Chapter 11
Management of Hyperosmotic Hyperglycemia

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Learning Objectives

1. Distinguish between diabetic ketoacidosis (DKA) and hyperosmotic hyperglycemic state (HHS).
2. Describe the management of HHS.
3. Identify the causes of HHS.

Clinical Vignette: A 58-year-old woman was found obtunded in a park, appearing profoundly dehydrated. A blood glucose check in the field was 1200 mg/dL. She was transported to the emergency department where her vital signs were: temperature 37.6 °C, BP 70/30 mmHg, HR 120 bpm, RR 18, O_2Sat 100% on RA.

A. **She clearly has a problem with elevated blood glucose—what are the two major hyperglycemic syndromes?**

Draw two overlapping circles in Fig. 11.1*; label the intersecting area "hyperglycemia," and label each circle "DKA" and "HHS."*

Teaching points

- Diabetic ketoacidosis (DKA) is an acute complication of diabetes mellitus type 1 (DM1). Deficiency of insulin prohibits muscle and liver cell glucose uptake. Insulin deficiency causes a shift from the normal carbohydrate metabolism to a state of fasting fat metabolism—lipolysis, which leads to ketoacidosis.
- Hyperosmolar hyperglycemic state (HHS) is associated with diabetes mellitus type 2 (DM2). Pancreatic production of insulin is sufficient to prevent ketoacidosis, but not adequate to cause glucose utilization.
- It takes one-tenth as much insulin to suppress ketoacidosis as it does to stimulate glucose uptake.

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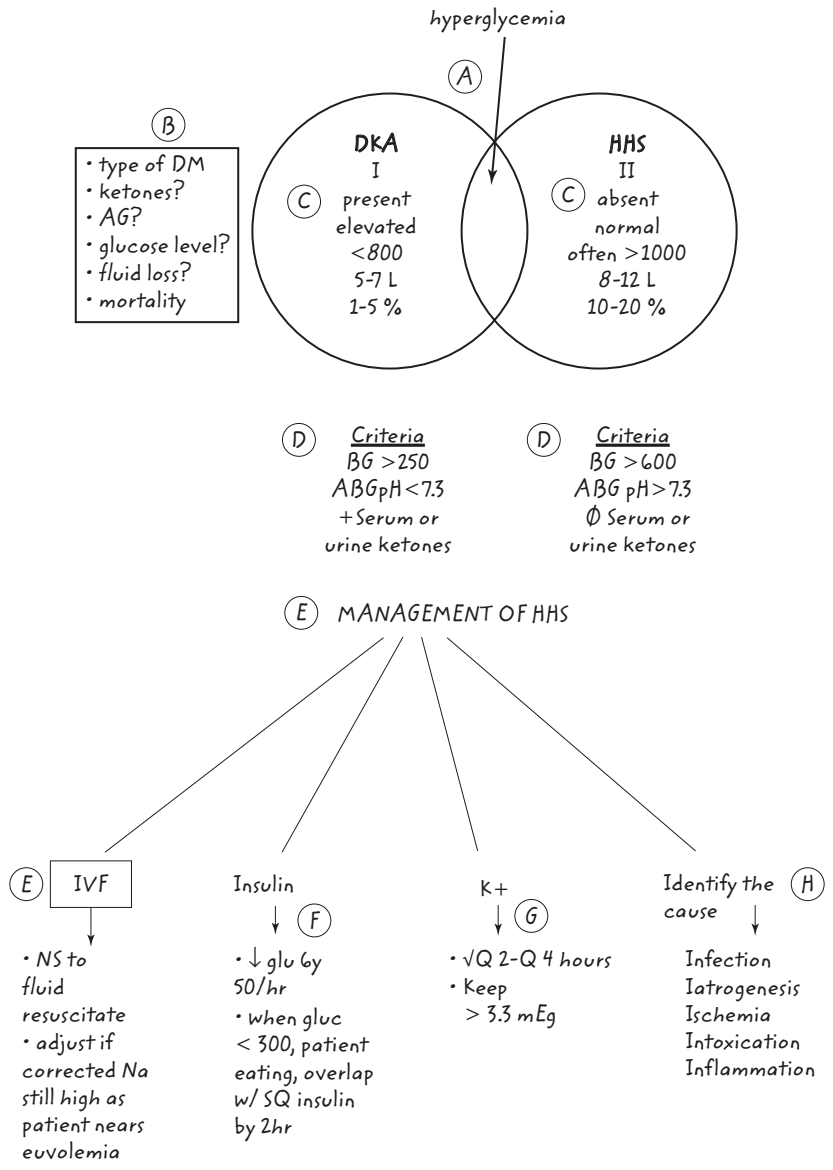

Fig. 11.1 Management of hyperosmotic hyperglycemia: A–H

B. **DKA and HHS have hyperglycemia in common, but the syndromes are different in several respects—what are some ways in which these syndromes are different?**

Write down the key distinguishing features in a column alongside the circles, making sure to include any not mentioned.

C. **For each of these variables, how do DKA and HHS typically present?**

Query learners about each of the characteristics and fill out the information for DKA and HHS as in Fig. 11.1.

