition.

**Table 5.2** Common causes of hypoglycemia in the ICU

| |
|---|
| Insulin |
| Oral hypoglycemic agents |
| Sepsis (including malaria) |
| Hepatic failure |
| Alcohol |
| Adrenal crisis (including steroid withdrawal) |
| Drugs |

**Table 5.3** Drugs associated with hypoglycemia

| |
|---|
| Insulin |
| Oral hypoglycemic agents |
| Gatifloxacin |
| Quinine |
| Artesunate derivatives |
| Pentamidine |
| Lithium |
| Propoxyphene |

- Many patients in the ICU have altered mental state and/or are under sedation, and hypoglycemic episode may remain unnoticed in these patients, and so, frequent blood glucose monitoring is essential in these groups of patients.
- Many patients in ICUs are on intravenous insulin infusion. Discontinuation or intolerance to enteral feeding and stopping parenteral nutrition without simultaneously stopping insulin lead to hypoglycemia.
- At lower glucose range and in low perfusion states, bed side glucometer lose their accuracy.
- Continuous blood glucose monitoring if available will help to detect hypoglycemia early.

## Suggested Reading

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