Teaching points

- Although both DKA and HHS involve hyperglycemia, the ketones in DKA create an anion gap.
- Because HHS has no ketoacidosis, there is no anion gap (unless the precipitant of HHS also causes a gap acidosis).
- Ketosis-prone DM2 is uncommon but tends to occur in patients who are Hispanic or African American (nearly 50%). The etiology of this acute, transient β-cell failure is not currently known.
- HHS develops over days to weeks compared to hours for DKA. Therefore, HHS has a greater hyperglycemia and concurrent fluid loss compared to DKA.
- Lack of insulin leads to hyperglycemia through two mechanisms: loss of cellular glucose uptake and inhibited hepatic gluconeogenesis. This leads to osmotic diuresis and subsequent dehydration.

D. **Your patient had a blood gas sent. Her pH was 7.4, and urine did not have ketones. Does she have DKA or HHS?**

Write down the DKA and HHS criteria below the circles to reinforce the key distinguishing factors. This patient has HHS.

E. **After determining that circulation, airway, and breathing (CAB) are stable, what is the most important first step in the management of this patient?**

Write out IVF, insulin, K+ and "Identify the cause" under management of HHS in Fig. 11.1. *Put a box around "IVF"—the most important initial treatment for this patient.*

Teaching points

- Three of these cornerstones (fluids, insulin, and potassium) need constant monitoring.
- Fluids are critical to restore intravascular volume and concurrently decreasing plasma osmolarity.
- The initial fluid should be normal saline (NS) even if patients are initially hypernatremic. This is because normal saline is hypo-osmotic (285 mOsm/L) relative to the hyperosmotic patient (>320 mOsm/L).

- The initial serum sodium in HHS may be low, normal, or high. High plasma osmolality pulls water out of cells, diluting serum sodium and causing hyperosmolar hyponatremia. Osmotic diuresis with loss of free water eventually leads to hypernatremia, often made worse by poor oral intake due to altered mental status.
- The "corrected" serum sodium is an estimate of what the serum sodium level will be once blood glucose comes down to the normal range.
- As the patient approaches euvolemia and if the "corrected" sodium still appears to be high, ½ NS may be used to avoid ongoing hypernatremia.
- A rule of thumb for fluid resuscitation is to correct one-half of the fluid deficit in the first 8–12 h and the rest in the following 12–36 h.

F. **How quickly should the blood glucose be brought down?**

Fill out the second column under "Insulin."

Teaching points

- A rule of thumb for intravenous insulin infusion is to decrease blood glucose by 50 mg/dL per hour.
- When serum glucose reaches 250–300 mg/dL, a long-acting SQ insulin may be administered 30 min before a meal (the patient must be able to eat) and 2 h before discontinuing the infusion. The overlap accounts for the time to onset for the long-acting insulin, which is approximately 2 h.
- HHS is resolved when osmolarity reaches <320 mOsm/kg and mental status returns to baseline.

G. **What will happen to the potassium level as you give insulin and fluid to this patient?**

Fill out the third column under "K^+"

Teaching points

- The initial serum potassium may be high, normal, or low. Hyperosmolarity and insulin deficiency cause potassium to shift out of cells. However, total body potassium is typically very low due to urinary losses from osmotic diuresis.
- Serum potassium will fall rapidly with correction of hyperosmolality and administration of insulin. Itshould be monitored every 2–4 h.
- Delay potassium replacement until the serum level falls <5 mEq/L. If potassium is <3.3 mEq/L, pause the insulin until it reaches 3.3 mEq/L.
- There is usually no indication for bicarbonate or phosphate repletion as these levels are typically normal and self-limited, respectively. However, you should carefully replete phosphate if there is cardiac dysfunction, anemia, respiratory depression, or a serum phosphate level <1.0 mg/dL.

H. **What could have precipitated our patient's HHS?**

Fill out the fourth column under "Identify the cause."

Teaching points

- Infection (~45%)—leukocytosis is common in HHS, even without an infection. Nevertheless, the source of infection should be investigated in all cases.
- Iatrogenesis—inadequate insulin therapy (~30%), dehydration, medication side effects (e.g., glucocorticoids, thiazide diuretics, sympathomimetic drugs, antipsychotics).
- Ischemia—myocardial infarction, stroke.
- Intoxication—illicit drugs (particularly cocaine), alcohol.
- Inflammation—pancreatitis, appendicitis, pregnancy, trauma.

Return to objectives and emphasize key points

1. Distinguish between diabetic ketoacidosis (DKA) and hyperosmotic hyperglycemic syndrome (HSS)
    - HHS is more typical in type 2 diabetic patients.
    - HHS is diagnosed by a blood glucose >600 mg/dL, arterial pH > 7.30, and absent serum and urine ketones.
2. Describe the management of HHS: asterisk columns 1–3 below "Management of HHS"
    - Start with fluid resuscitation.
    - Correct blood glucose and potassium abnormalities.
    - Remember to concurrently find and treat the precipitating factor.
    - HHS is resolved when osmolarity reaches <320 mOsm/kg and mental status returns to baseline.
3. Identify the causes of HHS: asterisk column 4 below "Management of HHS"
    - Infection
    - Iatrogenesis
    - Ischemia
    - Intoxication
    - Inflammation

Resources

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